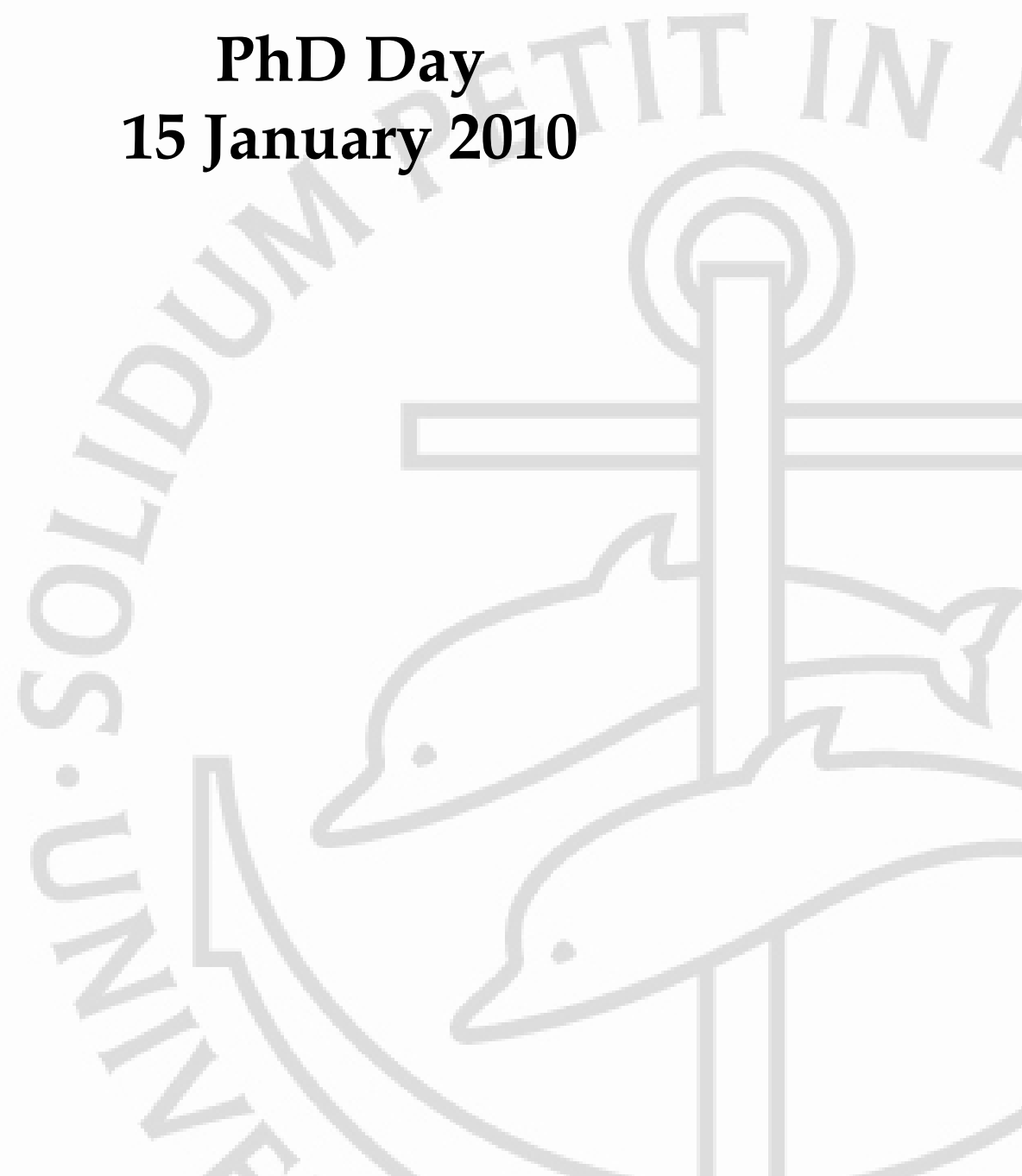
UNIVERSITY OF AARHUS
GRADUATE SCHOOL OF HEALTH SCIENCES

PhD Day
15 January 2010



Welcome

It is our pleasure to welcome students, faculty, and guests to the PhD Day 2010. We warmly thank all those who have taken the time to participate and help make the PhD Day a leading event in the training of our graduate students.

The world of science is by nature global and to go international is a key ambition of the PhD programme in Denmark. Aarhus Graduate School of Health Sciences acknowledges that internationalisation is a very important aspect of science, not least for the individual PhD student. One way to support internationalisation is by networking. The theme of the PhD Day 2010 is thus INTERNATIONAL NETWORKING. Nine PhD students coming from USA, England, Sweden, Switzerland, and France will spend a day with PhD students from Aarhus. They were invited by the respective Graduate Programmes and we trust that this day of science related as well as social activities will lead to new contacts, further networking and new collaborations across borders.

As is evident from the abstracts presented in this programme book the Aarhus Graduate School of Health Sciences provides a vibrant scientific environment ready to meet new challenges and offering many opportunities. The PhD students are central to research and research environments and the Organizing Committee is satisfied that this book shows the commitment and high quality research done at our Faculty.

The Organizing Committee and the Faculty of Health Sciences are confident that the PhD Day 2010 will be a success and we cordially welcome all participants.

Troels Staehelin Jensen
Chairman, Organizing Committe

Lise Wogensen Bach
Vice-Head, Aarhus Graduate School of Health Sciences

Søren Mogensen
Dean, Faculty of Health Sciences
Aarhus University

Contents

Welcome	3
Information	6
Program	7
The Skou Lecture	9
Aarhus Graduate School of Health Sciences	10
International office	11
The PhD Association	12
Association of Pregaduate Medical Research	13
The Student Counsellor	14
Library of Health Sciences	15
SunQnet - a network for female scientists	16
Sponsors	17
Session chairmen	18
Free communication program	
Session overview	
- Fogh Nielsen Prize	19
- oral	19
- posters	20
Abstracts	37
Index	234

Information

Practical information:

- Lunch will be held in the Lake Auditorium Building
- Posters will be shown in the Lake Auditorium Building; the Bartholin Building teaching wing room and auditoria 1 - 4; and the Victor Albeck Building.
- Posters should be hung between 15.00 and 16.00 on 14 January or 7.15-8.00 on 15 January. All posters must be taken down immediately after the closing of the conference.
- Oral presenters for sessions O1-O4 must meet in the auditorium concerned between 07.30 and 08.00 to put their PowerPoint presentation onto the auditorium hard disk.

Organizing committee:

- Gunna Christiansen, Institute of Medical Microbiology & Immunology
- Helene Nørrelund, Department of Endocrinology and Diabetes
- Iben Møller Jønsson, PhD student, Department of Paediatrics
- Jens Cosedis Nielsen, Department of Cardiological Medicine B
- Kimmo Jensen, Institute of Physiology and Biophysics
- Lise Wogensen Bach, Research Laboratory for Biochemical Pathology
- Maciej Bogdan Maniecki, PhD student, Department of Clinical Biochemistry
- Michael Mulvany, Head Graduate School of Health Sciences
- Niels Trolle Andersen, Department of Biostatistics, Institute of Public Health
- Thomas Vorup-Jensen, Institute of Medical Microbiology & Immunology
- Troels Staehelin Jensen (chairman), Department of Neurology and Danish Pain Research Center
- Troels Thim, PhD Student, Department of Cardiological Medicine B
- Vivi Schlünssen, Department of Environmental and Occupational Medicine, Institute of Public Health
- Tanja Hansen, PhD Administration

Prize committee:

- Chairman, Jens Chr. Djurhuus
- Co-chairman, Helene Nørrelund

Secretariat:

Inge Haislund Andersen, Forskeruddannelsen, The Faculty of Health Sciences, Vennelyst Boulevard 9, 8000 Aarhus C. IHA@SUN.AU.DK

Graduate School of Health Sciences, Aarhus University

PHD DAY 15 JANUARY 2010

International networking

Sessions held in Auditorium 1 in the Lake Auditorium unless otherwise indicated

14 January

15.00 – 16.00 Set up posters

15 January

7.15 – 8.00 Set up posters

Welcome

8.15 Søren Mogensen, Dean of Faculty

8.20 Maciej Maniecki, Chairman of the PhD Association

8.25 Troels S. Jensen, Chairman of the Organizing Committee – today's programme

8.30 Jonathan Webb, University of Oxford: "Establishing a dynamic doctoral program. A PhD student's perspective"

Poster session

9.15 Poster visits part one (two chairmen per group of 10 posters) and coffee
P01-P13: Lake Auditorium, P14-P28: Bartholin Building, P29-P36: Victor Albeck Building (all odd numbered sessions)

Oral communications

10.45 Parallel sessions (6 presentations, each presentation 10+5 min.)

Session O1	Chairmen: Raben Rosenberg & Ebba Nexø	Aud. 1
Session O2	Chairmen: Bente Jespersen & Christian Aalkjær	Aud. 2
Session O3	Chairmen: Leif Mosekilde & Lise Wogensen Bach	Aud. 3
Session O4	Chairmen: Jens Overgaard & Jytte Banner Lundemose	Aud. 4

12.15 Lunch

Poster session

13.00 Poster visits part two (two chairmen per group of 10 posters) and coffee
P01-P13: Lake Auditorium, P14-P28: Bartholin Building, P29-P36: Victor Albeck Building (all even numbered sessions).

14.00 Poster viewing

Skou Lecture Chaired by Søren Mogensen, Dean of Faculty

14.30 Nobel Laureate Timothy Hunt: "My Way into the Cell Cycle"

Fogh Nielsen prize competition Chaired by Søren Moestrup & Iben Møller Jønsson

15.15 PhD student Anna Krarup Keller
15.30 PhD student Anne Nyholm Holdensen
15.45 PhD student Casper Bindzus Foldager

Closing remarks

16.00 Lise Wogensen Bach, Vice-Head of Graduate School

Social programme

18.00 Dinner and presentation of prizes in 'Stakladen'
Festive speech by Jane Skov, PhD

22.00 Band and dance

The Skou Lecture

Tim Hunt is a 'Principal Scientist' (note, not THE principal scientist) at Cancer Research UK, Clare Hall Laboratories, in South Mimms, Herts (15 miles north of central London). Dr Hunt was born in 1943 and grew up in Oxford, but went up to Cambridge to read Natural Sciences in 1961. He did his Ph.D. in the Department of Biochemistry on "The Synthesis of Haemoglobin". He spent almost 30 years altogether in Cambridge, mostly working on the control of protein synthesis, with
spells in the USA; he was a postdoctoral Fellow at the Albert Einstein College of Medicine in 1968-70 and he spent summers at the Marine Biological Laboratory, Woods Hole from 1977 until 1985, teaching and doing research. In 1982, he discovered cyclins, which turned out to be "Key Regulator(s) of the Cell Cycle". This discovery led to a share of the Nobel Prize in Physiology or Medicine in 2001, together with Lee Hartwell and Paul Nurse.
Dr Hunt has helped write two books: together with Andrew Murray, he wrote "The Cell Cycle: An Introduction", and with John Wilson composed "Molecular Biology of the Cell: A Problems Approach" to accompany the textbook by Alberts *et al*. The latest edition of The Problems Book has just been published (2008). Apart from researching, writing and lecturing, Dr Hunt finds himself on numerous scientific advisory panels. He was a member of the EMBO panel that reviewed Cell and Molecular Biology in Austria and chaired the EMBO review panel for the French "Genopole" system. He was on the Scientific Advisory Board of the IMP in Vienna, and is a member of the advisory board of laboratories in Barcelona, Dundee, London, Madrid, Mishima, Oxford and Trieste. He chaired the Life Sciences Panel for selection of European Young Investigators under the aegis of the European Science Foundation, and is chairman of the council of EMBO. He actively promoted the idea of the European Research Council by lobbying commissioners and MPs in Brussels. Dr Hunt is a Fellow of the Royal Society, a Fellow of the Academy of Medical Sciences, a Foreign Associate of the National Academy of Sciences of the USA, a Member of EMBO, a Foreign Member of the American Academy of Arts and Sciences and a Member of Academia Europaea. He was knighted in June 2006. He is married to Mary Collins, who is Professor of Infection and Immunity at University College London. They have two children, Celia (13) and Agnes (9).

Aarhus Graduate School of Health Sciences

The Aarhus Graduate School of Health Sciences was established in 1996, and was based on a tradition of providing quality postgraduate courses started in the 1970s. The Graduate School has currently 500 PhD students enrolled, with 170 enrolled in 2009. The Graduate School is part of the Faculty of Health Sciences, which has four broad divisions: biomedical sciences, clinical sciences, public health and odontology. The Faculty has a total of about 400 professors and associate professors, with the clinical faculty members having joint appointments in the Aarhus University Hospital. The Graduate School has established eleven graduate programmes (*forskeruddannelsesprogrammer)* of high scientific quality which cover the whole range of the Graduate School's activities.

The University of Aarhus Graduate School of Health Sciences provides PhD training in all aspects of health sciences from basic research to the clinic. The integrated approach ensures that the overall aim of improving patient health care is obtained in a multidisciplinary manner without fragmentation of the research training process. Furthermore, this approach ensures a uniform quality of the PhD training program.

The Graduate School is led by a Head and vice-Head who are advised by the elected PhD Committee. The Graduate School Heads are assisted by the PhD administrator and the staff of the PhD office. The Graduate School holds about 80 courses each year, of which some are core courses taken by all PhD students, while the majority of courses are elective taken according to the needs of the particular PhD student. The Graduate School Heads are responsible for monitoring the quality of the courses and initiating new courses as required in collaboration with the graduate programmes.

It is the aim of the Graduate School that the individual PhD student completes a project at the highest international level, and that the work can be seen as a part of health science in its broadest terms. This focus builds on the Faculty's international expertise which stretches from basic biomedicine and molecular biological research to patient-oriented clinical investigations into molecular understanding of pathogenesis, diagnosis and treatment. New discoveries in these areas will therefore have an advantage for society, but also an important commercial perspective directed towards the Danish pharmaceutical and biotechnological industry. It is within this large and exciting environment that the Graduate School is able to offer a wide range of challenging PhD projects.

Michael J. Mulvany, Head of Graduate School
Lise Wogensen Bach, vice-Head of Graduate School

International office

Aarhus University has an international focus and makes targeted efforts to attract researchers and students from abroad. The University wants to recruit PhD students from among the best students in the world. The University also wants Danish PhD students to go abroad.

This international focus and the wish for increased international mobility among PhD students are also encouraged by the Aarhus Graduate School of Health Sciences.

How are we doing this?

First of all the University has a central International Help Desk (IHD) this is an office that provides service to international PhD scholars. It is a place where one can get practical and administrative help to solve problems arising in connection with the studies and work at Aarhus University, and residence in Denmark.

Furthermore, one can also obtain advice on how to solve problems with childcare and job-opportunities for spouses. The office provides a general service to all nine main academic areas, and refers questions to experts within or outside the University for more specific information.

One of these experts is the international officer at the Graduate School of Health Sciences. The international officer is a key person in the communication between the IHD and the many institutes at the Faculty of Health Sciences, and can assist with more specific questions. Most importantly the officer will communicate with the international PhD student before arrival in Aarhus, giving information about legalisation, forwarding our welcome package and the international PhD student will be offered a mentor, who will support the PhD student during the first weeks after arrival.

The PhD student will also be offered a free Danish course as soon as possible after arrival.

Since we are also encouraging Danish PhD students to work for shorter or longer periods of time in a laboratory abroad, we are planning to develop ‘what shall I do’ or ‘how to go abroad’ packages, which, hopefully, will avoid some of the problems the PhD students come across when planning their stay abroad. From 1 October 2009 it has been possible to earn ECTS points from your stay abroad if you hand in a report (1-3 months, 2 ECTS, 4-6 months, 4 ECTS).

For more information please look at our homepage: www.Health.au.dk/forskeruddannelsen

The international officer can be contacted at: khl@sun.au.dk

There are currently 65 international students at the Graduate School of Health Sciences, and the number is increasing month by month. The students come from all over the world, at the time being from 24 different nations.

Phdassociation.dk

All PhD students at SUN, AU are members Including You!

We work on issues concerning Your PhD:

Overall, the Phd association works on improving the PhD study at SUN, AU. We lobby for issues like PhD courses, teaching load, studying abroad etc.

Main activities:

- Collaboration with the Graduate School of Health Science
- Organizer of "After Work Meetings"
- Co-organizer of the annual PhD day

We look forward to seeing you at the next General Assembly the 1st of Februrary

Phdforeningen.dk

Studenterforskning.dk

Selskab for Medicinsk Studenterforskning

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Selskab for Medicinsk Studenterforskning (SMS, *Society of Pregaduate Medical Research*) is an independent organisation of medical students with interest in medical research.

The object of the society is to disseminate and facilitate pregraduate medical research.

SMS organizes courses in experimental surgery (pigs and rodents) and information events where medical students can meet potential supervisors for a future research year.

SMS will March 2010 host the second national Danish conference for pregraduate medical research, where pregraduate researchers nationwide are invited to present their research and network with other students. Find more information on www.kms2010.dk

At the annual general assembly, medical students and doctors who have carried out a pregraduate Research Year are elected to the board of the *Society of Pregaduate Medical Research*.

The society manages a web-site that coordinates research year projects and distributes contact between supervisors and potential prospective research year students.

www.studenterforskning.dk

Studenterforskning.dk

Selskab for Medicinsk Studenterforskning

Student counsellor for PhD students

Personal contact: Sanne Angel

phdstudievejleder@sun.au.dk

Phone: 8942 4448

Surviving you dissertation

From time to time it is more than a book title.

In the knowledge ~~of~~ that a PhD-study can be an overwhelming challenge, the Faculty of Health Science has established a student counsellor for Ph.D students.

Is it difficult to plan your daily work?

Are things not working?

Is it hard to collaborate with your supervisor?

Do you find your situation as a PhD student difficult or unsatisfactory?

I am always an interested listener.

The PhD student counsellor is a professional interlocutor. Conversations with the counsellor are confidential and anonymity is promised. It is not an alternative to the professional research supervision. By means of conversations, the counsellor can help students become aware of what they perceive as difficult and why. This is done in close collaboration with the secretary of The Graduate School of Health Sciences if the process related issues have administrative elements. The intention is to help PhD students gain clarity, come to terms with their situation or for them to see other opportunities, if they experience personal problems or other difficulties related to the process of working and studying as a PhD student. The counsellor can also assist students in making competent decisions on deliberate basis.

You are always welcome to contact the PhD student counsellor!
Sometimes sooner is better than latter, no problem is too small for a talk.

Det Sundhedsvidenskabelige Bibliotek – Library of Health Sciences

Your library!

www.statsbiblioteket.dk

The library provides help and guidance on information and literature search

- Fast and easy finding of and access to relevant literature
- E-alerts with table of contents from your favourite journals
- E-alerts matching the keywords of your project
- Individual instruction and help for literature search designed for your specific project
- PhD course '*Literature search in medical databases*'

Just contact us…

Library of Health Sciences
Aarhus University / The State and University Library
The Victor Albeck Building, Vennelyst Boulevard 4, 8000 Århus C

Phone: 8946 2362
E-mail: svb@statsbiblioteket.dk

SunQnet, et netværk for forskere ved Det Sundhedsvidenskabelige Fakultet, Aarhus Universitet. Netværket er et uformelt fagligt forum for, der primært har til formal at styrke kvindelige forskeres samarbejde på tværs af Fakultetets institutter, men alle er naturligvis velkomne til at deltage. Netværket henvender sig til forskere på alle niveauer inklusiv studerende. http://www.sunqnet.au.dk

frAU-female researchers at Aarhus University
Ved Aarhus Universitet findes desuden netværket frAU, som er et interfakultært netværk primært for kvindelige forsker (http://www.frau.au.dk:80/index.jsp). Dette netværk arrangerer løbende seminarer, kurser og møder ----og er græsrodsbevægelsen og inspirationskilden for arbejdet i universitetets task force for ligestilling: http://www.au.dk/ligestilling. Man tilmelder sig e-mail liste på frAU's hjemside (http://www.frau.au.dk:80/index.jsp).

Networks
SunQnet is a network for scientists employed at the Faculty of Health Science at the University of Aarhus. The network is an informal scientific forum, which primarily aspires to strengthen the collaboration between female researchers at the various institutes of the faculty. The network is directed to all researchers including students.
http://www.sunqnet.au.dk

frAU-female researchers at Aarhus University
The network frAU is an interdisciplinary platform for women scientists at Aarhus University (http://www.frau.au.dk:80/index.jsp). This network arranges seminars, courses and meetings ---- and is the source of inspiration for the work in the task force for equal opportunity at Aarhus University http://www.au.dk/ligestilling. To participate in the network one can join the e-mail list at frAU's home page

(http://www.frau.au.dk:80/index.jsp).

The organization committee for the PhD-day 2010 is grateful for the travel grants given by Lundbeck, Novo Nordisk A/S and Medtronic

Session chairmen

Fogh-Nielsen session Søren Moestrup & Iben Møller Jønsson

O01	Raben Rosenberg & Ebba Nexø
O02	Bente Jespersen & Christian Aalkjær
O03	Leif Mosekilde & Lise Wogensen Bach
O04	Jens Overgaard & Jytte Banner Lundemose
P01	Mads Dahl & NN
P02	Allan Flyvbjerg & Morten Ø. Jensen
P03	Thomas G. Jensen & Anneli Sandbæk
P04	Natalya Fedosova & Jens Otto Lunde Jørgensen
P05	Anders Børglum & Marianne Nordsmark
P06	Steffen Junker & Britt Elmedal Laursen
P07	Rikke Nørregaard & Jens Leipziger
P08	Niels Gregersen & Kirsten Lomborg
P09	Karen Dybkær & Christer Swan Andreassen
P10	Per Höllsberg & Ellen Aagaard Nøhr
P11	Toke Bek & Sussie Laustsen
P12	Jens Nyengaard & Claus Lindbjerg Andersen
P13	Lene Baad-Hansen & Hans Jürgen Hoffmann
P14	Gunna Christiansen & Jens Fedder
P15	Ulf Simonsen & Johan Palmfeldt
P16	Lise Lotte Hansen & Lars Dyrskjøt
P17	Poul Frost & Marianne Hokland
P18	Henning Andersen & Tine Brink Henriksen
P19	Jens Sandahl Christiansen & Lars Uhrenholt
P20	Maiken Stilling & Jens Rolighed Larsen
P21	Michael Borre & Lars Vinge Nygaard
P22	Vladimir Matchkov & Peter Vedsted
P23	Kim Overvad & Sten Rasmussen
P24	J. Michael Hasenkam & Samuel Alberg Thrysøe
P25	Karin Demtröder & Michael Mulvany
P26	Michael Rehling & Søren Risom
P27	Robert Fenton & Michael Sørensen
P28	Ann Wenzel & Jan Frystyk
P29	Jeppe Prætorius & Kjeld Hermansen
P30	Torben Clausen & Arne Møller
P31	Sven Poulsen & Reimar W. Thomsen
P32	Eva Bonefeld-Jørgensen & Morten Nielsen
P33	Jens Peter Kroustrup & Palle Villesen
P34	Kamille Smidt Rasmussen & Andreas Stauropoulos
P35	Søren Kjærgaard & Yvonne Eskildsen-Helmond
P36	Kari Tanderup & Steffen Thiel

Fogh Nielsen session. Chairmen: Søren Moestrup & Iben Møller Jønsson

FN Anna Krarup Keller. MICRODIALYSIS FOR DETECTION OF POSTOPERATIVE ISCHEMIA IN EXPERIMENTAL RENAL TRANSPLANTATION

FN Casper Foldager. EFFECTS OF COMBINED 3D- AND HYPOXIC CULTURING ON CARTILAGE-SPECIFIC GENE EXPRESSION IN HUMAN CHONDROCYTES

FN Anne Nyholm Holdensen. CRUCIAL DETERMINANT OF CA^{2+} TRANSPORT CYCLE RATE OF SERCA

Oral session 01. Chairmen: Raben Rosenberg & Ebba Nexø

O01.01 Mette Laursen. X-RAY CRYSTALLOGRAPHIC STUDIES OF HIGH AFFINITY BINDING OF CARDIAC GLYCOSIDES TO THE NA^+,K^+-ATPASE

O01.02 Anders Etzerodt. IDENTIFICATION OF THE PROTEASE RESPONSIBLE FOR THE PHORBOL ESTER INDUCED SHEDDING OF THE HEMOGLOBIN SCAVENGER RECEPTOR CD163

O01.03 Mette Juul Koefoed. IMPROVED INTEGRATION AND REMODELING OF BONE ALLOGRAFTS COATED WITH FREEZE-DRIED VIRAL VECTORS BASED ON ADENO-ASSOCIATED VIRUS (AAV)

O01.04 Tue Fryland. CHARACTERIZATION OF *BRD1* – A SUSCEPTIBILITY GENE FOR SCHIZOPHRENIA AND BIPOLAR DISORDER

O01.05 Marion Delenclos. OVER-EXPRESSION OF ALPHA-SYNUCLEIN DISRUPTS THE EXPRESSION PROFILE OF BASSOON, AN ACTIVE ZONE COMPONENT.

O01.06 Cathrine Søndergaard Baastrup. CENTRAL NEUROPATHIC PAIN AND ANXIETY IN AN EXPERIMENTAL MODEL OF SPINAL CORD INJURY

Oral session 02. Chairmen: Bente Jespersen & Christian Aalkjær

O02.01 Martin Broch-Lips. EFFECTS OF REDUCED CL^- CONDUCTANCE ON THE FUNCTION OF WORKING MUSCLE

O02.02 Ingunn Skogstad Riddervold. DOES EXPOSURE TO WOOD SMOKE AFFECT AIRWAY RESPONSES IN ATOPIC HUMANS?

O02.03 Anders Knudsen. IMPACT OF ISCHEMIC PRE- AND POSTCONDITIONING ON GENE EXPRESSION LEVELS IN THE RAT LIVER USING DNA MIKROARRAYS

O02.04 Morten Olsen. EDUCATIONAL ACHIEVEMENT AMONG LONG-TERM SURVIVORS OF CONGENITAL HEART DEFECTS: A DANISH POPULATION-BASED FOLLOW-UP STUDY

O02.05 Thomas Wittenborn. A NOVEL ANGIOGENESIS MOUSE MODEL FOR SCREENING FUNCTIONALIZED NANO-PARTICLES

O02.06 Kristian Altern Øvrehus. DIAGNOSTIC EVALUATION OF PATIENTS SUSPECTED OF CORONARY ARTERY DISEASE: EXERCISE TESTING OR CORONARY COMPUTED TOMOGRAPHIC ANGIOGRAPHY?

Oral session 03. Chairmen: Leif Mosekilde & Lise Wogensen Bach

O03.01 Louise Wamberg. EXPRESSION OF VDR MRNA IN ADIPOSE TISSUE IS AFFECTED BY ADIPOSE TISSUE LOCATION IN LEAN SUBJECTS

O03.02 Rasmus Sode-Carlsen. ONE YEAR OF GROWTH HORMONE THERAPY IMPROVES BODY COMPOSITION IN ADULTS WITH PRADER-WILLI SYNDROME

O03.03 Ane Bærent Fisker. VITAMIN A SUPPLEMENTATION AT BIRTH PRIMES THE RESPONSE TO SUBSEQUENT VITAMIN A SUPPLEMENTATION: A BENEFICIAL EFFECT FOR GIRLS

O03.04 Lars Erik Bartels. DENDRITIC CELLS FROM CROHN'S PATIENTS CAN MODULATE OWN

FUNCTION THROUGH HYDROXYLATION OF 25-HYDROXY VITAMIN D3

O03.05 Helene Kvistgaard. A NOVEL SILENT MUTATION IN THE *AVP* GENE MAY CAUSE REDUCED PROCESSING OF THE AVP PROHORMONE

O03.06 Anders Lindelof. WHY CAN OBESE ADOLESCENTS NOT ENGAGE IN HEALTHY HABITS? - THE STIGMA OF OBESITY AND THE MISSING DIALOGUE.

Oral session 04. Chairmen: Jens Overgaard & Jytte Banner Lundemose

O04.01 Kasper Toustrup. VALIDATION OF A HYPOXIC GENE EXPRESSION SIGNATURE ON XENOGRAFTS AND HUMAN HEAD AND NECK SQUAMOUS CELL CARCINOMAS (HNSCC)

O04.02 Peter Martin Hjørnet Kamper. TUMOR-INFILTRATING MACROPHAGES CORRELATE TO ADVERSE PROGNOSIS AND EPSTEIN-BARR VIRUS STATUS IN CLASSICAL HODGKIN LYMPHOMA.

O04.03 Malene Hvid Larsen. IL-25 IN ATOPIC DERMATITIS

O04.04 Anne Stidsholt Roug. A COMPARATIVE STUDY OF THE IMMUNOPHENOTYPE OF STEM CELLS IN AML FOCUSING ON ANTIGENS RELATED TO EARLY HEMATOPOIESIS

O04.05 Iben Møller Jønsson. IS THERE A NEW LIGHT AT THE END OF THE TUNNEL? A STUDY ON RECTAL PHYSIOLOGY IN HEALTHY CHILDREN AND CHILDREN WITH FAECAL INCONTINENCE.

O04.06 Tina Rask Emholdt. NEPHROGENIC SYSTEMIC FIBROSIS: A CASE STUDY FROM DENMARK

Poster session 01. Chairmen: Mads Dahl & Andreas Nørgaard Glud

P01.01 Steffen Møller-Larsen. IN-DEPTH ASSOCIATION ANALYSIS OF TOLL-LIKE RECEPTORS WITH ASTHMA AND RELATED ATOPIC DISORDERS

P01.02 Majbritt Hauge Kyneb. INVESTIGATION OF THE USE OF THE MEMBRANE RECEPTOR CD163 AS TARGET IN CYTOSTATIC TREATMENT OF AML

P01.03 Anne-Mette Bay Bjørn. MATERNAL USE OF PRESCRIBED GLUCOCORTICOIDS DURING PREGNANCY AND RISK OF CONGENITAL BIRTH DEFECTS: AN 11-YEAR POPULATION-BASED STUDY IN DENMARK

P01.04 Lars Peter Sørensen. VLDL-TG METABOLISM IN TYPE 2 DIABETES

P01.05 Philipp Harbig. METHODS FOR IMPROVING COMPLIANCE WITH MEDICINE INTAKE (MICMI): A VALIDATION OF QUESTIONNAIRE 'ELDERLY MEDICINE COMPLIANCE QUESTIONNAIRE (EMCQ)'

P01.06 Michael Winterdahl. HEPATIC BLOOD PERFUSION CAN BE ESTIMATED NON-INVASIVELY BY DYNAMIC PET USING GLUCOSE ANALOGS: VALIDATION OF A PORTAL VENOUS MODEL IN PIG STUDIES

P01.07 Emma Tina Bisgaard Olesen. VASOPRESSIN INDEPENDENT MEMBRANE TARGETING OF AQUAPORIN-2 BY PROSTAGLANDIN E2

P01.08 Kathrine Kleis Tilma. THE DIAMETER RESPONSE OF RETINAL VESSELS AFTER TOPICAL APPLICATION OF A PROSTAGLANDIN AGONIST AND A PROSTAGLANDIN SYNTHESIS INHIBITOR IN VIVO. PRELIMINARY RESULTS.

P01.09 Marianne Cathrine Rohde. STRESS RESPONSE IN SUDDEN INFANT DEATH; IN VITRO STUDIES OF FIBROBLAST CULTURES

Poster session 02. Chairmen: Allan Flyvbjerg & Morten Ø. Jensen

P02.01 Yonglun Luo. DEVELOPMENT OF A CLONED BRCA1 KNOCKOUT PIG MODEL

P02.02 Janne Lebeck. EXPRESSION OF HEPATIC AQUAGLYCEROPORIN 9 (AQP9) IS REGULATED IN RESPONSE TO CASTRATION AND PPARα- AGONIST TREATMENT

P02.03 Ebbe Bødtkjer. DISRUPTION OF THE NA^+,HCO_3^--COTRANSPORTER NBCN1 CAUSES HYPERTENSION: INTRACELLULAR ACIDIFICATION INHIBITS NO PRODUCTION AND RHO-KINASE DEPENDENT CA^{2+}-SENSITIVITY

P02.04 Pernille Munk Frandsen. ACTIVATION AND RECEPTOR STUDIES OF HUMAN MAST CELLS IN HEALTHY INDIVIDUALS AND PATIENTS WITH ASTHMA AND ALLERGY

P02.05 Hanne Vebert Olesen. CREATING A NATIONAL PATIENT DATABASE

P02.06 Irina Kruglikova. THE IMPACT OF CONSTRUCTIVE FEEDBACK ON TRAINING IN GASTROINTESTINAL ENDOSCOPY USING HIGH FIDELITY VIRTUAL REALITY SIMULATION. A RANDOMIZED CONTROLLED TRIAL

P02.07 Maria Jakobsen. VIRAL DELIVERY OF TNF-α TARGETED SHRNA MEDIATES RESOLUTION OF PSORIASIS IN THE XENOGRAFT TRANSPLANTATION MODEL

P02.08 Ida Sejersdahl Kirkegaard. EARLY FETAL GROWTH RATE, PLACENTA HORMONES AND PRETERM DELIVERY

P02.09 Helle Rosenberg. CO-REGULATION OF A BICARBONATE TRANSPORTER AND A KINASE IN THE MOUSE

Poster session 03. Chairmen: Thomas G. Jensen & Anneli Sandbæk

P03.01 Pernille Kure Vandborg. FOLLOW-UP OF NEONATAL NON-HAEMOLYTIC HYPERBILIRUBINEMIA IN DANISH TERM AND NEAR-TERM INFANTS WITH TOTAL SERUM BILIRUBIN (TSB) LEVEL ≥ 420 UMOL/L.

P03.02 Raffaella Mangnoni. NEURODEGENERATIVE DISEASES DUE TO MUTATION IN THE MITOCHONDRIAL HSP60 CHAPERONE: STUDIES OF THE PATHOPHYSIOLOGY USING MOLECULAR PROTEOMICS AND PHENOTYPE INVESTIGATION OF GENE-MODIFIED MICE

P03.03 Tine Qvistgaard. MESOANGIOBLASTS AS THERAPEUTIC STEM CELLS

P03.04 Helle Damkier. THE *SLC4A10* GENE PRODUCT IS A NA^+ DEPENDENT CL^-/HCO_3^- EXCHANGER IN A MAMMALIAN EXPRESSION SYSTEM

P03.05 Tina Storm. THE ROLE OF CUBILIN IN PROXIMAL TUBULAR REABSORPTION.

P03.06 Sabina Jelen. AQP9 IS NOT ESSENTIAL FOR AMMONIA UPTAKE OR UREA RELEASE IN THE LIVER

P03.07 Anders Peter Søndergaard. BIOMECHANICAL PROPERTIES OF THE CORNEA FOLLOWING UVA-RIBOFLAVIN CROSS-LINKING

P03.08 Nynne Sharma. TRANSCRIPTIONAL SILENCING AND PROTECTION OF DNA TRANSPOSON VECTORS WITH APPLICATIONS IN THERAPEUTIC GENE TRANSFER AND PIG TRANSGENESIS

P03.09 Thaneas Prabakaran. FABRY DISEASE, DIAGNOSTIC MARKERS AND THE MECHANISM OF ENZYME REPLACEMENT TREATMENT IN THE RENAL GLOMERULI

Poster session 04. Chairmen: Natalya Fedosova & Jens Otto Lunde Jørgensen

P04.01 Margrethe Smidth. EFFECTS OF AN ACTIVE IMPLEMENTATION OF A CHRONIC DISEASE MANAGEMENT PROGRAMME FOR PATIENTS WITH COPD.

P04.02 Berit Hvass Christensen. THE INFLUENCE OF MATERNAL WORK ON THE DEVELOPMENT OF ALLERGIC DISEASES - A PHD. PROJECT WITHIN THE DANISH NATIONAL BIRTH COHORT

P04.03 Anette Werner. THE EFFECT OF MENTAL TRAINING ON CHILDBIRTH - MEASURED ON PAIN EXPERIENCE AND OTHER BIRTH OUTCOMES

P04.04 Morsi Abdallah. INTRAUTERINE EXPOSURES AND CHILDHOOD PSYCHIATRIC DISORDERS

P04.05 Lena Aadal. REHABILITATION OF TARGETED DAILY LIFE COMPETENCES AS SITUATED LEARNING. INTENSIVE REHABILITATION OF PATIENTS WITH SEVERE TRAUMATIC BRAIN INJURY.

P04.06 Rune Dupont Birkler. A VALIDATED METHOD FOR THE EXTRACTION OF DRUGS FROM THE DRUGWIPE® DRUG-TESTING DEVICE AND CONFIRMATION BY LC-MS/MS

P04.07 Tine Steen Rubak. REGISTER-BASED COHORT STUDY OF INCIDENCE OF TOTAL HIP REPLACEMENT IN RELATION TO CUMULATIVE PHYSICAL WORK LOAD AMONG MALES IN DENMARK

P04.08 Marie Louise Tørring. THE WAITING TIME PARADOX: DANISH CANCER PATIENTS DIAGNOSED FAST HAVE HIGHER MORTALITY

P04.09 Marie Louise Svendsen. COMORBIDITY, QUALITY OF CARE, AND OUTCOME ACCORDING TO MEDICAL SPECIALTY IN STROKE UNITS: A NATIONAL POPULATION-BASED FOLLOW-UP STUDY

P04.10 Trine Brogaard. INTEGRATED SHARED CARE BETWEEN GENERAL PRACTICE, DISCHARGE HOSPITAL AND A SPECIALISED PALLIATIVE CARE TEAM FOR SERIOUSLY ILL CANCER PATIENTS.

P04.11 Morten Willert. EFFECTS OF A STRESS MANAGEMENT INTERVENTION ON ABSENTEEISM FROM WORK - RESULTS FROM A RANDOMIZED WAIT-LIST CONTROLLED TRIAL

P04.12 Hanne-Lise Falgreen Eriksen. PRENATAL EXPOSURE TO ALCOHOL AND TOBACCO: EFFECTS ON IQ AT AGE 5

Poster session 05. Chairmen: Anders Børglum & Marianne Nordsmark

P05.01 Kasper Lynghøj Christensen. A KETONE BODY AS ENDOGENOUS CARBONYL SCAVANGER?

P05.02 Trine Østergaard. ALTERNATIVE MRNA SPLICING OF THE HUMAN EGF RECEPTOR HER4

P05.03 Lisbeth Venø Kruse. THE HERITABILITY OF ATOPIC DISEASE – ESPECIALLY ALLERGIC RHINITIS

P05.04 Dang Quang Svend Le. 3-D PERFUSION CULTURE OF OSTEOGENIC STEM CELLS WITH MEDIA PERFUSION RATE DEPENDENT ON DIFFERENTIATION STAGES

P05.05 Thomas Guldager Knudsen. DIRECT EFFECT OF METHYLPREDNISOLONE ON RENAL SODIUM AND WATER TRANSPORT VIA THE PRINCIPAL CELLS IN THE KIDNEY

P05.06 Torsten Bloch Rasmussen. CLINICAL, GENETIC AND PROTEIN STUDIES IN ARRHYTHMOGENIC RIGHT VENTRICULAR CARDIOMYOPATHY

P05.07 Zhenping Liu. CHRONIC EFFECTS OF AMINO ACIDS ON THE FUNCTION OF THE INS-1E CLONAL BETA CELLS: AMINOACIDOTOXICITY AND BETA CELL DYSFUNCTION.

P05.08 René Frydensbjerg Andersen. IDIOPATHIC NEPHROTIC SYNDROME - OUTCOME IN DANISH PATIENTS

P05.09 Pia Møller Faaborg. ANORECTAL FUNCTION AFTER LONG-TERM USE OF TRANSANAL COLONIC IRRIGATION

Poster session 06. Chairmen: Steffen Junker & Britt Elmedal Laursen

P06.01 Gitte Aarøe Dam. EFFECTS OF BRANCHED-CHAIN AMINO-ACIDS ON AMMONIA METABOLISM IN SKELETAL MUSCLE IN PATIENTS WITH LIVER CIRRHOSIS AND HEALTHY CONTROLS

P06.02 Iben Blaabjerg Sundtoft. SHORT INTERPREGNANCY INTERVAL AS A RISK FACTOR OF SPONTANEOUS PRETERM BIRTH DUE TO LOW CERVICAL COLLAGEN

P06.03 Anne Petas Swane Lund Krarup. HYPOSENSITIVITY IN PATIENTS WITH BARRETT'S OESOPHAGUS: MECHANISMS AND IMPLICATIONS FOR TREATMENT

P06.04 Yu Wang. NAVIGATED PERCUTANEOUS TRANS-ILIAC LUMBOSACRAL FUSION : A FEASIBILITY STUDY USING 3D SURGICAL SIMULATION

P06.05 Anne Skakkebæk Jensen. NEUROPSYCHOLOGIC, NEURORADIOLOGIC, AND GENETIC ASPECTS OF KLINEFELTER´S SYNDROME

P06.06 Mie Hessellund Samson. TREFOIL FACTORS AT BIRTH AND IN THE HUMAN FETUS

P06.07 Casper Nielsen. QUANTITATIVE DETERMINATION OF D-LACTATE IN PLASMA ON THE MODULAR ANALYTICS P

P06.08 Stinne Pulkkinen Schmidt. MISFOLDING OF A DISEASE-ASSOCIATED VARIANT OF SHORT-CHAIN ACYL-COA DEHYDROGENASE LEADS TO OXIDATIVE STRESS AND FISSION OF THE MITOCHONDRIAL NETWORK

P06.09 Dorthe Mørck Mortensen. CALCINEURIN A IS UPREGULATED IN TACROLIMUS-TREATED

RENAL TRANSPLANT PATIENTS WITH STABLE ALLOGRAFT FUNCTION

Poster session 07. Chairmen: Rikke Nørregaard & Jens Leipziger

P07.01 Carina Henriksen. THE PATHOPHYLOGY OF RAPID-ONSET DYSTONIA PARKINSONISM: CELL CULTURE STUDIES AND PORCINE MODEL

P07.02 Ole Halfdan Larsen. THE COMBINATION OF RECOMBINANT FACTOR VIIA AND FIBRINOGEN CORRECTS COAGULATION IN A MODEL OF WHOLE BLOOD THROMBOCYTOPENIA

P07.03 Jonas Jensen. OSTEOGENIC POTENTIAL OF BIPHASIC CALCIUM PHOSPHATE WITH GROWTH FACTOR LOADED ELECTROSPUN POLYMER FIBERS

P07.04 Rita Maria Delgado Silva Marques. [ATP INHIBITS NA^+ ABSORPTION VIA BASOLATERAL P2 RECEPTORS IN MOUSE MEDULLARY THICK ASCENDING LIMB (MTAL)]

P07.05 Maiken Kudahl Larsen. SUDDEN DEATH – A RETROSPECTIVE GENETIC STUDY OF HEART DISEASE

P07.06 Christian Overgaard Steensen. WATER IS DISTRIBUTED PASSIVELY TO THE MUSCLES BUT THE BRAIN IS PROTECTED AGAINST EDEMA IN ACUTE HYPONATREMIA

P07.07 Katrine Emmertsen. LOW ANTERIOR RESECTION SYNDROME SCORE - A SYMPTOM-BASED SCORING SYSTEM FOR BOWEL DYSFUNCTION AFTER RESECTION FOR RECTAL CANCER.

P07.08 Trine Borup Andersen. COMPARISON OF WITHIN- AND BETWEEN-SUBJECT VARIATION OF SERUM CYSTATIN C AND SERUM CREATININE IN CHILDREN AGED 2-13 YEARS

P07.09 Eva Greibe. RAINBOW TROUT SPAWN VITAMIN B12 BINDING PROTEIN AND VITAMIN B12 MALABSORPTION

Poster session 08. Chairmen: Niels Gregersen & Kirsten Lomborg

P08.01 Christel Krøigaard. INVESTIGATION OF CALCIUM-ACTIVATED POTASSIUM CHANNEL OPENING FOR TREATMENT OF PULMONARY DISEASE

P08.02 Maj Lesbo. CARDIOPULMONARY FUNCTION IN PECTUS EXCAVATUM PATIENTS COMPARED TO HEALTHY CONTROL SUBJECTS.

P08.03 Lars Rolighed. EFFECT OF VITAMIN D TREATMENT I PATIENTS WITH PRIMARY HYPERPARATHYROIDISM.

P08.04 Jakob Østergaard. DIABETIC NEPHROPATHY AND THE COMPLEMENT SYSTEM

P08.05 Lau Brix. MAGNETIC RESONANCE IMAGING OF THE VOCAL CORDS DURING SINGING WITH HIGH SPATIAL AND TEMPORAL RESOLUTION USING RADIAL GOLDEN RATIO SAMPLING AND FAST RECONSTRUCTION ON A GRAPHIC CARD

P08.06 Karen Lorentzen. HYALURONIC ACID AND TSG-6 INTERACTIONS IN ANGIOPATHY

P08.07 Jesper Langhoff Hønge. RECELLULARIZATION OF AORTIC HEART-VALVE PROSTHESES IN VIVO

P08.08 Rikke Vestergaard. DOES OSTENE™ IMPROVE BONE HEALING COMPARED WITH BONE WAX AFTER STERNOTOMY?

P08.09 Aygen Øzbay. IMPAIRING EFFECTS OF CYCLOSPORINE AND TACROLIMUS ON INSULIN SECRETION AND TRANSCRIPTIONAL REGULATION IN RAT BETA-CELLS

P08.10 Jesper Brink Askov. EFFECT OF MITRAL VALVE RING ANNULOPLASTY ON IN VIVO CHORDAL TENSION

P08.11 Súsanna Við Streym Thomsen. THE STABILITY OF 25-HYDROXYVITAMIN D IN HUMAN BLOOD DURING DIFFERENT SAMPLING AND STORAGE CONDITIONS.

Poster session 09. Chairmen: Karen Dybkær & Christer Swan Andreassen

P09.01 Esben Søndergaard. ACUTE EFFECTS OF AEROBIC EXERCISE ON VLDL-TRIACYLGLYCEROL KINETICS

P09.02 Anette Luther Christensen. GRADUALLY CHANGING SEASONAL VARIATION OF

CARDIOVASCULAR DISEASES IN DENMARK FEATURING DYNAMIC LINEAR MODELS

P09.03 Lars Jakobsen. PRIMARY PERCUTANEOUS CORONARY INTERVENTION IN A REAL-LIFE POPULATION: COMPARISON WITH TRIAL FINDINGS

P09.04 Jens Holmer-Jensen. DIFFERENTIAL ACUTE EFFECTS OF MILK DERIVED PROTEINS ON POSTPRANDIAL LIPAEMIA IN OBESE NON-DIABETIC SUBJECTS

P09.05 Sophie Constantin Lütken. REGULATION OF RENAL AQUAPORINS AND SALT TRANSPORTERS IN LOW SODIUM DIET RATS WITH EXPERIMENTALLY INDUCED HEART FAILURE

P09.06 Hans Henrik Møller Nielsen. SCANDINAVIAN STUDY OF TRANSAPICAL CATHETERBASED AORTIC STENTVALVE TREATMENT VERSUS OPEN SURGERY

P09.07 Torben Harsløf. THE EXPRESSIONAND REGULATION OF BONE-ACTING CYTOKINES IN HUMAN PERIPHERAL ADIPOSE TISSUE IN ORGAN CULTURE

P09.08 Christian Daugaard Peters. CARDIOVASCULAR EFFECT OF IRBESARTAN IN NEWLY STARTED HEMODIALYSIS PATIENTS – A SUBSTUDY WITHIN THE SAFIR-STUDY.

P09.09 Thomas Krusenstjerna-Hafstrøm. INSULIN SENSITIVITY AND SUBSTRATE METABOLISM BEFORE AND AFTER TREATMENT IN PATIENTS WITH GROWTH HORMONE DEFICIENCY

P09.10 Troels Thim. BARE METAL STENTS CRIMPED ON PACLITAXEL COATED BALLOONS: PHARMAKOKINETIC PROFILES AND EFFECTS ON LATE LUMEN LOSS AND NEOINTIMA FORMATION

Poster session 10. Chairmen: Per Höllsberg & Ellen Aagaard Nøhr

P10.01 Marianne Bennetzen. ENDOCANNABINOID LEVELS ARE HIGHER IN THE ADIPOSE TISSIE OF OBESE WOMEN COMPARED WITH THOSE OF OBESE MEN

P10.02 Lea Brader. HEALTHY NORDIC DIET IN THE PREVENTION OF METABOLIC SYNDROME – THE AARHUS UNIVERSITY HOSPITAL (AUH) PART OF A MULTI-CENTRE STUDY (SYSDIET)

P10.03 Helle Damgaard Zacho. FUNCTIONAL VERSUS RADIOLOGICAL ASSESSMENT OF CHRONIC INTESTINAL ISCHEAMIA

P10.04 Charlotte Amalie Ihlo. PHARMACOKINETIC AND PHARMACODYNAMIC PARAMETERS OF DIFFERENT INSULIN PUMP STROKE FREQUENCIES. A RANDOMIZED CONTROLLED STUDY COMPARING SUBCUTANEOUS AND INTRAVENOUS ADMINISTRATION OF INSULIN ASPART.

P10.05 Karina Bech Cullberg. REDUCTION OF ANGIOGENIC FACTORS AFTER WEIGHT LOSS WITH OR WITHOUT AEROBIC EXERCISE IN OBESE SUBJECTS. A 12- WEEK RANDOMIZED INTERVENTION STUDY.

P10.06 Rasmus Pold. PSAMMOMYS OBESUS: A PROMISING ANIMAL MODEL OF TYPE 2 DIABETES

P10.07 Jacob Thorsted Sørensen. REGIONAL IMPLEMENTATION OF PRE-HOSPITAL DIAGNOSIS IN ACUTE ST-ELEVATION MYOCARDIAL INFARCTION AND DIRECT ADMISSION TO INTERVENTIONAL HOSPITAL: IMPACT ON SYSTEM DELAY

P10.08 Mads Brix Kronborg. LONG TERM CLINICAL OUTCOME AND LEFT VENTRICULAR LEAD POSITION IN CARDIAC RESYNCHRONIZATION THERAPY.

P10.09 Hua Chen. THE ACUTE EFFECT OF SULFAPHENAZOLE ON INTRACELLULAR CALCIUM AND REACTIVE OXYGEN SPECIES IN MESENTERIC SMALL ARTERIES OF DB/DB MICE

P10.10 Marta Bauerek. EFFECT OF DIETARY CHOLESTERYL ESTERS ON THE ABSORPTION OF CHOLESTEROL BY CACO-2 CELLS

Poster session 11. Chairmen: Toke Bek & Sussie Laustsen

P11.01 Ania Pietraszek. POSTPRANDIAL DYSMETABOLISM - THE EFFECTS OF MONOUNSATURATED VS. SATURATED LIPIDS ON LIPID AND CARBOHYDRATE METABOLISM AND INFLAMMATION IN HEALTHY 1ST DEGREE RELATIVES OF PATIENTS WITH TYPE 2 DIABETES

P11.02 Grazina Urbonaviciene. PLASMA ALPHA-DEFENSIN FOR PREDICTING CARDIOVASCULAR RISK IN PATIENTS WITH PERIPHERAL ARTERIAL DISEASE

P11.03 Jane Byriel Knudsen. INFECTIVE ENDOCARDITIS: A CONTINUOUS CHALLENGE. THE RECENT

EXPERIENCE OF A EUROPEAN TERTIARY CENTER

P11.04 Eigil Husted Nielsen. USEFULNESS OF NATIONAL PATIENT REGISTRY DATA AND RELIABILITY OF ICD-8 AND ICD-10 CODES FOR THE IDENTIFICATION OF PATIENTS WITH NEWLY DIAGNOSED CRANIOPHARYNGIOMA.

P11.05 Tanja Tvistholm Sikjær. TREATMENT OF HYPOPARATHYROIDISM WITH SUBCUTANEOUS PTH (1-84) INJECTIONS: EFFECTS ON MUSCLE FUNCTION AND QUALITY OF LIFE.

P11.06 Sofie Gry Pristed. CHANGES IN HEALTH-RELATED QUALITY OF LIFE AFTER GASTRIC BANDING

P11.07 Kim Munk. REMOTE ISCHEMIC PERCONDITIONING BY REPETITIVE NON-INJURIOUS LIMB ISCHEMIA IMPROVES LEFT VENTRICULAR FUNCTION AFTER STEMI IN PATIENTS WITH EXTENSIVE MYOCARDIUM AT RISK. ECHOCARDIOGRAPHIC RESULTS FROM THE REMOTE ISCHEMIC PERCONDITIONING IN STEMI TRIAL

P11.08 Maiken Glud Dalager. CT CORONARY ARTERY PLAQUE IMAGING, IMPACT OF DIFFERENT CONTRAST CONCENTRATIONS ON PLAQUE IDENTIFICATION

P11.09 Christian Høst. TESTOSTERONE ACUTELY SUPRESSES ADIPONECTIN LEVELS IN EXPERIMENTAL MALE HYPOGONADISM. A DOUBLE BLIND, RANDOMIZED, PLACEBO-CONTROLLED, CROSS-OVER STUDY.

P11.10 Bo Løfgren. INHIBITION OF THE MALATE-ASPARTATE SHUTTLE ABOLISHES CARDIOPROTECTION BY POSTCONDITIONING IN RAT HEARTS

Poster session 12. Chairmen: Jens Nyengaard & Claus Lindbjerg Andersen

P12.01 Christian Møller Pedersen. REMOTE ISCHAEMIC PRECONDITIONING PREVENTS SYSTEMIC PLATELET ACTIVATION ASSOCIATED WITH ISCHAEMIA-REPERFUSION INJURY IN MAN

P12.02 Dorte Guldbrand Nielsen. PHYSIOLOGY – IS IT IMPORTANT TO KNOW WHEN LEARNING TRANSTHORACIC ECHOCARDIOGRAPHY?

P12.03 Erik Grove. INCREASED WHOLE BLOOD PLATELET AGGREGATION IN CORONARY ARTERY DISEASE PATIENTS WITH A HIGH PLATELET TURNOVER

P12.04 Thais Almeide Lins Pedersen. LONG-TERM FOLLOW-UP AFTER SURGICAL CORRECTION OF COARCTATION OF THE AORTA: HIGH PREVALENCE OF CARDIOVASCULAR MORBIDITY

P12.05 Rasmus Haarup Lie. CYCLOSPORINE A ADMINISTERED IMMEDIATELY BEFORE REPERFUSION DOES NOT ELICIT CARDIO-PROTECTION IN AN IN-VIVO PORCINE MODEL OF ACUTE MYOCARDIAL INFARCTION.

P12.06 Ulla Kristine Møller. THE EFFECTS OF BREASTFEEDING AND AMENORRHEA ON CHANGES IN BONE MINERAL DENSITY POSTPARTUM. AN UNCONTROLLED FOLLOW-UP STUDY.

P12.07 Thomas Dalsgaard. [NOVEL OPENERS OF SMALL CONDUCTANCE CALCIUM-ACTIVATED POTASSIUM CHANNELS ENHANCES ENDOTHELIUM-DEPENDENT VASODILATATION IN PORCINE RETINAL ARTERIOLES]

P12.08 Mikkel Misfeldt. PERIVASCULAR GLIAL CELLS ARE INVOLVED IN TONE REGULATION OF PORCINE RETINAL ARTERIOLES IN VITRO

P12.09 Charlotte Strandhave. HAPTOGLOBIN PHENOTYPE PREDICTS LOW HEART RATE VARIABILITY IN PATIENTS WITH CHRONIC KIDNEY DISEASE

P12.10 Anders Koustrup Niemann. ACCURACY OF COMPUTATIONAL 3D MODELS USING ULTRASOUND AND MR

Poster session 13. Chairmen: Lene Baad-Hansen & Hans Jürgen Hoffmann

P13.01 Mads Kjølby. SORT1, THE CARDIOVASCULAR RISK GENE AT 1P13.3 IS A NOVEL REGULATOR OF HEPATIC LIPOPROTEIN EXPORT

P13.02 Krista Kjærgaard. CYSTATIN C IS AN ACCURATE AND REPRODUCIBLE MARKER OF RESIDUAL RENAL FUNCTION IN PERITONEAL DIALYSIS PATIENTS

P13.03 Maria Mærsk Nielsen. SATIATING EFFECTS OF MILK BUT NOT SUGAR- OR ARTIFICIAL-SWEETENED SOFT DRINKS AND WATER

P13.04 Ulla Kampmann Opstrup. VITAMIN D STATUS IN PATIENTS WITH TYPE 2 DIABETES – A CROSS-SECTIONAL STUDY

P13.05 Martin Majlund Mikkelsen. NO INCREASED OPERATIVE BLOOD LOSS IN PATIENTS WITH SEVERE AORTIC VALVE STENOSIS AND ACQUIRED VON WILLEBRAND SYNDROME UNDERGOING ELECTIVE AORTIC VALVE REPLACEMENT

P13.06 Jesper Fleischer. SELF-MONITORING OF AUTONOMIC NERVOUS FUNCTION AT HOME SHOW HIGHER VARIABILITIES WHEN COMPARED TO HOSPITAL TESTING

P13.07 Niklas Johan Alexander Telinius. ADRENERGIC INNERVATION OF THE HUMAN THORACIC DUCT

P13.08 Rebekka Vibjerg Bækgaard Thomsen. MECHANISMS UNDERLYING RESISTANCE TO ISCHEMIC PRECONDITIONING IN DIABTES MELLITUS.

P13.09 Michael Madsen. CO-TREATMENT WITH PEGVISOMANT AND A SOMATOSTATIN ANALOGUE (SA) IN SA-RESPONSIVE ACROMEGALIC PATIENTS

P13.10 Birgitte Kousholt. CARDIAC NATRIURETIC PEPTIDE THERAPY IN A PORCINE MODEL OF ACUTE MYOCARDIAL INFARCTION

Poster session 14. Chairmen: Gunna Christiansen & Jens Fedder

P14.01 Jette Ahrensberg. CHILDHOOD MALIGNANCIES - SYMPTOMS AND DELAY IN DIAGNOSIS AND TREATMENT.

P14.02 Merethe Kousgaard Andersen. THE OVERWEIGHT CHILD IN GENERAL PRACTICE - IDENTIFY, ASSESS, ADDRESS

P14.03 Lene Bastrup Jørgensen. IDENTIFICATION OF COPD PATIENTS' STRATEGIES FOR COPING WITH DYSPNOEA

P14.04 Jakob Kjeldgaard Jakobsen. TREATMENT OF FAECAL INCONTINENCE WITH SACRAL NERVE STIMULATION – IMPROVED FUNCTION WITH STIMULATION BILATERALLY

P14.05 Christina Malmose Stapelfeldt. THE DEVELOPMENT IN SICK-LEAVE AMONG YOUNG (<40 YEARS) NORWEGIAN AND DANISH ELDERCARE EMPLOYEES IN THE PUBLIC SECTOR BETWEEN 2000 AND 2010.

P14.06 Vibeke Bregnballe. FROM CHILD TO ADULT WITH CYSTIC FIBROSIS

P14.07 Morten Søndergaard Jensen. IS PRENATAL EXPOSURE TO PARACETAMOL, ASPIRIN AND IBUPROFEN A RISK FACTOR FOR CRYPTORCHIDISM?

P14.08 Ann Dyreborg Larsen. RISK OF NEGATIVE BIRTH OUTCOME WHEN EXPOSED TO ADVERSE PSYCHOSOCIAL WORK ENVIRONMENT DURING PREGNANCY.

P14.09 Mette Bach Larsen. DIAGNOSTIC DELAY IN CANCER IN PRIMARY HEALTH CARE -BEFORE AND AFTER THE INTRODUCTION OF FAST TRACK REFERRALS TO SECONDARY HEALTH CARE

P14.10 Marianne Lisby. THE EFFECT OF SYSTEMATIC MEDICATION REVIEW IN ELDERLY PATIENTS ADMITTED TO AN ACUTE WARD OF INTERNAL MEDICINE

Poster session 15. Chairmen: Ulf Simonsen & Johan Palmfeldt

P15.01 Julie Glavind. TIMING OF ELECTIVE CAESAREAN SECTION AND MORBIDITY OF THE NEWBORN

P15.02 Nellie Bering Zinther. ADHESION FORMATION, SHRINKAGE AND BIOMECHANICS OF PROSTHETIC MESHES AFTER LONG-TERM INTRA-ABDOMINAL IMPLANTATION IN A SHEEP MODEL.

P15.03 Bjarne Otto Rittig-Rasmussen. NECK PAIN, NECK TRAINING AND CORTICAL PLASTICITY.

P15.04 Dorte Rytter. MATERNAL INTAKE OF FISH OIL AND RISK FACTORS FOR THE METABOLIC SYNDROME IN THE 18 YEAR OLD OFFSPRING

P15.05 Trine Guldberg. DEVELOPMENT AND EVALUATION OF ELECTRONIC FEEDBACK, A TOOL FOR QUALITY ASSURANCE OF THE DIABETIC CARE IN GENERAL PRACTICE.

P15.06 Mette Trøllund Rask. DIAGNOSTIC CLASSIFICATION OF MEDICALLY UNEXPLAINED SYMPTOMS IN PRIMARY CARE

P15.07 Ioannis Basinas. EXPOSURE ASSESSMENT OF DUST AND PATHOGEN ASSOCIATED MOLECULAR PATTERNS (PAMPS) IN DANISH FARMS. THE SUS12 STUDY.

P15.08 Christian Wulff. THE EFFECT OF CASE MANAGEMENT IN COMPLEX CANCER PATHWAYS

P15.09 Hjördis Osk Atladottir. THE ASSOCIATION OF MATERNAL INFECTION REQUIRING HOSPITALIZATION DURING PREGNANCY AND AUTISM SPECTRUM DISORDER: AN EXPLORATIVE DANISH COHORT STUDY

P15.10 Kasper Grosen. PREDICTION OF THE CONSUMPTION OF OPIOID ANALGESICS FOLLOWING MINIMALLY INVASIVE CORRECTION OF PECTUS EXCAVATUM

Poster session 16. Chairmen: Lise Lotte Hansen & Lars Dyrskjøt

P16.01 Lise Juul. A PRACTICE-NURSE ADDRESSED INTERVENTION TO ENHANCE SELF-MANAGEMENT IN PEOPLE WITH TYPE 2 DIABETES. A RCT IN PRIMARY HEALTH CARE.

P16.02 Jens Christian Jensen. THE ODDER PROJECT: PREDICTORS OF MUSCULOSKELETAL PAIN, WITH EMPHASIS ON THOSE LEADING TO CONSULTATIONS IN PRIMARY CARE.

P16.03 Pia Kirkegaard. BY WHAT CRITERIA DO GENERAL PRACTITIONERS (FAMILY PHYSICIANS) ASSESS NEWLY DEVELOPED DECISION AIDS?

P16.04 Stine Yde Nielsen. Q-FEVER IN PREGNANCY AND FETAL CONSEQUENSES

P16.05 Lotte Ørneborg Rodkjær. SCREENING AND TREATMENT FOR DEPRESSION IS ASSOCIATED WITH A DECLINE IN DEPRESSION AMONG HIV-POSITIVES. A THREE-YEAR PROSPECTIVE FOLLOW-UP STUDY.

P16.06 Chunsen Wu. HEALTH OF CHILDREN BORN TO MOTHERS WITH PREECLAMPSIA – A POPULATION-BASED SIBLING-COHORT STUDY

P16.07 Charlotte Gjørup Pedersen. QUALITY OF CARE AND CRIME RATES AMONG PATIENTS WITH SCHIZOPHRENIA: A NATIONWIDE POPULATION-BASED FOLLOW-UP STUDY

P16.08 Gija Rackauskaite. ADD INSTITUTION CHANGE ORDER OF INSTITUTIONS VALIDATION OF DANISH GMFCS FAMILY REPORT QUESTIONNAIRE

P16.09 Grethe Elholm. THE EFFECT OF FARMING EXPOSURE ON CHANGES IN ATOPY OVER TIME

P16.10 Morten Charles. NEUROPATHY IN A POPULATION WITH SCREEN-DETECTED TYPE 2 DIABETES

Poster session 17. Chairmen: Poul Frost & Marianne Hokland

P17.01 Annette Langager Høgh. TRENDS IN ACE-INHIBITOR TREATMENT 1996 – 2003, AMONG DANISH PERIPHERAL VASCULAR RECONSTRUCTED PATIENTS

P17.02 Rikke Jørgensen. MEANINGFUL CHANGE WITH THE METHOD GUIDED SELF-DETERMINATION – A RANDOMISED CONTROLLED STUDY FOR PATIENTS DIAGNOSED WITH SCHIZOPHRENIA.

P17.03 Peter Agergaard. CAN 22Q11.2 DELETION BE DETECTED ON BEHALF OF A CLINICAL ASSESSMENT OF A PATIENT WITH CONGENITAL CARDIAC MALFORMATION?

P17.04 Anne Sophie Ågård. LONG-TERM IMPACT OF ACUTE CRITICAL ILLNESS AND ADMISSION TO INTENSIVE CARE UNIT. PATIENTS' AND RELATIVES' PERSPECTIVE

P17.05 Lisa Gregersen Østergaard. THE EFFECT OF MODERN REHABILITATIONSTRATEGIES FOR LUMBAR SPINAL FUSION PATIENTS - TWO RANDOMIZED CLINICAL STUDIES

P17.06 Bodil Bjørnshave. IS EVIDENCE-BASED EFFECT OF PULMONARY REHABILITATION (PR) – BASED ON SELECTED STUDYPOPULATIONS?

P17.07 Leanne Langhorn. EARLY REHABILITATION OF PATIENTS WITH POSTTRAUMATIC AMNESIA

IN THE INTENSIVE CARE UNIT

P17.08 Mai-Britt Guldin. DEVELOPMENT OF A PROGNOSTIC CLINICAL TOOL FOR SCREENING FOR COMPLICATED GRIEF IN GENERAL PRACTICE

P17.09 Anna Lamberg. REGISTRATION IN THE REGIONAL NMSC DERMATOLOGY DATABASE: COMPLETENESS OF REGISTRATION OF NON MELANOMA SKIN CANCER (NMSC) AND POSITIVE PREDICTIVE VALUE OF KEY VARIABLES REGISTERED IN THE DATABASE.

P17.10 Helle Svenningsen. DOES SEDATION INFLUENCE ON DELIRIUM AND POST-TRUMATIC STRESS DISORDER AS A RESULT OF HOSPITALIZATION IN INTENSIVE CARE - AN ONGOING PROJEKT

Poster session 18. Chairmen: Henning Andersen & Tine Brink Henriksen

P18.01 Asger Granfeldt. CARDIOPROTECTION BY POSTCONDITIONING IN VIVO INVOLVES LOCAL INHIBITION OF NEUTROPHILS

P18.02 Maria Bach Laursen. THE ROLE OF MIRNA AND AID IN B-CELL MALIGNANCIES

P18.03 Jette Lindorff Riis. CCL17 AND CCL27 ARE DIFFERENTIALLY EXPRESSED IN INFLAMMATORY SKIN DISEASES

P18.04 Trine Silkjær. VARIATIONS IN MITOCHONDRIAL DNA IN PATIENTS WITH ACUTE MYELOID LEUKEMIA

P18.05 Rasmus Boye Kjellerup. CHARACTERIZATION OF THE MAPK PHOSPHATASES IN SKIN INFLAMMATION

P18.06 Emilia Wiechec. COMPARATIVE STUDY OF DIFFERENT DIAGNOSTIC TECHNIQUES (AI, MLPA, FISH) IN BREAST CANCER PATIENTS WITH 1Q25.3 ALTERATIONS.

P18.07 Gao Hong. RIFAMPICIN-SOAKED SILVER-COATED DACRON VERSUS POLYTETRAFLOURETHYLENE GRAFTS FOR IN SITU REPLACEMENT OF EARLY DEEP STAPHYLOCOCCUS AUREUS GRAFT INFECTION IN A RANDOMIZED CONTROLLED TRIAL IN A PORCINE MODEL

P18.08 Bekka Anina Ozer Christensen. WOUND HEALING – A PROTEOMIC ANALYSIS OF ERYTHROPOIETIN'S EFFECT ON GRANULATION TISSUE ISOLATED FROM EPTFE IMPLANTS

P18.09 Jenny Blechingberg. REGULATION OF GENE EXPRESSION BY THE TET-PROTEIN FAMILY

P18.10 Troels Schepler. GROWTH INHIBITORY MICRORNAS SUPPRESSED BY THE WNT PATHWAY IN COLORECTAL CANCER

Poster session 19. Chairmen: Jens Sandahl Christiansen & Lars Uhrenholt

P19.01 Christopher Nordentoft Vejgaard. ARRAY BASED CHARACTERIZATION OF LEUKEMIC MODEL SYSTEMS

P19.02 Tomasz Kazimierz Wojdacz. METHYLATION SENSITIVE HIGH RESOLUTION MELTING (MS-HRM) FOR ASSESSMENT OF METHYLATION IN CLINICAL SAMPLES

P19.03 Lone Schmidt Sørensen. ABSTRAC INCORPORATION OF OMEGA-3 FATTY ACIDS INTO GRANULOCYTE CELL MEMBRANES WITHIN ONE WEEK OF ORAL SUPPLEMENTATIONT TITLE

P19.04 Anders Jensen. PHYLOGENETIC AND TAXONOMIC ANALYSIS OF GROUP C STREPTOCOCCI

P19.05 Tine Gregersen. GASTROINTESTINAL FUNCTION IN PATIENTS WITH CARCINOID SYNDROME

P19.06 Simon Lønbro Jensen. RESISTANCE TRAINING AND DIETARY SUPPLEMENTS AS INTERVENTION FOR REGAINING MUSCLE MASS FOLLOWING RADIOTHERAPY IN HEAD AND NECK CANCER PATIENTS.

P19.07 Malene Krag Kjeldsen. THE ROLE OF SOX4 IN MAILGNANT LYMPHOPOIESIS

P19.08 Johan Grankvist. METASTASES IN BREAST CANCER MRI OR PET/CT A CLINICAL COMPARISON

P19.09 Maria Luise Salskov-Iversen. CASPASE-5 IS UPREGULATED IN PSORIASIS

P19.10 Simon Rasmussen. THE ROLE AND MECHANISM OF AUTOPHAGY IN TOLL LIKE RECEPTOR 9 MEDIATED VIRAL RECOGNITION

Poster session 20. Chairmen: Maiken Stilling & Jens Rolighed Larsen

P20.01 Pernille Bach Jørgensen. TELOMERE DYNAMICS IN SPERMATOGENESIS

P20.02 Jakob Stegger. ANTHROPOMETRY AND RISK OF ACUTE CORONARY SYNDROME

P20.03 Lene Sundahl Mortensen. DIFFERENTIAL EFFECTS OF PROTEIN QUALITY ON POSTPRANDIAL LIPEMIA IN RESPONSE TO A FAT-RICH MEAL IN TYPE 2 DIABETES: COMPARISION OF WHEY, CASEIN, GLUTEN AND COD PROTEIN.

P20.04 Jens Ølholm. ANTI-INFLAMMATORY EFFECTS OF RESVERATROL ON MCP-1 EXPRESSION AND SECRETION IN HUMAN ADIPOSE TISSUE EXPLANTS

P20.05 Thomas Svava Nielsen. REGULATION OF LIPOLYSIS IN HUMAN MUSCLE AND ADIPOSE TISSUE

P20.06 Kristin Rós Kjartansdóttir. *IN VITRO* DERIVATION OF SPERMATOGENIC CELLS FROM HUMAN EMBRYONIC STEM CELLS

P20.07 Jeppe Grøndahl Rasmussen. HYPOXIA INCREASES EXPRESSION OF ANGIOGENIC AND ANTIAPOPTOTIC CYTOKINES IN HUMAN ADIPOSE TISSUE-DERIVED STEM CELLS

P20.08 Ruta Tuckuviene. PREDICTIVE VALUE OF PAEDIATRIC THROMBOSIS DIAGNOSES IN A NATIONWIDE HOSPITAL DISCHARGE REGISTRY

P20.09 Kristian Havmand. DILATION OF THE ASCENDING AORTA IN TURNER SYNDROME DURING SHORT-TERM FOLLOW-UP

P20.10 Emil Toft Brøndum. EDHF RESPONSE IN RESISTANCE ARTERIES FROM GASTRIC BYPASS PATIENTS

Poster session 21. Chairmen: Michael Borre & Lars Vinge Nygaard

P21.01 Charlotte Rotbøl Bøje. THE IMPORTANCE OF COMORBIDITY IN HEAD AND NECK CANCER

P21.02 Claus Tvedesøe. THE INFLUENCE OF HEAT ON EXTRAVASATION OF USPIO PARTICLES

P21.03 Tanja Eiersted Molzen. IDENTIFICATION OF ESSENTIAL GENES IN STREPTOCOCCUS PNEUMONIAE MENINGITIS

P21.04 Lykke Grubach. EPIGENETIC INHIBITION OF CBF-MUTATED LEUKEMIA - AN ONGOING STUDY

P21.05 Hanne Østergård Larsen. COMPARISON OF TRANSFECTION METHODS FOR SIRNA DELIVERY IN HEMATOPOIETIC SUSPENSION CELLS

P21.06 Ole Schmeltz Søgaard. IMPROVING THE IMMUNOGENICITY OF PNEUMOCOCCAL CONJUGATE VACCINE IN HIV-INFECTED ADULTS WITH A TLR9 AGONIST-ADJUVANT. A RANDOMIZED TRIAL

P21.07 Torben Stamm Mikkelsen. SHORTENING THE INFUSION TIME OF HIGH DOSE METHOTREXATE REDUCES THE ACCUMULATION OF ACTIVE METHOTREXATE POLYGLUTAMATES IN LEUKEMIA CELLS AND THE ANTILEUKEMIC EFFECTS

P21.08 Vanda Turcanova. HERPESVIRUS-INDUCED EXPRESSION OF A HUMAN ENDOGENOUS SUPERANTIGEN

P21.09 Anders Kirch Dige. ETHYLENE-DIAMINE-TETRA-ACETATE (EDTA) MIMICS THE EFFECT OF REGULATORY T CELLS IN SUPPRESSION ASSAYS: A POTENTIAL PITFALL WHEN USING AUTOMACS-SEPARATED CELLS

P21.10 Britta Weber. TREATMENT WITH ERLOTINIB SHOW A DRAMATIC EFFECT AND BRAIN ACCUMULATION IN A PATIENT WITH METASTATIC NON-SMALL CELL LUNG CANCER HARBOURING A MUTATION IN THE EGF-RECEPTOR

Poster session 22. Chairmen: Vladimir Matchkov & Peter Vedsted

P22.01 Stefan W. Harders. HIGH RESOLUTION SPIRAL CT OF SOLITARY PULMONARY NODULES. MORPHOLOGIC ASSESSMENT, DIAGNOSTIC ACCURACY AND INTER-RATER AGREEMENT.

P22.02 Thomas Reinert. WHOLE GENOME METHYLATION ANALYSIS IN BLADDER CANCER

P22.03 Anne-Cathrine Bareid Østby. COMMUNITY RESPIRATORY VIRUSES CAUSING ACUTE

RESPIRATORY DISEASE IN PATIENTS ADMITTED AT INTENSIVE CARE UNITS AND DEPARTMENTS OF HEMATOLOGY

P22.04 Lasse Sommer Kristensen. MAKING THE MOST OF METHYLATION SPECIFIC PCR EXPERIMENTS: HOW TO OBTAIN ALLELE-SPECIFIC INFORMATION

P22.05 Anders Petersen. NODAL AND EXTRANODAL MANIFESTATIONS OF DIFFUSE LARGE B-CELL LYMPHOMA DIFFER IN EXPRESSION OF SPECIFIC MICRORNAS

P22.06 Maria Bro Kloster. THE ROLE OF PAX5, BCL6, AND PRDM1 PROMOTERS AND ISOFORMS IN B CELL DIFFERENTIATION AND MALIGNANCIES

P22.07 Hans Linde Nielsen. CLINICAL EPIDEMIOLOGY AND MANIFESTATIONS OF *CAMPYLOBACTER CONCISUS* AND *CAMPYLOBACTER UPSALIENSIS*

P22.08 Niels Fristrup. RISK STRATIFICATION OF BLADDER CANCER PATIENTS USING A PANEL OF 6 PROGNOSTIC PROTEIN MARKERS

P22.09 Martin Skøtt. THE ANTI-INFLAMMATORY EFFECTS OF ALFA-MELATONIN STIMULATING HORMONE (ALFA-MSH) ON MULTIPLE ORGAN FAILURE IN RATS WITH OR WITHOUT CHRONIC KIDNEY DISEASE

P22.10 Thomas Greve. A CASE OF SEVERE SUBDURAL EMPYEMA CAUSED BY STREPTOCOCCUS INTERMEDIUS AND STREPTOCOCCUS PNEUMONIAE DETECTED BY LYTA PCR AND BINAX NOW, ONLY.

Poster session 23. Chairmen: Kim Overvad & Sten Rasmussen

P23.01 Maja Døvling Kaspersen. IDENTIFICATION OF MULTIPLE TYPES OF HUMAN PAPILLOMAVIRUSES AND HERPESVIRUSES IN SEMEN FROM SPERM DONORS

P23.02 Mette Møller Handrup. PLACING OF TUNNELED CENTRAL VENOUS CATHETERS PRIOR TO INDUCTION CHEMOTHERAPY IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA.

P23.03 Peder Fode. DETERMINATION OF COPY NUMBER VARIATIONS OF THE HUMAN β-DEFENSIN 3 GENE USING THREE INDEPENDENT METHODS

P23.04 Mette Bak Nielsen. EVALUATION OF PATIENTS OPERATED FOR LOCALLY RECURRENT RECTAL CANCER

P23.05 Thomas Damgaard Sandahl. A NATIONWIDE STUDY OF THE INCIDENCE AND SHORT-TERM MORTALITY RATE OF ALCOHOLIC HEPATITIS IN DENMARK FROM 1999–2008

P23.06 Lene Mølgård Hansen. EARLY DEATHS AND TREATMENT-RELATED MORTALITY IN CHILDHOOD ACUTE MYELOID LEUKAEMIA (AML) IN THE NORDIC COUNTRIES: 1984-2003

P23.07 Diem Bentzon. HEREDITARY PROSTATE CANCER IN MIDTJYLLAND: A STUDY OF GENETIC VARIANTS IN PROSTATE CANCER

P23.08 Carina Agerbo Rosenberg. CHARACTERISATION OF AGE-SPECIFIC T CELL RESPONSES FOLLOWING VACCINATION AGAINST HEPATITIS B VIRUS INFECTIONS

P23.09 Sine Nygaard Langerhuus. EFFECT OF FISH OIL SUPPLEMENTATION IN A PORCINE MODEL OF AORTIC VASCULAR PROSTHETIC GRAFT INFECTION

P23.10 Lise Saksø Mortensen. 4 D BIOLOGICAL IMAGING OF HYPOXIA IN HUMAN TUMOURS

Poster session 24. Chairmen: J. Michael Hasenkam & Samuel Alberg Thrysøe

P24.01 Jimmi Søndergaard. THE ACUTE MORBIDITY DURING RADIOTHERAPY OF BLADDER CANCER IN RELATION TO THE TREATMENT TECHNIQUE

P24.02 Pauliina Wright. A METHOD TO INDIVIDUALIZE ADAPTIVE PLANNING TARGET VOLUMES FOR DEFORMABLE TARGETS

P24.03 Lars Toft Nielsen. TLR SIGNALING INCREASES IMMUNOGENICITY OF RETROVIRAL HIV-1 VACCINE CANDIDATE

P24.04 Magdalena Julia Dabrowska. IMPACT OF GROWTH FACTOR INDEPENDENCE 1 IN HUMAN T-CELL LYMPHOMAS; PATHOGENIC POTENTIAL IDENTIFIED BY INSERTIONAL MUTAGENESIS IN A MURINE T-CELL LYMPHOMA MODEL

P24.05 Trine Tramm. PROGNOSIS IN PATIENTS WITH UNTREATED, NODE-NEGATIVE EARLY BREAST CANCER: - USING AN ALGORITHM DEVELOPED FROM AND APPLIED TO FORMALIN FIXED, PARAFFIN EMBEDDED TISSUE (FFPE).

P24.06 Anders Christian Larsen. INCIDENCE OF VENOUS THROMBOEMBOLIC DISORDERS IN UPPER GASTROINTESTINAL CANCER

P24.07 Kåre Gotschalck Sunesen. IMMUNOSUPPRESSIVE DISORDERS AND RISK OF ANAL SQUAMOUS CELL CARCINOMA: A NATIONWIDE COHORT STUDY IN DENMARK, 1978-2006

P24.08 Emil Kofod-Olsen. HUMAN HERPESVIRUS-6B PROTEIN U19 STABILIZE AND INACTIVATE P53.

P24.09 Søren Beck. THE INNATE IMMUNE SYSTEM RECOGNIZES CYTOPLASMIC DNA IN A SEQUENCE DEPENDENT MANNER

Poster session 25. Chairmen: Karin Demtröder & Michael Mulvany

P25.01 Karen Louise Thomsen. TUMOR NECROSIS FACTOR-ALPHA ACUTELY UP-REGULATES UREA SYNTHESIS *IN VIVO* IN RATS - A HEPATIC ELEMENT OF INFLAMMATORY CATABOLISM

P25.02 Charlotte Christie Petersen. REACTIVATION VERSUS PRIMARY CYTOMEGALOVIRUS INFECTION IN CHRONIC LYMPHOCYTIC LEUKEMIA PATIENTS

P25.03 Caroline Winther Tørring. HOW EPSTEIN-BARR VIRUS MAY INITIATE MULTIPLE SCLEROSIS

P25.04 Line Reinert. TOLL LIKE RECEPTORS (TLR2/9) INDUCED ANTIVIRAL ACTIVITY AGAINST HSV-2

P25.05 Christoffer Sølling. ERYTHROPOIETIN (EPO) ATTENUATES ACUTE RENAL DYSFUNCTION IN A PORCINE MODEL OF ISCHEMIA-REPERFUSION INJURY.

P25.06 Ditte Andreasen Søborg. OCCURRENCE AND CHARACTERIZATION OF VIRULENCE GENES AMONGST NATURALLY OCCURRING ENVIRONMENTAL BACTERIA

P25.07 Louise Brøndt Hartlev. UNBIASED STEREOLOGICAL ESTIMATION OF CARTILAGE AND SUBCHONDRAL BONE IN HUMAN OSTEOARTHRITIC FEMORAL HEADS

P25.08 Susie Mikkelsen. RIG-I-MEDIATED ACTIVATION OF P38 MAPK PROCEEDS THROUGH A PATHWAY DEPENDENT ON TRAF2, TAK1, AND P38 KINASE ACTIVITY: IMPACT ON TYPE I IFN PRODUCTION AND ACTIVATION OF DENDRITIC CELLS

P25.09 Ulrik Vindelev Elstrøm. CONE-BEAM CT AND DEFORMABLE REGISTRATION FOR MONITORING ANATOMIC CHANGES AND EXPLORATION OF ADAPTIVE STRATEGIES IN RADIOTHERAPY OF HEAD AND NECK CANCER

P25.10 Søren Egedal Degn. A QUANTITATIVE ASSAY FOR MAP19, THE ALTERNATIVE SPLICE PRODUCT OF THE MASP-2 GENE

Poster session 26. Chairmen: Michael Rehling & Søren Risom

P26.01 Vagn Erik Lisbjerg Johnsen. 3D-MOTION CAPTURE OF GAIT IN PARKINSON'S DISEASE TREATED WITH DEEP BRAIN STIMULATION

P26.02 Nina Dyrberg Lorenzen. A COMPARISON OF TWO DIFFERENT SURGICAL RESURFACING TECHNIQUES

P26.03 Anders Dohn. THE NEURAL FOUNDATION OF ABSOLUTE PITCH ABILITY

P26.04 Kasper Severinsen. THE TRIGGER TRIFECTA AND CONFORMATIONAL TRANSITIONS IN THE HUMAN SEROTONIN TRANSPORTER

P26.05 Louise Munk Rydtoft. MR STUDIES AT 16.4 T OF NEURITE DENSITY AND PLAQUE DEPOSITION IN A MOUSE MODEL OF ALZHEIMER'S DISEASE

P26.06 Dan Sonne Pedersen. METALLIC GOLD TREATMENT INDUCES NEUROPROTECTIVE ASTROCYTOSIS AND EVOKES STEM CELL RESPONSE IN A RODENT MODEL OF MULTIPLE SCLEROSIS

P26.07 Rune Thomsen. OTIMIZING THE BOYDEN CHAMBER ASSAY FOR ASTROCYTIC CELLS.

P26.08 Henriette Thisted. PREAMISSION ANTIDIABETIC TREATMENTS AND MORTALITY AFTER ISCHEMIC STROKE IN PATIENTS WITH DIABETES MELLITUS: A NATIONWIDE POPULATION-BASED FOLLOW-UP STUDY

P26.09 Fabia Febbraro. STUDY OF THE RELATION OF IRON AND α-SYNUCLEIN AT TRANSLATIONAL AND POST-TRANSLATIONAL LEVEL: IMPLICATIONS FOR PARKINSON'S DISEASE

Poster session 27. Chairmen: Robert Fenton & Michael Sørensen

P27.01 Marie Bagger Bohn. MECHANICAL STABILITY OF ACL RECONSTRUCTION IN AN EXPERIMENTAL PORCINE MODEL

P27.02 Kristina Dupont Hougaard. REMOTE ISCHEMIC PERCONDITIONERING IN ACUTE STROKE: AN ENDOGENEOUS MODEL TO GENERATE NEUROPROTECTION.

P27.03 Line Bie Mertz. ANGELMAN SYNDROME IN DENMARK. GENOTYPE COMPARED WITH PHENOTYPE

P27.04 Hans Gjørup. THE MORPHOLOGY OF THE NEUROCRANIUM, SPLANCHNOCRANIUM AND CERVICAL COLUMN IN PATIENTS WITH HYPOPHOSPHATAEMIC RICKETS.

P27.05 Kari Konstantin Nissen. MULTIPLE SCLEROSIS AND THE IMPACT OF A SPECIFIC ENDOGENOUS RETROVIRUS ON HUMAN CHROMOSOME X

P27.06 Dariusz Orlowski. AUTOMETALLOGRAPHIC (AMG) ENHANCEMENT OF THE GOLGI-COX STAINING AND ITS USE FOR HIGH RESOLUTION VISUALIZATION OF DENDRITES AND SPINES

P27.07 Stephen Austin. REMISSION, METACOGNITIVE PROCESSES AND QUALITY OF LIFE- OUTCOMES FROM OPUS TRIAL. A 10 YEAR FOLLOW-UP OF A RANDOMIZED MULTI-CENTRE TRIAL OF INTENSIVE EARLY INTERVENTION VERSUS STANDARD TREATMENT FOR PATIENTS WITH FIRST EPISODE SCHIZOPHRENIA SPECTRUM DISORDER

P27.08 Vibeke Fuglsang Bliksted. SOCIAL COGNITION IN FIRST-EPISODE SCHIZOPHRENIA: THEORY OF MIND AND SOCIAL PERCEPTION

P27.09 Kåre Sanden Ettrup. A PORCINE MODEL OF HYPOTHALAMIC DEEP BRAIN STIMULATION FOR THE TREATMENT OF MORBID OBESITY.

P27.10 Kathrine Just Andersen. CHARACTERIZATION OF BASAL GANGLIA DYSFUNCTION IN A RODENT MODEL OF PARKINSON'S DISEASE

Poster session 28. Chairmen: Ann Wenzel & Jan Frystyk

P28.01 Lene Vammen Søndergaard. CLONED GöTTINGEN MINIPIGS SHOW REDUCED INTER-INDIVIDUAL VARIATION IN BEHAVIORAL TESTS

P28.02 Thomas Maribo. LOW BACK PAIN PATIENTS EXPERIENCE LOWER PAIN INTENSITY AFTER EXTENSIVE PHYSICAL TESTING

P28.03 Torben Albert Devantier. ASSOCIATIONS BETWEEN DEPRESSION AND CARDIOVASCULAR DISEASE IN PATIENTS WITH LATE ONSET SINGLE EPISODE MAJOR DEPRESSIVE DISORDER

P28.04 René Ernst Nielsen. COMPARISON OF THE EFFECTS OF SERTINDOLE AND OLANZAPINES ON COGNITION (SEROLA)

P28.05 Annette Ingeman. QUALITY OF CARE AND MEDICAL COMPLICATIONS AMONG PATIENTS WITH STROKE: A FOLLOW-UP STUDY

P28.06 Jannik Jakobsen. GENERATION OF EGFP PIGS REVEALED A NOVEL TWO FACED FUNCTION OF THE SLEEPING BEAUTY TRANSPOSASE.

P28.07 Kaare Meier. SPINAL CORD STIMULATION, A 3-YEAR EXPERIENCE

P28.08 John Brincks. OVERGROUND GAIT TRAINING OR ROBOTIC GAIT PRACTISE? NO SUPERIOR GAIT INTERVENTION WAS DETERMINED FOR SUBACUTE PATIENTS WITH STROKE. A PILOT STUDY

P28.09 Faramarz Jadidi. EFFECT OF STIMULUS LOCATION ON INHIBITORY RESPONSES IN HUMAN JAW-CLOSING MUSCLES

P28.10 Simon Hjerrild. CEREBRAL INVOLVMENT IN CHRONIC HEPATITIS C VIRUS INFECTION ASSESSED BY MRI

Poster session 29. Chairmen: Jeppe Prætorius & Kjeld Hermansen

P29.01 Sanna Lemming Kjær. CONTEXTUAL NEGATIVE CUES APPEAR IMPORTANT FOR INDUCTION OF INCREASED STATE OF ANXIETY IN PRENATALLY STRESSED RATS

P29.02 Marianne Toft Vestermark. STRONTIUM SUBSTITUTED BIOACTIVE GLASS AS COATING FOR ORTHOPAEDIC IMPLANTS.

P29.03 Sabrina Maria Gade Sundbye. P25α EXPRESSION IN MODELS OF EXCITOTOXICITY

P29.04 Jennifer Heather Christensen. POST-OPERATIVE COURSE AFTER REMOVAL OF LOWER THIRD MOLARS: EFFECT OF LONG-DURATION ANAESTHETIC AND ANTI-INFLAMMATORY TREATMENT ON PAIN AND SWELLING

P29.05 Hanna Järnum. GENDER AND AGE DEPENDENCE OF CINGULUM AND CORPUS CALLOSUM IN HEALTHY VOLUNTEERS ASSESSED BY DIFFUSION TENSOR IMAGING: A VIRTUAL DISSECTION STUDY

P29.06 Eduardo Garza. SONATA ANALGESICA: IS MUSIC-INDUCED ANALGESIA JUST A CONSEQUENCE OF THE PLACEBO EFFECT?

P29.07 Kristian Sandberg. LOCALIZATION OF CORTICAL AREAS INVOLVED IN CONSCIOUS PROCESSING DURING BINOCULAR RIVALRY USING MEG

P29.08 Christopher Joseph Bailey. CONCURRENT MEASUREMENT IN THE RAT OF THE EPIDURAL ELECTROENCEPHALOGRAM AND BRAIN GLUCOSE CONSUMPTION USING μPET: DEVELOPMENT OF METHODS

P29.09 Trine Christensen. GENE EXPRESSION PROFILING OF VENTRAL HIPPOCAMPAL GRANULAR CELL LAYER IN RATS EXPOSED TO CHRONIC MILD STRESS

Poster session 30. Chairmen: Torben Clausen & Arne Møller

P30.01 Leslie Foldager. USING LOGIC REGRESSION TO IDENTIFY SNP INTERACTIONS BASED ON INDIVIDUALLY TIME-MATCHED CASE-CONTROL DATA

P30.02 Ivana Konvalinka. SYNCHRONIZATION IN JOINT ACTION: FROM TAPPING TO FIRE-WALKING

P30.03 Malene Hørnø Schmidt. ASSESSMENT OF A NEW COMPOSITE DENTAL RESTORATIVE MATERIAL

P30.04 Kaare Dyre Palnum. USE OF MEDICAL PROPHYLAXIS AND CLINICAL OUTCOME IN PATIENTS WITH ISCHEMIC STROKE: A NATIONWIDE FOLLOW-UP STUDY

P30.05 Jan Hendrik Rölfing. ERYTHROPOIETIN'S OSTEOGENIC POTENCY IN POSTEROLATERAL FUSION

P30.06 Jesper Ougaard Schønnemann. RASCH-ANALYSIS OF THE DANISH VERSION OF THE DISABILITIES OF ARM, SHOULDER AND HAND QUESTIONNAIRE.

P30.07 Bjørn Petersen. MUSICAL EAR TRAINING WITH COCHLEAR IMPLANTS

P30.08 Louise Buur Lund. IDENTIFICATION/ CHARACTERISATION OF SIGNALLING PATHWAYS INVOLVED IN P25α INDUCED α-SYNUCLEIN DEPENDENT DEGENERATION

P30.09 Joel Fredrik Astrup Aanerud. SEROTONIN RECEPTORS IN THE HUMAN BRAIN

Poster session 31. Chairmen: Sven Poulsen & Reimar W. Thomsen

P31.01 Sanne Kragh Kjær. IS TREATMENT OUTCOME ASSOCIATED WITH COGNITIVE DYSFUNCTIONS IN OCD?

P31.02 Kasra Zainali. THE EFFECT OF GOLD PARTICLES IN SHEEP ALLOGRAFT

P31.03 Kristine Rømer Thomsen. ELUCIDATING THE FUNCTIONAL NEUROANATOMY OF SOCIAL PLEASURE

P31.04 Martin Gottliebsen. REVERSIBEL EPIPHYSIODESE - STAPLING VERSUS TENSION BAND PLATING TECHNIQUE

P31.05 Caspar Skau Madsen. EXPERIMENTAL PAIN MODEL WITH TOPICAL CAPSAICIN AND CONTACT HEAT EVOKED POTENTIALS

P31.06 Anne Hansen. SPASTICITY AND PAIN FOLLOWING STROKE: A PROSPECTIVE STUDY

P31.07 Juozas Petruskevicius. CEMENTATION OF FEMORAL COMPONENT WITH PROXIMAL CENTRALIZER. ANALYSIS OF CEMENT PENETRATION IN CANCELLOUS BONE

P31.08 Kåre Eg Severinsen. LONG TERM EFFECTS OF PROGRESSIVE RESISTANCE TRAINING VS. HIGH INTENSITY ENDURANCE TRAINING ON REHABILITATION OF WALKING IMPAIRMENT AFTER STROKE: A ONE YEAR FOLLOW-UP

P31.09 Mette Buhl Callesen. DOPAMINE AGONIST INDUCED PATHOLOGICAL GAMBLING IN PARKINSON'S DISEASE

Poster session 32. Chairmen: Eva Bonefeld-Jørgensen & Morten Nielsen

P32.01 Tue Hartmann. PRETREATMENT MR-SCANNING IN OCD

P32.02 Andreas Schröder. SPECIALISED TREATMENT FOR PEOPLE WITH SYNDROMES OF SEVERE BODILY DISTRESS: A RANDOMISED CONTROLLED TRIAL

P32.03 Linda Locht. METALLIC SILVER INDUCES INFLAMMATORY RESPONSES IN THE MOUSE BRAIN

P32.04 Birgitte Fuglsang Kjølby. CONTRAST AGENT CONCENTRATION MEASUREMENTS IN MAGNETIC RESONANCE PERFUSION WEIGHTED IMAGING

P32.05 Henriette Klit. CHARACTERIZATION OF CENTRAL POST-STROKE PAIN (CPSP)

P32.06 Jasna Furtula. MUNIX PERFORMED ON BRACHIAL BICEPS MUSCLE WITH QUANTITATIVE AND QUALITATIVE ASSESSMENT OF FORCE

P32.07 Signe Groth Renvillard. NEUROPSYCHOLOGICAL IMPAIRMENT AND HIGH PREVALENCE OF DEPRESSION IN PATIENTS WITH CHRONIC HEPATITIS C VIRUS.

P32.08 Thomas Urban. PATIENT DISCOMFORT IN IMMEDIATE IMPLANT PLACEMENT IN MOLAR REGIONS IN ASSOCIATION WITH THREE REGENERATIVE TECHNIQUES

P32.09 Jimmi Nielsen. 10-YEAR TRENDS IN THE TREATMENT AND OUTCOMES OF PATIENTS WITH FIRST-EPISODE SCHIZOPHRENIA

Poster session 33. Chairmen: Jens Peter Kroustrup & Palle Villesen

P33.01 Mette Sørensen. EFFECTS OF STATINS ON ORTHOPAEDIC IMPLANT FIXATION

P33.02 Esben Laugesen. PULSE PRESSURE AND AMBULATORY ARTERIAL STIFFNESS INDEX PREDICT CARDIOVASCULAR DISEASE IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

P33.03 Frederik Hvid-Jensen. 17 YEAR FOLLOW-UP OF 4706 GASTROESOPHAGEAL REFLUX PATIENTS; MORTALITY AND COMPLICATIONS.

P33.04 Sidse Kringelholt. VASOACTIVE EFFECTS OF PROSTAGLANDIN RECEPTOR AGONISTS IN ISOLATED INTRAOCULAR PORCINE CILIARY ARTERIES.

P33.05 Line Mayland Kolstrup. HEMODYNAMIC EFFECTS OF THREE INOTROPIC STRATEGIES IN THE IMMATURE HEART

P33.06 Anne Roslev Bukh. BACTERIAL TRANSLOCATION AND IMMUNE ACTIVATION IN HIV- AND NON-HIV-INFECTED PERSONS

P33.07 Trine Dalsgaard. GENE THERAPY OF PKU

P33.08 Kim Henningsen. BEHAVIORAL AND MOLECULAR CORRELATIONS IN THE RAT CHRONIC MILD STRESS MODEL OF DEPRESSION.

P33.09 Line Andersen. ASSESSMENT OF PRESYMPTOMATIC CHANGES IN CEREBRAL TISSUE PERFUSION IN MUTATION CARRIERS OF FAMILIAL FRONTOTEMPORAL DEMENTIA, MEASURED WITH MRI

P33.10 Merete Ipsen. HOW MUCH DO MEDICAL SPECIALISTS TEACH IN THE HOSPITALS? INDICATORS OF EDUCATIONAL EFFORT IN THE DANISH SPECIALIST TRAINING.

Poster session 34. Chairmen: Kamille Smidt Rasmussen & Andreas Stauropoulos

P34.01 Pia Damgaard Colding. EFFECTS OF THREE INOTROPIC STRATEGIES ON THE METABOLISM IN

THE IMMATURE MYOCARDIUM

P34.02 Julie Mackenhauer. PREVALENCE AND CHARACTERISTICS OF NON-LACTATE AND LACTATE EXPRESSORS IN SEPTIC SHOCK

P34.03 Jesper Damsgaard. VIRAL MENINGITIS – A STUDY OF POST-INFECTIOUS COGNITIVE DYSFUNCTION AND ASSOCIATED NEUROPATHOLOGY

P34.04 Astrid Hjelholt Nielsen. IMMUNE CELLS IN HUMAN SALPINX INFECTED WITH *CHLAMYDIA TRACHOMATIS S*EROVAR D COMPARED TO UNINFECTED SALPINX.

P34.05 Anne Leegaard. PRESSURE PAIN TRESHOLD IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS

P34.06 Adjmal Nahimi. SEROTONERGIC MODULATION OF EXOGENOUS L-DOPA-DERIVED DOPAMINE RELEASE IN RATS WITH UNILATERAL 6-OHDA LESIONS REVEALED WITH MICRO-PET IMAGING.

P34.07 Katrine Hygum. IN MICE TRANSCOBALAMIN STANDS IN FOR HAPTOCORRIN

P34.08 Stine Maria Lund Andersen. TOPICAL APPLICATION OF VALRUBICIN HAS A BENEFICIAL EFFECT ON DEVELOPING SKIN TUMORS.

P34.09 Bjørn Borsøe Christensen. STRUCTURALLY GRADED POLYCAPROLACTONE HYBRID SCAFFOLDS FOR HYALINE CARTILAGE REPAIR

P34.10 Tue Asger Kruse Rasmussen. INCREASED LEVELS OF IL-21 AND IL-23 CORRELATE TO DISEASE ACTIVITY AND IL-23 ALSO TO RADIOGRAPHIC PROGRESSION IN RHEUMATOID ARTHRITIS

Poster session 35. Chairmen: Søren Kjærgaard & Yvonne Eskildsen-Helmond

P35.01 Katrine Nielsen. ALDEHYDE DEHYDROGENASE ACTIVITY AS A MARKER FOR GRAFT QUALITY IN AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR HEMATOLOGICAL MALIGNANCIES

P35.02 Ole Møller Hansen. THE EFFECT OF CELL SEEDING DENSITY ON CARTILAGE REGENERATION IN MATRIX-ASSISTED CHONDROCYTE IMPLANTATION IN A RABBIT MODEL

P35.03 Katrine Schou. BACTERIAL AND VIRAL MENINGITIS - CLINICAL MANIFESTATIONS, COURSE AND SEQUELAE

P35.04 Morten Würtz. PATIENTS WITH PREVIOUS DEFINITE STENT THROMBOSIS HAVE A LARGER FRACTION OF IMMATURE PLATELETS AND A REDUCED ANTIPLATELET EFFECT OF ASPIRIN

P35.05 Mette Julsgaard Nielsen. MEDICAL TREATMENT OF CROHN'S DISEASE PATIENTS PRIOR TO AND DURING PREGNANCY

P35.06 Kristina Bennet Emdal. THE ROLE OF HER4 IN ESTROGEN-RESPONSIVE AND ANTIESTROGEN-RESISTANT HUMAN BREAST CANCER

P35.07 June Anita Ejlersen. THE DIAGNOSTIC VALUE OF 2D-STRAIN STRESS ECHOCARDIOGRAPHY IN CHEST PAIN PATIENTS WITH SUSPECTED CORONARY ARTERY DISEASE

P35.08 Louise Jensen. PLASMA CALPROTECTIN PREDICTS MORTALITY IN PATIENTS WITH ST-SEGMENT ELEVATION MYOCARDIAL INFARCTION TREATED WITH PRIMARY PERCUTANEOUS CORONARY INTERVENTION

P35.09 Lotte Abbildgaard. WILM'S TUMOR GENE 1 (WT1) AS A TUMOR-MARKER IN CHILDHOOD ACUTE MYELOID LEUKEMIA (AML) - DETERMINATION OF THE NORMAL VALUES OF WT1 IN CHILDREN.

Poster session 36. Chairmen: Kari Tanderup & Steffen Thiel

P36.01 Chen Muwan. FREE RADICALS GENERATED BY 3-D TANTALUM SCAFFOLD ANTAGONIZE THE CYTOTOXIC EFFECT OF DOXORUBICIN

P36.02 Søren Schou Olesen. EVIDENCE OF ALTERED CEREBRAL PAIN PROCESSING IN CHRONIC PANCREATITIS - A PILOT STUDY

P36.03 Nis Borbye Pedersen. VASOPRESSIN-MEDIATED SIGNALING IN THE DISTAL CONVOLUTED TUBULE REGULATES PHOSPHORYLATION OF THE THIAZIDE-SENSITIVE NA^+-CL^-

COTRANSPORTER (NCC) AT TWO CONSERVED THREONINE RESIDUES

P36.04 Ayfer Topcu. EFFECT OF REFLEXOLOGY, HOMEOPATHY, AND TRADITIONAL MEDICAL TREATMENT IN ASTHMA: A RANDOMIZED CONTROLLED, PARALLEL-GROUP TRIAL

P36.05 Nicklas Heine Staunstrup. TRANSGENIC PIG MODELS

P36.06 Hanne Bjerregaard Møller. PHOSPHORYLATION REGULATED ENDOCYTOSIS OF THE WATER CHANNEL AQUAPORIN-2

P36.07 Christian Fynbo Christiansen. COMORBIDITY AND MORTALITY IN INTENSIVE CARE UNIT PATIENTS – A POPULATION-BASED COHORT STUDY

P36.08 Elise Røge Nielsen. EFFECT OF HYPOXIA ON THE FUNCTION AND REGEULATION OF THE ADENOSINE A_{2A} RECEPTOR

P36.09 Kaspar René Nielsen. POLYMORPHISMS IN INFLAMMATORY MEDIATORS - RELATION TO DISEASE ACTIVITY AND SURVIVAL IN B-CELL DISEASES

Antal: 376 **FN: Fogh Nielsen; O: Oral communiation; P: Poster presentation**

Session	Name	Abstract
FN	Anna Krarup Keller	MICRODIALYSIS FOR DETECTION OF POSTOPERATIVE ISCHEMIA IN EXPERIMENTAL RENAL TRANSPLANTATION *A.K. Keller[1], T.M. Jørgensen[2], K. Ravlo[1], T.K. Nielsen[1], L.H. Olsen[2], L.B. Stolle[3]* [1]Institute of Clinical Medicine, [2]Department of Urology, Aarhus University Hospital, [3]Department of Plastic Surgery, Aarhus University Hospital Purpose: We designed an experimental renal transplantation model and evaluated microdialysis as a detector of induced postoperative ischemia, a feared complication that when caused by vascular thrombosis usually leads to graft loss. Materials and Methods: Two microdialysis catheters were placed in the left kidney in 16 pigs, one in the renal cortex and one fixed on the renal capsule. Two-hour baseline measurements were made at steady state, the kidney was removed afterwards and subjected to warm and cold ischemia. It was subsequently re-anastomosed end to end in situ and reperfused for 5 hours. Pigs were then randomized into a total renal artery occlusion or controls. Results: At baseline there were no changes in local metabolites (glucose, glutamate, glycerol and lactate) and no significant difference between the groups. Glycerol increased 4-fold in each group during cold ischemia but there were no pivotal alterations in other metabolites. After kidney reperfusion glycerol decreased and all metabolites were in steady state after 1 hour. At 30 minutes after postoperative ischemia was introduced there were significant increases in all kidneys in ischemia vs steady state reperfusion levels of cortical lactate, glutamate, glycerol and the lactate-to-glucose ratio ($p < 0.001$). No metabolic changes were seen in controls. Conclusions: Microdialysis detected significant metabolic changes after postoperative ischemia in pigs with experimental renal transplantation, while no metabolic changes were observed in controls. In the future microdialysis may become a valuable tool for postoperative observation of transplanted kidneys, probably with major impact on early graft survival.
FN	Casper Foldager	EFFECTS OF COMBINED 3D- AND HYPOXIC CULTURING ON CARTILAGE-SPECIFIC GENE EXPRESSION IN HUMAN CHONDROCYTES *C.B. Foldager[1, 2], S. Munir[1], M. Ulrich-Vinther[1], K. Søballe[1], C. Bunger[1], M. Lind[2]* [1]Orthopaedic Research Lab, Aarhus University Hospital, [2]Sports Trauma Clinic, Aarhus University Hospital INTRODUCTION Articular cartilage is known to have a very limited potential of self-repair. Native chondrocytes reside in a 3D network and are exposed to low oxygen tensions. In vitro culturing and expansion of chondrocytes are essential in many treatment strategies of cartilage defects. We hypothesize that in vitro culturing in a native-like 3D and hypoxic environment favors expression of cartilage specific genes. MATERIALS AND METHODS Chondrocytes were isolated from normal cartilage of 12 individuals. The cells were divided into monolayer or 3D culturing synthetic scaffolds. Cell seeding densities were 20,000 cells/cm^2 in monolayer and $5x10^6$ cells/mL in scaffolds. 24 hours after seeding, the cells for baseline measurements were harvested. Remainders were divided in three groups for incubation in 21%, 5% or 1% oxygen. RNA extractions were performed 1, 2 and 6 days after baseline. Quantitative RT-PCR was performed using assays for collagen type (COL) 1, 2, aggrecan (AGC), sox9, and beta-actin (ACTB). Results are presented relative to the hypoxia stable reference genes beta2-microglobulin and ribosomal protein L13a. RESULTS

Combined culturing in 3D and severe hypoxia (1%) resulted in a significant increase in COL2 and AGC expression that was most pronounced at 6 days. ACTB expression decreased from one to six days in monolayer but increased 3D. Sox9 expression increased significantly in hypoxia, while no difference was observed between 3D and monolayer.
CONCLUSION
These new results suggest that early chondrocyte-seeding on scaffolds with subsequent hypoxic culturing would provide optimal regenerative properties of implanted chondrocytes in cartilage repair treatments.

FN Anne Nyholm Holdensen

CRUCIAL DETERMINANT OF CA^{2+} TRANSPORT CYCLE RATE OF SERCA

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Ion translocation by the sarcoplasmic reticulum Ca^{2+}-ATPase depends on large movements of the A-domain, but the driving forces have yet to be defined. The A-domain is connected to the ion-binding membranous part of the protein through linker regions.
We have determined the functional consequences of changing the length of the linker between the A-domain and transmembrane helix M3 ("A-M3 linker") by insertion and deletion mutagenesis at two sites. It was feasible to insert as many as 41 residues (polyglycine and glycine-proline loops) in the flexible region of the linker without loss of the ability to react with Ca^{2+} and ATP and to form the phosphorylated Ca_2E1P intermediate, but the rate of the energy-transducing conformational transition to E2P was reduced by >80%. Insertion of a smaller number of residues gave effects gradually increasing with the length of the insertion. Deletion of two residues at the same site, but not replacement with glycine, gave a similar reduction as the longest insertion. Insertion of one or three residues in another part of the A-M3 linker that forms an α-helix ("A3 helix") in E2/E2P conformations had even more profound effects on the ability of the enzyme to form E2P.
These results demonstrate the importance of the length of the A-M3 linker and of the position and integrity of the A3 helix for stabilization of E2P and suggest that, during the normal enzyme cycle, strain of the A-M3 linker could contribute to destabilize the Ca_2E1P state and thereby to drive the transition to E2P.

O01.01 Mette Laursen

X-RAY CRYSTALLOGRAPHIC STUDIES OF HIGH AFFINITY BINDING OF CARDIAC GLYCOSIDES TO THE NA^+,K^+-ATPASE

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The Na^+,K^+-ATPase is a membrane bound ion pump, which transports Na^+ and K^+ across the plasma membrane in all animal cells and thereby maintains chemical gradients required for cell excitability, cellular uptake of ions, nutrients and neurotransmitters, and regulation of cell volume and intracellular pH. Cardiac glycosides are specific and potent inhibitors of the Na^+,K^+-ATPase. They are naturally found in many plants and toad venoms and have been used for centuries in medical treatment of congestive heart failure and atrial fibrillation. During the last decades, endogenous cardiac glycoside-like compounds have been identified in low concentrations in mammals and are believed to possess a hormone-like function and have been related to several diseases, such as hypertension and cancer.
Despite a long history and an extended therapeutic application of cardiac glycosides, their binding mode to the Na^+,K^+-ATPase is still elusive. The aim of this project is to determine the structural basis for the specificity and high affinity binding of cardiac glycosides with the Na^+,K^+-ATPase. We intend to compare crystal structures of the Na^+,K^+-ATPase in complex with different cardiac glycosides and thus reveal the

molecular determinants for the ligand recognition.
We have succeeded in crystallizing pig kidney Na^+,K^+-ATPase in complex with several cardiac glycosides. We will present the preliminary results on the comparison of those complexes. Since the datasets, collected so far, have relatively low-resolution, we continue working on the optimization of the crystallization conditions for Na^+,K^+-ATPase complexes.

O01.02 Anders Etzerodt

IDENTIFICATION OF THE PROTEASE RESPONSIBLE FOR THE PHORBOL ESTER INDUCED SHEDDING OF THE HEMOGLOBIN SCAVENGER RECEPTOR CD163

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The hemoglobin scavenger receptor CD163 is a 130 kDa transmembrane protein exclusively expressed on cells of the monocytic lineage. Cleavage of CD163 from the cell surface produces a soluble CD163 plasma protein (sCD163) and correlation between increased sCD163 plasma concentration and severity of various infectious and inflammatory diseases has been established. Previous data indicate that the cleavage of CD163 is sensitive to inflammatory stimuli and that shedding is due to an extracellular cleavage site located close to the transmembrane region. In the present study we present new evidence identifying a specific protease to be responsible for the phorbol 12-myristate 13-acetate-induced release of sCD163 in transfected human embryonic kidney cells by inhibiting enzyme activity using metalloprotease inhibitors or small interfering RNA to knock down ADAM17 expression. Our data contributes to the understanding of the complex mechanisms involved in regulation of CD163 and its role in inflammation.

O01.03 Mette Juul Koefoed

IMPROVED INTEGRATION AND REMODELING OF BONE ALLOGRAFTS COATED WITH FREEZE-DRIED VIRAL VECTORS BASED ON ADENO-ASSOCIATED VIRUS (AAV)

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Bone allografts tend to fracture a few years after implantation due to a lack of vascularization and remodeling. To prevent these complications we have developed allografts coated with vectors based on adeno-associated virus (AAV) (Nat Med 11: 291-297, 2005; Mol Ther 12: 212-8, 2005). In this approach the vectors are freeze-dried onto the cortical surface of the bone without loosing infectivity. Murine femoral allografts coated with a marker gene (LacZ) are capable of transducing adjacent inflammatory cells and osteoblasts in the fracture callus following transplantation. While the LacZ carrying vector had no effect on bone healing, the delivery of Bone Morphogenetic Protein signals via a constitutively active Alk2-gene induced endochondral bone formation directly on the allograft surface. One month post-implantation there was evidence of remodeling of the new woven bone and massive osteoclastic resorption of the cortical surface. Micro computed tomography (mCT) analysis after 6 weeks of healing demonstrated a significant increase in new bone formation. We will now investigate the possible effect of VEGF overexpression in conjunction with a gene with effect on formation of connective tissue (FGF) using 3D magnetic resonance imaging (MRI) at 3 and 6 weeks to study the importance of new vessel formation during early osteogenesis.

O01.04 Tue Fryland

CHARACTERIZATION OF *BRD1* – A SUSCEPTIBILITY GENE FOR SCHIZOPHRENIA AND BIPOLAR DISORDER

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Several studies have identified the bromodomain containing 1 (BRD1) gene as a susceptibility gene for schizophrenia and bipolar disorder. The gene encodes a co-transcription factor BRD1 which has recently been identified as a mediator in the MOZ/MORF complex. This project aims to identify and explore BRD1 genomic binding sites and epigenetic regulatory functions in HEK293 cells by extensive DNA microarray profiling. We want to clarify the effects of over-expression and knock down of BRD1 in HEK293 cells using mRNA expression microarrays. Also, we want to perform ChIP microarray to identify genomic target sites for BRD1. For expression arrays, we have made stable cell lines expressing a long and a short splice variant of BRD1 representing BRD1 mRNA up-regulation. We show that we are able to knock down endogenous BRD1 protein and mRNA using RNA interference. We perform immunoprecipitation of BRD1-V5 fusion protein using anti-V5 antibody conjugated beads as an initial step to "tag ChIP". A preliminary ChIP promoter microarray identified several genes affecting multiple pathways important in the pathophysiology of schizophrenia and bipolar disorder underlining the initial genetic association studies. Here we present the promoter of abelson helper integration site, AHI1 as a potential BRD1 binding site. Two studies have previously identified the AHI1 gene to associate with schizophrenia.

O01.05 Marion Delenclos

OVER-EXPRESSION OF ALPHA-SYNUCLEIN DISRUPTS THE EXPRESSION PROFILE OF BASSOON, AN ACTIVE ZONE COMPONENT.

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Alpha-synuclein (α-syn) is one of the main constituents of Lewy bodies (LB) and plays an important role in the pathology of Parkinson's disease (PD). Overexpression of α-syn causes PD, but the pathogenic mechanism remains elusive. In vivo, α-syn has been associated with synaptic vesicles (SV) and its expression has been found to correlate with changes in synaptic plasticity, suggesting a role in neurotransmitter release. Here we over expressed α-syn rat and monkey brains using viral vectors to characterize the relation between α-syn and the vesicular machinery in Parkinsonian animals. Using immunohistochemical approaches, we studied different markers of SV as well as proteins present in the active zone. Active zones are specialized regions of the presynaptic plasma membrane where SV dock and fuse to release neurotransmitter. Bassoon, a high molecular weight component, participates in the active zone formation and the scaffolding of molecules involved in SV recycling. When toxic levels of α-syn accumulated in axons, bassoon was enriched and associated with α-syn in both species. However, accumulation of α-syn did not affect the SV per se, and staining for SV related proteins such as SV2, synaptophysin and MUNC 13 remained unchanged. Thus, bassoon expression is specifically disrupted in presence of high levels of α-syn. Importantly, when we extended our analysis to post-mortem samples of human suffering of PD, we observed in fact that accumulation of insoluble α-syn in LB and neurites colocalized with bassoon. In conclusion, our data suggest that the disruption of the targeting of bassoon induced by α-syn may play a role in the neurodegenerative process in PD.

O01.06 Cathrine Søndergaard Baastrup

CENTRAL NEUROPATHIC PAIN AND ANXIETY IN AN EXPERIMENTAL MODEL OF SPINAL CORD INJURY

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Anxiety is an important comorbidity in patients suffering from chronic pain. However, in animals the connection between persistent pain and anxiety has only sparingly been investigated. The current study aimed to investigate whether anxiety-

like behavior in animals is concomitant with chronic pain and if they develop simultaneously. Furthermore we investigated if anxiety-like behavior and/or central pain could be reversed by analgesic or anxiolytic drugs. Central neuropathic at level pain was induced in female Sprague-Dawley rats by spinal cord contusion. Mechanical hypersensitivity was assessed by applying von Frey filaments, and anxiety-like behavior was assessed using the elevated plus maze. Animals with a spinal cord contusion injury exhibited mechanical hypersensitivity as well as increased anxiety-like behavior 4 weeks post surgery. NaCl 0.9%, midazolam (0.5mg/kg; i.p.), morphine (3mg/kg; i.p.) and pregabalin (30 mg/kg; i.p.) were administered to all animals in a balanced schedule before exposing them to either the elevated plus maze (one group) or the mechanical hypersensitivity assay (another group). Animals were tested in randomized order and treatment was blinded to experimenter. Results will be presented.
Preliminary results suggest that spinal cord injured rats concomitantly develop anxiety-like behaviour and mechanical hypersensitivity, but can both be reversed by analgesic treatment (morphine and Pregabalin), as shown in a peripheral model of neuropathic pain? And will sham operated animals be unaffected by the analgesic?. I.e. can anxiety-like behaviour in the neuropathic pain model indirectly be a result of pain?

O02.01 Martin Broch-Lips

EFFECTS OF REDUCED CL^- CONDUCTANCE ON THE FUNCTION OF WORKING MUSCLE

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During muscle activity extracellular K^+ ($[K^+]_o$) increases due to the action potentials propagating on the muscle membrane. This rise in $[K^+]_o$ has the potential to reduce excitability due to a depolarization of the membrane potential (Vm) and hence slow inactivation of the Na^+-channels. The maintenance of excitability and thus force production therefore depends on a compensatory regulation of the muscle membrane excitability.
In our lab it has been shown that muscle membrane Cl^- conductance (G_{Cl}), or the ease of which Cl^- passes the muscle membrane, is down-regulated during activity and could potentially relief some loss of excitability. This observation is, however, at odds with previous studies showing that reductions in G_{Cl} decreases muscle performance.
In this study we demonstrate that muscles contractile endurance during intense activity was improved by a moderate reduction $[Cl^-]_o$. However, a large reduction in the $[Cl^-]_o$ had little effect. This biphasic effect of lowered $[Cl^-]_o$ and hence lowered G_{Cl} on muscle performance was related to the combined effect of an increased excitability, a reduced ability to re-accumulate K^+ lost from the fibres during excitation and a decreased ability to clamp the membrane potential at the normal resting value when $[K^+]_o$ increases. Altogether, the study strongly indicate that the hazardous effect of $[K^+]_o$ on muscle excitability and potentially on high intensity muscle endurance is very dependent on the G_{Cl}.

O02.02 Ingunn Skogstad Riddervold

DOES EXPOSURE TO WOOD SMOKE AFFECT AIRWAY RESPONSES IN ATOPIC HUMANS?

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Wood smoke consists of a complex mixture of compounds and contributes widely to environmental air pollution. Growing evidence suggests that wood smoke air pollution among other causes acute inflammation in the respiratory system, increases the incidence of asthma and allergic diseases. The study objective was to characterize airway responses after a controlled human exposure to wood smoke. Twenty non-smoking atopic human participants with normal lung function and

normal bronchial reactivity were in a double-blinded study at random exposed for 3 h at three different exposure conditions; filtered air (control exposure) and wood smoke with a particulate matter (PM) concentration at 200 and 400 µg/m^3. An experimental set-up with a wood-burning facility was used to generate wood smoke emissions inside the climate chamber where participants were exposed for 3½ hour under controlled environmental conditions.
Health effects were evaluated in relation to changes in different lung function measures: peak expiratory flow (PEF), forced expiratory volume in the first second (FEV_1), and forced vital capacity (FVC). The results will be presented and discussed at the PhD day.

O02.03 Anders Knudsen

IMPACT OF ISCHEMIC PRE- AND POSTCONDITIONING ON GENE EXPRESSION LEVELS IN THE RAT LIVER USING DNA MIKROARRAYS

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Background and aims: Ischemic pre- and postconditioning increase the ability of the liver, to tolerate ischemia/reperfusion injuries. The mechanism behind this phenomenon is unknown. The aim of the present study was to examine how ischemic pre- and postconditioning affects the whole genome expression using DNA microarray analysis.
Methods: Twenty-eight male Wistar rats were randomized into five groups: (A) control; (B) ischemic; (C) ischemic preconditioning; (D) ischemic postconditioning; and (E) combined ischemic pre- and postconditioning. All rats except the control group were subjected to 30 min of liver ischemia. Ischemic preconditioning consisted of 10 min of inflow occlusion and 10 min of reperfusion. Ischemic postconditioning consisted of three cycles of 30 sek inflow occlusion and 30 sek of reperfusion. Liver biopsy and blood samples were collected after 30 min of reperfusion. Total RNA was extracted from the biopsy and used to determine the full genome expression.
Results: ALAT increased significantly in groups B-E compared to group A ($p = 0.010$). SAM two class unpaired analysis was used to identify genes significantly up or down regulated. Expression levels were significantly changed in 308 genes in group (A) vs. (B); 1212 genes in (A) vs. (C); 5015 genes in (A) vs. (D) and 4331 genes in (A) vs. (E).
Conclusion: Ischemic conditioning changes gene expression profiles in the rat liver. Ischemic pre- and postconditioning seems to have an identical effect on gene expression. Subsequent pathway analysis identified several genes and networks which could be involved in the protective effects of ischemic conditioning.

O02.04 Morten Olsen

EDUCATIONAL ACHIEVEMENT AMONG LONG-TERM SURVIVORS OF CONGENITAL HEART DEFECTS: A DANISH POPULATION-BASED FOLLOW-UP STUDY

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Background: Congenital heart defects (CHD) have been associated with neurodevelopmental impairment, but little is known about CHD patients' adult educational attainments.
Methods and Results: Using administrative databases, we identified all Danish

patients with a primary CHD diagnosis born from January 1, 1977 to January 1, 1991 who lived to age 13. We retrieved data on gestational age and potential extracardiac defects (ECD). As a comparison cohort, we randomly sampled 10 persons per CHD patient. We obtained information on educational attainment from Denmark's Database for Labour Market Research. The study population was followed until achievement of specific educational levels or until death, emigration or end of study (January 1, 2006). We estimated the hazard ratio (HR) of attaining educational levels, conditional on completing preceding levels, using discrete time Cox regression adjusting for socioeconomic factors. Analyses were repeated for a subcohort of patients and controls born at term. We identified 2,986 CHD patients. Their probability of completing compulsory basic schooling was approximately 10% lower than control individuals' [adjusted HR = 0.87(95% CI: 0.83-0.92)]. Their subsequent probability of completing secondary school was lower than controls', both for all CHD patients [adjusted HR = 0.74(95% CI: 0.69-0.80)] and for the subcohort [adjusted HR = 0.80(95% CI: 0.73-0.86)]. The probability of attaining a higher degree, conditional on completion of youth education, was not affected [adjusted HR = 0.92 (95% CI: 0.79-1.07)].
Conclusions: The probability of completing both basic and secondary school was reduced among long-term CHD survivors.

O02.05 Thomas Wittenborn

A NOVEL ANGIOGENESIS MOUSE MODEL FOR SCREENING FUNCTIONALIZED NANO-PARTICLES.

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Background :
As a common denominator for many pathological conditions such as atherosclerosis and tumor progression, the angiogenesis process can serve as a target for diagnosis and treatment when investigating these diseases. Developing blood vessels are known to be fragile and leaky, introducing an opening into the Extravascular Extracellular Space (EES), which may be exploited to introduce Ultrasmall Superparamagnetic Iron Oxide (USPIO) particles into the EES. Attaching different ligands to the surface of particles can functionalize these to target matrix proteins, proteoglycans or other components of the EES and hence identify areas with leaky vessels/angiogenesis.
Aims:
1) To establish a functional angiogenesis mouse-model which will serve as a screening system for USPIO-particles.
2) To visualize injected USPIO particles in this model.
3) To functionalize USPIO particles to evade the immune system and specifically target the area of angiogenesis.
Results:
By implanting discs of foreign material (Poly-Capro-Lactone (PCL)) underneath the skin of mice and leaving the implants for 1-6 weeks we have been able to observe the process of neovascularization within the implant. After 6 weeks the implant had become completely infiltrated by cells and neovessels. This novel angiogenesis model will now be used to screen functionalized USPIO-particles by optical imaging. Comparing this to MRI and Histology of the animals will reveal correlations between the different detection systems.
Perspectives:
Developing multifunctionalized USPIO particles targeted for neovascularization will enable diagnosis, monitoring and/or treatment of angiogenesis-related diseases in a

non-invasive manner.

O02.06 Kristian Altern Øvrehus

DIAGNOSTIC EVALUATION OF PATIENTS SUSPECTED OF CORONARY ARTERY DISEASE: EXERCISE TESTING OR CORONARY COMPUTED TOMOGRAPHIC ANGIOGRAPHY?

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In patients suspected of coronary artery disease (CAD) we assessed the diagnostic sensitivity and specificity of exercise testing using 1) ST-changes alone and 2) ST-changes, angina and hemodynamic variables, against coronary computed tomographic angiography (CTA). Quantitative invasive coronary angiography (QCA) was used as reference (>50% coronary lumen reduction). A positive exercise test was defined as 1) development of significant ST-changes (≥1mV measured 80 ms from the J-point), and 2) occurrence ≥1 of the following exercise test variables: ST-changes ≥1mV measured 80 ms from the J-point, angina, ventricular arrhythmia (run of ≥3 premature ventricular beats), and ≥20 mmHg drop in systolic blood pressure during the test. A positive CTA was defined as a coronary lumen reduction ≥50%. In 100 patients 61 ±9 years, 50% men and a 29% prevalence of significant CAD, the diagnostic sensitivity and specificity (95% confidence interval) of exercise testing using ST-changes were 45% (53-87) and 63% (61-84), respectively, whereas the inclusion of all test variables yielded a sensitivity of 72% (53-87) and a specificity of 37% (26-49). The CTA diagnostic sensitivity of 96% (82-100) and specificity of 80% (69-89), however, were superior to any of the exercise test strategies. In conclusion, the diagnostic sensitivity of exercise testing significantly improves if all test variables are used as compared to ST-changes exclusively are considered in patients with suspected CAD. Furthermore, the superior diagnostic performance of CTA for the detection of significant CAD may favour CTA as a first-line diagnostic test in patients suspected of CAD.

O03.01 Louise Wamberg

EXPRESSION OF VDR MRNA IN ADIPOSE TISSUE IS AFFECTED BY ADIPOSE TISSUE LOCATION IN LEAN SUBJECTS

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Objective: Low levels of plasma 25-(OH)-vitamin-D_3 are common in obesity. Adipocytes have specific vitamin D receptors (VDR) and adipose tissue is believed to be the main storage site for vitamin D. We aimed to evaluate the abundance of VDR in adipose tissue, measured as the expression of VDR mRNA, in lean and obese individuals. Also we wished to investigate any differences in different compartments of adipose tissue.

Methods: Paired samples of visceral (VAT) and subcutaneous (SAT) adipose tissue biopsies and blood samples were obtained from 10 obese women (age 43,2 ± 9.5 years; BMI, 44,2 ± 4,3 kg/m^2) undergoing laparoscopic gastric banding for obesity and from 10 lean women (age 44,5 ± 6,3 years; BMI 22,5 ± 0,9 kg/m^2) undergoing laparoscopic surgery for gynecological reasons.

Results: All obese and 60,0 % of lean subjects were deficient of 25(OH)D_3, defined as plasma levels < 75 nmol/l. (mean 24,8 nmol/l vs.64,8 nmol/l, p= 0,051). Mean levels of VDR mRNA in SAT was significantly higher in lean compared to obese subjects:0,596 ± 0,617 vs. 0,056 ± 0,055, (p=0,022). Levels of VDR mRNA was similar in VAT: 0,080 ± 0,055 vs. 0,079 ± 0,087, (p = 0,98). In lean individuals levels of VDR mRNA was significantly higher in SAT compared to VAT: 0,596 ± 0,617 vs 0,080 ± 0,055 (p=0,03).

Conclusion: Vitamin D deficiency is common, even in lean subjects. Expression of

VDR mRNA is higher in subcutaneous adipose tissue than in visceral adipose tissue in lean individuals, and in SAT of lean subjects the expression is greater than in SAT of obese subjects. The metabolism of 25(OH)-vitamin D may differ between various adipose tissue compartments and between individuals with different fat mass.

O03.02 Rasmus Sode-Carlsen

ONE YEAR OF GROWTH HORMONE THERAPY IMPROVES BODY COMPOSITION IN ADULTS WITH PRADER-WILLI SYNDROME

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Introduction: Prader-Willi syndrome (PWS) presents clinically with a multitude of findings, including abnormal body composition and partial growth hormone (GH) deficiency. Until now three studies with non-optimal design and/or patient materials have reported beneficial effects upon body composition of GH treatment in adults with PWS.

Aim: The aim of this study was to confirm and substantiate the results from previous studies.

Patients and methods: 40 patients, 22 women, 18 men, age 29 years (16-41) (median and range) with genetically verified PWS participated in a multinational Scandinavian study. The patients were randomized to treatment with GH (0.6 – 0.8 mg daily) (NorditropinSimpleXx®) or placebo for 12 months. Insulin-like growth factor-I (IGF-I) and body composition (dual x-ray absorptiometry (DXA)) were measured at baseline and after 12 months.

Results: The change in IGF-I was +122 vs. + 5 µg/L (GH vs. placebo) ($p<0.001$). Body fat changed -2.05 vs. +2.60 kg ($p<0.001$) and lean body mass +2.39 vs. -0.00 kg ($p=0.006$).

Conclusion: In this first large scale, long-term placebo-controlled study the improvement in body composition by GH treatment in adults with PWS was confirmed. No side effects were observed. Whether these findings persists during long-term therapy and translates into significant clinical benefits for this particular patient group remain to be elucidated.

O03.03 Ane Bærent Fisker

VITAMIN A SUPPLEMENTATION AT BIRTH PRIMES THE RESPONSE TO SUBSEQUENT VITAMIN A SUPPLEMENTATION: A BENEFICIAL EFFECT FOR GIRLS

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Background and objectives: Within a randomised trial of vitamin A supplementation (VAS) at birth conducted at a demographic surveillance site in Guinea-Bissau all children received a follow-up visit after the first year and were offered VAS (FU-VAS). There was no effect of VAS at birth on overall mortality before 1 year of age. Based on recent observations we tested the hypothesis that VAS at birth primes the response to subsequent doses of VAS.

Design: We examined whether the mortality between 1 and 3 years of age differed according to VAS or placebo at birth and FU-VAS.

Results: Of 4345 infants enrolled in the original trial, 3646 lived in the study area at 1 year of age and 2958 received FU-VAS. Between 1 and 3 years of age, 112 children died. After FU-VAS, girls who had VAS at birth had lower mortality than girls who had placebo; the MRR being 0.37 (95% CI 0.16 to 0.87). In contrast, among girls who did not receive FU-VAS, VAS at birth had no significant effect on mortality compared with placebo at birth (1.67 (0.81 to 3.41)). Hence, in the second and third

year of life the effect of VAS at birth was different in girls who had or had not received FU-VAS (p for homogeneity=0.01). In boys there was no difference; the MRR for VAS versus placebo at birth was 0.73 (0.35 to 1.51) after FU-VAS, and 0.57 (0.23 to 1.42) in those who did not receive FU-VAS. This resulted in a significant interaction between sex, VAS at birth and FU-VAS (p=0.04).
Conclusions: The present results suggest that VAS at birth primes the response to subsequent VAS in girls. This may have implications for VAS distribution policies.

O03.04 Lars Erik Bartels

DENDRITIC CELLS FROM CROHN'S PATIENTS CAN MODULATE OWN FUNCTION THROUGH HYDROXYLATION OF 25-HYDROXY VITAMIN D3

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Objective
Crohn's disease (CD) is associated with vitamin D deficiency. The circulating form is the inactive 25-hydroxy vitamin D (25-D3) which is activated by 1-α-hydroxylase into 1,25-dihydroxy vitamin D (1,25-D3). It is established that dendritic cells (DC) express 1-α-hydroxylase which in healthy individuals modulate immune functions in a tolerogenic direction. However 1-α-hydroxylase expression is elevated in colonic biopsies from CD patients and a dysfunction of this enzyme might play a role in CD.
Methods
Peripheral blood was drawn from six patients with established CD. Monocytes were separated through adhesion to plastic flasks and differentiated into DC by IL-4 and GM-CSF and matured by LPS. Under differentiation cultures were stimulated with either 25-D3 or 1,25-D3. Maturation was evaluated by flow cytometry measuring the expression of surface markers and DC function was evaluated with allogen MLR.
Results
After treatment with 1,25-D3 DC reduced the expression of CD80 (with 33%, p=0.03), CD83 (with 54%, p=0.03), CD86 (with 44%, p=0.03) and HLA-DR (with 62%, p=0.03). The expression of CD14 increased by a factor eight after vitamin D3 treatment (p=0.03). Similar observations were made after 25-D3 stimulation. DC stimulated with both types of vitamin D3 showed decreased ability to activate lymphocytes from an allogen donor (for both, $p<0.01$).
Conclusion
DC from CD patients responded to both 25-D3 or 1,25-D3 treatment by reduced maturation, which in both cases lead to a decreased activation of lymphocytes. Thus our findings indicates that DC from CD-patients are capable of activating vitamin D3 to modulate own activity and control immunoreactions.

O03.05 Helene Kvistgaard

A NOVEL SILENT MUTATION IN THE *AVP* GENE MAY CAUSE REDUCED PROCESSING OF THE AVP PROHORMONE

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Autosomal dominant Familial Neurohypophyseal Diabetes Insipidus (adFNDI) is caused by mutations in the gene encoding the AVP prohormone. We have identified a unique point mutation (g.1924G>A) in the AVP gene, which is the first silent mutation found in a kindred with apparent adFNDI.
The aim of the study was to test if the mutation results in production of abnormal AVP prohormone, which fails to fold efficiently thereby exerting a dominant negative effect in a similar manner as other adFNDI mutations. Additionally, we

wished to test if the silent mutation represents a splicing mutation as it changes the second nucleotide of exon 3 possibly part of its 5´ splice site.
Clinical studies of two members of the kindred confirmed the diagnosis of adFNDI. Expression constructs containing a minigene including all exons and intron 2 of the AVP gene both with and without the mutation were constructed. Heterologous expression in mammalian cell lines was performed. Preliminary results indicate that the mutation may cause a reduced amount of immunoreactive AVP in the cell culture medium as determined by radioimmunoassay analysis.
This mutation is the first silent mutation reported in the AVP gene. We demonstrate that it is associated with a typical FNDI phenotype. Further cell studies are needed to confirm this association. These will include RT-PCR and further investigations of the intracellular processing of the AVP prohormone. We hope to demonstrate that a silent mutation can have a dominant negative effect like missense mutations, if it affects splicing, and thereby lead to misfolding of the resulting aberrant protein.

O03.06 Anders Lindelof WHY CAN OBESE ADOLESCENTS NOT ENGAGE IN HEALTHY HABITS? - THE STIGMA OF OBESITY AND THE MISSING DIALOGUE.

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Background: obesity is considered a threat to public health. Sedentary activities and unhealthy diet are associated with obesity and the focal point of treatment strategies. These strategies have poor effect and new approaches are needed. It has been hypothesized that instead of focusing solemnly on diet and exercise habits attention should be drawn to factors stimulating such habits.
Aim: to explore factors influencing the behavior of obese adolescents.
Material and method: a qualitative study. 12 obese adolescents and their parents are observed for four years with yearly interviews and field observations.
Results: obese adolescents have a wish for losing weight. They try to change lifestyle, but cannott sustain healthier eating and exercising habits. This failure might be due to the way obesity is managed among friends and families.
We found that obese adolescents and their families and friends all avoid situations where the adolescent's obesity is put into attention. This is both a verbal and a behavioral avoidance. Shame, guilt, and embarrassment are used to explain this avoidance
As the adolescents avoid these situations they cannot involve family and friends in their obesity. I.e. they cannot get support to reduce weight, and they cannot seek comfort when emotionally troubled, e.g. when being bullied or gaining weight.
Perspectives: to engage in lasting lifestyle changes obese adolescents need social support. We argue that the possibilities of losing weight will increase if the adolescent is able to non-judgmentally deal with his obesity among friends and families. Such articulation cannot be achieved today and should be integrated in future treatment strategies.

O04.01 Kasper Toustrup VALIDATION OF A HYPOXIC GENE EXPRESSION SIGNATURE ON XENOGRAFTS AND HUMAN HEAD AND NECK SQUAMOUS CELL CARCINOMAS (HNSCC)

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Aim:
To evaluate the in vivo-impact of a previously suggested in vitro-derived Hypoxic Gene Expression Signature (Sorensen et al, 362-366, Radiotherapy and Oncology, 2005).
Background:
Hypoxic tumours are associated with more aggressive phenotypes and increased resistance to radiotherapy. In HNSCC this resistance can be reduced by the use of hypoxia modifying therapy. A promising strategy to identify candidate patients for

this therapy is to be guided by hypoxia-responsive gene-expressions.
Methods:
We converted three relevant cell lines into a xenograft-model. Prior to extirpation of each tumour (n=22), the mice were infused with exogenous tracers (pimonidazole and ^{18}F-FAZA) to expose hypoxic and non-hypoxic areas respectively. Each area was identified and tumour tissue dissected. RNA was extracted from cells representing each area, and gene expressions were calculated by qPCR. Similar procedure was performed on a small series of five human HNSCC.
Results:
The previously suggested in vitro-derived hypoxic signature constituted 30 genes with two more genes added on the basis of literature studies. A median-increased gene expression in the suggested hypoxic areas compared to the normoxic areas was observed in all but two genes. 15 genes were more than two-fold median up-regulated in 2 out of 3 xenograft-lines ($P < 0.05$). Studies are ongoing to apply the signature genes on human HNSCC.
Conclusion:
By verifying a significant up-regulation of our signature genes in suggested hypoxic areas of HNSCC-xenografts, we underline the relevance of these genes as hypoxic markers not only in vitro but also in vivo. Further studies on well described cohorts of HNSCC-patients are ongoing.

O04.02 Peter Martin Hjørnet Kamper

TUMOR-INFILTRATING MACROPHAGES CORRELATE TO ADVERSE PROGNOSIS AND EPSTEIN-BARR VIRUS STATUS IN CLASSICAL HODGKIN LYMPHOMA.

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Background:
Classic Hodgkin lymphoma (cHL) is characterized by a minority of neoplastic cells surrounded by a heterogeneous background of non-neoplastic cells. CD68 and CD163 are antigens expressed by cells belonging to the monocytes/macrophage lineage. Both a high CD68 and CD163 expression have been suggested to have pro-tumoral effects. The aim of the present study was to correlate the expression of CD68+ and CD163+ LAMs with clinico-pathological features and prognosis in a cohort of previously untreated HL patients.
Methods:
A tissue microarray was constructed with paraffin embedded tissue specimens from 286 cHL cases. CD68 and CD163 expression was assessed immunohistochemically and the degree of intratumoral LAM infiltration was scored using point grid counting. Clinical data were obtained from clinical records.
Results:
The median age was 37 yrs (range: 6-86 yrs). The M:F ratio was 1.2.
At univariate level a high CD68 and CD163 expression correlated with an adverse impact on overall survival ($p=0.001$ and 0.04, respectively). A high CD68 expression was also found to correlate with an inferior event-free survival ($p=0.04$). At multivariate level, a high CD68 expression retained a significant predictive impact on OS ($p=0.006$). In addition, we demonstrated that both a high CD68 and CD163 expression were related to the presence of EBV in the neoplastic cells ($p=0.0004$ and 0.0001, respectively).
Conclusions:
In cHL, a high expression of the macrophage/monocyte related antigens CD68 and CD163 correlates with adverse outcome and with the presence of EBV in the tumour cell population.

O04.03 Malene Hvid

IL-25 IN ATOPIC DERMATITIS

Larsen

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Atopic dermatitis (AD) is a chronic, relapsing inflammatory skin disease estimated to affect 10–20% of children and 1–3% of adolescents in the Western world. The underlying immunological mechanism is not fully elucidated, however the immune response has traditionally been characterized as Th2-like.

The novel cytokine IL-25 (IL-17E) has been associated with the development of asthma, another atopic disease. These results led us to hypothesize that IL-25 could play a potential role in AD. We have previously shown that IL-25 are indeed present within the skin of AD patients. Further, some of the IL-25 positive cells are characterized as large mononuclear cells present along the basal membrane of the skin lesions.

Since dendritic cells are present in increased numbers in AD skin lesions we wished to determine if these cells could be responsible for IL-25 production. We therefore isolated monocytes from the skin and stimulated these cells with IL-4 and GMCSF for 7 days to develop DCs. These cells were then examined for the presence of a panel of cells markers including e.g. HLA-DR, CD11c, CD80 and CD83 using flow cytometry, which confirmed that the cells had indeed developed a DC phenotype. We then examined if the cells had the potential to produce IL-25 using intracellular flow cytometry. These results showed that between 25-60% of the dendritic cells indeed produced IL-25. Thus, our results confirm that DCs, which are present in large numbers in the skin of AD patients, has the potential to produce IL-25.

O04.04 Anne Stidsholt Roug

A COMPARATIVE STUDY OF THE IMMUNOPHENOTYPE OF STEM CELLS IN AML FOCUSING ON ANTIGENS RELATED TO EARLY HEMATOPOIESIS

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Background: In AML malignant myeloid precursor cells cause proliferation of undifferentiated cells. Malignant stem cells surviving chemotherapy cause relapse. We have performed an immunophenotypic (IP) characterization of blasts in AML involving a comparison of antigens related to stemcellness including MICL, CD96, CD123 and CD133. Methods: MNC from diagnosis, remission and relapse from 50 AML patients were analyzed by 4-color flow cytometry. Boolean gating involved determination of the IP of viable CD45low/SSClow cells. RQ-PCR and Western blotting were performed to validate RNA content and protein expression for the CD96 and MICL genes. Results: We analyzed the CD34- and CD34+ patients separately. While the broad expression of CD123 precluded further analysis within the CD34 subsets, MICL, CD96 and CD133 were differentially expressed on CD34- and CD34+ AML patients. CD96 and CD133 were positively correlated to the CD34 expression (CD96: r2=0.36, p=0.01 and CD133; r2=0.72, p< 0.001), MICL displayed a negative correlation to CD34 (MICL: r2=-0.44, p=0.001). In addition, MICL expression was more pronounced and less heterogeneous within the CD34- subset. Conclusion: We have observed a differential expression of CD34 to be important in describing the expression of a series of candidate LSC antigens. Within the CD34- subset of patients, the MICL protein expression suggests that AML arises from a small pool of leukemic SC within this subset. In addition, we observed an equally stable expression of CD123 in both CD34+ and CD34- AML cases, suggesting this antigen as a universal marker for leukemic SC, irrespective of CD34 expression.

O04.05 Iben Møller Jønsson

IS THERE A NEW LIGHT AT THE END OF THE TUNNEL? A STUDY ON RECTAL PHYSIOLOGY IN HEALTHY CHILDREN AND CHILDREN WITH FAECAL INCONTINENCE.

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Although benign in nature, functional faecal incontinence is psychologically malignant causing considerable distress and low self-esteem for the effected children. The physiology behind this condition is incompletely understood. We have shown the existence of three spontaneous motility patterns in children with overactive bladder which differed from the pattern of healthy adults. It is unknown whether these are present in healthy and faecally incontinent children.
Aim: To characterise the patterns of rectal motor activity in children with faecal incontinence and compare them with healthy children. Furthermore, to describe the association between the autonomous nervous system and rectal motility.
Materials and Methods: 20 children with faecal incontinence and 12 healthy children from 7yrs to 12yrs are to be included and undergo a 24-hour rectal manometric recording and 24-hour Holter monitoring. Duration and type of rectal motility patterns will be registered. Heart rate variability will be calculated on the basis of the Holter monitering and used as a measurement for autonomous activity.
Perspectives: The study will hopefully increase the understanding of the rectal physiology in healthy children and children suffering from faecal incontinence and potentially lead to new treatment strategies.

O04.06 Tina Rask Emholdt

NEPHROGENIC SYSTEMIC FIBROSIS: A CASE STUDY FROM DENMARK
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Purpose
To identify patients with nephrogenic systemic fibrosis (NSF) among patients with severe kidney disease, to whom MRI scan with gadolinium based contrast agent (GBCA) has been administered at least once at Skejby Hospital, during the period January 1997 to February 2009.
Methods and Materials
Case study. 565 patients with kidney disease, who had been exposed to different GBCAs: Omniscan®, Dotarem®, Magnevist®, Vasovist®, Multihance®, and Gadovist®, were included in this study. Careful inspection of patient records revealed 32 patients where the suspicion of NSF was raised. The patients have been thoroughly examined by an experienced dermatologist.
Results
Surprisingly, 18 patients were diagnosed with NSF, mean age 53 years and subjected to 1-5 consecutive dosages of GBCA. The 18 patients were differently affected with NSF: from minor skin changes to major disseminated lesions, joint restrictions and pain. Among deceased patients there has been a suspicion of NSF in 16 cases.
We found three patients where Gadovist or Dotarem seemed to be the main cause of NSF.
Conclusion
This retrospective investigation has revealed 18 new cases of NSF. As consequence, a national investigation in Denmark is now initiated. Gadovist® or Dotarem® has not previously been the main course of NSF.

P01.01 Steffen Møller-Larsen

IN-DEPTH ASSOCIATION ANALYSIS OF TOLL-LIKE RECEPTORS WITH ASTHMA AND RELATED ATOPIC DISORDERS
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Toll-like receptors (TLRs) are pathogen sensing receptors responsible for initiating innate and adaptive immune responses against a range of pathogens. The atopic phenotype is frequently associated with a TH2 type of T helper cells whereas TLRs are strong inducers of the TH1 type highlighting these receptors as interesting targets for therapy and general research aimed at describing the pathophysiology related to atopy and allergy.

We have previously reported association of two viral sensing receptors, TLR7 and TLR8, to asthma and related atopic disorders. Most significant associations were seen for variants rs179008 (TLR7) and rs2407992 (TLR8) - both are of putative functional significance.

In this study we do an in-depth association analysis of TLR7 and 8 in which we take into consideration a considerably larger proportion of the genetic variability of these genes by adopting a tag-SNP approach. We also include TLR1, 3, 6, 9 and 10. We analyze the previously used as well as additional cohorts by a combination of case/control and family-based association studies thus providing an increased power.

P01.02 Majbritt Hauge Kyneb

INVESTIGATION OF THE USE OF THE MEMBRANE RECEPTOR CD163 AS TARGET IN CYTOSTATIC TREATMENT OF AML

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Despite intensive chemotherapy and bone marrow transplant only 40% of patients with acute myeloid leukemia (AML) survive more than five years.

Immunoconjugates, in which a toxin is conjugated to a cancer-specific antibody, comprise new promising strategies for treatment of cancer. Ideally this targeting strategy allows delivery of the toxic substance directly to the cancer cells without affecting the healthy tissues, i.e. the systemic side effects related to conventional chemotherapy are diminished.

In the present study we will investigate if it is possible to use the membrane receptor CD163 as target for cytostatic treatment of AML. CD163 is the receptor for endocytosis of haptoglobin-hemoglobin complexes and is only present on cells of monocytic lineage, with highest expression on anti-inflammatory macrophages. The receptor is also expressed on some myelomonocytic forms of AML of the FAB-type M4 and M5 and it is these AML-subtypes we attempt to target in this study.

Initially we will in various in vitro assays investigate the binding, endocytosis and growth inhibiting effect of a toxin-conjugated CD163-binding compound to humane cancer cell lines expressing the receptor. Subsequently we will establish growth of a suitable CD163-positive humane AML cell line in immunedeficient mice (NOD/SCID) and eventually we will investigate the effect of treatment with the drug candidate. We also aim for using the mouse model with primary AML cells isolated from AML patients for evaluation of the drug candidate.

P01.03 Anne-Mette Bay Bjørn

MATERNAL USE OF PRESCRIBED GLUCOCORTICOIDS DURING PREGNANCY AND RISK OF CONGENITAL BIRTH DEFECTS: AN 11-YEAR POPULATION-BASED STUDY IN DENMARK

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Background: Glucocorticoids are first-line drugs for treatment of a variety of conditions in women of childbearing age.

Objective: To examine the association between use of prescribed glucocorticoids

(inhaled, oral, or topic preparations) during pregnancy and risk of congenital birth defects among the off-spring.
Design: Population-based prevalence study.
Setting: All pregnant women who gave their first live-birth after 20th gestational week in the Central and the North Denmark Regions from 1 January 1997 to 31 December 2007.
Methods: We linked data from the Danish Medical Birth Registry and the regional prescription databases to obtain information of prescriptions for reimbursed glucocorticoids filled during the period from 30 days before pregnancy until delivery.
Results: Among 84,130 women giving first live-birth, we identified 5,500 (6.5%) women who redeemed at least one prescription of glucocorticoids during pregnancy. We registered 374 (6.8%) birth defects among off-springs of users of glucocorticoids compared to 4,711 (6.0%) birth defects among off-springs of non-users [crude prevalence odds ratio (POR)=1.14 (95% confidence interval (CI) 1.03; 1.28)]. We found the highest prevalence of birth defects (8.3%) among users of oral glucocorticoid [crude POR=1.25 (95%CI 1.01; 1.54)] compared to a prevalence of 6.4% in users of inhalation [POR=1.14 (95%CI 0.94; 1.38)].
Conclusion: Our findings suggest that users of glucocorticoids during pregnancy have an increased risk of birth defects among off-springs. We do not know whether our findings are causal or may be explained by some confounding factors.

P01.04 Lars Peter Sørensen

VLDL-TG METABOLISM IN TYPE 2 DIABETES

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Background
A complication of type 2 diabetes is diabetic dyslipidemia, which is an important and common riskfactor for cardiovaskular disease. Recent evidence suggest that the lipid and lipoprotein abnormalities are metabolically interrelated, and that a fundamental defect is an overproduction of VLDL-TG. However, recearch in VLDL-TG kinetics have been limited due to methological problems. The aim of this study was to study the physiological basis of this metabolic dyslipidemia using ex vivo labeled VLDL-TG tracers.
Methods
11 healthy men and 11 men with type 2 diabetes, matched for age and BMI, were included. VLDL-TG production rate (Ra) and clearance (Cl) was determined in the basal state (2 hours) and during a euglycemic hyperinsulinemic glucose clamp (5 hours) using primed-constant infusion of ^{14}C VLDL-TG tracer.
Results
VLDL-TG Ra ($\mu mol \cdot min^{-1}$) was lower in the healthy men compared to the men with type 2 diabetes in both the basal state (46.7 (33.8-123.2) vs. 89.3 (49.0-155.1), P = 0.030) and during hyperinsulinemia (34.2 (17.9) vs. 60.0 (26.2), P = 0.014) while there was no difference in VLDL-TG clearance ($ml \cdot min^{-1}$) between the groups in the basal state (55.2 (18.9) vs. 50.2 (19.5), P = 0.549) or during hyperinsulinemia (44.7 (16.2) vs. 44.6 (18.2), P = 0.988).
Conclusion
Our data demonstrate, that the hypertriglyceridemia observed in diabetic dyslipemia is a result of increased VLDL-TG production rather than decreased clearance.

P01.05 Philipp Harbig

METHODS FOR IMPROVING COMPLIANCE WITH MEDICINE INTAKE (MICMI): A VALIDATION OF QUESTIONNAIRE 'ELDERLY MEDICINE COMPLIANCE QUESTIONNAIRE (EMCQ)'

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Objective: Noncompliance with medicine intake is a major problem for medicine treatment. Methods for Improving Compliance with Medicine Intake (MICMI) is a research project to evaluate compliance with medicine intake in an elderly population. The aim of the project is to compare different registration and intervention methods. One of the registration methods is the questionnaire EMCQ, which has been validated in a pilot project. Research design and methods: A randomized study involving 2 pharmacists and 1 nurse and including 22 participants aged at least 65 years. Compliance was assessed under blinded condition by pill count and EMCQ at two home visits. EMCQ includes 14 questions and is based on Morisky 4-item, compliance-questionnaire-rheumatology and COMPASS questionnaire. Results: In 17 out of 22 participants there is a concordance in [non]-compliance measured by EMCQ and pill count. 1 participant has better compliance in EMCQ than in pill count, 2 participants have lower compliance in EMCQ than in pill count and 1 person was noncompliant in pill count, but compliant in EMCQ. Conclusion: EMCQ can be used in research for measuring compliance with medicine intake.

P01.06 Michael Winterdahl

HEPATIC BLOOD PERFUSION CAN BE ESTIMATED NON-INVASIVELY BY DYNAMIC PET USING GLUCOSE ANALOGS: VALIDATION OF A PORTAL VENOUS MODEL IN PIG STUDIES

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Hepatic perfusion can be quantified by kinetic analysis of the time-activity curves (TACs) in liver tissue measured by dynamic PET in relation to the tracer input from the hepatic artery (HA) and the portal vein (PV) measured by blood sampling. In humans, blood sampling from the PV is not possible. The purpose of the study was to examine if a portal model can replace portal sampling for the estimation of hepatic perfusion. We used [^{11}C]methyl-glucose, MG[1], [^{18}F]fluoro-2-deoxy-galactose, FDGal[2], and [^{18}F]fluoro-2-deoxy-glucose, FDG[1]. In pigs studies TACs from the portal vein and the femoral artery were measured by blood sampling, following iv injection. Dispersion and delay from arterial TAC to portal TAC was described by a portal model with a single parameter, β[3]. Average values of β were estimated for each glucose analog. For each injection: 1) a simulated tissue TAC was calculated using the measured dual-input TAC and a one-tissue compartment model with a 'true' perfusion; 2) a non-invasive dual-input TAC was calculated; 3) hepatic perfusion was estimated using the simulated tissue TAC and the non-invasive PV-model dual input. The relative deviation was not significantly different from zero for any of the three glucose analogs. In conclusion, hepatic perfusion can be quantified non-invasively by dynamic PET with glucose analogs using glucose analog specific average values of β for the portal venous model. For clinical use in humans, arterial blood sampling may be replaced by scan data from the abdominal aorta[4], which will make the method completely non-invasive.
1) Munk et al, 2001; 2) Sørensen et al, 2008; 3) Munk et al, 2003; 4) Keiding et al, 2000.

P01.07 Emma Tina Bisgaard Olesen

VASOPRESSIN INDEPENDENT MEMBRANE TARGETING OF AQUAPORIN-2 BY PROSTAGLANDIN E2

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Water permeability (Pf) of the kidney collecting duct (CD) can be increased by vasopressin induced trafficking of aquaporin-2 (AQP2) to the apical plasma membrane (APM) of principal cells. However, previous studies on isolated perfused

tubules indicate that prostaglandin E2 (PGE2) also increases Pf of the CD under certain conditions. Therefore, we hypothesized that PGE2 acting on one of the known prostanoid receptors (EP1-4) can regulate the APM abundance of AQP2 independently of vasopressin.
Methods: A Madine-Darby canine kidney (MDCK) cell line stably transfected with AQP2 was used for all studies. The cells were experimentally treated using PGE2 as described below. For immunocytochemistry (IC), cells were grown on coverslips until confluent, stimulated with PGE2, fixed and labelled using an AQP2 antibody. For quantitative biotinylation studies, APM proteins were biotinylated, purified and samples immunoblotted to determine the fraction of biotinylated AQP2 under different conditions; this is an assessment of the fraction of AQP2 on the APM.
Results: Immunoblotting revealed the presence of EP2 and EP4 but not EP3 in our MDCK cells. Biotinylation studies demonstrated that the APM abundance of AQP2 is significantly increased after 40 min stimulation with PGE2 at concentrations of 10^{-9}M (1,8±0,1), 10^{-8}M (2,8±0,2), 10^{-7}M (3,4±0,5) and 10^{-6}M (4,3±0,2) compared to controls (1±0,04)(n=4). IC in cells stimulated for 10, 20, 40 and 80min with PGE2 (10^{-7}M) indicated a max effect at 40min.
Conclusion: PGE2 increases the APM abundance of AQP2 in a time and concentration dependent manner in MDCK cells. This could have implications for the treatment of nephrogenic diabetes insipidus.

P01.08 Kathrine Kleis Tilma

THE DIAMETER RESPONSE OF RETINAL VESSELS AFTER TOPICAL APPLICATION OF A PROSTAGLANDIN AGONIST AND A PROSTAGLANDIN SYNTHESIS INHIBITOR IN VIVO. PRELIMINARY RESULTS.

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Background:
Disturbances in the retinal blood flow are involved in the pathophysiology of the major sight threatening diseases, including diabetic retinopathy. These disturbances are assumed to be due to deficient tone regulation of retinal resistance arterioles. In vitro studies have shown that prostaglandins are involved in this tone regulation, but it is unknown whether this finding can be transferred to clinical practise.
Methods:
Ten normal persons and ten age matched (20-35 years) type 1 diabetic patients with minimal diabetic retinopathy were studied. The test persons were randomized to receive either the prostaglandin F2α agonist Xalatan or the prostaglandin synthesis inhibitor Voltaren twice per day for one week. The baseline diameter of retinal arterioles and the diameter change during isometric exercise (pressure autoregulation) of a retinal arteriole was measured before and at the end of the treatment period using the Retinal Vessel Analyzer.
Results:
In both normal persons and in patients with diabetic retinopathy the prostaglandin agonist Xalatan induced a significant contraction and the prostaglandin synthesis inhibitor Volataren a significant dilation of the basal diameter of the measured retinal arteriole.
Conclusions:
The diameter of retinal resistance arterioles can be modified by short term topical treatment with agonists and antagonists to prostaglandin F2α agonist. This suggests that these compounds can be used for the treatment of diseases where disturbances in retinal perfusion is part of the disease pathogenesis.

P01.09 Marianne Cathrine Rohde

STRESS RESPONSE IN SUDDEN INFANT DEATH; IN VITRO STUDIES OF FIBROBLAST CULTURES

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We searched for variations in cellular stress response systems in cases of Sudden Unexpected Death in Infancy (SIDS), which have been associated with hyperthermia. The expression of genes coding for proteins in the cellular stress response and in the antioxidant systems was investigated in vitro by trying to mimic physiological stress full events.
Cells from children who died of unnatural known causes (controls) were compared with cells from children who died suddenly and unexpected and where the cause of death was unexplained (cases). Fibroblast cultures have been established from Achilles-tendons sampled during post mortem examinations. Fibroblast cultures were exposed to hyperthermia (40°C) and harvested at several time points during a 24 hours period. In order to investigate stress-response profiles, selected stress markers (Heat shock proteins: Hsp70 (cytosolic) and Hsp60 (mitochondrial); Antioxidants: HO-1 (cytosolic) and SOD2 (mitochondrial)) were evaluated using quantitative real-time PCR methods. Relative mRNA expressions were measured under stressed and unstressed conditions.The stress response profiles demonstrated large inter-individual variation in both groups, but most pronounced for the SIDS group. However, both groups showed significant changes over time as a response to stress, compared to base levels. The SIDS group though showed a higher response to stress than controls. We found some association with prone position when found and the level of stress response.
The results may indicate that SIDS cases over expressed heat shock factors in some situations of stress, compared to the control group we analysed.

P02.01 Yonglun Luo DEVELOPMENT OF A CLONED BRCA1 KNOCKOUT PIG MODEL
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Introduction: Mutations in BRCA1 gene are the underlying cause of breast cancer (BC) in most inherited forms of breast and ovarian cancers. Due to the similarities in biological processes and metabolism between pigs and human, a BC pig model may aid in elucidating the pathogenesis of BC. The purpose of this study is to generate a cloned BRCA1 knockout (KO) pig model using recombinant adeno-associated virus (rAAV) and Handmade cloning (HMC). Methods: A rAAV/BRCA1 KO construct was generated as described by Kohli et al (2004). 1.5×10^6 cells (fetal Yucatan fibroblasts) were transduced with rAAV/BRCA1 KO virus. Stable clones were selected with G418 (1 mg/ml) and further screened by PCR and Southern blot analysis (SBA). BRCA1 KO clones were chosen for HMC-SCNT pig cloning. Results: A rAAV/BRCA1 KO viral vector was generated deleting 55 bp in the BRCA1 gene upon targeting. Transduction resulted in ~350 G418 resistant clones, of which ~35% were BRCA1 KO. However, when these KO clones were further expanded for SBA, most clones stopped growing, and sufficient genomic DNA could only be purified from a few clones. One of the clones (ID: 1G7) was characterized to be only $BRCA1^{+/-}$. This clone is currently undergoing HMC in Beijing Genomics Institute (BGI), Shenzhen, China. Discussion: In this study, we have observed an extraordinary high targeting rate of the BRCA1 gene (~35%). According to our knowledge, this is the highest targeting rate reported for rAAV based or traditional vector based gene KO methods. This high targeting efficiency is probably due to the lack of repeated sequences in the targeting construct as the entire construct is made up from unique BRCA1 exon 11 sequences.

P02.02 Janne Lebeck EXPRESSION OF HEPATIC AQUAGLYCEROPORIN 9 (AQP9) IS REGULATED IN RESPONSE TO CASTRATION AND PPARα- AGONIST TREATMENT
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Increased hepatic glucose production plays a pivotal role in the pathophysiology of

diabetes mellitus. AQP9 has been suggested to facilitate the transport of glycerol into hepatocytes where it can be used as a gluconeogenic substrate. Hence, the regulation of AQP9 and thereby glycerol uptake could be a potential modulator of hepatic glucose production. This study aims to investigate the role of castration and PPARα – agonist (WY14643) administration in regulation of hepatic AQP9 protein expression in male rats. 25 days post-operative, the castrated rats had a 1.5 fold increase in hepatic AQP9 ($p < 0.02$) abundance. Furthermore, the castrated rats displayed a 53% reduction in plasma glycerol together with a small but statistically significant increase in plasma glucose when compared with controls. In rats treated for 10 days with WY14643 (3 mg/kg/day), immunoblotting showed a 2.6-fold decrease in expression of hepatic AQP9 ($p < 0.001$). Immunohistochemical analysis revealed a marked decrease of AQP9 in the periportal zone, whereas AQP9 expression in the perivenous zone appeared unchanged. There were no changes in plasma glucose levels. We conclude that hepatic AQP9 expression increases in response to castration in male rats and that this is accompanied by a decrease in plasma glycerol and increase in plasma glucose. Moreover, treatment with a PPARα –agonist results in a marked decrease and redistribution of hepatic AQP9 protein.

P02.03 Ebbe Bødtkjer

DISRUPTION OF THE NA^+,HCO_3^--COTRANSPORTER NBCN1 CAUSES HYPERTENSION: INTRACELLULAR ACIDIFICATION INHIBITS NO PRODUCTION AND RHO-KINASE DEPENDENT CA^{2+}-SENSITIVITY

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Hypertension is a major cardiovascular risk factor influenced by vascular tone. We provide here the first direct evidence that arterial tone is affected by membrane acid-base transport with implications for blood pressure regulation. Knockout of Na^+,HCO_3^--cotransporter NBCn1 (slc4a7) acidified mesenteric artery smooth muscle and endothelial cells and reduced NO-mediated relaxations and rho-kinase dependent smooth muscle Ca^{2+}-sensitivity. NBCn1 knockout mice were mildly hypertensive at rest, displayed an attenuated blood pressure response to NO-synthase and rho-kinase inhibition and were resistant to developing angiotensin II hypertension. NO levels were reduced in arteries from NBCn1 knockout mice while dilation to the NO-donor S-nitroso-N-acetylpenicillamine, the endothelial Ca^{2+}-response to acetylcholine and endothelial NO-synthase expression were unaffected. With CO_2/HCO_3^- absent, no differences were observed between arteries from NBCn1 knockout and wild type mice. Using a functional genetics approach to induce sustained intracellular acidification, we show a novel direct interaction between intracellular pH and blood pressure regulation.

P02.04 Pernille Munk Frandsen

ACTIVATION AND RECEPTOR STUDIES OF HUMAN MAST CELLS IN HEALTHY INDIVIDUALS AND PATIENTS WITH ASTHMA AND ALLERGY

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The human mast cell is a central effector cell in the innate immune response and plays a key role in the allergic inflammatory process. Present studies are limited as mature mast cells are difficult to isolate from human tissue in sufficient quantities. Mast cells express several receptors including the high affinity receptor (FcεRI) and Toll like receptors (TLRs). These receptors can activate the mast cell and are thus considered important in mediator release causing asthma.

The objectives of this study are to characterize some of the receptors that activate mast cells. These include FcεRI, TLR2 and TLR4. We want to analyze the release of

inflammatory mediators like prostaglandin D_2, histamine and several cytokines. Furthermore we wish to analyze the effect of known proinflammatory mediators like IFN-γ on the response after stimulation of the receptors.

Another objective is to characterize the profile of expressed mRNA in mast cells from healthy individuals and patient with type-1 allergy. This will be done by use of microchips. From this study we expect to achieve new knowledge about some of the differences between mast cells from healthy and allergic individuals.

P02.05 Hanne Vebert Olesen

CREATING A NATIONAL PATIENT DATABASE

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Aim. To create a patient registry for patients with cystic fibrosis. The registry should provide an overview of the single patient for use in the daily clinic as well as a database of all patients for purposes of quality control and research.
Methods. Study of other patient registries. Identification of relevant variables and specification of common definitions where applicable. Selection of reference values for calculation of predicted values for lung function parameters. Developement of database and queries.
Results. Working registry with clinical implications for the single patient (evaluation of lung function and anthropometric variables over time). Three yearly reports produced for center based and national quality control. Identification of further variables to add in the future.
Conclusion. Benefit for the single patient because of increased awareness of trends in vital parameters (graphic presentations). Quality in treatment has improved because certain problems have been identified and treatment has been optimized in several areas (nutrition, antibiotic treatment).

P02.06 Irina Kruglikova

THE IMPACT OF CONSTRUCTIVE FEEDBACK ON TRAINING IN GASTROINTESTINAL ENDOSCOPY USING HIGH FIDELITY VIRTUAL REALITY SIMULATION. A RANDOMIZED CONTROLLED TRIAL

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Background: Recently, virtual-reality (VR) computer simulators have been used to enhance traditional endoscopy teaching. Previous studies have demonstrated validity of these systems. However, to date no simulator-training curricula have been designed and there is very little evidence on the impact of external feedback on acquisition of endoscopic skills. The aim of the present study was to assess the impact of external feedback on the learning curves on a VR colonoscopy simulator using inexperienced trainees. Materials and methods: Twenty two trainees, without colonoscopy experience were randomized to a group which received structured feedback provided by an experienced supervisor and a controlled group. All participants performed 15 repetitions of task 3 from the Introduction colonoscopy module of the Accu Touch Endoscopy simulator. Retention/transfer tests on simulator were performed 4-6 weeks after the last repetition. The proficiency levels were based on the performance of 8 experienced colonoscopists. Results: All subjects were able to complete the procedure on the simulator. There were no perforations in the feedback group vs. 7 in the non-feedback group. Subjects in the feedback group reached expert proficiency levels in percentage of mucosa visualized and time to reach the cecum significantly faster compared with the control group. None of the groups demonstrated significant degradation of performance in simulator retention/transfer tests. Conclusion: Concurrent feedback given by supervisor concur an advantage in acquisition of basic colonoscopy skills and achieving of

proficiency level as compared to independent training.

P02.07 Maria Jakobsen

VIRAL DELIVERY OF TNF-α TARGETED SHRNA MEDIATES RESOLUTION OF PSORIASIS IN THE XENOGRAFT TRANSPLANTATION MODEL

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TNF-α is a well known target in psoriasis treatment and biologic treatments targeting TNF-α are already clinically used against psoriasis and psoriasis arthritis. To test the hypothesis that TNF-α in skin can be stably down-regulated by RNAi, we designed a panel of shRNAs targeting human TNF-α. One shRNA in particular showed high potency in down-regulation of TNF-α protein expression in vitro and was selected for in vivo studies. In vivo studies were carried out in the xenograft mouse model in which human psoriatic plaques keratome skin biopsies were transplanted onto SCID mice. Grafted psoriatic skin was exposed to viral vector-encoded TNF-α shRNAs by a single intradermal injection of purified lentiviral vectors. Biopsies were taken three weeks after injection. qPCR-based measurements of TNF-α mRNA in skin treated with lentiviral vector-encoded TNF-α shRNA demonstrated a 29% reduction in the level of TNF-α mRNA. Moreover, the epidermal thickness of the human psoriatic plaques was reduced with 22% relative to mice treated with lentiviral vectors encoding an irrelevant shRNA. Our results demonstrate that lentiviral vector-encoded TNF-α shRNAs have the potential to down-regulate TNF-α production both in vitro and in vivo. Phenotypic changes in shRNA-treated psoriatic skin suggest that TNF-α-encoding RNA is a valid therapeutic target in psoriasis treatment. Currently, we are working on substitution of the lentiviral vector for an AAV vector for the delivery of shRNAs as the AAV vector is based on the non-pathogenic adeno-associated virus.

P02.08 Ida Sejersdahl Kirkegaard

EARLY FETAL GROWTH RATE, PLACENTA HORMONES AND PRETERM DELIVERY

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Objective To evaluate the placenta hormones pregnancy-associated plasma protein-A (PAPP-A) and free β-human chorionic gonadotropin (β-hCG) and the growth rate of the fetus from the first to the second trimester in relation to preterm delivery.
Methods All 9450 singleton pregnant women, who attended the prenatal screening program between January 2005 and December 2007, and gave birth at Aarhus University Hospital, Denmark, were included. PAPP-A and free β-hCG was measured in the first trimester. Early fetal growth rate was estimated by $(GA_{20} - GA_{12})/Days_{calendar,}$ where GA_{12} reflects the gestational age in days calculated from CRL at 12 weeks scan, GA_{20} reflects the gestational age in days calculated from BPD at 20 weeks scan and $Days_{calendar}$ is the actual number of days between the two scans.
Results Early fetal growth rate > the 90th centile was associated with preterm delivery (OR 1.9; 95% CI, 1.5 – 2.4) and so was both PAPP-A < 0.3 MoM (OR 2.4; 95% CI, 1.4 – 4.0) and free β-hCG < 0.3 MoM (OR 2.1; 95% CI, 1.0 – 2.4). For pregnancies with PAPP-A < 0.4 MoM and fetal growth rate < the 10th centile the OR for preterm delivery increased to 3.3 (95%CI 1.5 – 7.5) compared with those with PAPP-A and early fetal growth rate within the normal range. All associations persisted, when restricting to spontaneous deliveries.
Conclusion Rapid early fetal growth rate, low PAPP-A, and low free β-hCG are independent risk factors for preterm delivery. If, in addition to a low PAPP-A, early fetal growth rate is slow the risk of preterm delivery was even higher than for a low PAPP-A alone, and we believe that the presence of this combination should increase

clinical awareness.

P02.09 Helle Rosenberg

CO-REGULATION OF A BICARBONATE TRANSPORTER AND A KINASE IN THE MOUSE

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Dicistronic or polycistronic transcription is common in prokaryotes but in eukaryotes it is considered a relatively rare phenomenon except in C. elegans where up to 15 % of the genome may be transcribed in polycistronic units. In mammals there are few reports indicating that dicistronic transcription also occurs. In prokaryotes the polycistronic genes code for functionally interacting proteins. In mammals it is not known whether the genes in dicistronic transcripts are also functionally related. In this study we report on studies of co-regulation of the two genes Slc4a7 - encoding electroneutral sodium bicarbonate cotransporter NBCn1 important for buffering excess intracellular H^+ and the NEK10 - encoding the never in mitosis kinase 10 of unknown function. In a bioinformatic search we found the two genes to be closely mapped on the genome across a number of eukaryotic species. We thus hypothesized, that they might be transcribed as a discistronic mRNA. In a genetrap mouse model heterozygous mutation in the promoter region of the Slc4a7 causes decreased levels of NBCn1 and NEK10 mRNA and homozygous mutation in that region causes disappearance of both NBCn1 and NEK10 mRNA. In potassium depletion of SVJ129 mice, kidney thick ascending limb NBCn1 and NEK10 mRNA are both up-regulated. In contrast in the inner medulla neither of the genes were regulated (negative control). In a Northern blot probed with NBCn1 only one band of app. 8 KB was found. It was possible to detect a transcript using forward primer in NBCn1 and reverse primer in NEK10. These data suggest the presence of dicistronic transcription of NBCn1 and NEK10 and coordinated regulation of the two genes.

P03.01 Pernille Kure Vandborg

FOLLOW-UP OF NEONATAL NON-HAEMOLYTIC HYPERBILIRUBINEMIA IN DANISH TERM AND NEAR-TERM INFANTS WITH TOTAL SERUM BILIRUBIN (TSB) LEVEL ≥ 420 UMOL/L.

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Background: Severe and extreme hyperbilirubinemia in the newborn carries a substantial risk of permanent neurological sequelae. There are only few follow-up studies of children with gestationel age (GA) ≥ 35 weeks with severe neonatal hyperbilirubinemia, and the results are not consistent. The question whether infants with severe hyperbilirubinemia, who have minor acute neurological symptoms or are asymptomatic in the neonatal period, will suffer from long term sequelae remains controversial.

Aim: To assess possible developmental impairment in Danish children born 2004-2007 with GA ≥ 35 weeks and neonatal non-haemolytic hyperbilirubinemia (TSB ≥ 420 umol/l) compared with a matched non-bilirubin exposed control group.

Methods: The study group (n=213) is identified by linking electronically stored laboratory data to the Danish personal identification number (CPR). The control group (n=208) is matched on sex, age, GA and municipality of residence through the Danish birth registry. The families (n=421) were mailed the Ages and Stages Questionnaire (ASQ), which is a parent completed questionnaire ment as a screening tool to identify children with developmental delay. It consists of six questions in each of five developmental sections: fine motor skills, gross motor skills, communication, problem solving and personal-social skills. It is completed partly by the parents recall on the child's abilities and partly after testing certain skills with the child.

Results: The overall response rate was 75 %: 79 % (n=169/213) for the study group, 70% (n=146/208) for the control group. Data will be analyzed using multipel linear regression. Preliminary results will be presented.

P03.02 Raffaella Mangnoni

NEURODEGENERATIVE DISEASES DUE TO MUTATION IN THE MITOCHONDRIAL HSP60 CHAPERONE: STUDIES OF THE PATHOPHYSIOLOGY USING MOLECULAR PROTEOMICS AND PHENOTYPE INVESTIGATION OF GENE-MODIFIED MICE

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Mitochondria are the primary energy-generating system and are involved in many catabolic and anabolic metabolisms. To maintain activity of mitochondrial proteins cells rely on efficient protein quality control (PQC) systems keeping protein misfolding under control. Neuronal health relies heavily on mitochondrial functionality and integrity, so alteration of mitochondrial physiology are linked to several neurodegenerative disorders and ageing.

The mitochondrial chaperone Hsp60 assists folding of mitochondrial proteins and its absence is not compatible with cell survival in yeast and mice. Decreased levels of Hsp60 substrate proteins perturb mitochondrial metabolism and develop with time into mitochondria dysfunctions specifically in neurons, finally resulting in neurodegeneration. Mutations in the HSPD1 gene coding for Hsp60 in humans are associated with an autosomal dominant form of hereditary spastic paraplegia (SPG13) and with an autosomal recessive inherited hypomyelinating leucodystrophy (MitCHAP60 disease).

We have produced heterozygous Hsp60 knockout mice carrying a genetrap insertion in intron 2 in one allele of the murine Hspd1 gene, and display half levels of Hsp60. The animals will be evaluated for behavioural tests, histological analyses and quantitative mitochondrial proteome profiling in neuronal tissues.

We will use this mouse model to shed light on cellular surveillance systems coping with stress challenges and to pinpoint critical features of these systems. We expect that our investigations will contribute to a better understanding of these processes and can give ideas on how to delay or turn back pathological processes involving mitochondrial dysfunction.

P03.03 Tine Qvistgaard

MESOANGIOBLASTS AS THERAPEUTIC STEM CELLS

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INTRODUCTION Mesoangioblasts are mesodermal stem cells. They are easy to expand, they retain high differentiation potential, and they are obvious candidates for therapeutic application. This project explores the osteogenic and skeletal myogenic potentials of mesoangioblasts. The aim is to use these cells for experimental reconstruction of oro-facial bone defects and regenerative treatment of Duchenne Muscular Dystrophy.

METHODS Mesoangioblasts are evaluated for attachment, proliferation and differentiation on granules of calcium phosphate (HA/TCP) in culture. Mesoangioblasts (+/- BMP2) attached to such granules are inserted in vivo or in situ to assess osteogenic differentiation. For therapeutic application against Duchenne Muscular Dystrophy, mesoangioblasts are engineered into retroviral packaging cells for in situ transduction of dystrophic fibers with microdystrophin. Methods for delivery of cells are monitored histochemically to deliver cells efficiently to all affected sites of the body. All in vivo work is done on mice.

RESULTS Mesoangioblast attachment to HA/TCP was observed to depend on

serum levels, granula size and composition. Cells expressing BMP2 have been developed and are compared with original mesoangioblasts in vitro et vivo. Mesoangioblast packaging cells have been engineered and are currently tested for their efficiency using an egfp-expressing retroviral vector. We found intracardial injection of labeled mesoangioblasts to distribute cells systemically, including delivery to oro-facial bone.

P03.04 Helle Damkier

THE *SLC4A10* GENE PRODUCT IS A NA^+ DEPENDENT CL^-/HCO_3^- EXCHANGER IN A MAMMALIAN EXPRESSION SYSTEM

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The slc4a10 gene encodes an electroneutral Na^+-dependent HCO_3^- importer for which the stoichiometry is unsettled and the amino acids defining the translocation sites are unknown. We aimed to explore this using stably slc4a10-transfected fibroblasts. Slc4a10 induced a significant Na^+-dependent recovery of intracellular pH (pH_i) upon acidification in the presence of CO_2/HCO_3^- as assessed by pH sensitive (BCECF) fluorometry. The increase in the intracellular Na^+ concentration during pH_i recovery was larger in slc4a10-expressing cells than control cells using the Na^+ sensitive fluorophore CoroNa Green and gave rise to an estimated Na^+:HCO_3^- stoichiometry of 1:2. Cl^- is most likely the counter ion maintaining electroneutrality, as 1) Na^+-dependent pH_i recovery was eliminated in Cl^--depleted cells, 2) acute extracellular Cl^- removal lead to a larger alkalization in slc4a10-transfected cells than in control cells, and 3) the DIDS-sensitive and Na^+-dependent $^{36}Cl^-$ efflux during pH_i recovery was significantly greater in acidified slc4a10-transfected cells than in control cells. Charged amino acids specific to slc4a gene family members that transport Na^+ and are expected to move more HCO_3^- molecules per turnover were targeted by site directed mutagenesis. Na^+-dependent pH_i recovery was reduced in each of the single amino acid mutated cell lines compared to wild type slc4a10-transfected cells and completely eliminated in quadruple mutant cells. In conclusion, the data suggest that slc4a10 expressed in mammalian cells encodes a Na^+-dependent Cl^-/HCO_3^- exchanger in which four specific charged amino acids seem necessary for ion translocation.

P03.05 Tina Storm

THE ROLE OF CUBILIN IN PROXIMAL TUBULAR REABSORPTION.

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Imerslund-Gräsbeck syndrome (IG-S or MGA1) is a rare autosomal recessive disorder. IG-S is characterized by selective malabsorption of intestinal intrinsic factor-vitamin B_{12} and consequently causes megaloblastic anaemia. Cases of IG-S have been reported all over the world and generally present in early childhood. Genetic defects causing IG-S have been identified in the genes encoding either of the receptor proteins cubilin (CUBN) and AMN (Amn). These constitute the receptor complex cubam, which facilitates dietary vitamin B_{12} absorption. In addition to the intestinal expression, both receptor proteins have been identified in renal proximal tubule cells. Cubilin is, in collaboration with megalin, here, suggested to be involved in reabsorption of a panel of ligands including transferrin, vitamin D-binding protein, and apolipoprotein A-I (apoA-I) from the glomerular ultrafiltrate. IG-S cases are therefore excellent for studying the role of cubilin in proximal tubular reabsorption. The aim of this Ph.D. project is to illuminate the role of cubilin through genotype-phenotype correlations observed in these patients. Genotypes will be determined through direct sequencing of the CUBN and Amn genes and phenotypes through immunochemical analyses of collected urines, and immunohistochemical analyses of kidney biopsies if possible. Preliminary results from immunohistochemical analyses on a collected kidney biopsy indicate an essential role for cubilin in correct trafficking of the receptor partner AMN, and in

reabsorption of transferrin and apoA-I. Additional identification of genotype and proteins excreted in the urine will help to further clarify the role of cubilin.

P03.06 Sabina Jelen

AQP9 IS NOT ESSENTIAL FOR AMMONIA UPTAKE OR UREA RELEASE IN THE LIVER

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Aquaporin 9, a water channel also permeable for various small solutes like glycerol, urea and ammonia is exclusively expressed in the basolateral membrane in hepatocytes. The role of AQP9 in the liver is not fully characterized. AQP9's localization in the sinusoidal membrane, the major site for urea/ammonia turnover, together with it's ability to facilitate transport of these solutes, suggests a function in ammonia and/or urea uptake or release.
In the presented study physiological relevance of an AQP9 role in ammonia and/or urea transmembrane exchange in the liver was examined in wild type (WT) and AQP9-knockout mice. Since ammonia and urea are byproducts of amino acid metabolism we challenged the hepatic system with elevated doses of glutamine (short term ammonia/urea elevation) or treated with high protein diet (long term ammonia/urea elevation). Single administration of 2mmol/100 g body weight glutamine by gavage evoked elevation of ammonia. No significant difference in plasma, liver and brain concentration of ammonia and urea, respectively, was detected between knockout and wild type mice. These results provide evidence against a physiological role of AQP9 in facilitating ammonia and urea transport following short term elevation of ammonia.
To test a possible role of AQP9 in long term ammonia and urea homeostasis we apply high protein diet treatment. Experiment currently is in progress.

P03.07 Anders Peter Søndergaard

BIOMECHANICAL PROPERTIES OF THE CORNEA FOLLOWING UVA-RIBOFLAVIN CROSS-LINKING

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Introduction:
UVA-mediated riboflavin collagen cross-linking (CXL) has recently been introduced to stabilize progressive keratoconus. Further, a reduction of corneal swelling has been observed empirically following CXL, making the treatment an option for patients suffering from endothelial dysfunction, including Fuchs dystrophy.
Purpose:
To describe the biomechanical properties of the cornea following CXL. The compressibility of the cornea (swelling pressure) and shear strength will be examined. Normal and CXL-treated corneas ex vitro are tested using custom-made equipment, measuring swelling pressure and shear (force) simultaneously. Further, examination of corneal laser/microkeratome-cut sub segments allows depth dependency of the treatment to be examined. The experiments will initially be conducted in vitro in a porcine model, followed by human ex vitro studies. The null-hypotheses of the study are that CXL will neither reduce the swelling pressure nor increase shear strength.
Materials and methods:
Porcine and human corneas are treated with the CXL-procedure. Fellow eyes are used as controls. A modified biotester has been developed for this project; measuring compression (swelling) in one axis, while measuring shear force in the perpendicular axis simultaneously.
Perspective:
Through biomechanical studies of corneal swelling pressure and shear force, we aim to gain further insight into previously less described biomechanical parameters of the cornea under physiological conditions and following CXL. Current treatment protocols may thereby be optimized and benefit from this basic research PhD

project.

P03.08 Nynne Sharma

TRANSCRIPTIONAL SILENCING AND PROTECTION OF DNA TRANSPOSON VECTORS WITH APPLICATIONS IN THERAPEUTIC GENE TRANSFER AND PIG TRANSGENESIS

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DNA transposon vectors are new promising integration tools with many desirable properties. These include easy and inexpensive production together with efficient transgene integration, and DNA transposons have today become widely studied vectors for transgenesis and therapeutic gene transfer. A potential obstacle, however, for integrating vectors is transcriptional repression of the element and its genetic cargo. The aim of this work was therefore to study and compare the levels of transcriptional silencing of transgenes carried by different transposon elements, and use the knowledge to design novel protected vectors with applications in therapeutic gene transfer and in genetic engineering of transgenic pig disease models.
In the study, experiments have been performed with the Sleeping Beauty (SB), the piggyBac (PB), and the Tol2 transposon, which are all known to transpose efficiently in mammalian cells. SB, PB and Tol2 transposon vectors encoding a fluorescence reporter gene and a drug-resistance selection gene have been cloned, and transposition activity has been tested in murine embryonal cells. Furthermore, insulators, which are DNA elements that can serve as genetic barriers to chromosomal position effects, have been incorporated into the vectors to test for possible protection. Expression analysis of stably transfected cell lines will establish the silencing level of the different transposon vectors and show if vectors containing insulator sequences are protected against silencing.
Results from this study will contribute significantly to the knowledge of transcriptional silencing of DNA transposon elements and hopefully lead to improved DNA transposon-based vectors.

P03.09 Thaneas Prabakaran

FABRY DISEASE, DIAGNOSTIC MARKERS AND THE MECHANISM OF ENZYME REPLACEMENT TREATMENT IN THE RENAL GLOMERULI

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Fabry disease is an X-linked lysosomal storage disease caused by deficiency of alpha-Galactosidase A (α-Gal A) activity. The reduced enzymatic activity results in accumulation of globotriaosylceramide in renal endothelial, glomerular and tubular cells. This leads to end stage organ failure. Enzyme replacement therapy (ERT) results in significant clearance of the cellular deposits throughout the body and kidney.
The aim is to study the renal genotype-phenotype correlations in Fabry patients and to study mechanisms by which α-Gal A is taken up by podocytes. Genotypes are determined by sequencing the α-Gal A gene and the renal pattern will be determined through immunohistochemical analyses of collected urines and renal biopsies. Correlations between phenotype-genotype are in progress. Furthermore, one of the major issues is to determine which patients to treat with ERT and when to institute treatment. The disease is very heterogenous and a number of patients, especially females do not develop symptoms until late in life. It is therefore important to identify mutations, which do or do not induce early onset of the disease. To identify potential receptors for the cellular uptake of α-Gal A in podocytes, an immortalized cell line will be used. Receptors will be identified by affinity chromatography, followed by immunofluorescence and Western blotting studies. Preliminary results indicate that there is more than one receptor involved in the α-Gal A uptake in the podocytes. Clarifying the mechanisms by which α-Gal A is taken up in podocytes would be beneficial for future ERT.

P04.01 Margrethe Smidth

EFFECTS OF AN ACTIVE IMPLEMENTATION OF A CHRONIC DISEASE MANAGEMENT PROGRAMME FOR PATIENTS WITH COPD.

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Healthsystems will manage more people with chronic diseases as lifeexpectancy increases and treatment options improve. As need for resources increases, it will be vital that a targeted strategy for healthcare to the growing group is developed so all are offered professional and efficient treatment and that resources are used equitable. A proactive strategy will secure the need of the whole population is served and not only acute needs of patients.
The study concentrates on the process of implementation and effects of Region Midtjylland's programme for COPDpatients. An active implementationstrategy for chronic disease management programme is designed based on literature and methods proven effective in implementing new ways of working with different stakeholders. It is an intervention study approx. 4000 COPDpatients will be clusterrandomised after blocrandomisation of the GPpractice. 15 GPpractices in Ringkøbing-Skjern Municipality will be randomised to receive the focused implementation or to an "as usual" group. With data from registers and a questionnaire survey the effect on COPDpatients selfreported health, evaluation of the healthsystem and changes in distribution of healthresources will be analysed. How healthprofessionals in hospital, communitycare and GPpractices perceive the implementation and how it influences their conception, interactions and culture will be illustrated in an interviewsurvey of stakeholders.
We expect to see the active implementation of the coordinated, structured and effective effort induce coherence, better quality of treatment, make efficient use of healthresources, enhance healthprofessionals' competences and increase patientsatisfaction.

P04.02 Berit Hvass Christensen

THE INFLUENCE OF MATERNAL WORK ON THE DEVELOPMENT OF ALLERGIC DISEASES - A PHD. PROJECT WITHIN THE DANISH NATIONAL BIRTH COHORT

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The prevalence of allergic diseases has increased in the last 40 years. In spite of thorough research the reason for this increase is not fully understood. Animal studies show that prenatal exposure can induce allergic diseases in the offspring. The purpose of this study is to explore whether occupational exposure to allergens and other asthmatogens during pregnancy is associated with the development of allergic disease in the offspring. Population and data material derives from The Danish National Birth Cohort ("Better health for mother and child", DNBC). The cohort includes data from more than 100.000 pregnant women in Denmark and was established in the years 1996- 2002 to contribute to the knowledge on how pregnancy affects health of the child. In this study the 60.000 women who have answered the 7 year electronic questionnaire, will be included. The cohort contains information about prenatal occupation and the children's prevalence of wheeze, asthma and allergic diseases at 1½ and 7 years. Additional information about occupational exposure during pregnancy will be provided via Asthma specific Job Exposure Matrixes and the Danish Ministry of Employment's DREAM Database. Additional information about health outcomes will be provided in The Danish National Birth Registry, and The Danish National Patient Registry. It is our hope that this study will

contribute to further knowledge about the impact of occupational exposure during pregnancy on the development of allergic diseases. This knowledge might be important in the future working environment councelling og pregnant women.

P04.03 Anette Werner

THE EFFECT OF MENTAL TRAINING ON CHILDBIRTH - MEASURED ON PAIN EXPERIENCE AND OTHER BIRTH OUTCOMES

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BACKGROUND: LABOUR PAIN IS A CHALLENGE TO THE PARTURIENT WOMAN. PAIN RELIEF METHODS DURING BIRTH ARE LIMITED AND OFTEN ASSOCIATED WITH SIDE EFFECTS. SEVERAL STUDIES INDICATE THAT A MENTAL TRAININGS METHOD, SELF HYPNOSIS, HAS A POSITIVE IMPACT ON THE LABOUR PAIN AND OTHER BIRTH OUTCOMES.
AIM: THE AIM OF THE STUDY IS TO EXAMINE THE EFFECT OF A SHORT ANTENATAL COURSE IN SELF HYPNOSIS
PRIMARY ON: THE USE OF EPIDURAL ANALGESIA DURING BIRTH
SECONDARY ON: LENGTH OF BIRTH, BIRTH PROGRESSION AT ARRIVAL AT BIRTH DEPARTMENT, BIRTH EXPERIENCE, MEDICAL INTERVENTIONS DURING BIRTH, HEMORRHAGE DURING BIRTH, SALIVA CORTISOL PROFILE, INFECTION, POSTNATAL DEPRESSION, BREASTFEEDING DURATION, CHILD'S CONDITION AND WELLBEING AT BIRTH AND 6 MONTHS LATER, FUTURE MODE OF DELIVERY
METHOD: THE STUDY IS DESIGNED AS A RANDOMISED, CONTROLLED, SINGLE BLINDED, SINGLE CENTER TRIAL USING A 3 ARM GROUP DESIGN. THE INTERVENTION GROUP RECEIVES 3 ANTENATAL CLASSES IN SELF HYPNOSIS INCLUDING AUDIO COMPACT DISCS FOR HOMEWORK. THE ACTIVE COMPARATOR GROUP ALSO RECEIVES 3 ANTENATAL CLASSES AND AUDIO COMPACT DISCS FOR HOMEWORK. THIS PROGRAM INCLUDES A MIXTURE OF TRAINING IN DIFFERENT RELAXATION METHODS AND MINDFULNESS. THE CONTROL GROUP ONLY RECEIVES ORDINARY ANTENATAL CARE AND NO ADDITIONAL INTERVENTIONS. THE DATA COLLECTION WILL BE BASED ON QUESTIONNAIRES, REGISTER DATA, MEDICAL RECORDS AND BIOLOGICAL MATERIAL. IT IS PLANED TO INCLUDE 361 PARTICIPANTS IN THE HYPNOSIS GROUP, 361 PARTICIPANTS IN THE PLACEBO EFFECT GROUP AND 168 PARTICIPANTS IN THE CONTROL GROUP - IN TOTAL 890.
CLINICALTRIALS.GOV PROTOCOL RECORD M-20080200

P04.04 Morsi Abdallah

INTRAUTERINE EXPOSURES AND CHILDHOOD PSYCHIATRIC DISORDERS

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BACKGROUND:
Evidence suggests that Autism Spectrum Disorders (ASD's) have a large genetic component and a complex heterogeneous inheritance pattern. In this study, the relationship between inflammatory responses of the immune system and genetic susceptibility, prenatally and postnatally in early childhood period, is investigated.
HYPOTHESIS:
The main hypothesis of this study is that inflammation/infection in mother or child during pregnancy and early childhood period is associated with ASD in genetically susceptible children. To test this hypothesis, the proposed study will analyze the association between i) inflammation/infection in child during pregnancy by measuring inflammatory markers obtained from samples of amniotic fluid, ii) inflammation/infection in child after birth, by measuring inflammatory markers obtained from samples of Phenylketonuria (PKU) blood spots and iii) susceptible genotypes of child for development of ASD.
MATERIAL AND METHODS:

For analyzing the associations mentioned above, a Danish historic birth cohort (HBC) created at Statens Serum Institute, Copenhagen, will be utilized. Cases and controls of ASD are retrieved from different Danish national registers and identified within the HBC. Inflammatory markers of interest will be measured using Luminex techniques. For identification of genotypes of child, Illumina methodology will be used.
Relevant statistical methodologies including regression analyses, Cox proportional hazard models and mixed-model analysis of variance models are used with correcting for multiple testing.
PERSPECTIVES:
Results from this study will contribute directly to the general understanding of the pathophysiology of ASD.

P04.05 Lena Aadal

REHABILITATION OF TARGETED DAILY LIFE COMPETENCES AS SITUATED LEARNING. INTENSIVE REHABILITATION OF PATIENTS WITH SEVERE TRAUMATIC BRAIN INJURY.

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Background: In Denmark annually about 120 people need highly specialized neurorehabilitation after a severe traumatic brain injury (TBI). Given that patients with severe TBI have changed abilities to (re)learn, and that the objective of neurorehabilitation is to regain an independent and meaningful everyday life, two levels of pedagogical challenges exist: Helping the patient regain or compensate for changed learning abilities and supporting the patient in relearning or compensating for lost competencies.
Objective: To develop a model, that may foster participation by synthesizing insights from "situated learning" theory with neuropsychological research that illuminates the patients' changed learning abilities.
Methods: Qualitative study. Theoretical analysis and synthesis of "situated learning theory", neuropsychological theory and empirical studies of cognitive and emotional functioning following a TBI. Lave and Wenger's "situated learning" theory describes learning as a relational process situated in a practice community. A severe TBI can change both the competencies involved in the learning process and the ability to participate. Considering rehabilitation as relearning requires that the special learning competencies of patients with severe TBI are determined.
Results/conclution: Because of their changed abilities to (re)learn, patients with severe TBI pose challenges in terms of being active participants in the "rehabilitation practice community." This study highlighted six main categories that need to be considered in developing a practice which fosters relearning: Perception, attention, memory, language, physical competencies and emotion/model of behaviour

P04.06 Rune Dupont Birkler

A VALIDATED METHOD FOR THE EXTRACTION OF DRUGS FROM THE DRUGWIPE® DRUG-TESTING DEVICE AND CONFIRMATION BY LC-MS/MS

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Introduction: In recent years, the demand for a fast, easy, and reliable drug test has increased. Many commercially available tests are based on immunochromatographic methods requiring visual reading, which is essentially subjective[1]. It is therefore recommended to make a conformation analysis by GC-MS or LC-MS[2]. Presently available drug tests also suffer other drawbacks like lack of specificity and accuracy[3]. Together with the cross-reactivity seen with some legal drugs, this further backs the call for a confirmatory analysis of the drug testing device. We present a validated method for confirming the result from the DrugWipe® drug test.
Methods: Eight of the most common drugs of abuse were selected. The DrugWipe®

drug tests were spiked on cutoff level. The immunochromatographic test strip was extracted with acidified methanol containing deuterated internal standards. The methanol was evaporated and the residue was dissolved in eluent and analyzed using LC-MS/MS apparatus.
Results: All analyzed drugs were extracted from the DrugWipe® drug test at recovery rates reaching 90%. All analytes demonstrated fine baseline separation achieved within a 6 minutes run time. Experiments on matrix effects showed no ion suppression, nor interference between the analyzed compounds.
Conclusion: The method is useful when a positive drug test has to be confirmed and no reference material is available. It discards false positive tests when no drugs of abuse are detected. The method was successfully applied to DrugWipe® drug tests received from local nightclubs in Aarhus, Denmark.
1) Clin. Chem., 2002, 48, 1, 174-176
2) Forensic Sci. Int., 2001, 121, 37-46
3) ROSITA-2 final report, May 2006

P04.07 Tine Steen Rubak

REGISTER-BASED COHORT STUDY OF INCIDENCE OF TOTAL HIP REPLACEMENT IN RELATION TO CUMULATIVE PHYSICAL WORK LOAD AMONG MALES IN DENMARK

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Introduction. Primary osteoarthritis (OA) may lead to disability, and is a leading cause of total hip replacement (THR) in the West. Earlier studies have relied on self-reported exposures, some on self-reported outcome, and none have used cumulative exposures for the entire work life. We investigated the risk of primary OA leading to a THR 1996-2006 in relationship to cumulative exposures estimated for the period 1964-1996.
Methods and population. We did a nation-wide register-based cohort study comprising 782,511 men born in Denmark 1935-1964, with at least 10 years of full-time employment before 1996, and still living January 1, 1996. Followed-up was done in the National Patient Registry from 1996 to 2006. An industry exposure matrix was developed. Cumulative exposure was calculated for all persons. Risk of THR was estimated by Cox proportional hazard regression, controlled for age at start of follow-up (AF). AF and cumulative exposure were analysed as continuous variables.
Results. During follow-up 6675 cases appeared. Incidence rate ratios (IRR) are reported with 95% confidence intervals. An increase of ten point years yielded a crude IRR of 1.26, and an IRR 1.04 (1.02 – 1.06) when adjusted for AF.
Discussion. Even with a crude exposure assessment as this, there seemed to be a higher risk of total hip replacement with increasing cumulative exposure. Strengths were the independent exposure assessment, complete follow-up, and complete information of all employment 1964-1995. We were able to control for age at start of follow-up, but not for other relevant confounders, eg. trauma.

P04.08 Marie Louise Tørring

THE WAITING TIME PARADOX: DANISH CANCER PATIENTS DIAGNOSED FAST HAVE HIGHER MORTALITY

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BACKGROUND: Delay in the diagnosis of cancer is generally considered unacceptable. However, observational studies often show an inverse association between the length of the diagnostic interval and mortality. Paradoxically, patients diagnosed more rapidly have higher mortality rates than patients with longer wait in the primary and secondary health care sector.

AIM: To examine whether the waiting time paradox is manifest in the Danish health care system.
MATERIALS & METHODS: The study was based on data on hospital discharge diagnoses for the 2004-2005 period, extracted from population-based healthcare databases in the former County of Aarhus, Denmark. All patients with a first-time diagnosis of breast, skin, lung, prostate, and colorectal cancer were identified and confirmed by each patient's General Practitioner (GP), who provided a detailed description of the diagnostic pathway. Diagnostic interval was defined as time duration from first presentation of symptom to GP until date of diagnosis. Proportional hazard regression was used to estimate 3-year mortality rate ratios for 15-29 days compared with 0-14, 30-89, and 90+ days of duration, adjusting for gender and age.
RESULTS: We identified 1270 cancer patients. Mortality varied across cancer diagnosis. There were no associations between duration and mortality for breast and skin cancer. For lung, prostate, and colorectal cancer a short diagnostic interval (0-14 days) was associated with highest mortality.
CONCLUSION: The waiting-time-paradox is manifest in Denmark. We speculate that GPs and hospital doctors are able to distinguish more or less aggressive malignancies and organise the course of referral accordingly.

P04.09 Marie Louise Svendsen

COMORBIDITY, QUALITY OF CARE, AND OUTCOME ACCORDING TO MEDICAL SPECIALTY IN STROKE UNITS: A NATIONAL POPULATION-BASED FOLLOW-UP STUDY

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Background: Stroke unit care improves patient outcome, but the importance of medical specialty in stroke units remains uncertain.
Objectives: To assess whether stroke unit setting (neurologic versus non-neurologic) is associated with quality of care and outcome among stroke patients , and whether these associations depend on comorbid disease.
Methods: In a national population-based follow-up study, we identified 45521 stroke unit patients during 2003-2008. Primary outcomes were quality of care (fulfillment of evidence-based acute care criteria), mortality, length of stay, and readmission. Charlson Comorbidity Index was used to measure comorbidity. The analyses were adjusted for patient and service characteristics and clustered by stroke units.
Results: Stroke unit patients in neurologic settings had higher odds of receiving early antiplatelet therapy (OR 1.78, 95% CI 1.20-2.65), and lower odds of receiving early physiotherapy- (OR 0.67, 95 % CI 0.46-0.99) and occupational therapy assessment (OR 0.64, 95 % CI 0.47-0.87), than patients in non-neurologic settings. No other results, including results for patient outcome, reached statistical significance. However, stratified for comorbid disease, patients in neurologic settings with moderate comorbid disease had increased risk of 1-year mortality (OR 1.18, 95% CI 1.02-1.36) and non-statistically significantly increased risk of 30-day mortality and hospital readmission.
Conclusions: Stroke unit setting may affect the timing of essential management processes in the early phase of stroke. A trend toward adverse outcome among patients with moderate comorbid disease in neurologic stroke unit settings needs further investigation.

P04.10 Trine Brogaard

INTEGRATED SHARED CARE BETWEEN GENERAL PRACTICE, DISCHARGE HOSPITAL AND A SPECIALISED PALLIATIVE CARE TEAM FOR SERIOUSLY ILL CANCER PATIENTS.

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Background: Traditionally, the GP has had the full responsibility for the palliative care of terminally ill cancer patients who are cared for at home. Like in other countries, changes have been made to the organization of palliative care in Denmark: Hospices have been established in some, and specialized palliative care teams in most areas.
Recent research indicates that there is a problem when it comes to communication between the hospital and primary care. The discharge process often leaves the patient feeling "left in limbo".
Aim:To describe a group of palliative patients and their use of the health care system. To assess the consequences for patients, relatives and health care professionals of 3 different ways of organizing palliative care.
Method:Comparison of 2 ways of organizing palliative care versus usual care: 1.Usual discharge with regular discharge letter to the GP. 2.Discharge with referral to a specialist palliative care team. This is a patient-centred shared care model in which the palliative care team plans the patient's treatment and care. 3.Discharge where an extra effort is made to improve the communication between primary and secondary care. This is a shared care model focusing on support of the primary care professionals. The model will be pilot-tested in this study.
Results:Data collection began in April 2008 and will commence in December 2009. Primary endpoints will, among others, be whether patients' and relatives' wishes regarding preferred place of death of the patient are fulfilled. There will be no conclusions ready for presentation in January 2010. However, we will have experience with regard to study design and inclusion of patients.

P04.11 Morten Willert

EFFECTS OF A STRESS MANAGEMENT INTERVENTION ON ABSENTEEISM FROM WORK - RESULTS FROM A RANDOMIZED WAIT-LIST CONTROLLED TRIAL

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Background: High levels of work-related stress are associated with rising levels of absenteeism from work. The effect of a stress management intervention on absenteeism is investigated.
Methods: 102 participants were randomized to either the Intervention (I) or the Waitlist control (WLC) group. Self-reported data on absenteeism, defined as days full or part time absent from work within the previous three months, were obtained at baseline and 3, 6 and 9 months follow-up. Register-based data from the DREAM database were drawn from randomization and 48 weeks ahead. The DREAM database contains weekly information on granted sickness absence compensation and disability benefits. Treshold to enter DREAM is sick leave for two consecutive weeks. Statistical analyses were performed with the Mann- Whitney U test and Cox regression. Data are reported with 95% confidence intervals.
Results: On self-reported absenteeism the I-group median was 11(3-25) days absent in the three months preceding the post-intervention measurement. The median of the WLCgroup in the same interval was 45(19-60). This difference was found to be statistically significant (p=0.02). On cumulative number of weeks registered in the DREAM database in weeks 1–16, the I-group had a median of 7(0-13) weeks, while the WLC-group median was 12(8-16) weeks. This difference was not significant (p=0.15). Survival analysis for weeks 1–48 revealed a hazard ratio of 1.24(0.70–2.21) favouring the I-group, with a corresponding p-value of p=0.46.
Conclusions: The intervention appears effective in lowering self-reported days absent from work. From the register-based records no significant results were obtained.

P04.12 Hanne-Lise

PRENATAL EXPOSURE TO ALCOHOL AND TOBACCO: EFFECTS ON IQ AT

Falgreen Eriksen AGE 5

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Objectives: To examine the effects of alcohol consumption and tobacco smoking in pregnancy on child IQ at the age of 5. Background: Both alcohol drinking and tobacco smoking in pregnancy has been associated with later cognitive deficits in the child. However, neither the effects of low to moderate doses of alcohol, nor the combined effects of alcohol and tobacco are well elucidated. Both issues need clarification, since a concurrent, moderate use of both substances is likely to be more common than high consumption of either separately, in particular among pregnant women. Methods: Participants were sampled from the Danish National Birth Cohort according to a study design in which varying levels and patterns of alcohol intake in pregnancy were represented. At 60-64 months of age, the children were examined with a battery of cognitive tests, including a short form of The Wechsler Preschool and Primary Scale of Intelligence – Revised. The study included a total of 1784 mother-child pairs. Results: Preliminary analyses found smoking of >10 cigarettes/day to be associated with a decrement of 2.4 IQ points (95% CI= -4.22- -.54) compared to non-smokers in a multiple linear regression model adjusted for main confounders, including maternal IQ. No effects of an average intake of 1-8 drinks per week were found, nor did alcohol and tobacco interact. Conclusion: The preliminary analyses of this study indicated smoking more than 10 cigarettes per day in pregnancy to have a fairly substantial negative impact on offspring IQ whereas a low to moderate intake of alcohol did not seem to compromise test performance.

P05.01 Kasper Lynghøj Christensen A KETONE BODY AS ENDOGENOUS CARBONYL SCAVANGER?

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The development of age-associated diseases, such as diabetes and Alzheimer's disease, as well as biological aging is probable caused by long term accumulation of damaged biopolymers due to reactive oxygen species (oxidative stress) and highly reactive carbonyl species (carbonyl stress). Oxidative stress and carbonyl stress are closely intertwined and both leads to undesirable modifications and degradation of (vital) proteins (e.g. mitochondrial) via a range of non-enzymatic reactions. To slow down this aging process much research is currently directed towards understanding the initiation and progression of the deleterious processes, in which depletion of endogenous scavengers (antioxidants) seem to play a crucial part.
Recently, we discovered a fast reaction between the endogenous ketone body acetoacetate, which is generated as the body utilizes fat as ATP-source, and a highly reactive endogenous carbonyl specie: methylglyoxal. Methylglyoxal is known to afford pathological changes e.g. by the formation of so-called advanced glycation end-products (AGE's). Interestingly, the onset and progression of diabetic complications has partly been blamed the formation of methylglyoxal and AGE's. Our recents findings therefore lead to the novel hypothesis that acetoacetate might play a role as a hitherto unknown scavenger of the highly cytotoxic methylglyoxal in vivo and thus might have a beneficial impact by slowing the initiation and progression of age related diseases.

P05.02 Trine Østergaard ALTERNATIVE MRNA SPLICING OF THE HUMAN EGF RECEPTOR HER4

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The epidermal growth factor (EGF) system is of importance in relation to development and growth of many types of cancers and drugs targeting these receptors are emerging. Human EGF Receptor 4 (HER4) is alternatively spliced into the isoforms, CYT1 and CYT2 where the difference is that CYT2 lacks exon 26. CYT1 is able to activate the PI3K/Akt pathway, whereas CYT2 is not. It has been shown that the CYT1 isoform is associated with cell growth, whereas the CYT2 isoform is associated with apoptosis.
The mechanism behind the alternative splicing of HER4 into CYT1 and CYT2 isoforms is unknown. In this project I will construct a minigene containing exon 25, 26 and 27 with intervening introns. I will quantify the splice products of the minigene by Q-PCR. By site directed mutagenesis I will change specific sequences of the minigene and monitor the splicing capability of the mutated minigene. This will identify the regulatory sequences involved in controlling the alternative splicing mechanism. Characterization of these sequences will enable me to pull down the proteins interacting with them. In future experiments the proteins involved in splice site determination in HER4 will be investigated.
Understanding the mechanism of alternative splicing of HER4 will be of importance for the understanding of the role of the two variants, CYT1 and CYT2, in development of cancer and resistance towards anti-cancer drugs.

P05.03 Lisbeth Venø Kruse

THE HERITABILITY OF ATOPIC DISEASE – ESPECIALLY ALLERGIC RHINITIS
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Abstract
Allergic Rhinitis (AR) is the most common of the atopic diseases, and is characterized by mucosal inflammation induced by allergen exposure. AR has increased in prevalence over the last 40 years. Today 10-30% of adults and up to 40% of children suffers from AR. Typical symptoms are itching, blockage and drip due to inflammation of nasal mucosa, often accompanied by conjunctivitis. The pathogenesis is multifactorial with a substantial genetic etiologic component. Previous genetic studies have revealed one major chromosomal candidate region (LOD = 2,38) and eight minor candidate regions (LOD = 1,04-1,63).
Our aim in this study is 1) to clarify whether these regions are true susceptibility regions, 2) to gain enough statistical strength to identify the specific risk genes trough fine scale genetic mapping and 3) to identify new chromosome regions containing risk genes by complete genome scanning. These goals will be approached trough ascertainment and analysis of a large group of sib-pair families with hay-fever.
We have included and clinically characterized 130 Danish sib-pair families (546 individuals) in the study. DNA was extracted from venous blood and genotyping was preformed using in total 429 microsatellite markers. In the analyses we will include genotypes from 36 originally collected AR sib-pair families. These families are a subgroup of 134 Danish nuclear families in PhD project by Ulla Christensen: "The heritability of atopic disease – Especially atopic dermatitis".
Presently sample analysing and data interpreting is ongoing. This is expected to last into autumn 2010

P05.04 Dang Quang Svend Le

3-D PERFUSION CULTURE OF OSTEOGENIC STEM CELLS WITH MEDIA PERFUSION RATE DEPENDENT ON DIFFERENTIATION STAGES
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Fluid shear stress on cells is important to stimulate differentiation and synthesis of

mineralized matrix. In this study, we divide the culturing into periods with low and high fluid shear stress, respectively. We hypothesize that a given low/high ratio regime will provide a good protocol for cell colonization and differentiation, thereby improving dynamic culturing conditions to obtain the highest mineralization rate.
Porous polycaprolactone scaffolds were made with fused deposition modelling (FDM) The macroporous FDM geometry was generated with a CAD program and executed using a Bioscaffolder (Syseng, Germany). Scaffolds have a thickness of 5 mm and diameter of 10 mm.
We employ a large sample number (N = 72) perfusion setup that allows for easy withdrawal of scaffolds. hMSC-TERT cells (43. passage) are seeded at a density of 2×10^6cells/scaffold and statically cultured for one day prior to low flow perfusion culture (0.02 mL/min). Both static and perfusion culture will be in DMEM at 37°C, 5% CO_2.
All scaffolds are seeded at day 0 and statically cultured for one day and then cultured with a low perfusion rate. Subsequently, at four time-points, 8 samples are transferred to a high perfusion rate culture and 8 samples are removed for analysis. A sample batch is removed at day 1 to inspect seeding efficiency. Every third day, beginning from day 3, 8 scaffolds are withdrawn for testing ALP/DNA ratio, 3 for live/dead stains using confocal microscopy and μ-CT scanning, and 8 scaffolds are transferred to the high flow perfusion regime (0.7 mL/min). At day 12, the remaining 32 scaffolds will all be in the high perfusion regime and will remain in culture for a total of four weeks.

P05.05 Thomas Guldager Knudsen

DIRECT EFFECT OF METHYLPREDNISOLONE ON RENAL SODIUM AND WATER TRANSPORT VIA THE PRINCIPAL CELLS IN THE KIDNEY

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Glucocorticoids influence renal concentrating and diluting ability. We tested the hypothesis that methylprednisolone (MP) treatment increased renal water and sodium absorption by increased absorption via the aquaporin 2 water channels and the epithelial sodium channels, respectively.
The effect of MP was measured during fasting in a randomized, placebo-controlled, single-blinded cross-over study of 15 healthy humans. The subjects received a standardized diet on day 1, fasted for 24 hours during day 2, and received MP 500 mg IV on day 3. The effect variables were urinary excretions of aquaporin2 (u-AQP2), the β-fraction of the epithelial sodium channel (u-$ENaC_\beta$), cyclic-AMP (u-cAMP), prostaglandin E_2 (u-PGE_2), free water clearance (C_{H2O}), fractional excretion of sodium (FE_{Na}), and plasma concentrations of vasopressin (p-AVP), angiotensin II (p-Ang II), aldosteron (p-Aldo), atrial natriuretic peptid (p-ANP), and brain natriuretic peptid (p-BNP).
MP treatment increased u-AQP_2, u-$ENaC_\beta$ and p-AVP significantly, but did not change u-c-AMP, C_{H2O} and FE_{Na}. U-PGE_2, P-Ang II and p-BNP were unchanged. MP increased u-AQP2 and u-ENaC. Neither the vasopressin-c-AMP-axis, nor changes in the activity in the renin-angiotensin-aldosterone system nor the natriuretic peptide system seem to bear a causal relationship to the increase in either u-AQP2 or u-ENaC. Most likely the effect is mediated via a direct effect of MP on the principal cells in the distal part of the nephron. The lack of increase in urinary output and sodium excretion most likely can be attributed to the diuretic and natriuretic properties of the increased secretion of ANP shortly after the infusion of MP.

P05.06 Torsten Bloch Rasmussen

CLINICAL, GENETIC AND PROTEIN STUDIES IN ARRHYTHMOGENIC RIGHT VENTRICULAR CARDIOMYOPATHY

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Background: Arrhythmogenic right ventricular cardiomyopathy (ARVC) is a hereditary heart muscle disease. The disease induces malignant ventricular tachyarrhythmias and is a major cause of sudden cardiac death. Genetic investigations of ARVC patients have identified mutations in genes encoding desmosomal proteins. Desmosomes are intercellular junctions abundant in the myocardium and epidermis. It is believed that impaired cell-to-cell adhesion of cardiac myocytes plays a major role in the pathogenesis of ARVC.

Aim: To investigate the effects of mutations detected in desmosomal genes on levels of protein and mRNA. Clinical, genetic and protein studies will be compared to establish if specific expression profiles of desmosomal proteins in skin and heart tissue are correlated with phenotype.

Methods: Mutation screening by direct sequencing in 5 desmosomal genes (DSP, PKP2, DSG2, DSC2, JUP). In patients carrying a suspected disease-associated mutation: semi-quantitative determination of desmosomal proteins in epidermal and endomyocardial biopsies by use of immunohistochemistry. Primary keratinocytes from ARVC patients are cultured in order to investigate levels of mRNA and proteins by means of qPCR and immunoblotting.

Preliminary results: Sixty-two index patients underwent physical examination and genotyping. Thirty-nine sequence-variants were detected of which 32 were considered to be disease-associated while 7 were believed to be single nucleotide polymorphisms. Further clinical and genetic investigations of family members are ongoing. Patient samples have been obtained from half of the patients. Assays for protein and mRNA investigations are currently under development.

P05.07 Zhenping Liu

CHRONIC EFFECTS OF AMINO ACIDS ON THE FUNCTION OF THE INS-1E CLONAL BETA CELLS: AMINOACIDOTOXICITY AND BETA CELL DYSFUNCTION.

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Background: Glucose and fatty acids play a key role in the modulation of normal insulin secretion and pancreatic beta-cell function. We hypothesize, that increased levels of AAs may contribute to the beta cell dysfunction in type 2 diabetes with increased basal insulin secretion (BIS) and impaired glucose-stimulated insulin secretion (GSIS).

Aims: To investigate the long-term effects of selected AAs on the function of the clonal beta cell line, INS-1E cells.

Materials and methods: The INS-1E cells were grown in a modified RPMI 1640 medium. Every second day the INS-1E cell medium was exchanged with RPMI 1640 containing AAs according to the protocol. After 72h, INS-1E cells were incubated for 60 min in the modified KRB containing 3.3 or 16.7 mM glucose. The medium was collected for insulin analysis (RIA).

Results: Incubation for 48h and 72h with L-leucine, L-lysine, L-proline did not change the insulin output from INS-1E cells. DL-homocysteine (1000 μM) decreased insulin output from INS-1E cells after 48-h and 72-h, respectively. After 72 h incubation with L-leucine, L-lysine, L-proline and DL-homocysteine, BIS from INS-1E cells was increased. GSIS from INS-1E cells treated with 1 to 10 mM of L-leucine, L-lysine, or L-proline was impaired. DL-homocysteine suppressed GSIS of INS-1E cells but only at the concentration of 1000 μM.

Conclusions: Chronic exposure to L-leucine, L-lysine and L-proline increased BIS and inhibited GSIS from INS-1E cells. DL-homocysteine at physiological concentration significantly enhanced BIS. Elevation of plasma AAs may play a pathogenic role for the dysfunction of beta cells.

Key words: Insulin secretion in vitro; L-amino acid; Toxicity

P05.08 René Frydensbjerg Andersen

IDIOPATHIC NEPHROTIC SYNDROME - *OUTCOME IN DANISH PATIENTS*

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Background: Nephrotic syndrome (NS) is generally accepted to have an excellent long-term outcome but the road to stable remission is often complicated. Our objectives were to evaluate the outcome and highlight the chronic nature of idiopathic NS in children.
Methods: We reviewed the medical records of 58 (28 f) patients with idiopathic NS admitted to 4 Paediatric Departments from 1997 to 2009. The incidence was 1.85/100.000. Median age 6.5 yrs (range 1.2 - 14.2 yrs). Mean follow-up was 5 yrs. Relapse was 3 consecutive days with 3+ on dipstick. Complications besides cushingoid changes were included. Outcome measures were renal function, blood pressure (BP), proteinuria and the use of medication.
Results: Steroid resistance (SR) was seen in 9% (5/58). In the steroid sensitive (SS) group 75% (40/53) had relapse. The average relapse number was 5.1 (range 0 - 23). Of all SS patients, 57% (30/ 53) had frequent relapses or were steroid dependent (FQ/SD group). The relapse rate in the FQ/SD group was 1.2 relapse/year compared to 0.26 relapse/year in non-FQ/SD group. Of the 30 FQ/SD patients 21 had a total of 26 complications. In the non-FQ/SD group 13 complications were seen in 10 patients. Of the five SR patients, one developed renal failure. 2 patients had persistent low grade proteinuria (< 0.5 g/day). BP was normal. At follow-up all SS patients had normal renal function and BP. At last visit 14 patients in the FQ/SD group were treated with immunosuppressive drugs.
Conclusions: Although we demonstrate a favorable long-term renal outcome only a minority of the patients had a mild disease course without relapses or complications to the treatment or to the disease itself.

P05.09 Pia Møller Faaborg

ANORECTAL FUNCTION AFTER LONG-TERM USE OF TRANSANAL COLONIC IRRIGATION

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Aim: The increased use of transanal colonic irrigation (TAI) warrants study of its effects on anorectal function after long-term use.
Method: Anorectal physiology tests were performed in 12 patients with chronic idiopathic constipation (CC) and 10 with idiopathic faecal incontinence (FI) (median 55 years (range 21-70)) before and after median 68 (range 32-113) months use of TAI.
Results: In CC median rectal volume at urge to defecate increased from 121 (70-264) to 268 ml (69-484) (p=0.05). In contrast, rectal compliance, volume at first sensation, maximum tolerable rectal volume, anal sensory level, median anal resting and squeeze pressures were unaltered. In FI median volume at urge to defecate increased from 125 (range 50-221) to 158 ml (range 97-287) (p=0.033) and maximum tolerable rectal volume increased from 156 (80-321) to 253 ml (162-332) (p=0.047). Median anal resting pressure decreased from 48 (29-100) to 32 cmH2O (12-79) (p=0.011) and anal squeeze pressure decrease from 69 (30-107) to 38 cmH2O (30-70) (p=0.017). Anal sensory level, rectal volume at first sensation and rectal compliance were unaltered.
Conclusions: As rectal compliance was unaltered, we find it likely that the increased rectal volume tolerability is explained by patients getting used to irrigation rather than by changes in mechanical rectal wall properties. Since anal sphincter function deteriorated in FI only, we suggest that this is due to the natural history of FI rather than side effects from long term use of TAI.

P06.01 Gitte Aarøe Dam

EFFECTS OF BRANCHED-CHAIN AMINO-ACIDS ON AMMONIA METABOLISM IN SKELETAL MUSCLE IN PATIENTS WITH LIVER CIRRHOSIS AND HEALTHY CONTROLS

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Background and Aims

Branched-chain amino acids (BCAA) are used to prevent hepatic encephalopathy in cirrhotic patients. The main effect takes place in muscle where BCAAs provide carbon-skeletons for the TCA-cycle. This enhances the conversion of alfa-ketoglutarate to glutamine which accordingly lowers the arterial concentration of ammonia. We studied the effect of BCAA on ammonia metabolism across the leg-muscle.

Methods

12 patients with cirrhosis and 6 healthy subjects fasted overnight. Catheters were inserted into the femoral artery (A) and vein (V). Muscle blood flow (F) was determined by dye dilution principle. Blood flow and A and V concentrations of ammonia and amino acids were measured before an oral load of BCAA and after 1 and 3 hours. The uptake and release of ammonia and amino acids were calculated as F(A-V).

Results

Baseline arterial concentration of ammonia was significantly higher in patients than in healthy controls (mean 99 vs. 63 µmol/L). The arterial concentration of ammonia increased significantly in both groups 1 hour after administration of BCAA.

Mean base-line uptake of ammonia in muscles was higher in patients than in healthy subjects (8.3 vs. 3.2 µmol/min). This uptake increased to 10 µmol/min in healthy subjects and to 17 µmol/min in patients.

The uptake of ammonia and BCAA was followed by an increased release of glutamine . In healthy subjects the net-balance changed from uptake (14µmol/min) to release of 61 (1 hour) and 48 (3 hours) In patients, baseline release was 19 µmol/min and increased to 56 (1 hour) and 150 (3 hour).

Conclusions

BCAA led to an increased uptake of ammonia by muscle and was followed by release of glutamine.

P06.02 Iben Blaabjerg Sundtoft

SHORT INTERPREGNANCY INTERVAL AS A RISK FACTOR OF SPONTANEOUS PRETERM BIRTH DUE TO LOW CERVICAL COLLAGEN

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OBJECTIVE: The incidence of preterm birth is increasing and continues to be a significant cause of neonatal mortality and morbidity. A short interpregnancy interval is a risk factor of early spontaneous preterm birth, with the strongest association found within interpregnancy intervals shorter than 6 months.

Cervix uteri consist predominantly of fibrous connective tissue (85%-90%). Cervical collagen concentration decreases during pregnancy, a prerequisite for vaginal delivery. Correlation between cervical insufficiency and a low cervical collagen concentration has been shown in former studies.

The aim of this study is to describe the normalization of cervical collagen after labor.

METHODS: Cervical biopsies were collected from 15 women three, six, nine, and twelve months post partum. The biopsies were analyzed for the hydroxyproline concentration to express the concentration of collagen. The post partum hydroxyproline concentration was compared to the concentration in a control group consisting of 96 women with no pregnancy within the last twelve months.

RESULTS: The difference in collagen concentration is found to be statistically significant three and six months after birth compared to the control group (50.2 (31.8;57.7)µg/mg dry weight; p<0.01, 58.1 (48.6;65.5)µg/mg dry weight vs. 65.0 (48.6;76.1)µg/mg dry weight. No significant difference in collagen concentration was found nine and twelve months after birth compared to the control group.
CONCLUSIONS: Cervical collagen is markedly lower three and six months post partum. The lower collagen concentration may explain the association between short interpregnancy interval and preterm labor.

P06.03 Anne Petas Swane Lund Krarup

HYPOSENSITIVITY IN PATIENTS WITH BARRETT'S OESOPHAGUS: MECHANISMS AND IMPLICATIONS FOR TREATMENT

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Objective: Information on visceral sensation in patients with Barrett's oesophagus may contribute to our understanding of the disease. The study objective was to describe the sensation to multimodal pain stimulation in the metaplastic part and the normal part of oesophagus in these patients.
Methods: Fifteen patients with Barrett's oesophagus and 15 healthy volunteers were subjected to mechanical, thermal and electrical pain stimuli of the oesophagus. Both the metaplastic part and normal were examined. Pain scores, referred pain areas, contractile responses and evoked brain potentials to electrical stimulations were recorded.
Results: Patients were hyposensitive to mechanical (45.1 ml versus 38.8 ml; P=0.02) and heat stimulation (18 versus 14 sec; P=0.048) when stimulating the metaplastic area. Four patients but no controls experienced nausea instead of pain in response to distension (P=0.03). No indication of abnormalities in the pain processing of the central nervous system was present, as the responses were similar between groups to electrical pain stimuli bypassing the receptors (maximum intensity 13.6 mA versus 13.8 mA; P=0.7), the referred pain areas (P-values all>0.3), or evoked brain potentials (amplitudes P=0.1 and latencies P=0.7). No differences in sensitivity to stimulations in the normal tissue were found between groups.
Conclusion: Patients with Barrett's oesophagus are hyposensitive in the metaplastic part of the oesophagus likely due to abnormalities affecting peripheral nerves. Hence, a lower threshold for endoscopy should be considered if patients with Barrett's oesophagus report even slight oesophageal pain.

P06.04 Yu Wang

NAVIGATED PERCUTANEOUS TRANS-ILIAC LUMBOSACRAL FUSION : A FEASIBILITY STUDY USING 3D SURGICAL SIMULATION

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Objective. To verify the feasibility of a novel navigated minimally invasive procedure for lumbosacral fusion.
Methods. CT data of 60 patients was included. The DICOM format image files of each case were imported to mimics 12.3 software (materialise Inc., Belgium), and a 3D model was reconstructed and used for surgical simulation. S1 pedicle screw placement was simulated, and a working corridor, through which discectomy and bone grafting could be performed, was designed to be a 10 mm-diameter cylinder. If both the corridor and the screw trajectory could be accommodated in the sacral ala without overlapping with each other and penetration of any wall of the sacrum, the feasibility of the approach could be verified for the case. After verifying the feasibility of the approach, the feasibility of performing discectomy and bone grafting through the approach was also evaluated .
Results. 3D modeling and surgical simulation were successfully completed in all cases, the feasibility of the procedure was verified in all cases. It was found in 4 cases that the cross-section of the corridor partly overlapped with the iliosacral joint. The

mean length of the corridors was 58.00±5.09 mm, the mean length of the screw trajectories was 51.00±6.55 mm. The mean ratio of the area that curettes can reach to the total area of the disc was 0.721±0.065 (range, 0.57 – 0.894), 0.956±0.045 (range, 0.8 – 1) and 0.945±0.058 (range, 0.813 – 1) in the axial, coronal and sagittal planes respectively.
Conclusion. The results of this study verified the feasibility of the navigated percutaneous trans-iliac lumbosacral fusion from both anatomical and operative perspective.

P06.05 Anne Skakkebæk Jensen

NEUROPSYCHOLOGIC, NEURORADIOLOGIC, AND GENETIC ASPECTS OF KLINEFELTER´S SYNDROME

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Background: Klinefelter syndrome (KS) is the most common sex-chromosome disorder in men with a prevalence of 1 in 660 men. Men with the syndrome have an ekstra X-chromosome. The syndrome is associated with cognitive and behavioral dysfunction and also with hypogonadism. Magnetic resonance imaging have pointed to different volumetric alterations in several brain structures. Several genetic factors involving the X-chromosome have been suggested to influence the neuropsychological phenotype in men with KS. Aim: The aim of this project is to investigate the following: 1. Whether KS is associated with volumetric alterations in brain structures and an altered brain activity in attempt to assess the neuroanatomic and neurofunctional basis for the altered neuropsychological phenotype seen in KS. 2. Whether genetic factors involving the X-chromosome influence cognition, brain morphology and brain activity in men with KS. 3. Whether testosterone treatment improves cognition and behaviour in men with KS.
Methods: We include 100 men with KS of whom 50 recieve testosterone treatment and 100 age-matched control men. Subjects are administered a battery of standardized neuropsychological tests to cover cognitive domains and domains of personality. We use magnetic resonance imaging to measure total and regional brain volumes and functional magnetic resonance imaging to measure brain activity, while subjects are performing an attention-demanding cognitive task. The genetic testing includes the parental origin of the supernumeary X-chromosome, the pattern of X-chromosome inactivation, androgen receptor (AR) CAG_n repeat length, and a gene expression profile of brain-expressed genes.

P06.06 Mie Hessellund Samson

TREFOIL FACTORS AT BIRTH AND IN THE HUMAN FETUS

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Objective. Trefoil factors (TFF1-3) are 7-12 kDa peptides secreted by mucosal surfaces. Changing levels of expression reflect in serum concentrations. Serum levels of TFF2 and 3 are highly elevated in pregnant women. We report the occurrence of TFFs in cord blood at birth.
Material and methods. Using in house ELISA methods, serum concentrations of TFF1-3 were measured in 92 pairs of samples of cord blood from newborns and blood from their mothers obtained at birth. On selected samples size exclusion chromatography was used to investigate molecular forms.

Results. Serum from cord blood contained considerably less TFF2 and 3 than did serum from mothers (median 108 and 1196 pmol/L, 17.8% and 15.7% of mothers median). Yet median concentrations of TFF2 and 3 in cord blood were 140% and 850% of that in blood donors. There was no difference in concentrations of TFF1 amongst newborns, mothers and donors. We found positive correlations between concentrations of the same TFF in the newborn and the mother, and between TFF2 and 3 in mothers and newborns respectively. The sex of the newborn had no impact on any of the concentrations of TFFs. Size exclusion chromatography showed no major difference between molecular forms present in cord blood, mothers and donors. For TFF1 and 3 high molecular forms were present in addition to the monomer. Most TFF2 was present as a molecule slightly larger than recombinant TFF2.
Conclusions. All TFFs are present in cord blood, TFF2 and 3 in high concentrations compared to blood donors, but low compared to mothers. The results further emphasize a possible role for TFFs in relation to childbearing and newborns, a role that remains to be clarified.

P06.07 Casper Nielsen

QUANTITATIVE DETERMINATION OF D-LACTATE IN PLASMA ON THE MODULAR ANALYTICS P

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Background. D-Lactate the isomer of L-Lactate is normally present in blood at nanomolar concentration. Millimolar concentrations of D-Lactate can arise due to excess intestinal microbial production under anaerobic conditions. Methods. We used the D-Lactic Acid kit from Biocontrol Systems, Italy on the Modular Analytics P, Roche Diagnostics, Germany. In the reaction D-Lactate is oxidized to pyruvate by NAD+ in the presence of D-Lactate dehydrogenase. The formed pyruvate is converted to L-Alanine in the presence of L-glutamate and ALT. The amount of NADH formed in the coupled reaction, measured by the change in absorbance at 340 nm, is proportional to the concentration of D-Lactate. The sample volume was 10 µL. Blood samples were collected from pigs with gut ischemia in tubes with fluoride-citrate mixture. Results. The assay was linear in the range from 0,17 – 4,50 mmol/L. The analytical recovery was 95-104%. The detection limit was 0,03 mmol/L. Within-run imprecision based on duplicates of 40 plasma samples was 3,88 % for samples in the concentration range 0,044-0,422 mmol/L. Within-run, between-run and total imprecision for two aqueous D-Lactate controls run in duplicates twice a day for 15 days were 3,29 %, n/a, 4,39 % (mean = 0,484 mmol/L) and 1,08 %, 1,55 %, 2,17 % (mean = 1,998 mmol/L). The concentration of D-Lactate in plasma samples was stable for 4 days at 2-8°C and long term stable at -20°C or -80°C. There was no interference from L-Lactate concentrations up to 20 mmol/L. Conclusions. The developed D-Lactate assay on the Modular Analytics P is a precise and convenient method for the determination of D-Lactate concentrations for routine clinical purposes.

P06.08 Stinne Pulkkinen Schmidt

MISFOLDING OF A DISEASE-ASSOCIATED VARIANT OF SHORT-CHAIN ACYL-COA DEHYDROGENASE LEADS TO OXIDATIVE STRESS AND FISSION OF THE MITOCHONDRIAL NETWORK

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Background: Short-chain acyl-CoA dehydrogenase deficiency (SCADD) is a rare recessively inherited disorder affecting the mitochondrial fatty acid β-oxidation. Patients are usually presenting neuromuscular features such as developmental delay, hypotonia, seizures, as well as a general failure to thrive. Methods: To study

the pathogenesis of SCADD, we have transiently transfected human astrocytes with wild-type cDNA or cDNA carrying the disease associated variation c.319 C>T. Transfected cells were analyzed for protein aggregates by Western blotting. SCAD localization, production of reactive oxygen species (ROS), as well as mitochondrial morphology was analyzed by confocal laser scanning microscopy. Results and conclusion: Cells transfected with the variation c.319 C>T revealed aggregating SCAD protein with negligible amounts of soluble protein, compared with the wild-type cells. This is the first time SCAD protein aggregations have been observed ex vivo. How cells respond to these misfolded SCAD proteins have not yet been characterized. Here we show that the misfolded SCAD proteins localize to the mitochondria as expected, and that the expression is associated with an increased production of ROS, coupled to an altered mitochondrial morphology. Accordingly, we suggest a pathogenic mechanism involving toxic species of the misfolded variant SCAD protein, which can lead to mitochondrial dysfunction. We therefore propose that the amount of toxic species of variant SCAD protein, and thereby the expressivity of the disease, may be controlled by yet unknown endogenous and/or exogenous stress factors in patients with the severe variation c.319 C>T in the SCAD gene.

P06.09 Dorthe Mørck Mortensen

CALCINEURIN A IS UPREGULATED IN TACROLIMUS-TREATED RENAL TRANSPLANT PATIENTS WITH STABLE ALLOGRAFT FUNCTION

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Tacrolimus (FK) exerts its immunosuppressive action by inhibiting calcineurin phosphatase (CaN).

Our group has previously demonstrated that FK decreases CaN activity in patients early after renal transplantation. However, in stable kidney transplant recipients, this inhibition was hardly seen during treatment with FK.

We included 20 stable kidney transplant recipients receiving FK. Blood samples were drawn at trough level (T:0) and 2h post dose (T:2). Included were also 10 healthy non-medicated subjects.

T-lymphocytes were isolated using an E-rosette method and a fluorometric DNA assay was used to quantify T-lymphocytes. Gene expression (mRNA molecules/cell) of CaN Aα and Aβ were measured using real time PCR. CaN activity was measured as the release of ^{32}P from a phosphorylated peptide. IFN-γ was determined in whole blood by an ELISA method.

No difference in the gene expression of the two CaN A isoforms within the T-lymphocyte were found, but CaN Aβ was significantly up-regulated in kidney transplant recipients compared to 10 healthy controls.

CaN activity in T-lymphocytes were significantly inhibited at T:2 compared to T:0 ($p=0.02$) in the stable kidney transplant recipients. Compared to the healthy controls there were no significant difference.

We demonstrated that after long-term treatment with FK the gene expression of CaN A in the T-lymphocytes are up-regulated compared to healthy controls. This up-regulation resulted in a higher trough CaN activity level in the T-lymphocytes in the FK treated group and 2 hours post dose it was similar to the healthy controls. This resulted in the production of IFN-γ being unaffected of the immunosuppressive treatment.

P07.01 Carina Henriksen

THE PATHOPHYLOGY OF RAPID-ONSET DYSTONIA PARKINSONISM: CELL CULTURE STUDIES AND PORCINE MODEL

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Rapid-onset Dystonia Parkinsonism (RDP) is an autosomal dominantly inherited neurological movement disorder characterized by abrupt onset of dystonia, usually with signs of Parkinsonism. RDP is caused by missense mutations in the a3-isoform (ATP1A3 gene) of the Na^+,K^+-ATPase. a3 is the major isoform of Na^+,K^+-ATPase expressed in neurons, but a convincing hypothesis for the pathophysiological mechanism underlying the development of the disease is missing and a contribution to a better understanding of this mechanism is the aim of the Ph.D. project. It is possible that the pathogenesis is entirely related to lack of Na^+,K^+-ATPase function (haploinsufficiency), but it is also possible that dominant negative interactions from the mutated protein may be important. By use of cell culture, RDP mutations will be analyzed to evaluate their influence on the function of the Na^+,K^+-ATPases. Some of the mutations have been found to reduce the Na^+ affinity of the Na^+,K^+-ATPase, which might lead to an increase in the intracellular Na^+ concentration. It is a goal to establish a transgenic mini pig overexpressing Na^+,K^+-ATPase a3 with an RDP mutation causing reduced Na^+ affinity, thus allowing us to test the negative dominance hypothesis. One of the tools I need is the neuron specific promoter of the a3-isoform, and here I will present the result of my attempt to clone this promoter from pig. Furthermore the tissue specific expression patterns of the isoforms (a1, a2 and a3) of the Na^+,K^+-ATPase at the transcriptional level will be shown, including expression in specific parts of the porcine brain as well as the developmental pattern.

P07.02 Ole Halfdan Larsen

THE COMBINATION OF RECOMBINANT FACTOR VIIA AND FIBRINOGEN CORRECTS COAGULATION IN A MODEL OF WHOLE BLOOD THROMBOCYTOPENIA

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Successful and effective haemostatic intervention in thrombocytopenia might be based on a combination of haemostatic agents. The present study aimed to explore the haemostatic effect of a fibrinogen concentrate (Haemocomplettan®) in combination with recombinant factor VIIa (rFVIIa, NovoSeven®) in a validated laboratory model of thrombocytopenia in whole blood (WB). Blood from 10 healthy volunteers was drawn into 3.2% citrate with the addition of corn trypsin inhibitor 18.3 µg/ml to inhibit artificial contact factor activation. Thrombocytopenia in WB was produced as previously reported (Ann Hematol. 2007 Mar;86(3):217-21). Thrombocytopenic WB (mean platelet count 29 × 10^9/l (range 6-52)) was spiked in vitro with buffer (control), platelets (+50×10^9/L), rFVIIa (2µg/mL), or fibrinogen (2mg/mL) as well as the combination of fibrinogen (2mg/mL) and rFVIIa (2µg/mL). Dynamic WB clot formation profiles were recorded by ROTEM® Thrombelastometry using activation with minimal amounts of tissue factor. Thrombocytopenia model WB was characterised by a reduced maximum velocity (MaxVel, 5.73mm×100/s (mean)) and maximum clot firmness (MCF, 35.8mm). Fibrinogen as well as rFVIIa increased the MaxVel and MCF and the combination showed an additive effect increasing the MaxVel (10.8mm×100/s) and MCF (43.3mm) comparable to the effect of fresh platelets (MaxVel,8.9mm×100/s; MCF,45.2mm). The data suggest that fibrinogen in combination with rFVIIa provide an additive haemostatic effect in thrombocytopenia, and may hold the potential to serve as an effective alternative treatment option to platelet transfusion.

P07.03 Jonas Jensen

OSTEOGENIC POTENTIAL OF BIPHASIC CALCIUM PHOSPHATE WITH GROWTH FACTOR LOADED ELECTROSPUN POLYMER FIBERS

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Introduction: Two used components in regeneration of bone are the osteoconductive CaPs and osteoinductive growth factors such as BMP-2. We aimed at achieving controlled release of BMP-2 as well as supplying osteoconductive material to the bone formation site. Materials and Methods: Electrospun PLGA fibers loaded with BMP-2 were mixed with two different calcium phosphate ceramics, Nanostim and Calcibon. Both ceramics are moldable during implantation. To incorporate the BMP-2 into the PLGA fibers a water-in-oil emulsion electrospinning was performed. The fiber morphology was analyzed using scanning electron microscopy and presence of protein within fibers were visualized using fluorescent proteins and confocal microscopy. hMSC-TERT cell proliferation and differentiation were analyzed on the fibers. In addition to development and characterization of the scaffold with SEM, microCT and BMP2 release kinetics, an in vitro cell study was performed to evaluate nanofibers alone without the ceramic component. Results: Fluorescence microscopy revealed uniform fibers with proteins inside. We found no increase in proliferation and differentiation into osteogenic cells, when hMSC-TERTs were seeded on the BMP-2 loaded fibers as well as when cells were affected only by the BMP-2 release from the fibers. A homogenous mixture of the fibers with the calcium phosphates were achieved, but insufficient BMP-2 were released from the fibers to be detected using BMP-2 ELISA assay. Conclusion: A new scaffold comprised of electrospun fibers containing BMP-2 mixed in a moldable CaP was developed. However, impaired release of BMP-2 resulted in an inconclusive osteogenic effect of the scaffold in vitro.

P07.04 Rita Maria Delgado Silva Marques

ATP INHIBITS NA^+ ABSORPTION VIA BASOLATERAL P2 RECEPTORS IN MOUSE MEDULLARY THICK ASCENDING LIMB (MTAL)

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Extracellular nucleotides regulate epithelial transport via luminal and basolateral P2 receptors. Renal epithelia abundantly express P2 receptors which mediate significant inhibition of solute absorption. Recently, we found several P2 receptors in the mTAL including luminal and basolateral $P2Y_2$ receptors. In addition we found evidence for a basolateral P2X receptor. It is currently not known if extracellular nucleotides influence transport in this segment. In this study we use isolated perfused TAL from mice to electrically measure Na^+ absorption. By microelectrodes we determined the transepithelial voltage (V_{te}) and the transepithelial resistance (R_{te}) and via these the transepithelial Na^+ absorption (equivalent short circuit current, I_{sc}). Results: Non-stimulated TALs show large transepithelial transport and were characterized by: V_{te}: +9.03±0.44 mV, (lumen-positive), R_{te}: 8±1.1 Ω cm^2, I_{sc}: 1404±21.4 μA/cm2 (n=16). As expected, luminal furosemide (100 μM) completely blocked this transport. Basolateral ATP (100 μM, for 10 minutes) acutely (within 1 minute) reduced the absorptive I_{sc}. After 3 minutes a maximal reduction was measured and amounted to 19.6±2.8% (n=8). In most experiments transport inhibition was sustained during the application of ATP. Basolateral UTP, a $P2Y_2/P2Y_4$ receptor agonist was without effect as was adenosine. These data define that basolateral ATP exerts a significant inhibition of Na^+ absorption in mouse mTAL. Our data point to a P2X receptor-mediated mechanism. Intriguingly, these data add yet another example of P2 receptor mediated inhibition of tubular transport in intact renal epithelium.

P07.05 Maiken Kudahl Larsen

SUDDEN DEATH – A RETROSPECTIVE GENETIC STUDY OF HEART DISEASE

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Introduction: Several cases of sudden death on basis of genetic heart disease have inspired to a retrospective study. The aim of this study is to examine inherited heart

disease from selected forensic autopsies.
Materials and methods: Purified DNA from blood of approximately 180 selected autopsies will be examined. The following genetic heart diseases will be emphasized; long QT-syndrome and Brugada syndrome due to defects in cardiac ion channel proteins, catecholaminergic polymorph ventricular tachycardia due to defects in the ryanodine receptor, arrhythmogenic right ventricular cardiomyopathy due to defects in the desmosome proteins, hypertrophic, dilated and restrictive cardiomyopathy due to defects in the contractile proteins.
Results: Two cases of sudden cardiac death due to genetic heart disease are presented; a 25 year-old man, with a microscopic diagnosed hypertrophic cardiomyopathy, had a mutation in the myosin binding protein C (MYBPC3) and a 21 year-old woman with a normal heart, had a mutation, F29L in the HERG gene associated with long QT 2 syndrom.
Discussion: Mutations in the genes of the above mentioned proteins are known to present as arrhythmia or sudden death. Diagnosed cases of sudden cardiac death in the Danish population are few, despite the estimated higher number of cases in the literature. The perspective of the study is to determine the molecular cause of sudden cardiac death in order to intervene and prevent sudden cardiac death in relatives to cases with proven genetic heart disease.

P07.06 Christian Overgaard Steensen

WATER IS DISTRIBUTED PASSIVELY TO THE MUSCLES BUT THE BRAIN IS PROTECTED AGAINST EDEMA IN ACUTE HYPONATREMIA

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BACKGROUND: Acute hyponatremia can cause severe cerebral dysfunction with high mortality and morbidity. Brain edema is the proposed reason. Several authors have claimed that all cells reduce their volume in hypotone stress by regulatory volume decrease (RVD). RVD might protect the brain, but recently, we have shown that global RVD is unlikely to happen in a clinical relevant model of hyponatremia in pigs (Study l). Because, the muscles contain the greatest bulk of water in the body we hypothesized that water is distributed passively to the muscles but not to the more vulnerable brain in acute hyponatremia.
METHODS: Pigs were randomized to hyponatremia (n=8) or control (n=7). Hyponatremia was induced over 7 hours using DDAVP and infusion of 2.5 % glucose. Serial MRI was used to determine in vivo water content simultaneously in the brain and muscle.
RESULTS: Plasma [Na^+] was decreased from 138(SD=1) to 123(SD=2) mmol/l with a proportional decrease in plasma osmolality. In controls, the plasma [Na^+] was 137 mmol/l(SD=2). Moderate hyponatremia induce a significant increase in brain and muscle water content compared to controls ($P<0.05$). Water increase in the muscles was as expected from the decreased extracellular osmolality ($P=0.74$). In the brains the water increase was 40 % less than expected ($P=0.02$).
CONCLUSION: Hyponatremia induce a significant increase in brain and muscle water in this model. Whereas the water distribution to the muscles was passive (no RVD), the water increase in the brains was only 60 % of expected, probably because of RVD. The results are consistent with the lack of global RVD and this might help protecting the brain from more serious edema.

P07.07 Katrine Emmertsen

LOW ANTERIOR RESECTION SYNDROME SCORE - A SYMPTOM-BASED SCORING SYSTEM FOR BOWEL DYSFUNCTION AFTER RESECTION FOR

RECTAL CANCER.

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Introduction: Low anterior resection (LAR) for rectal cancer often results in severe bowel dysfunction (Low Anterior Resection Syndrome (LARS)) with incontinence, urgency and frequent bowel movements. Several studies have investigated functional outcome. Unfortunately, functional results have been described without a consistent terminology hereby complicating the comparison of results. The aim of this study was to develop and validate a scoring system based on symptoms and impact on quality of life (QoL).

Methods: Questionnaires were mailed to 1212 former LAR patients. The associations between items and impact on QoL were computed by binomial regression analyses. Based on clinical knowledge and the association with QoL, the most important items were selected and regression analysis was performed to find the adjusted risk ratio (RR) for each item. Individual score values were designated each item, and added to form the LARS-score. The score was divided into "No LARS", "Minor LARS" and "Major LARS". The validity was tested by ROC curves and the Spearman's rank correlation.

Results: In total 1020 patients responded. The five most important items were: "Incontinence for flatus", "Soiling", "Frequency of bowel movements", "Clustering of stools" and "Urgency". The range of the score was 0-42 with the limits of 0-20 (No LARS), 21-29 (Minor LARS) and 30-42 (Major LARS). The score showed good correlation and a high sensitivity (72.54%) and specificity (82.52%) for identifying patients with Major LARS.

Conclusion: We have constructed a valid and reliable LARS-score that is correlated to impact on QoL. This is a simple tool for a quick clinical evaluation of the severity of LARS.

P07.08 Trine Borup Andersen

COMPARISON OF WITHIN- AND BETWEEN-SUBJECT VARIATION OF SERUM CYSTATIN C AND SERUM CREATININE IN CHILDREN AGED 2-13 YEARS

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Background: Previously, data has not been reported on both the within-subject (SD_I) and the between-subject (SD_G) variation of cystatin C in children. Thus, this study aims to determine this biological variation including analytical variation (SD_A) of both cystatin C and creatinine to characterize the two analytes as renal function markers in children.

Methods: On two consecutive days blood samples for duplicate analysis of cystatin C (nephelometric, Dade Behring) and creatinine (enzymatic, Roche) were obtained from 30 children (11 females and 19 males, mean age 8.3 range 2-13 years) referred for GFR measurement by ^{51}Cr-EDTA clearance. For determination of the between-subject variation only children with normal GFR (n=21) were included. Data were adjusted for the well known age-related increase in creatinine.

Results: (Given as coefficients of variation). Within-subject variations were identical for both analytes (6.4%). Between-subject variation was 11.1% for cystatin C and 28.4% for creatinine, though decreasing to 20.1% after adjusting for age. The analytical variation was 1.7% and 2.5% for cystatin C and creatinine, respectively. The index of individuality ($IOI=SD_I/SD_G$) was 0.65 for cystatin C and 0.25 for creatinine, though increasing to 0.36 after adjusting for the age-adjustment.

Conclusions: Within-subject variation was identical and low for cystatin C and creatinine suggesting that the two are equally suitable for serial monitoring of renal function in children. Based on the low IOI, neither analyte, however, seems suitable as a screening marker of renal function in a healthy population of children using population-based reference intervals.

P07.09 Eva Greibe

RAINBOW TROUT SPAWN VITAMIN B12 BINDING PROTEIN AND VITAMIN B12 MALABSORPTION

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Background: Vitamin B12 (B12) deficiency is associated with anaemia, nerve damage and cognitive decline and is a common condition among the elderly. We have recently developed - and launched for routine use - an absorption test for free B12, named CobaSorb. However, we still need a standardized assay to measure a patients ability to absorb food bound B12. The major challenge is to find a B12 binding protein suitable to act as proxy for food bound B12. Our approach was to investigate food items normally eaten unprepared.

Materials and Methods: The supernatants of homogenized spawn from different fish were incubated with 57Co-labelled B12. For measurement of B12 binding capacity, affinity studies and pH-sensitivity experiments; charcoal precipitation was used to remove excess labelled B12. For characterization of B12 binders, gelfiltration was performed, and glycosylation status was estimated by concanavalin A sepharose precipitation. The protein was purified by affinity chromatography on B12-coupled sepharose followed by gelfiltration.

Results: From an initial screening, the rainbow trout spawn was selected for further analysis based on a high content of B12 binding protein. The structural and functional characteristics of the protein was compared to the human B12 binders; TC, HC and IF, and found to share the structural characteristics of HC with regard to glycosylation, size, affinity for B12-analogs and sensitivity towards low pH.

Conclusions: The findings suggest that the B12 binder from rainbow trout spawn could be a suitable proxy for food bound B12 in a B12 food absorption test. Clinical studies are needed to clarify its potential in diagnosis of B12 malabsorption.

P08.01 Christel Krøigaard

INVESTIGATION OF CALCIUM-ACTIVATED POTASSIUM CHANNEL OPENING FOR TREATMENT OF PULMONARY DISEASE

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Pulmonary arterial hypertension (PAH) is a life-threatening disease characterized by abnormal constriction of pulmonary arteries, proliferative vasculopathies, and finally organ failure. Present treatments do not sufficiently prevent PAH and therefore there is interest in new pharmacological approaches. We hypothesized that an increase in calcium-activated potassium (K_{Ca}) channel expression could be observed as a compensatory mechanism to counteract PAH. For this purpose we investigated the expression of small (SK), intermediate (IK) and large (BK) conductance K_{Ca} channels in lungs of normotensive/normoxic rats (n=6) and chronic hypobaric hypoxic rats (n=7) that develop PAH and right ventricular hypertrophy. Bronchioles and intrapulmonary arteries were isolated and the expression of K_{Ca} channels investigated by QPCR, immunohistochemistry and Western blotting. IK and SK3 immunoreaction was found in the arterial endothelium and bronchial epithelium. At mRNA level, K_{Ca} channels were expressed in the following order in rat bronchioles and arteries: BKβ1>>SK1>IK_{Ca}=BKα>SK3>>SK2. In arteries, BKβ1 mRNA and BKα mRNA and protein expression was upregulated by hypoxia. IK mRNA expression was higher in arteries than bronchioles and unaltered in tissue from chronic hypoxic rats. mRNA for SK1, SK2 and SK3 was unaltered by hypoxia, whereas SK3 protein was upregulated in arteries exposed to hypoxia. In conclusion, in the chronic hypoxic rat both SK3, BK β1 and BKα was upregulated in pulmonary arteries. In recent studies we found that K_{Ca} openers dilate pulmonary arteries and with the present results this suggests that drugs opening K_{Ca} channels may be beneficial for the treatment of PAH.

P08.02 Maj Lesbo

CARDIOPULMONARY FUNCTION IN PECTUS EXCAVATUM PATIENTS COMPARED TO HEALTHY CONTROL SUBJECTS

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Background:

Pectus excavatum, a relatively common deformity of the anterior chest wall, is often associated with: fatigue, discomfort, tachypnea and dyspnea.

- The question is therefore whether there is reason to believe that surgical correction of pectus excavatum will influence the cardiopulmonary function or just provide cosmetic and psychological improvements.

Aim:

To compare results from cardiopulmonary patient-examinations performed during a 6 months period prior to and post surgery with healthy age matched controls.

Materials and methods:

Patients, N= 41; Control subjects, N= 21. All between 11 and 18 years old.

Cardiopulmonary tests performed:

MRI scan to determine Haller index, Cardiopulmonary exercise test, Echocardiography, Spirometry, Questionnaire.

Results:

Prior to surgery the difference in Haller Index between the two groups were highly significant (Patients 5.3±2.3, Controls 2.7±0.3, P=0.00)). In the cardiopulmonary exercise test we also found a significant difference in Maximum Cardiac Index with a patient value of 6.6±1.3 and control value of 7.9±1.8 l/min/m^2 (P=0.03). Data collected 6 months post surgery trend towards a difference in preliminary results.

Conclusion:

A significant difference between the two groups was found in maximum cardiac index.

This indicate, that patients born with pectus excavatum may suffer from a compromised filling of the right sided cavities of the heart, which leads to a decreased stroke volume and therefore affects the cardiac output. This fits the complaints of fatigue, discomfort, tachypnea and dyspnea during exercise.

P08.03 Lars Rolighed

EFFECT OF VITAMIN D TREATMENT I PATIENTS WITH PRIMARY HYPERPARATHYROIDISM

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Introduction.

Vitamin D has become a favorite topic in many recent studies. Vitamin D is of great importance in the regulation of calcium homeostasis due to its effects on intestinal calcium absorption and mineralization of calcified tissues. Increasing interest in vitamin D insufficiency with connection to various diseases has heightened the need for randomized controlled trials analyzing effects of vitamin D treatment. In primary hyperparathyroidism (PHPT) changes in the metabolism of vitamin D have been shown in several studies: 1) Reduction of plasma 25-OHD. 2) Reduction in half-life of 25-OHD. 3) Elevated 1, 25$(OH)_2$D suggesting a substrate-product relationship of the activity of 1α-hydroxylases. 4) Polymorphous VDR coding genes, leading to reduced VDR mRNA, which may lead to decreased vitamin D sensitivity in parathyroid adenoma cells. 5) Decreased parathyroid hormone (PTH) after vitamin D treatment.

Methods.
We are conducting a randomized controlled clinical trial with PHPT patients. Fifty patients will be enrolled and randomized to daily treatment with vitamin D (2800 IE) or placebo. Patients are examined and followed in 52 weeks. Operation for PHPT after 25 weeks.

Examinations.
Parathyroids: size and function. Muscular tissue: strength, balance, biopsies, EMG and biochemical markers. Fatty tissue: Biopsies, biochemical markers and body composition. Bone metabolism: Biopsies, DXA, QCT and biochemical markers. Well-being: Questionnaire SF-36 and WHO-5. Blood pressure: 24-hour measurement.

Results.
Final results are not available. We are still including patients and only about half of the patients have been included so far.

P08.04 Jakob Østergaard DIABETIC NEPHROPATHY AND THE COMPLEMENT SYSTEM

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Background and aim
Diabetic nephropathy is still the most common cause of end-stage renal disease in many western countries. Better treatments and tools for identification of patients at high risk are very much needed. The complement system and in particular mannose-binding lectin (MBL) seems important to diabetic nephropathy. In mice, we have previously shown that absence of MBL protects the kidneys from diabetic changes. We have also found that absence of C3 surprisingly does not protect the kidneys to diabetic changes to the extent that MBL deficiency did. In the present study we wanted repeat the design in genetically more homogeneous animals i.e. animals backcrossed for 12 generation. Also, we want to test whether the effects of MBL depend on mouse strain.
Methods
We used both C57BL/6J MBL knock-out and SV129EVSV MBL knock-out mice to evaluate the kidney changes after three months of experimental type 1 diabetes. Diabetes was induced by streptozotocin in multiple low-dose, intra-peritoneal, injections. In both strains, non-diabetic wild-type (WT) animals and non-diabetic MBL-knock-out animals were used as controls. Renal growth was measured. Glomerular volume is measured by light microscopy. Mesangial volume and glomerular basement membrane thickness are measured by electron microscopy. Renal mRNA expressions of transforming growth factor β, connective tissue growth factor, collagen IV, fibronectin, vascular endothelial growth factor A (VEGF-A), vascular endothelial growth factor receptor, and nephrin are measured by real-time PCR. Localisation of complement factors is determined by immunehistochemistry. Kidney function is evaluated 24 h albumin excretion rate.

P08.05 Lau Brix MAGNETIC RESONANCE IMAGING OF THE VOCAL CORDS DURING SINGING WITH HIGH SPATIAL AND TEMPORAL RESOLUTION USING RADIAL GOLDEN RATIO SAMPLING AND FAST RECONSTRUCTION ON A GRAPHIC CARD

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Background: Magnetic resonance imaging (MRI) imaging has a limited spatial and temporal resolution. Non-Cartesian sampling strategies have shown to be useful for real-time applications providing high spatial and temporal resolution in combination with parallel imaging methods like k-t SENSE. One sampling strategy is to use a constant azimuthal profile spacing of 111.246° (the Golden Ratio). With this method it is possible to vary spatial and temporal resolution after data acquisition. The purpose of the work was to test this approach in a dynamic study of the vocal cords during different song techniques.
Methods: A Philips Achieva 1.5T MRI system was programmed to acquire non-Cartesian radial k-space profiles based on the Golden Ratio. A time-resolved 2D balanced-TFE CINE sequence (128x128 matrix, 2.34x2.34x3.0 mm2, TR=5.1, TE=2.5, 256 samples/profile, 16 coils and a total scan time of 32.9s) was applied to a professional singer. A coronal slice plane was placed along the vocal cords during the acquisition. Raw radial MRI data profiles were reconstructed by k-t SENSE on a Nvidia GTX 280 graphics card. By visual evaluation the optimal number of radial profiles was found for an acceptable temporal resolution and artifact level.
Results: 10.000 radial profiles were acquired. 34 profiles were found to be the optimal number for imaging of the vocal chords during singing.
Conclusion: Non-cartesian sampling strategies based on the Golden Ratio showed promising results of imaging the moving vocal cords in a volunteer. Thus, this study is an indication that MRI can be applied to moving objects in the scanner hereby making images of moving organs possible.

P08.06 Karen Lorentzen HYALURONIC ACID AND TSG-6 INTERACTIONS IN ANGIOPATHY

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Background: Diabetic angiopathy is characterized by increased production of extracellular matrix (ECM) components. We focus on hyaluronic acid (HA), a large non-sulphated glycosaminoglycan that is stabilized by HA binding proteins in the ECM. We focus on Inter-α-trypsin Inhibitor (IαI) and tumor necrosis factor α stimulated gene 6 (TSG-6). TSG-6 functions as a catalyst transferring heavy chains (HC) of IαI onto HA, thereby assisting ECM stabilization.
Hypothesis: Hyaluronan levels and stabilization in the tunica media (TM) influence SMC differentiation that contributes to the increased ECM production leading to diabetic angiopathy.
Aim: To investigate HC•HA crosslink in normal conditions as well as in diabetic angiopathy.
Methods: We use transgenic mice (TG) with elevated HA levels in TM and non-transgenic (WT) siblings. RNA expression is investigated by qPCR and protein expression by immunohistochemistry (IHC), western blot (WB) and ELISA.
Results: We show a significant (p=0,02) decrease of TSG-6 mRNA in aorta from 10-month old HAS-2 TG mice (n=8) vs WT (n=7). We see a similar tendency (non-significant) by IHC in TM however we can't detect TSG-6 in TM by WB.
As TSG-6 is the only known catalyst shuttling HCs from IαI onto HA, the amount of HC•HA is a measure of the activity of TSG-6. By WB we estimate that the expression of HC2 is similar in TG and WT mice.
We are developing an ELISA towards TSG-6 to make a more precise quantification of the TSG-6 content, and an ELISA for TSG-6 activity, measuring only the HCs bound to HA. Currently we are doing pilot experiments that look promising.
Conclusion: Increased levels of HA alone do not result in altered HC2 cross-linking patterns.

P08.07 Jesper Langhoff Hønge RECELLULARIZATION OF AORTIC HEART-VALVE PROSTHESES IN VIVO

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Background: Conventional glutaraldehyde treated bioprosthetic heart valves are non-viable with limited durability and early calcification, especially in children. Deoxycholic acid (DOA) treated, decellularized porcine heart valves allows recellularization without calcification in the pulmonary position in sheep. We aimed to study DOA treated heart valves in the aortic position in a longterm porcine model.
Material & Method: Twelve 90kg pigs received a DOA heart valve prosthesis in the aortic position. 6 months postoperatively, the valves were explanted and subjected to gross pathology examination, High Resolution (HR) X-ray imaging and histological evaluation.
Results: Five pigs survived the observation period. Three pigs had minor thrombotic depositions located at the commisural area. HR X-ray imaging demonstrated almost complete absence of calcification. Complete fibroblast recellularization of the stent adjacent area was observed in all valves. Variable ingrowth of endothelial-like cells and fibroblasts in the basal part of the cusps were seen in three valves. Immunohistochemistry staining demonstrated a limited immunogenic cell response.
Conclusion: DOA treated heart valves implanted in the aortic position in pigs allows slowly recellularization of host cells after six months. Only limited amounts of thrombotic material and calcification were observed. This study supports the findings seen in other studies and indicates that DOA treated heart valves may be used as alternative to glutaraldehyde valve prostheses in heart valve surgery.

P08.08 Rikke Vestergaard

DOES OSTENE™ IMPROVE BONE HEALING COMPARED WITH BONE WAX AFTER STERNOTOMY?

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Does Ostene™ improve bone healing compared with Bone wax after sternotomy?
Background:
Bone wax is used in cardiac surgery to reduce intraoperative bleeding by applying it to the spongiosa after sternotomy. However, Bone wax is non-absorbable and stays in the wound, reducing bone healing and increasing risk of sternal bone infection. To solve this problem a new biocompatible, absorbable hemostatic agent (Ostene™) was introduced, which is claimed not to reduce bone healing Ostene™ . The aim of this study was to compare sternal bone healing after sternotomy in pigs treated with Bone wax or Ostene™ .
Methods:
In total 24 Danish Landrace/Yorkshire pigs a midline sternotomy was performed. The pigs were allocated to three study groups: Bone wax, Ostene™ or Control (no treatment). After one hour of sterile exposure to open air, the sternum was closed using steel wires, a stainless steel screw through the two first costae and finally sub- and intracutaneous skin sutures. Six weeks later the animals were euthanized and their sternum removed for CT-scans to asses bone density (mg/ccm) as a measure of bone healing.
Results:
Bone density in the Ostene™ group (277 ±31 mg/ccm) was significantly higher compared with the Bone wax group (122 ±36 mg/ccm), but no statistically significant difference (p=0.9) was found between the Ostene™ group and Control group (280 ±61 mg/ccm).
Conclusion:
Ostene™ did not reduce sternal bone healing compared with controls. Bone wax impaired bone healing significantly compared with controls/Ostene ™.

P08.09 Aygen Øzbay

IMPAIRING EFFECTS OF CYCLOSPORINE AND TACROLIMUS ON INSULIN SECRETION AND TRANSCRIPTIONAL REGULATION IN RAT BETA-CELLS

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Introducing calcineurin inhibitors cyclosporine (CsA) and tacrolimus (Tac) into the field of transplantation has improved the outcome of organ transplants, but complications such as post-transplantation diabetes mellitus (PTDM) cause morbidity and impairment of survival rates. The pathogenic mechanisms behind PTDM and the contribution of each calcineurin inhibitor remain controversial.
We incubated rat beta-cells at various glucose concentrations and various amounts of CsA, Tac and vehicle for 6 and 24 hours. Our aim was to measure insulin, calcineurin and transcriptional markers involved in beta-cell function.
Both drugs primarily impaired insulin secretion while insulin content remained unaltered. Tac was able to inhibit basal ($p<0.05$) but not glucose stimulated insulin secretion after 6 hours of exposure, however after 24 hours, both agents equally inhibited basal and stimulated ($p<0.05$) insulin secretion. Calcineurin activity was decreased by both drugs during all conditions. Only CsA yielded slight alterations in calcineurin and insulin mRNA, while very high doses of the drug tended to increase expression levels of apoptosis associated genes Bax/Bcl2, as well as SREBP-1c. NFATc1-4 levels were not decreased notably by either drug. We found augmented acute diabetogenic effects of Tac in comparison to CsA, however prolonged exposure revealed similar effects for both drugs. The diminished insulin output was mirrored by decreased calcineurin activity, yet multiple pathways are possibly involved. Despite similarities in diabetogenicity, CsA had more negative impact on transcriptional markers essential for beta-cell function.

P08.10 Jesper Brink Askov

EFFECT OF MITRAL VALVE RING ANNULOPLASTY ON IN VIVO CHORDAL TENSION

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Introduction and aims:Reconstructive surgery on the mitral valve (MV) leaflets or chordae tendineae (CT) often entails an annuloplasty ring to fixate the repaired MV and relieve the repaired tissue from tensile stresses. The aim of this study was to assess the impact of mitral annuloplasty in terms of change in chordal tension.
Materials and methods: Four 80 kg pigs received a size 32 Carpentier Edwards Physio Ring annuloplasty. CT tension in the secondary chordae on the anterior leaflet was recorded by dedicated miniature force transducers before and after ring implantation along with standard hemodynamic parameters. The distances between the anterior papillary muscle, posterior and anterior annulus and the commissures were assessed using sonomicrometry ultrasound crystals.
Results: Preliminary results suggest a 21% average reduction of maximum systolic tension in the secondary CT of the anterior leaflet following ring implantation. Changes in systolic subvalvular and annular geometries were detected along with this reduction in maximum systolic chordal tension.
Conclusion: These preliminary data indicate that the Physio ring reduces maximum tension in the secondary CT. This might be a reflection of the flat diastolic shape of the Physio ring, causing significant changes in the subvalvular geometry; especially the papillary muscle position relative to the mitral annulus. Final results will be available by January 2010.

P08.11 Súsanna Við Streym Thomsen

THE STABILITY OF 25-HYDROXYVITAMIN D IN HUMAN BLOOD DURING DIFFERENT SAMPLING AND STORAGE CONDITIONS.

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Background: The effect of different storage conditions on the pre-analytic stability of 25-hydroxyvitamin D (25OHD) is largely unknown.
Aim: To investigate the stability of 25OHD in whole blood, sampled in different glass tubes (serum versus EDTA-plasma) and stored at different conditions (room temperature vs. refrigerator) prior to processing.
Material and Methods: In a cross-sectional design, we drew blood samples from 14 healthy adult into 3 serum- and 3 EDTA-plasma glass tubes. Samples were treated in three different ways: 1) centrifuged and frozen immediately, 2) kept for three days at room temperature before centrifuging and freezing, or 3) stored in a refrigerator (+5^{o}C) for three days before centrifuging and freezing. Thereafter, all samples were frozen at - 80^{0}C for a minimum of 1 week before analysis using isotope dilution liquid chromatography–tandem mass spectrometry (LC-MS/MS).
Results: Serum samples frozen immediately were considered as gold standard and had a mean value of 95±27 nmol/l. The percentage retrieval exceeded 90% for all methods investigated. Compared with gold standard, EDTA tubes kept refrigerated showed a higher correlation coefficient (r= 0.882, p<0.001) and had a higher retrieval (%) than serum tubes kept at +5^{o}C (r= 0.841, p<0.001). However, when stored at room temperature, samples collected in serum tubes correlated slightly better with the gold standard (r= 0.876, p<0.001) than did the EDTA-tubes (r= 0.847, p<0.001).
Conclusion: If immediate processing is not possible, the best result is obtained with EDTA-tubes kept refrigerated, whereas serum tubes can be used if samples are stored at room temperature.

P09.01 Esben Søndergaard

ACUTE EFFECTS OF AEROBIC EXERCISE ON VLDL-TRIACYLGLYCEROL KINETICS

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Introduction: Lipids are important substrates for oxidation in the basal fasting state and during exercise. Studies have demonstrated that aerobic exercise mediates a delayed onset decrease in very-low-density-lipoprotein triglyceride (VLDL-TG) concentration in plasma. But the acute effects on VLDL secretion and oxidation remain unclear.
Aim: To estimate the acute effects of exercise on VLDL-TG secretion, clearance and oxidation.
Methods: 16 young, lean, healthy individuals (8 men and 8 women) were recruited (age 20-30 years, BMI < 25 kg/m^2). The subjects were studied under basal fasting conditions and during 90 min of cycling exercise at 50% of VO2max. VLDL-TG kinetics was assessed using a primed-constant infusion of ex-vivo labelled [1-14C] VLDL-TG. Fractional VLDL-TG derived fatty acid oxidation was measured by $^{14}CO_2$ trapping from expired air.
Results: During exercise (50% of VO2max), there was a statistically significant decrease in VLDL-TG secretion rate from 39.9± 22.7 µmol/min to 31.4±21.5 µmol/min (p = 0.04. The total VLDL-TG oxidation rate was unchanged [basal: 19.5±13.8 µmol/min; exercise: 22.9±20.2 µmol/min (p = 0.22)]. The contribution of VLDL-TG oxidation to total energy expenditure (EE) fell to 3.2±4.5 % compared to 13.7±9.3 % in the basal fasting state (p < 0.001). There were no gender related differences in VLDL secretion or oxidation.
Conclusions and perspectives: Fatty acids from VLDL-TG are a quantitative important substrate for lipid oxidation under basal fasting conditions. During exercise, the oxidation of VLDL-TG is unchanged, but we demonstrate a lower VLDL production rate, which may contribute the delayed onset hypotriglyceridemia seen after exercise.

P09.02 Anette Luther Christensen

GRADUALLY CHANGING SEASONAL VARIATION OF CARDIOVASCULAR DISEASES IN DENMARK FEATURING DYNAMIC LINEAR MODELS

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Clarification of the temporal pattern of frequencies in cardiovascular diseases (CVD) may be an essential in establishing the etiology of CVD as well as improving prophylactic treatments. These patterns, called seasonal variation, are often modelled by statistical models such as the COSINOR models, the geometrical models or regression models and are often parameterized by a symmetric curve around the median frequency with a single maximum and a single minimum. However, such models assume the seasonality being constant during a period of observation, hence, the influence of changes in risk factors, e.g. life style factors, and treatment is neglected. The majority of findings suggest that during winter the frequency of CVD is highest, whereas during summer the frequency is lowest. Furthermore, it has been reported that ageing and weather conditions may influence the seasonal variation.
We hypothesize that the seasonal variation in CVD changes gradually during the period from 1977 to 2009. This is exemplified by analysing daily frequencies of incident venous thromboembolisms (VTE) in the Danish population, which encounters more than 93,000 cases, when restricted to not having prior cancer diagnoses or any diagnoses within three months of diagnosis of VTE. Hence, we aim to specify a model which handles gradual changes in the seasonal variation during a period of years featuring dynamic linear models. These models should set standard for modelling seasonal variation in epidemiological studies. Furthermore, we aim to investigate the association between weather conditions, e.g. humidity and precipitation, and the seasonality of CVD as well as the effect of ageing utilizing.

P09.03 Lars Jakobsen

PRIMARY PERCUTANEOUS CORONARY INTERVENTION IN A REAL-LIFE POPULATION: COMPARISON WITH TRIAL FINDINGS

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Background: Primary percutaneous coronary intervention (pPCI) is the recommended treatment of ST-Elevation Myocardial Infarction (STEMI). The efficacy of pPCI is documented in a number of randomised controlled trials, among these the Danish DANAMI-2 trial. However, translating RCT results into real life settings is a challenge as the external validity is often impaired.
Methods: We did a population-based follow-up study in the Central Denmark Region. We compared 1320 consecutive patients from West Danish Heart Registry treated with pPCI between April 2004 and December 2006 to the 686 patients treated with pPCI in the DANAMI-2 trial. The main outcome measure was the composite endpoint of all-cause mortality, reinfarction and stroke at 30 days, 1 and 2 years.
Results: The real-life population had a more adverse baseline risk profile including older age, higher comorbidity and a longer duration of symptoms. The cumulative incidence of the composite endpoint after 1 and 2 years was 17.8 % and 22.0 % respectively in the real-life population compared with 13.6 % and 17.3 % in the DANAMI-2 population. After adjustment the differences persisted after 1 year (adjusted HR=1.8, 95% CI: 1.3-2.6), and 2 years (adjusted HR=1.7, 95% CI: 1.2-2.3). The results in the real-life patients eligible according to the DANAMI-2 criteria were comparable to the results in the DANAMI-2 trial.
Conclusion: Real-life patients had a more adverse baseline prognostic profile and a poorer clinical outcome compared with the DANAMI-2 patients. However, the prognosis in the real-life patients eligible according to the DANAMI-2 criteria was comparable to the results obtained in the DANAMI-2 patients.

P09.04 Jens Holmer-Jensen

DIFFERENTIAL ACUTE EFFECTS OF MILK DERIVED PROTEINS ON POSTPRANDIAL LIPAEMIA IN OBESE NON-DIABETIC SUBJECTS

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Objective: We investigated the acute postprandial (480m) effects of milk derived proteins on responses of triacylglycerol, insulin, glucose and free fatty acids following a fat-rich mixed meal.
Methods: 11 obese non-diabetic males and females randomly consumed a meal on four different days. Meals consisted of an energy free soup added 100g of butter, 95g of white bread and one of four 45g milk protein preparations, either casein-glyco-macro-peptide (CGMP), whey isolate (WI), whey hydrolysate (WH) or alpha-lactalbumin (AL). A standard diet (55 % carbohydrates, 30% fat, 15% protein) was consumed on the day prior to test day. Triacylglycerol responses were measured in plasma and in the chylomicron-rich fraction and in the chylomicron-poor fraction. Incremental area under the curve (iAUC) was calculated and differences was assessed. Results: No significant incremental differences over the 480m postprandial period was seen for triacylglycerol, insulin, glucose or fatty acids across treatment groups. However, WH elicited a higher insulin iAUC compared to WI and AL during the initial 30m ($p<0.05$) and, further, WH elicited a higher insulin iAUC compared to CGMP during the first postprandial hour ($p<0.05$).
CONCLUSION: The effects of the four milk derived proteins on postprandial triacylglycerol, glucose, insulin and free fatty acids during the 480m postprandial phase in obese non-diabetic individuals do not differ. WH, though, elicited a significantly larger insulin iAUC compared to WI and AL during the first half hour and a higher insulin iAUC during the first hour compared to CGMP. The difference was not reflected in glucose, free fatty acid or triacylglycerol responses.

P09.05 Sophie Constantin Lütken

REGULATION OF RENAL AQUAPORINS AND SALT TRANSPORTERS IN LOW SODIUM DIET RATS WITH EXPERIMENTALLY INDUCED HEART FAILURE
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Heart failure (HF) is a common complication to myocardial infarction (MI) and is associated with increased plasma vasopressin levels and renal AQP2 protein abundance as well as sodium and water retention. Thus reduced sodium intake is often recommended. To examine the underlying renal molecular mechanisms in low-output HF, male rats were subjected to ligation of the left anterior descending artery. The following MI and HF were confirmed with echocardiography at day seven. During the last seven days of experiment all the rats were fed a low sodium diet and treated with dDAVP (20 ng/h s.c.) or vehicle. The rats were divided into four groups: Sham (n=6); Sham+dDAVP (n=6); HF (n=5), HF+dDAVP (n=6). In dDAVP treated groups the protein expression of AQP2 and p(S256)-AQP2 abundance and renal salt transporters increased, but surprisingly HF rats on low sodium diet did not increase protein levels of water and salt transporters despite of increased plasma aldosterone levels, the finding being most profound in inner medulla. In conclusion, the findings support that sodium restriction may be important as a powerful clinical tool against renal water and sodium retention associated with low-output HF.

P09.06 Hans Henrik Møller Nielsen

SCANDINAVIAN STUDY OF TRANSAPICAL CATHETERBASED AORTIC STENTVALVE TREATMENT VERSUS OPEN SURGERY
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Background:
Aortic valve stenosis is a common cause of mortality and morbidity among the elderly. Most patients need valve surgery when the valve area decreases to a critical size. The procedure is demanding and up to one third of patients are deemed inoperable due to high risk. The development of new artificial valves - stentvalves - have given way for minimal invasive surgical procedures, that allows aortic valve replacement, of patients inoperable via conventional technique. Transapical Aortic Valve Replacement was introduced at our institution in 2006 for conventional inoperable patients. The results are encouraging, but there is a need for more detailed evaluation, before it can be considered an equal alternative to conventional surgery.
Aim:
The sim of the study is to compare the new transapical aortic stentvalve treatment with conventional surgical intervention in patients with severe aortic valve stenosis.
Study design:
Prospective randomized trial.
Material:
Inclusion of all patients with aortic valve stenosis aged 75 years and over, considered operable via conventional as well as transapical technique. Exclusion criteriae: prior heart surgery, need for revascularisation(PCI/CABG), dialysis.
Methods:
Patients will be randomized to either conventional surgery or transapical aortic stentvalve treatment. Primary endpoint will be a combined end-point consisting of death, CVI and/or renal failure with need for any dialysis, 1 month after index treatment.
Results:
11 patients included.
Conclusion:
The study results will provide information about the safety and quality of the new procedure, and hopefully be a guide in determining the procedure of choice in the future

P09.07 Torben Harsløf

THE EXPRESSIONAND REGULATION OF BONE-ACTING CYTOKINES IN HUMAN PERIPHERAL ADIPOSE TISSUE IN ORGAN CULTURE

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The cross-talk between bone and fat is an area of increasing interest. We investigated the expression and regulation of bone-acting cytokines in human peripheral adipocytes.
Human subcutaneous adipose tissue was aspirated from lean women during cosmetic surgery. Samples were divided into several aliquots, pre-incubated in for 24h, and subsequently cultured with IL-1β, TNF-α, cortisol, troglitazone, or control medium. Gene expression of BMP2, CTGF, OPG, RANKL, and TGFβ was determined at the mRNA level using real-time PCR. Target gene expression was normalized to the level of three house-keeping genes.
IL1-β, TNFα and cortisol significantly increased the expression of CTGF (ratio of medians of stimulation vs. control 1.65-2.01, $p<0.01$ for all) and OPG (ratio of medians of stimulation vs. control 1.62-3.10, $p<0.01$ for all) and significantly decreased the median expression of TGFβ (ratio of medians of stimulation vs. control 0.44-0.48, $p<0.001$ for all). The expression of BMP2 was not affected.
Troglitazone did not significantly alter the expression of any of the investigated cytokines.
This study for the first time shows that human peripheral adipocytes express the bone-acting cytokines, BMP2, OPG and RANKL. Previous studies show that IL1β, TNFα, and cortisol have adverse effects on bone quality. Our study suggests that this could be mediated by decreased production of TGFβ by peripheral adipocytes,

however, the increased production of OPG and CTGF would be assumed to counteract this effect. Studies investigating the effects in bone marrow adipocytes could further enlighten the topic.

P09.08 Christian Daugaard Peters

CARDIOVASCULAR EFFECT OF IRBESARTAN IN NEWLY STARTED HEMODIALYSIS PATIENTS – A SUBSTUDY WITHIN THE SAFIR-STUDY.

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Background: SAFIR is a multicenter study begun in April 2009 primarily designed to investigate whether an angiotensin II receptor antagonist (ARB) can preserve residual renal function among newly started hemodialysis patients (HD-pt.). This substudy within SAFIR focuses on cardiovascular disease (CVD) mechanisms and prevention. Patients with chronic renal failure suffer from a high risk of CVD and CVD mortality is markedly above what is seen in the general population. Several studies suggest that ARBs have a favourable effect on CVD that can not be explained solely by the blood pressure lowering effect of these drugs, but seems to originate from the ability of ARB to reduce arterial stiffening via inhibition of fibrosis and inflammation.

Hypotheses: ARB has a beneficial effect on the cardiovascular system in newly started HD-pt. causing:
Stable or less cardiac hypertrophy.
Less arterial stiffening.
Improvement of intra-dialysis hemodynamics.

Methods: 80 HD-pt. are recruited from dialysis centres in Skejby, Randers, Horsens, Viborg, Aalborg and Fredericia. Patients are randomized for treatment with either ARB (irbesartan) or placebo and followed for 1 year. Blood pressure is closely monitored and a systolic blood pressure level at 135-140 mmHg is the target among all patients. Blood- and urine sampling are done throughout the whole study period. Cardiac status is evaluated by echocardiography at entry and at the end of the study. The degree of arterial stiffness is measured noninvasively by applanation tonometry. Hemodynamic parameters during dialysis are obtained using ultrasound flow devices connected to the HD-machines.

Perspectives: Reduction of CVD-burden in HD-pt.

P09.09 Thomas Krusenstjerna-Hafstrøm

INSULIN SENSITIVITY AND SUBSTRATE METABOLISM BEFORE AND AFTER TREATMENT IN PATIENTS WITH GROWTH HORMONE DEFICIENCY

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Background: Growth hormone deficiency (GHD) is a disease caused by a lack of pituitary production of growth hormone, in adults typically because of a benign pituitary tumor. The chronic lack of growth hormone induces mutiple changes in body metabolism which are reversible by growth hormone treatment. We are now able to measure intracellular lipid content in liver and muscle using 1H-MR spectroskopy. Growth hormone treatment of GHD patients has direct and acute effect in both liver and muscle but the association between intracellular lipid content and insulin sensitivity is still unknown.
Aim: To characterize the treatment related changes in insulin sensitivity, substrate metabolism and intrahepatic-intramyocellular lipids in patients with growth hormone deficiency (GHD) before and after 3 months treatment with growth hormone.
Methods: 12 adult patients, recently diagnosed with growth hormone deficiency and

12 healthy controls matched on age, gender and BMI were investigated. Intramyocelluar, intrahepatic and intraabdominal lipid content were assesed using 1H-MR-spectroskopy, insulin sensitivity were calculated using HOMA, and lean body mass and body fat percentage were found using DEXA scan.

P09.10 Troels Thim

BARE METAL STENTS CRIMPED ON PACLITAXEL COATED BALLOONS: PHARMAKOKINETIC PROFILES AND EFFECTS ON LATE LUMEN LOSS AND NEOINTIMA FORMATION

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Background: Small prospective clinical trials have demonstrated the efficacy of paclitaxel-iopromide coated balloons in preventing restenosis in the coronary and peripheral arteries. Today, there is little data on the concomitant use of this technology along with bare metal stents. We tested the effect of a novel strategy, bare metal stent mounted on drug coated balloon to prevent restenosis in the porcine coronary injury model.

Methods: Different paclitaxel-iopromide formulations were used and their effects were compared to non-coated balloons. Bare metal stents (MeoFlex, MeoMedical) were crimped on all balloons and used to stent normal coronary arteries at a 1.1-1.2 stent to artery ratios. All animals were followed for 28 days for final angiograms and histopathology.

Results: There was no difference between groups in coronary artery diameters or stent to artery ratios at stent deployment. At 28 days, late lumen loss and neointima area were reduced in paclitaxel-iopromide groups compared to the control group. There were no adverse events in the experiment. Minimal amounts of fibrin and inflammatory cell infiltrates were seen in single sections in both coated balloon catheter groups but not in the control group.

Conclusion: The application of Paclitaxel along with a bare metal stent appears to significantly decrease restenosis compared to the regular non-coated balloon without delaying healing significantly.

P10.01 Marianne Bennetzen

ENDOCANNABINOID LEVELS ARE HIGHER IN THE ADIPOSE TISSIE OF OBESE WOMEN COMPARED WITH THOSE OF OBESE MEN

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Background: The endocannabinoid system consists of the cannabinoid receptors, the endogenous ligands that bind to these receptors, and the enzymes that synthesise and degrade the ligands. Obesity is associated with an over-activity of the endocannabinoid system. To clarify possible depot and gender differences, we investigated the peripheral endocannabinoid levels in the adipose tissue from two depots of obese men and women.

Materials and methods: Paired samples from subcutaneous adipose tissue (SAT) and visceral adipose tissue (VAT) were obtained from 10 obese women (age: 37.6 ± 2.3yr; BMI: 45.7 ± 1.2kg/m2) and 10 obese men (age: 37.9 ± 1.6yr; BMI: 45.3 ± 1.1kg/m2). We investigated the tissue with liquid-chromatography mass-spectrometry and RT-real time PCR.

Results: We found increased levels of both 2-arachidonoylglycerol (2-AG) ($p<0.05$) and anandamide ($p<0.05$) in both SAT and VAT of women compared with those of men. And both 2-AG and anandamide tended to be lower in the AT from VAT compared with SAT though this was only statistically significant for women ($p<0.05$,

2-AG and p<0.01, anandamide). We also found higher gene expression of FAAH in VAT than in SAT for both men and women (p<0.05).
Discussion: Because FAAH can degrade both endocannabinoids, the higher levels of FAAH in VAT compared with SAT can likely account for the difference in endocannabinoid levels in SAT and VAT. What took us by surprise, where the general difference between men and women of the same level of adiposity. A possible explanation for this phenomenon could be the inherent differences in the oestrogen and testosterone levels.

P10.02 Lea Brader

HEALTHY NORDIC DIET IN THE PREVENTION OF METABOLIC SYNDROME – THE AARHUS UNIVERSITY HOSPITAL (AUH) PART OF A MULTI-CENTRE STUDY (SYSDIET)

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Background: Sedentary lifestyle and increasing obesity have resulted in an alarming increase of metabolic syndrome (MeS). MeS can be described as clustering of risk factors, i.e. insulin resistance, central obesity, dyslipaemia, and high blood pressure, which links it to an increased risk of type 2 diabetes and cardiovascular disease. The traditional Nordic diet contains many food items including rape seed oil, berries, fruit, vegetables, whole grain and fish, which may favourably affect MeS. However, there are no studies available testing if a "healthy Nordic diet" (HN-diet) can reduce the main metabolic abnormalities of MeS. Thus, the beneficial health potential of a HN-diet in the prevention of MeS needs to be explored.
Aims: to evaluate the effects of a HN-diet on major abnormalities in MeS i.e. to 1) find out if a HN-diet could improve insulin sensitivity and other metabolic/physiological abnormalities in MeS, 2) identify new early markers for MeS, 3) study the effects of a HN-diet on gene expression, 3) study the effects of a HN-diet on lipid and metabolite profiles.
Method: The study is a controlled randomized parallel multi-centre dietary intervention involving 320 participants with MeS included from the 5 Nordic countries (40 recruited at AUH). The participants will be randomized to a HN-diet or a diet habitually consumed in Nordic countries for 6 month. At the major visits (0, 12 and 24 weeks) the participants will collect urine samples, complete a food diary and undergo clinical examination incl. blood pressure, body composition, adipose tissue biopsy, fasting blood samples and OGTT. In addition, postprandial lipaemia will be studied at 0 and 12 weeks at AUH.

P10.03 Helle Damgaard Zacho

FUNCTIONAL VERSUS RADIOLOGICAL ASSESSMENT OF CHRONIC INTESTINAL ISCHEAMIA

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Introduction The diagnosis chronic intestinal ischaemia(CII) is based on the clinical symptoms postprandial pain and weight loss combined with abnormal findings during angiography. Despite the well-known poor correlation between symptoms and morphology, physiologic tests are rarely performed.
It is possible to measure the total splanchnic blood flow (SBF) before and after a test-meal. The aim of this study was to correlate the SBF and angiogrpaphy.
Materials and methods Forty-six consecutive patients suspected of CII were investigated. The routine investigation included angiography and measurements of the SBF before and after a test-meal. Measurements of the total SBF were performed using the "Fick-principle". ^{99m}Technetium labelled Mebrofenin® was used as a tracer. Digital subtraction angiography was performed.
Results Agreement between SBF and angiography was found in 44 of 46 patients. Mean baseline SBF for all patients were 985 mL/min, total range (525 to 1932) and within the reported normal range. The mean postprandial increase in SBF was 480 mL/min (-130 to 1353), thus 36 patients were categorised as normal by both

angiography and SBF. Ten patients were suspected of CII due to a postprandial rise in SBF< 250 mL/min. In this group, eight patients had angiography also indicating CII, they were all referred to revascularisation. Two patients had abnormal SBF but normal angiography.
Discussion Agreement between SBF and Angiography was seen in 44/46 patients. In the two patients with discordent findings the affection of the intestinal arteries may be too distant or too subtle to be visualised on angiography, and these patients may benefit from medical treatment instead.

P10.04 Charlotte Amalie Ihlo

PHARMACOKINETIC AND PHARMACODYNAMIC PARAMETERS OF DIFFERENT INSULIN PUMP STROKE FREQUENCIES. A RANDOMIZED CONTROLLED STUDY COMPARING SUBCUTANEOUS AND INTRAVENOUS ADMINISTRATION OF INSULIN ASPART.

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Objective:
To study the pharmacokinetics and pharmacodynamics after subcutaneous bolus injections ones an hour (SBI), continuous subcutaneous insulin infusion (CSII), and continuous intravenous insulin infusion (CIII).
Research Design and Methods:
Ten patients with type 1 diabetes mellitus were given insulin aspart (IAsp) by SBI, CSII, and CIII, respectively. The insulin doses were individualized. A euglucaemic clamps aiming at near normal plasma glucose (pg) was performed.
Results:
A sinus variation of s-IAsp over time was found ($p < 0.0001$). However mean s-IAsp, and thus bioavailability (BA), did not differ significantly between SBI, CSII, and CIII ($p = 0.17$).
Variation of s-IAsp over time was significantly higher after CIII compared to SBI ($p= 0.023$) and CSII ($p = 0.013$).
Small, statistical significant differences were seen in mean GINF following the three administration modalities with mean pg highest and mean GINF lowest after CIII.
Conclusions:
We found small, but statistical significant differences in pharmacokinetics and pharmacodynamics after subcutaneous bolus injections once an hour (SBI), continuous subcutaneous insulin infusion (CSII), and continuous intravenous insulin infusion (CIII). The differences were small and most probably without clinical significance. Thus, more advanced insulin pump setting might not be reflected in a clinically important biodynamic response.

P10.05 Karina Bech Cullberg

REDUCTION OF ANGIOGENIC FACTORS AFTER WEIGHT LOSS WITH OR WITHOUT AEROBIC EXERCISE IN OBESE SUBJECTS. A 12- WEEK RANDOMIZED INTERVENTION STUDY.

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Objective: Obesity is associated with increased adipose tissue. To supply the growing adipose tissue with nutrients and oxygen, the vasculature responds by increasing the number and/or size of blood vessels. This expansion of the vasculature is dependent on vascular endothelial growth factor-A (VEGF-A) and angiopoietin-1 (Ang-1). One of the recently identified secreted factors from adipose tissue, angiopoietin-like protein-4 (ANGPTL-4), is found to be a potent anti-angiogenic factor.
Design: 1. Exercise-only (12-weeks of exercise), 2. Hypocaloric diet (8 weeks of very-low-energy-diet (VLED) followed by 4-weeks weight maintenance diet) and 3. Hypocaloric diet and exercise (8 weeks VLED + 4-weeks weight maintenance diet

combined with exercise throughout the 12-weeks).
Measurements: Serum levels of VEGF-A, ANG-1 and ANGPTL-4 were analyzed by ELISA. Moreover, gene expression of these angiogenetic factors was determined in adipose tissue biopsies by RT-PCR.
Results: ANG-1 concentration significantly decreased by 28% (P=0,002), and a tendency of decreased VEGF-A concentration was observed by 23% (P=0,054), after weight loss. However ANGPTL-4 levels increased significantly after weight loss by 31% (P=0,028). No significant changes of the gene expression of these angiogenetic factors were observed.
Conclusion: Our data show that plasma VEGF-A, ANG-1 and ANGPTL-4 levels are influenced by body adiposity and by weight changes, indicating the involvement of these factors in angiogenesis and in the expansion of adipose tissue that takes place in obesity. It is suggested that interaction with these angiogenetic factors may be a future treatment possibility for the obese state.

P10.06 Rasmus Pold

PSAMMOMYS OBESUS: A PROMISING ANIMAL MODEL OF TYPE 2 DIABETES

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Background: Psammomys Obesus (the Israeli sand rat) is a gerbil that in its natural environment feeds on low calorie diet. If the gerbil is introduced to normal rat chow it develops diabetes within 3-5 days. The aim was to determine if Psammomys Obesus fed on a normal chow diet for a short period would develop insulin resistance and β-cell changes when compared with gerbils fed on a low calorie diet.
Results: In gerbils fed on a normal diet for two weeks we found a significantly marked decrease in glucose infusion rate and ΔRd during the clamp when compared with gerbils on LED. Despite the high levels of insulin during the clamp the endogenous glucose production was only suppressed about 30% in both LED fed group and normal chow diet fed group. We found an increased β-cell mass in the normal diet fed gerbils and islets was depleted for insulin compared with LED fed gerbils.Methods:After an acclimatization period on low energy diet one group was fed on a low calorie diet (2.38 kcal/g) and the second group was fed on a normal chow diet (3.31 kcal/g). After one week the gerbils underwent surgery in order to have catheters inserted. They recovered on their allocated diets for another week and then they underwent a hyperinsulinemic euglycemic clamp (insulin infusion rate 35mU/kg/min) to measure whole body glucose uptake and to fully supress the endogenous glucose production.
Conclusion: The marked decrease in glucose infusion rate and ΔRd in gerbils fed normal diet demonstrate peripheral insulin resistance. The insulin resistance may have caused a compensatory increase in β-cell mass in gerbils fed normal diet.

P10.07 Jacob Thorsted Sørensen

REGIONAL IMPLEMENTATION OF PRE-HOSPITAL DIAGNOSIS IN ACUTE ST-ELEVATION MYOCARDIAL INFARCTION AND DIRECT ADMISSION TO INTERVENTIONAL HOSPITAL: IMPACT ON SYSTEM DELAY

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Prehospital diagnosis enables STEMI patients to be transferred directly to a PCI centre, eliminating treatment delay associated with initial admission at non-PCI hospitals. Reports on the benefit of such systems for early diagnosis have been published; however, there is limited information on the efficacy and success of expanding the networks to cover larger regions.

Aim:
To describe the share of STEMI-patients diagnosed in the ambulance and rerouted directly to a PCI centre in a 3-year period and the associated reduction in treatment delay.
Methods:
Prehospital ECG evaluation and phone interview by a cardiologist in patients with signs or symptoms of STEMI. In 2004 telemedicine was introduced in the region and gradually implemented in the ambulances, by 2006 covering the entire region. From 2004-2007 1024 consecutive STEMI patients in the study region were admitted at Skejby Hospital for primary PCI. All data were prospectively registered.
Results:
Prehospital rerouting to direct admission at PCI-centre: In early 2004: 43% of patients, In late 2006: 78% of patients
Prehospital ECG recording and telemedicine performed: In early 2004: 11% of patients, In late 2006: 73% of patients
Ambulance call to balloon inflation (mean time in minutes):
Telemedicine and rerouting: Rural area: 99 min. Urban area: 90 min.
No rerouting: Rural area: 173 min. Urban area: 140 min
Conclusion:Introduction of prehospital diagnosis and rerouting of STEMI patients in a large region:
1) is possible and feasible, even in a real-life setting with no special effort to introduce the technology
2) is associated with a significant and sustained reduction in treatment delay of > 1 hour

P10.08 Mads Brix Kronborg

LONG TERM CLINICAL OUTCOME AND LEFT VENTRICULAR LEAD POSITION IN CARDIAC RESYNCHRONIZATION THERAPY

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Background: In most CRT candidates the site of latest LV activation is lateral or posterior. Pacing at the site of latest activation has been suggested to give the best resynchronization. Previous studies have reported conflicting results in the effects of different LV lead positions (LV-PS) on echocardiographic and clinical outcomes.
Objectives: To identify the predictive value of a presumed optimal LV-PS on the long term clinical outcome in patients with CRT.
Methods: Clinical information was collected from patient files in consecutive patients treated with CRT from 1997 to 2007. A presumed optimal LV-PS was defined as a position between two and five o'clock in the short axis circumference and basal or mid-ventricular in the long axis. Symptomatic response was defined as improvement in NYHA class (≥1) and echocardiographic response as an improvement in LVEF of ≥ 5 % absolute.
Results: We included 567 patients (median age 66 years, 453 (80%) male). The LV-PS was optimal in 334 (59%) patients. The HR for all cause mortality with an optimal LV-PS was unadjusted 0.79 (0.59-1.06) and adjusted 0.99 (0.71-1.40). The OR for symptomatic response with an optimal LV-PS was unadjusted 1.13 (0.79-1.64) and adjusted 1.05 (0.67-1.64), and the OR for echocardiographic response was unadjusted 1.60(1.02-2.49) and adjusted 1.42 (0.88-2.31).
Conclusions: A presumed optimal LV-PS between two and five o'clock in the short axis circumference and basal or mid-ventricular in the long axis is not associated with a lower mortality or a better clinical response in patients treated with CRT.

P10.09 Hua Chen

THE ACUTE EFFECT OF SULFAPHENAZOLE ON INTRACELLULAR CALCIUM AND REACTIVE OXYGEN SPECIES IN MESENTERIC SMALL ARTERIES OF DB/DB MICE

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We have tested whether sulfaphenazole, a specific cytochrome P450 2C9 inhibitor, can improve the endothelial dysfunction of db/db mice (a model of type 2 diabetes). Furthermore, we aim to test whether the intracellular calcium ($[Ca^{2+}]_i$) transients and production of reactive oxygen species (ROS) are abnormal in these mice, and whether treatment with sulfaphenazole is affecting release of ROS. Obese db-/- mice and lean db+/- littermates were sacrificed after cervical dislocation. Small mesenteric arteries were dissected and mounted for $[Ca^{2+}]_i$ and ROS measurements. To measure $[Ca^{2+}]_i$ in endothelial cells, the vessel was first perfused intraluminally with 5 µM Calcium Green-1 and 3 µM Fura-red for 1 h. Then it was mounted on a wire myograph and examined using a confocal laser scanning microscope (LSM 5 PASCAL EXCITER, Zeiss, Germany). 50.8±6.8 % and 20.0±5.4 % of endothelial cells were found to respond to 0.5 µM ACh in db+/- and db-/- mouse arteries respectively. Incubation with 10 µM sulfaphenazole significantly enhanced the percentage of responding endothelial cells in db-/- rings ($p<0.05$). When measuring ROS production, the vessel was mounted in the same confocal myograph setup. CM-H_2DCFDA was used to quantify intracellular ROS concentration. The CM-H_2DCFDA fluorescence was significantly higher in arteries from db-/- mice compared to db+/- mice ($p<0.05$). Sulfaphenazole treatment significantly reduced the fluorescence signals. The above data suggest that sulfaphenazole may enhance endothelial dysfunction by increasing intracellular calcium within endothelial cells and decreasing ROS production in mesenteric small arteries of db-/- mice.

P10.10 Marta Bauerek

EFFECT OF DIETARY CHOLESTERYL ESTERS ON THE ABSORPTION OF CHOLESTEROL BY CACO-2 CELLS

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Background: Atherosclerosis is associated with high plasma LDL-cholesterol level. Clinical studies show that plant sterol treatment induces a reduction in serum LDL levels in mild hypercholesterolemic subjects. Therefore dietary plant sterols are recommended as adjunctive lifestyle treatment for hypercholesterolemia. While the absorption of intraluminal cholesterol and plant sterols is well described, the fate of dietary cholesteryl esters is unknown. Aim: To evaluate the effect of dietary cholesteryl esters on cholesterol absorption in human intestinal Caco-2 cell line. Methods: Cells were incubated in micellar solutions of ^{3}H cholesterol with or without unlabeled cholesteryl oleate. After specified incubation time media were discarded. Cells were washed with PBS and lysed in 0.1% SDS. ^{3}H cholesterol uptake was evaluated by determination of radioactivity in the cellular debris using liquid scintillation. To investigate cholesteryl ester uptake, cells were incubated with micelles containing ^{3}H cholesteryl oleate and analyzed as described above. Results: We showed that cells incubated with cholesterol micelles had accumulated 30% more cholesterol compared to cells incubated with micelles containing cholesterol and ester. It appears that inclusion of cholesteryl oleate in the micelles decreases the uptake of micellar cholesterol by CaCo-2 cells. Compared to cells incubated with cholesterol micelles, cells incubated with oleate micelles absorbed approx. 2-fold less labeled sterol. This suggests that uptake of the ester was significantly less than that of cholesterol. Conclusion: Our results indicate that cholesteryl oleate interferes with uptake of micellar cholesterol.

P11.01 Ania Pietraszek

POSTPRANDIAL DYSMETABOLISM - THE EFFECTS OF MONOUNSATURATED VS. SATURATED LIPIDS ON LIPID AND CARBOHYDRATE METABOLISM AND INFLAMMATION IN HEALTHY 1ST DEGREE RELATIVES OF PATIENTS WITH TYPE 2 DIABETES

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Type 2 diabetes (T2D) is a common disease associated with multiple complications and an increased risk of cardiovascular morbidity and mortality. 1st degree relatives of patients with T2D have an increased risk of developing T2D. This risk can be modified by the ingested diet: a diet rich in saturated fat increases the risk, while a diet rich in monounsaturated fat protects from development of T2D. The pathogenesis of T2D is partly explained by fasting dyslipidemia, postprandial dysmetabolism and impaired metabolic flexibility. Partly, it is explained by chronic low-grade inflammation in peripheral tissue. The dysmetabolism and inflammation are correlating entities exerting their influence through common pathways. This is established in patients with T2D, but sparsely studied in healthy relatives.
In this project we will study postprandial dysmetabolism, inflammation, oxidative stress, adipocytokines, inkretines, appetite regulating hormones and the expression of the genes involved in above mentioned. We will compare healthy 1st degree relatives of patients with T2D with healthy controls with no family history of T2D and look into differences in the response to meal stimulation with saturated and monounsaturated fat. The subjects will be examined with a hyperinsulinaemic euglycaemic clamp and a DEXA scan. Before and after the meal stimulation, we will take blood samples and perform muscle and adipose tissue biopsies. The biopsies will be used for studies of a vast number of genes.
The project will give us knowledge about the interaction between the intermediate metabolism and the innate immune system early pre-diabetic stages.

P11.02 Grazina Urbonaviciene

PLASMA ALPHA-DEFENSIN FOR PREDICTING CARDIOVASCULAR RISK IN PATIENTS WITH PERIPHERAL ARTERIAL DISEASE

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Background and Objective: Alpha-defensins are natural antibiotics made by neutrophils that have been reported to modulate cholesterol metabolism, vascular function, and associate with the presence and severity of atherosclerosis. We hypothesized that raised levels of plasma alpha-defensin could be useful in predicting cardiovascular (CV) outcomes in patients with peripheral arterial disease (PAD).
Methods: The study included 415 patients with PAD. Plasma alpha-defensin was measured by radioimmunoassay. The relationship between baseline plasma alpha-defensin levels and time to future CV events was assessed using Cox Proportional Hazard analysis.
Results: After a median time of follow-up of 43 months 210 patients reached the composite CV end point (17 death, 52 coronary, 26 cerebrovascular and 115 peripheral events). Cox-regression analysis showed that an increased level of plasma alpha-defensin was significantly associated with an increase in the risk of CV events to 1.66 (95% CI 1.08-2.55). After adjustment for age, gender, BMI, systemic hypertension, diabetes mellitus, smoking status, previous MI, total cholesterol, symptoms of leg ischemia, hs-CRP, use of β-blockers and angiotensin converting enzyme inhibitors plasma alpha-defensin levels retained its prognostic importance (HR=1.86; 95% CI 1.15-3.02). In this multivariable model plasma alpha-defensin ($p=0.012$) and previous MI ($p=0.001$) were independent predictors of CV events.
Conclusions: Elevated levels of plasma alpha-defensin were related to increased risk for CV events in PAD patients. Whether it provides independent prognostic information compared with other inflammatory markers will have to be assessed.

P11.03 Jane Byriel Knudsen

INFECTIVE ENDOCARDITIS: A CONTINUOUS CHALLENGE. THE RECENT EXPERIENCE OF A EUROPEAN TERTIARY CENTER

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Background and aim of the study: To monitor infective endocarditis (IE) before and after the condition was brought into focus in hospitals in the Aarhus region of Denmark.

Materials and methods: The prospective study included all 172 IE patients referred to the regional tertiary center during 2000-1 and 2005-6.

Results: A 137% increase in IE patients took place from 2000-1 to 2005-6 ($p < 0.01$). However, the delay from onset of symptoms to admission remained one month, with further prolongation of one week ($p < 0.05$) in 40% who had pre-hospital antibiotic treatment. Preceding health care instrumentation was recorded in 37% with ascending trend from 2000-1 to 2005-6. Six-month mortality was alarmingly high although the increase from 16% to 26% was non-significant. Independent predictors were prosthetic valve IE ($p = 0.02$), age ($p = 0.03$) and co-morbidity ($p = 0.05$); all three features increased over the five year interval.

Conclusions: Increased regional hospital attention to IE seemed to facilitate admission to our center. However, this did not improve survival, apparently because of unchanged admission delay and increasing age, co-morbidity, and prosthetic valve IE. Admission delay and health care induced IE are susceptible to modification. Future measures should therefore in particular focus on high-risk patients, improved education of GPs, and on facilitated access for the primary health care to blood culture and echocardiography.

P11.04 Eigil Husted Nielsen

USEFULNESS OF NATIONAL PATIENT REGISTRY DATA AND RELIABILITY OF ICD-8 AND ICD-10 CODES FOR THE IDENTIFICATION OF PATIENTS WITH NEWLY DIAGNOSED CRANIOPHARYNGIOMA

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Background: We wanted to identify patients with craniopharyngioma (CPH), but no Danish CPH-specific database exists.

Aim: To evaluate the National Patient Registry (NPR), selected ICD-8 and ICD-10 codes, and various search strategies in relation to identifying CPH patients.

Methods: The study period was 1985-2004. Four ICD-8 and three ICD-10 codes were applied to searches in the NPR and the local Neurosurgery, Endocrinology and Paediatrics registries (HDR), as well as the North Jutland County registry (COR). Medical files were reviewed, and each patient was assigned to one of the categories´A-G: A: verified CPH, B: probable CPH, C: benign cyst, D: unclassifiable cyst, E: old CPH, F: other disease and G: file not found.

Results: The North Jutland HDR, COR and NPR searches identified 74 patients, among whom the NPR identified 95% of A/B patients. From a DK-total of 684 records, 607 (89%) were reviewed and 207 assigned to categories A (159), B (26), C (17), or D (5). Category A/B criteria were fulfilled by 66% of those with NPR code 226.21 and by 62% with code D35.2. Sensitivities of 226.21 and D.35.3 were 93% and 87% for category A/B. PPVs were 66% and 62%. Sensitivities of the best code-department combinations were 0.73-0.94 with PPVs of 0.62-0.84.

Conclusions: The NPR was a useful source for identifying new CPH patients. Codes 226.21 and D35.3 showed high sensitivities but only moderate PPVs. Even the best search strategy should include a thorough review of medical records to exclude false positive cases.

P11.05 Tanja Tvistholm Sikjær

TREATMENT OF HYPOPARATHYROIDISM WITH SUBCUTANEOUS PTH (1-84) INJECTIONS: EFFECTS ON MUSCLE FUNCTION AND QUALITY OF LIFE

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Hypoparathyroidism is the only hormonal insufficiency state that is not treated by replacing the missing hormone. Conventional therapy includes treatment with calcium and 1a-hydroxylated vitamin D in order to relieve the hypocalcaemic symptoms. However, recent studies have shown that calcium homeostasis can be well regulated by PTH replacement therapy in patients with hypoparathyroidism.
Aim: The aim of the study is to assess whether PTH (1-84) posses advantages compared to conventional treatment in patients on muscle function, quality of life, calcium homeostasis, bone metabolism, and body composition.
Design: A double-blinded randomized placebo-controlled parallel-group trial comparing the effect of PTH (1-84). In the study, PTH treatment is added to conventional therapy with active vitamin D and calcium. A total of 60 patients with hypoparathyroidism are included. Duration is 6 months.
Outcome measures:
Muscle- and balance function: Effects of treatment on muscle strength and balance function are determined using a dynamometer and a stadiometer and through muscle biopsies, EMG and by biochemical measures. Quality of life: Effects measured by using the SF-36v2- and the WHO-Five Well-Being Index (WHO-5)-survey. Calcium homeostasis, bone metabolism, and body composition. Effects are measured by calcitropic hormones, biochemical markers of bone turnover, and iliac crest biopsies. In addition, bone mineral density and body composition is measured by DXA and Q CT scans. Perspective: As hypoparathyroidism is a life-long lasting disease, it is important to optimize treatment regimes according to the well being of patients and to minimize the risk of side effects.

P11.06 Sofie Gry Pristed CHANGES IN HEALTH-RELATED QUALITY OF LIFE AFTER GASTRIC BANDING

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BACKGROUND: Gastric surgery has been used for many years to treat morbid obesity. Morbid obesity is associated with co-morbidities, social stigmatization and reduced health related quality of life (HRQOL). HRQOL consists of multiple dimensions. When using the standardised questionnaire Short Form 36 (SF-36) emphasis is placed upon physical, emotional and social functioning. The SF-36 is through eight specific scales designed to provide assessment involving generic health concepts that are not specific to age, the illness or condition of the patient.
OBJECTIVE: To examine changes in HRQOL of life one and five years after gastric banding.
METHODS: A descriptive follow-up study. HRQOL is assessed using SF-36. The questionnaire was applied to the patients preoperational and one and five years postoperational.
RESULTS: Preoperatively the patients reported lower HRQOL as compared to the normal population in all of the eight domains, data not shown. Significant differences between the pre- and one-year postoperative HRQOL were found for all subscales except social function, role emotional and mental health, in favour of the postoperative HRQOL. Physical function 27.2 (95% CI 16.6;37.8; P<0.001). Role physical 40.5 (95% CI 20.6;60.3; P<0.05). Bodily pain 14.3 (95% CI 1.4;27.2; P<0.05). General health 15.7 (95% CI 8.6;22.8; P<0.001). Vitality 18.3 (95% CI 11.3;25.4; P<0.001). Social function 10.1 (95% CI -0.3;20.6; P=0.07). Role emotional 14.3 (95% CI -4.0;32.6; P=0.2). Mental health 5.1 (95% CI -2.8;13.1; P=0.2).
The final analysis concerning five year follow-up are still being prepared.

P11.07 Kim Munk REMOTE ISCHEMIC PERCONDITIONING BY REPETITIVE NON-INJURIOUS LIMB ISCHEMIA IMPROVES LEFT VENTRICULAR FUNCTION AFTER STEMI IN

PATIENTS WITH EXTENSIVE MYOCARDIUM AT RISK.
ECHOCARDIOGRAPHIC RESULTS FROM THE REMOTE ISCHEMIC PERCONDITIONING IN STEMI TRIAL

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Background: Remote ischemic perconditioning (rIPerC) i.e. episodes of distan organ ischemia while the heart suffers lethal ischemia, decreases infarct size and improves left ventricular (LV) function in animal models.

Objectives: To assess the effects of rIPerC, as an adjunct to primary PCI, on LV function in STEMI-patients.

Methods: In a andomized study, during ambulance transfer, patients with STEMI were allocated to rIPerC+primary PCI (n=145), or primary PCI alone (n=147). Outcome measures were global systolic longitudinal strain (GLS) of LV by speckle tracking-echocardiography and ejection fraction and volumes by 2D and 3D-echocardiography.

Results: The groups had comparable baseline characteristics. Overall, no difference was found in LV function, including myocardial strain analysis, on day one and after one month between patients assigned to rIPerC+PPCI and PPCI alone. Among patients with first LAD-MI, rIPerC-treated patients had a higher LVEF than those treated with PPCI alone, at day one (51±11% vs. 46±11%, p=0.034) and after 30 days (55±8% vs. 50±11%, p=0.037). In patients with extensive ^{99}Tc-sestamibi-SPECT-assessed myocardium at risk (>34 % of LV), those treated with rIPerC had a higher ejection fraction than those treated conventionally (51±7% vs. 45±9%, p=0.011) after one month.

Conclusion: Series of upper limb ischemia during transfer to PPCI improved residual LV function in the subset of patients with first LAD-STEMI and in STEMI-patients with extensive myocardium-at-risk.

P11.08 Maiken Glud Dalager

CT CORONARY ARTERY PLAQUE IMAGING, IMPACT OF DIFFERENT CONTRAST CONCENTRATIONS ON PLAQUE IDENTIFICATION

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Background: Characterizing non-calcified coronary plaques is a potential of coronary CT angiography (CCTA). CT-density characterized by Hounsfield Units (HU) may classify non-calcified plaques as fibrous or lipid-rich, but the intraluminal density caused by the iodine concentration in the contrast influences HU in the plaques in vitro. The influence of contrast density on HU in plaques in vivo is unknown.

Objective: To test if plaque characterization by CCTA depends on contrast density.

Methods: Two CCTA-scans using contrast with high and low iodine concentration were performed in 14 male coronary artery disease patients. Eleven non-calcified and 13 calcified plaques were identified and invasively confirmed by intravascular ultrasound (IVUS).

Results: A significant difference in luminal attenuation was achieved with the two types of contrast; 326[284;367] (High) and 118[103;134] (Low) HU (P<0.00001). In non-calcified plaques mean HU-values decreased from 48[28;69] to 11[-4;25] HU (P=0.004) when decreasing the contrast density. This decrease reclassified three plaques from fibrous (high) to lipid rich (low). Calcified plaques decreased less, but significant in HU-values from 770[622;919] HU to 675[496;855] HU (P=0.02) when

decreasing the contrast density.
Conclusion: Non-calcified plaques can be identified and classified by CCTA. The HU of both non-calcified and calcified plaques were significantly affected by the luminal contrast density. Changing the contrast density led to a change in sub-typing of non-calcified plaques. Characterization and classification of non-calcified plaques by absolute CT values therefore requires standardization of contrast protocols.

P11.09 Christian Høst

TESTOSTERONE ACUTELY SUPRESSES ADIPONECTIN LEVELS IN EXPERIMENTAL MALE HYPOGONADISM. A DOUBLE BLIND, RANDOMIZED, PLACEBO-CONTROLLED, CROSS-OVER STUDY.

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Context: Testosterone (T) decreases levels of circulating adiponectin (ADPN) and subforms in several setting of male hypogonadism. It is, however, still unclear whether this effect can be attributed to direct effects of T; likewise, T´s temporal effects on ADPN levels remain equivocal.
Objective: We investigated the effect of acute T substitution on ADPN and subform levels in experimental male hypogonadism.
Subjects and methods: 12 healthy young normal-weight men were examined on 4 occasions. In a double blind, placebo controlled and randomized cross-over study they received GnRH treatment on three occasions one month before trial days in order to achieve hypogonadal T levels. Acute substitution was performed with gel containing either physiological or supra physiological T or placebo. Total ADPN and ADPN subforms were measured using an in-house assay.
Results: In the eugonadal control arm ADPN was significantly suppressed compared to all hypogonadal arms, $P<0.00005$. By repeated measures statistics with ADPN as dependent variable, time*treatment (T) suppressed ADPN levels significantly in the treatment arms under basal conditions ($P=0.047$), whereas a trend was observed during both basal and hyperinsulinemic conditions ($P=0.085$).
Conclusion: We show, for the first time, that acute T substitution suppresses ADPN levels in male hypogonadism. During insulin stimulation, however, this effect diminished and was no longer significant. Thus, T suppresses ADPN levels acutely in hypogonadism, but insulin counterbalances this effect in the non treatment arms leaving the net decrement in ADPN levels equal during all four conditions.

P11.10 Bo Løfgren

INHIBITION OF THE MALATE-ASPARTATE SHUTTLE ABOLISHES CARDIOPROTECTION BY POSTCONDITIONING IN RAT HEARTS

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Objective: To investigate the importance of the malate-aspartate shuttle (MAS) for cardioprotection by ischemic postconditioning (iPCON). Furthermore, to study whether iPCON modulates metabolism of glutamate, a key metabolite of the MAS.
Methods: Four groups of isolated rat hearts were perfused and subjected to 40 min of global ischemia followed by 120 min reperfusion. iPCON was induced by 6 cycles of 10 sec reperfusion/10 sec ischemia. To inhibit the MAS the amino acid transaminase inhibitor aminooxyacetate (AOA: 0.025 mM) was administered during reperfusion. Hearts were allocated to 4 groups: 1) Control; 2) iPCON; 3) Control + AOA and 4) iPCON + AOA (n=10 in each group) and infarct size and left ventricular function were evaluated. Changes in coronary effluent and interstitial (microdialysis) glutamate were measured. In separate experiments intracellular glutamate $[Glu]_i$ was determined using radioactive tracer technique.
Results: iPCON reduced infarct size by 37% ($p<0.05$) when compared to control.

Inhibition of the MAS by AOA abolished the infarct reducing effect by iPCON ($p<0.001$). AOA did not affect infarct size in control hearts. Left ventricular function changed in parallel with infarct size. Myocardial release of glutamate was significantly decreased during iPCON ($p<0.001$) compared to controls. iPCON increased $[Glu]_i$ by 39% ($p<0.01$) compared to control. There were no differences in $[Glu]_i$ following 45 min reperfusion when comparing iPCON and control hearts, suggesting increased glutamate utilization in iPCON hearts.
Conclusion: Activity of the MAS is crucial for cardioprotection by iPCON. The mechanisms underlying iPCON includes myocardial glutamate metabolism.

P12.01 Christian Møller Pedersen

REMOTE ISCHAEMIC PRECONDITIONING PREVENTS SYSTEMIC PLATELET ACTIVATION ASSOCIATED WITH ISCHAEMIA-REPERFUSION INJURY IN MAN

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Background Modulating ischaemia-reperfusion (IR) injury may improve outcomes following ischaemia. In man, remote ischaemic preconditioning (RIPC) reduces myocardial injury following surgery although the mechanisms of RIPC remain poorly understood. We tested the hypothesis that RIPC reduced in vivo platelet activation after experimental IR injury in man. Methods Twenty-four healthy male subjects were randomised to undergo RIPC (a cuff inflated to 200 mmHg around the dominant upper arm for 5 minutes on 3 occasions, separated by 5 minutes of reperfusion) or sham, 30 minutes prior to induction of IR injury (a cuff inflated to 200 mmHg around the non-dominant upper arm for 20 minutes). In addition, 12 healthy males were randomised to sham+IR injury or sham+sham. Platelet-monocyte aggregation (PMA) was assessed using flow cytometery of whole blood at baseline, following RIPC, and 5 and 45 min following IR injury. Results There were no differences in PMA at baseline. Compared to baseline (25.7%), PMA was significantly increased at 5 (31.6%) and 45 (31.8%) min following sham+IR injury ($P=0.04$ for both) but not when IR injury was preceded by RIPC. Compared with baseline, neither sham nor RIPC alone had any effect on circulating PMA.
Conclusion: Systemic platelet activation occurs following IR injury in man. RIPC abolishes the increase in platelet activation associated with IR injury. Our findings support a role for platelet activation in the pathophysiology of IR injury and the mechanism of action of RIPC.

P12.02 Dorte Guldbrand Nielsen

PHYSIOLOGY – IS IT IMPORTANT TO KNOW WHEN LEARNING TRANSTHORACIC ECHOCARDIOGRAPHY?

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Background:
Transthoracic echocardiography (TTE) is an important non-invasive diagnostic tool in cardiology providing immediate dynamical information on cardiac structures and function. TTE is also a complex examination demanding high technical and interpretation skills of the physician. It is assumed that factors of importance for learning such skills include basal biological knowledge as well as perceptual-motor skills.
Research question:
To explore how knowledge of physiology is correlated with perceptual-motor and interpretation skills in TTE.
Hypothesis:

Physiology knowledge has an influence on skills level among novices, but not among intermediate or experts echocardiographers.
Material and method:
The study includes 45 doctors at three different levels of expertise; 15 novices, 15 intermediates and 15 experts.
We evaluate technical skills of all participants performing a TTE on a standardized patient. Pictures are stored digitally and two experts score the pictures on a checklist comparing these to a golden standard examination of the same patient.
We examine interpretation skills of the participants interpreting one TTE case showing a common and serious TTE condition. Participants then make a description of the TTE findings and fill out a checklist on possible pathologies.
Physiology knowledge is assessed by a 30 item multiple choice test of physiology of relevance to echocardiography.
Physiology knowledge will finally be compared to the results of TTE skills of the 3 groups of expertise.
Conclusion:
Data collection is accomplished and analysis is ongoing.

P12.03 Erik Grove

INCREASED WHOLE BLOOD PLATELET AGGREGATION IN CORONARY ARTERY DISEASE PATIENTS WITH A HIGH PLATELET TURNOVER

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Immature platelets reflect platelet production and turnover. We have previously shown that immature platelet levels are increased in patients with acute coronary syndromes. In this study we aimed to evaluate the presence of immature platelets in patients with stable coronary artery disease (CAD) and to investigate the importance of immature platelets to platelet aggregation in whole blood.
We included 177 CAD patients on aspirin monotherapy, including 85 type 2 diabetics. Immature platelets were detected by flow cytometry. Serum levels of thrombopoietin, soluble P-selectin and thromboxane B_2 were measured with ELISA. Whole blood platelet aggregation was determined using five agonist concentrations: arachidonic acid (0.5 and 1.0 mM), ADP (10 µM) and collagen (1.0 and 2.0 µg/mL). Immature platelet levels significantly correlated with platelet aggregation induced by all agonists ($r=0.21$-0.36, $p<0.01$) and with thrombopoietin levels ($r=-0.24$, $p=0.0014$) and P-selectin ($r=0.17$, $p=0.0276$). In diabetics, thrombopoietin ($p=0.0001$) and P-selectin levels ($p=0.0049$) were increased. Arachidonic acid induced residual platelet aggregation was also higher in diabetics ($p<0.01$) and serum thromboxane B_2 levels were less efficiently suppressed by aspirin ($p<0.0001$).
Immature platelet levels consistently correlated with increased platelet aggregation in whole blood. In diabetics, aspirin seems to confer a biochemically less efficient platelet inhibition. This may explain previous clinical findings of a reduced cardiovascular protection from aspirin in diabetics. Immature platelets may contribute to thrombus formation in patients with CAD and might increase the risk of cardiovascular events.

P12.04 Thais Almeide Lins Pedersen

LONG-TERM FOLLOW-UP AFTER SURGICAL CORRECTION OF COARCTATION OF THE AORTA: HIGH PREVALENCE OF CARDIOVASCULAR MORBIDITY

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Introduction: Coarctation of the aorta (CoA) is related to high cardiovascular

mortality and morbidity despite a successful surgical treatment. Late cardiovascular complications include recoarctation and systemic hypertension. The mechanisms behind those complications are poorly understood.
Objectives: to determine the prevalence of late complications 23 to 40 years after operation for CoA and clarify the pathophysiological mechanisms for the increased cardiovascular morbidity.
Methods: 246 patients were operated between 1965 and 1985, 178 of them are alive. Of those, 68 (mean age 41 Y) have been examined with: Anamnese; Clinical examination; ECG; Bicycle test + blood samples (renin, angiotensin II, aldosteron, BNP, ANF); 24 hour BP measurement; Echocardiography: colour Doppler, TDI and 3D; MRI; QOL (SF-36®). 40 additional patients will be examined in a near future and compared to 30 healthy controls.
Preliminary results: 38 (55%) had no follow-up; 30 (44%) had high BP at consultation (> 140/90 mmHg); 19 (28%) had hypertension on a 24-hour BP measurement (> 140/90 mmHg during daytime or > 135/85 over 24 hours); 16 (23%) had excessive BP response on bicycle test (SP ≥ 200 mmHg), 9 normotensives at rest; 9 (13%) had severe recoarctation on echocardiography and/or MRI and were referred to reintervention; 29 (42%) were referred to BP control or treatment; 31 (45%) were enrolled in a clinical and echocardiographic control.
Conclusions: Even successful repaired coarctation of the aorta is associated with excessive mortality and morbidity such as arterial hypertension and recoarctation, which often will need reintervention. Careful follow-up must be carried out for all patients.

P12.05 Rasmus Haarup Lie

CYCLOSPORINE A ADMINISTERED IMMEDIATELY BEFORE REPERFUSION DOES NOT ELICIT CARDIO-PROTECTION IN AN IN-VIVO PORCINE MODEL OF ACUTE MYOCARDIAL INFARCTION.

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Cyclosporine A has recently gained great interest in the research field of cardio-protection due to its ability to inhibit a mitochondrial folding protein which plays a pivotal role in ischemia reperfusion injury.
Method: Forty-eight pigs were randomized into three groups: Control group (Con, n=19), Cyclosporine group: Cyclosporine A 10mg/kg i.v. 5 minutes prior to reperfusion (Cyclo, n=19), Preconditioning group: Two cycles of 10min ischemia (Precon, n=10). The study was divided into a microdialysis protocol (n=32) and a coronary flow protocol (n=16). All pigs underwent 40min regional ischemia in the LAD territory followed by 180min reperfusion.
Results: The infarct sizes were: Con 51.4±16.5%, Cyclo 47.3±15.7%, Precon 2.4±3.6%. Con ↔ Cyclo: NS. Con ↔ Precon: Δ= 49.0% (35.2:62.7), Cyclo ↔ Precon: Δ=44.9% (31.1:58.6), both p<0.0001.
In the Cyclo and Precon groups the extracellular lactate concentration was significantly lower at 12, 14 and 16min of reperfusion: Con ↔ Cyclo Δ12= 1.34mmol/l (0.05:2.6) p<0.05, Δ14= 1.54mmol/l (0.3:2.8) p<0.01, Δ16 = 1.56mmol/l (0.3:2.9) p<0.01. Enhanced reflow was seen in the Cyclosporine and Precon group though only significantly different in the precon group at 12 and 14min of reperfusion: Con ↔ Precon: Δ12= 57.9 ml/min (28.4:97.3), p=0.01 and Δ14= 57.3 ml/min (16.7:99.1), p=0.01.
Discussion: Cyclosporine A had no ameliorating effect on infarct size. The accelerated lactate clearance in the Cyclo and Precon groups was largely explained by the concurrently enhanced reflow. Since a low pH protects the mitochondria at reperfusion, the accelerated lactate clearance may have worked in opposition to the putative beneficial effect of Cyclosporine.

P12.06 Ulla Kristine Møller

THE EFFECTS OF BREASTFEEDING AND AMENORRHEA ON CHANGES IN BONE MINERAL DENSITY POSTPARTUM. AN UNCONTROLLED FOLLOW-UP STUDY.

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Background: The postpartum period presents great challenges to the maternal calcium and skeletal homeostasis due to breastfeeding and low oestrogen levels. The relative impact of each of these factors on the reversible bone loss is unknown.
Aim: Elucidate the effects of breastfeeding and amenorrhea on changes in bone mineral density (BMD) postpartum.
Design: An uncontrolled follow-up study. 88 Caucasian women had BMD and sex hormones measured at 3 visits during a 9 month period after giving birth to a healthy child. Measurements were performed at 0.5, 4, and 9 months postpartum.
Methods: We studied correlations between length of breastfeeding and amenorrhea and changes in BMD.
Results: Overall, BMD decreased between visit 1 and 2 ($p<0.001$) with a subsequent increase between visit 2 and 3 ($p<0.001$). Length of breastfeeding as well as amenorrhea correlated negatively with changes in BMD between each visit ($p<0.04$) i.e., women who breastfeed and/or had amenorrhea for longest had the largest changes in BMD. Between visit 1 and 3 length of amenorrhea was the best and only predictor for BMD changes in whole body (41%, $p=0.001$) and lumbar spine (44%, $p<0.001$). On the other hand, neither of these indices could together or individually explain changes in the hip ($p>0.366$). Levels of sex hormones changes significantly over time ($p<0.001$). Prolactin correlated negatively with length of amenorrhea ($p<0.001$) and positively with changes in BMD whole body, lumbar spine and the hip ($p<0.04$) throughout the study.
Conclusion: Length of the breastfeeding and amenorrhea is of importance to changes in BMD and is most likely explained by changes in plasma levels of prolactin.

P12.07 Thomas Dalsgaard

NOVEL OPENERS OF SMALL CONDUCTANCE CALCIUM-ACTIVATED POTASSIUM CHANNELS ENHANCES ENDOTHELIUM-DEPENDENT VASODILATATION IN PORCINE RETINAL ARTERIOLES

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The present study investigated whether a selective opener of calcium-activated potassium channels of small (SK_{Ca}) and intermediate (IK_{Ca}) conductance, NS309, or a selective opener of $SK_{Ca}2$ and $SK_{Ca}3$ channels, CyPPA, enhanced endothelium-dependent vasodilatation in porcine retinal arterioles. Localization of $SK_{Ca}3$ protein and IK_{Ca} protein was examined by immunolabeling. Endothelial cell calcium was measured by fluorescence imaging. For functional studies, concentration-response experiments with bradykinin, NS309, and CyPPA, were constructed from isometric tension recordings in microvascular myographs. $SK_{Ca}3$ and IK_{Ca} protein was found localized to the endothelium. Bradykinin, but not NS309, increased endothelial cell calcium. Incubation with NS309 or CyPPA enhanced bradykinin relaxation, which was abolished by blocking SK_{Ca} channels with apamin. In the presence of NS309 or CyPPA, inhibition of NO synthase with asymmetric dimethylarginine and/or cyclooxygenase with indomethacin markedly reduced bradykinin relaxation. Bradykinin relaxation was completely abolished with inhibition NO synthase and cyclooxygenase together with a NO scavenger, oxyhaemoglobin. In porcine retinal arterioles, $SK_{Ca}3$ and IK_{Ca} protein is localized to the vascular endothelium. Bradykinin increases endothelial cell calcium followed by opening of SK_{Ca} and IK_{Ca} channels. Without altering endothelial cell calcium NS309 enhances bradykinin relaxation by activation of SK_{Ca} channels, which is mediated by NO and prostaglandins. These results implicate that opening SK_{Ca} channels improves

endothelium-dependent relaxation and makes them a potential target for treatments aimed at restoring retinal blood flow.

P12.08 Mikkel Misfeldt

PERIVASCULAR GLIAL CELLS ARE INVOLVED IN TONE REGULATION OF PORCINE RETINAL ARTERIOLES IN VITRO

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PERIVASCULAR GLIAL CELLS ARE INVOLVED IN TONE REGULATION OF PORCINE
RETINAL ARTERIOLES IN VITRO

Introduction
Disturbances in the retinal microcirculation secondary to impaired tone control of retinal arterioles are involved in the pathophysiology of several sight threatening diseases including diabetic retinopathy. Therapeutic intervention on these diseases requires a detailed knowledge of the functional and anatomical elements involved in the regulation of tone in retinal arterioles.

Methods
Porcine retinal arterioles (mean diameter 150 mM) were studied. Segments with a length of approximately 2 mm and a rim of approximately 2 mm retinal tissue preserved on each side of the vessel were mounted in a wire myograph (DMT). The preparation was loaded with the calcium sensitive fluorophore Oregon Green, and the vessel was pre-contracted with 1 uM of the prostaglandin analogue U46619.

Results
ATP and adenosine induced a similar concentration dependent relaxation of retinal arterioles ($p<0.01$). Blocking the degradation of ATP with the ectonucleotidase inhibitor AOPCP right shifted the vasodilating effect of ATP ($p<0.05$). During relaxation with ATP, but not with adenosine, fluorescence increased in the perivascular cells.

Conclusions
ATP induced vasorelaxation of porcine retinal arterioles is mediated through a distinct layer of perivascular cells located immediately outside the vascular smooth muscle cells. These cells might be related to the perivascular glial cells that have previously been shown to be involved in the pathophysiology of retinal vascular disease.

P12.09 Charlotte Strandhave

HAPTOGLOBIN PHENOTYPE PREDICTS LOW HEART RATE VARIABILITY IN PATIENTS WITH CHRONIC KIDNEY DISEASE

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Introduction:
Three major phenotypes for the haptoglobin (Hp) gene have been identified: Hp 1-1, Hp 2-2 and Hp 2-1. Hp 2-2 is associated with a poor outcome in several clinical conditions, such as diabetic nephropathy, due to a phenotype-dependent antioxidant capacity. Heart rate variability (HRV) may be an important predictor of mortality in patients with chronic kidney disease (CKD) due to increased risk of sudden cardiac death.
Aim:
To examine if Hp 2-2 is associated with a low HRV in patients with CKD.

Methods:
Patients (n = 61) were recruited from our outpatient clinic. They were eligible if they had a plasma creatinine level between 1.70 and 4.52 mg/dL for more than 3 months. The Hp phenotype was determined using a high-performance liquid chromatography. Furthermore, a 24-hour Holter recording was obtained in order to analyse 24-h HRV indices in the time domain.
Results:
The CKD patients were divided in three groups according to haptoglobin phenotypes: Hp 1-1 (n=12), Hp 2-1 (n=32), and Hp 2-2 (n=17). They were comparable regarding gender, plasma creatinine, BMI and haemoglobin, whereas there was significantly lower age (p=0.03) and plasma PTH (p=0.05) in the group of patients exhibiting Hp 2-2.
The HRV parameter SDNN was 129 ms (+ 43) in Hp 1-1 patients, 126 ms (+ 36) in Hp 2-1 patients, and 102 ms (+ 31) in Hp 2-2 patients (p = 0.02). Furthermore, SDANN was 111 ms (+ 45) in Hp 1-1 patients, 114 ms (+ 35) in Hp 2-1 patients, and 92 ms (+ 30) in Hp 2-2 patients (p = 0.04).
Conclusion:
CKD patients with Hp 2-2 had a significantly lower HRV compared to Hp 1-1 and Hp 2-1 patients. Thus, this phenotype may identify a group of CKD patients at high risk of sudden cardiac death.

P12.10 Anders Koustrup Niemann

ACCURACY OF COMPUTATIONAL 3D MODELS USING ULTRASOUND AND MR

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To facilitate a dialysis session an arteriovenous anastomosis (a-v fistula) is created between the radial artery and the cephalic vein changing the blood flow dramatically. Hemodynamic conditions cannot be visualized directly using current imaging modalities. Magnetic Resonance Imaging (MRI) and Computed Tomography (CT) are the golden standards for generating imagery suitable for data segmentation in order to generate 3D computational models. Hitherto, ultrasound has been unsuitable for this purpose due to problems with reproducibility caused by the extreme sensitivity of the technique. We have developed a method to obtain accurate image stacks using ultrasound relying on a step motor for providing a constant rate of advancement in the z-direction. We scanned an in vitro model using MR and ultrasound. The in vitro model consisted of two tubes with a side-to-side anastomosis between the two tubes comparable to an in vivo fistula. The images were segmented using ScanIP (Simpleware, Exeter, UK). The radius of the "vessels" of the model was measured on both MR and Ultrasound images using Matlab R2008a. The radii were known at the in- and outlets to be 2 and 3 mm, respectively. However, inside the "fistula chamber" itself, dimensions were unknown objectively but were estimated using cross-sectional areas converted to a fictional radius. Differences between the two imaging modalities were small with a maximal difference of 0.5 mm and average difference of 0.14 mm between ultrasound and MRI. Using the new technique to move the ultrasound transducer at a known rate produces highly accurate models suitable for generating 3D models for computational simulations.

P13.01 Mads Kjølby

SORT1, THE CARDIOVASCULAR RISK GENE AT 1P13.3 IS A NOVEL REGULATOR OF HEPATIC LIPOPROTEIN EXPORT

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Recent genome-wide association studies (GWAS) revealed strong association of hypercholesterolemia and myocardial infarction with a SNP on human chromosome 1p13.3. This locus covers three genes: SORT1, CELSR2 and PSRC1. We demonstrate that sortilin, encoded by SORT1, is an intracellular sorting receptor for apolipoprotein (apo) B100 that facilitates hepatic export of apoB100-containing lipoproteins. Absence of sortilin in gene-targeted mice reduces secretion of lipoproteins from the liver and ameliorates the hypercholesterolemic phenotype in low-density lipoprotein (LDL) receptor-deficient mice. In contrast, sortilin overexpression stimulates hepatic release of lipoproteins and increases plasma LDL levels. Our data uncovered a novel regulatory pathway in cholesterol homeostasis and demonstrate that SORT1 represents the cardiovascular risk gene on 1p13.3.

P13.02 Krista Kjærgaard

CYSTATIN C IS AN ACCURATE AND REPRODUCIBLE MARKER OF RESIDUAL RENAL FUNCTION IN PERITONEAL DIALYSIS PATIENTS

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Background: Measurement of residual renal function is important but the methods for determination are associated with problems, and the reproducibility of GFR estimations is not known. Our aim was to clarify variation and reproducibility of the available clearance methods using
plasma and renal clearances of 51Cr-EDTA as standards for total and renal clearances.
Methods: 12 stable peritoneal dialysis patients with urine output > 300 ml/24h underwent 2 separate and identical investigations approx. 1 week apart. 51Cr-EDTA was injected, and blood samples were drawn 6 times in 24h giving a plasma activity curve. Blood samples drawn 3h after 51Cr-EDTA injection were analysed for Cystatin C, creatinine, urea and albumin. Urine and dialysate were collected in the same period for measurement of creatinine, urea and 51Cr-EDTA activity. Total clearance based on MDRD-6 was compared to plasma clearance of 51Cr-EDTA, and mean of creatinine and urea renal clearance (CuC) and renal clearance of Cystatin C calculated as eGFR=-0.70+22*(1/Cystatin C) (CysC) were compared to renal clearance of 51Cr-EDTA (r51Cr).
Results: Paired t-tests on log-transformed data showed no statistical significant difference between methods regarding reproducibility but a significant difference between absolute values of CuC and r51Cr of doubtful clinical relevance.
Conclusion: Compared to r51Cr CysC seemed to be an accurate and reproducible method for calculation of residual renal function in peritoneal dialysis patients with no urine collection necessary.

P13.03 Maria Mærsk Nielsen

SATIATING EFFECTS OF MILK BUT NOT SUGAR- OR ARTIFICIAL-SWEETENED SOFT DRINKS AND WATER

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Energy-containing drinks may not convey proper satiety. As a result obesity and diabetes may occur due to the excessive amount of energy consumed. We seek evidence linking drinks to insufficient satiety and excessive energy intake as well as the mechanisms underlying this association. Methods: Our study is a crossover, intervention trial with 24 overweight subjects. After an overnight fast a 500ml drink (sucrose-sweetened soft drink (SSD), aspartam-sweetened soft drink (ASD), milk or water) was served. Blood-samples and satiety measured with visual analogue scales were collected at baseline and every 30 minutes. After four hours an ad libitum meal

was served and the energy intake calculated. Results: Compared to water milk caused 94% higher satiety (P= 0.008). The effects of the SSD were no different than water. There was significant increase of glucose after intake of the SSD compared to the ASD (P=0.0004), milk (P=0.0001) and water (P<0.0001). Ghrelin was significant lower after intake of milk than after water (P=0.008), and there was a tendency (not significant) towards Ghrelin being less decreased by the soft drink preloads compared to milk. However between the four preload drinks there were no significant differences in energy intake. Conclusion: Our study supports the notion that milk is more satiating than the equicaloric SSD, the ASD and water. The decrease of Ghrelin following milk intake is reflected in subjective satiety. Also the increase in glucose after intake of SSD did not increase satiety. However no significant differences in energy intakes between the four preloads support the notion that energy in drinks may cause higher total energy intake.

P13.04 Ulla Kampmann Opstrup

VITAMIN D STATUS IN PATIENTS WITH TYPE 2 DIABETES – A CROSS-SECTIONAL STUDY

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Vitamin D deficiency is a worldwide problem and causes rickets, osteomalacia and osteoporosis. The discovery that most organs and immune cells in the body have vitamin D receptors and that some also have the capacity to metabolize 25-hydroxyvitamin D to 25-dihydroxyvitamin D has provided new insights into the effects of vitamin D. Thus there is increasing evidence that vitamin D metabolism affects the risk of diabetes. However, most observational studies concern vitamin D status among healthy subjects and the risk of developing diabetes.

In this study we want to describe vitamin D status in a Danish cohort of patients with type 2 diabetes and to investigate the relation between vitamin D concentrations and glycemic control, measured by HbA_{1c}.

The participants in this cross-sectional study were patients with type 2 diabetes from the outpatient clinic at Silkeborg Regional Hospital. The recruitment period was from June 2008 to March 2009. 152 patients over 18 years of age we included. Exclusion criteria were malabsorption and renal failure (Urea > 12 mmol/l). 107 of the patients (70%) participated in a questionnaire survey concerning social class, medical conditions, vitamin D and calcium intake, sun exposure, smoking habits and physical activity. Blood samples were collected once in the period from November 2008 to March 2009.

Data is currently in preparation.

Perspectives: An inverse correlation between 25-hydroxyvitamin D concentrations and glycemic status would indicate that treatment of vitamin D insufficiency might be an easy and cost-effective method to improve metabolic control and prevent the serious complications associated with diabetes.

P13.05 Martin Majlund Mikkelsen

NO INCREASED OPERATIVE BLOOD LOSS IN PATIENTS WITH SEVERE AORTIC VALVE STENOSIS AND ACQUIRED VON WILLEBRAND SYNDROME UNDERGOING ELECTIVE AORTIC VALVE REPLACEMENT

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Introduction: Aortic valve stenosis can cause acquired von Willebrand syndrome (AvWS) and increase risk of bleeding from the gastrointestinal tract, skin and mucous membranes. Whether patients with AvWS have excessive blood loss during aortic valve replacement is unclarified. We hypothesized that patients with aortic

valve stenosis and AvWS undergoing elective solitary aortic valve replacement had a higher intraoperative and total blood loss within 24 hours of surgery as compared to patients without AvWS.
Methods: We consecutively enrolled 45 patients with severe aortic valve stenosis (orifice area 2) undergoing elective aortic valve replacement. To identify patients with preoperative AvWS we measured the von Willebrand factor ristocetin cofactor activity, the von Willebrand factor antigen level and the ratio of vWF ristocetin/vWF antigen. We also registered information on intraoperative and total blood loss within 24 hours of surgery. The blood loss was then compared between groups using the Mann-Whitney test.
Result: AvWS was found in 33% (15/45) patients. Baseline data did not differ significantly between groups with regard to age, gender, level of comorbidities and s-thrombocytes, APTT and INR. Patients with AvWS neither had excess intraoperative blood loss (375 ml [interquartile range 100-450 ml] vs 350 ml [interquartile range 250-500 ml], p=0.59) nor total blood loss (695 ml [interquartile range 450-850 ml] vs 752 ml [575-1035 ml], p=0.41) as compared to patients without AvWS.
Conclusion: Patients with aortic valve stenosis and acquired AvWS do not have increased blood loss during elective aortic valve replacement as compared to patients without acquired AvWS.

P13.06 Jesper Fleischer SELF-MONITORING OF AUTONOMIC NERVOUS FUNCTION AT HOME SHOW HIGHER VARIABILITIES WHEN COMPARED TO HOSPITAL TESTING

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Background: Cardiovascular autonomic neuropathy (CAN) is a frequent and potentially harmful complication of diabetes, and patients may suffer debilitating symptoms from all organ systems. Early detection and risk stratification of the individual patient may facilitate referral to correct treatment at the correct time. Because of the technical setups available today, testing for CAN is only recommended at the point-of-care office or in a clinical laboratory setting. The aim of this study was to evaluate feasibility of self-monitoring at home of autonomic function. Method: Ten healthy subjects were included (age 35 +/- 4, BMI 26 +/- 4). Participants underwent in-hospital testing for CAN before and after home monitoring. For 6 consecutive days twice a day participants measured autonomic function at home including inhalation/exhalation E:I ratio, response going from lying to standing 30:15 ratio and the Valsalva ratio. Self-monitoring at home was assessed using a handheld prototype device Vagus™ (Medicus Engineering Ltd, Denmark). Results: All participants were able to use the hand-held device. The mean difference between laboratory testing and self-monitoring was -0,024 (95% CI:-0.08-0.04); 0,095 (95% CI:-0.05-0.23); -0,097 (95% CI:-0.22-0.03); -17,5 (95% CI:-25 - -9.7) when E:I, 30:15, Valsalva ratio and SDNN(5 min) were measured respectively. Conclusions: The evaluations showed no significant difference between laboratory testing and self-monitoring at home. However, all tests but the response going from lying to standing (30:15 ratio) showed a tendency towards higher variabilities (indicating a lower level of stress) when testing at home as compared to hospital testing.

P13.07 Niklas Johan ADRENERGIC INNERVATION OF THE HUMAN THORACIC DUCT

Alexander Telinius

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Introduction
The lymphatic system consists of a vast network of vessels extending throughout the body. The role of this one-way transport system is twofold, 1) to maintain normal interstitial fluid volume and protein concentration gradient and 2) serving as a conduit for lymphocytes to the lymph nodes. By regulating the balance of tissue fluid the lymphatic system is one of the most important safety factors in preventing oedema. Our current knowledge of the innervation of lymphatic vessels is sparse and based primarily on animal studies.

Hypothesis
We hypothesize that the thoracic duct in humans has a functional adrenergic innervation.

Material and Methods
Thoracic ducts (n=17) were harvested during oesophageal cancer surgery. All vessels were mounted in a wire myograph (DMT 610M) for isometric force recordings. Cumulative concentration-response curves (CCRC) were created for noradrenaline (1nM-10µM) in all vessels except one. The last vessel was stimulated using electrodes with the purpose to depolarize the nerves in the vessel wall to release neurotransmitters.

Results
Maximal average tension produced after NA was 2.67 ± 0.34 N/m equalling 26.7 ± 3.8 mmHg. The maximal absolute tension produced was 4.46 ± 0.63 N/m, equivalent to 39.4 ± 6.3 mmHg.
The vessel stimulated with field stimulation responded with contractions identical with NA and 82% and 94% of the maximal average and absolute tension generated by NA, respectively.

Summary
We have shown that the human thoracic duct has adrenoceptors which can be stimulated by adding exogenous NA and upon nerve terminal depolarisation. We conclude that nerves can generate contractions at physiological relevant pressures.

P13.08 Rebekka Vibjerg Bækgaard Thomsen

MECHANISMS UNDERLYING RESISTANCE TO ISCHEMIC PRECONDITIONING IN DIABTES MELLITUS.

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BACKGROUND: Remote ischemic conditioning is a novel concept of protection against ischemia-reperfusion injury. The effectors of cardioprotection released by ischemic preconditioning is dialyzable and cross-species transferable from humans to rabbit hearts. The efficacy of ischemic preconditioning is decreased in diabetes mellitus, and in animal models an increased stimulus is required in order to induce cardioprotection. It is not clear whether the mechanism underlying reduced efficacy of ischemic preconditioning in diabetes is related to the production of a medication cardioprotective factor or a reduced ability to respond to the factor at the receptor site.
AIM of the study is to identify mechanisms underlying the attenuated activation of endogenous cardioprotective pathways by rIPC in diabetes mellitus.
METHOD: Bloodsamples are drawn from diabetic and non-diabetic testpersons before and after they undergo two intensities of rIPC stimuli; i.e. 4x5 minutes + 2x10 minutes inflation of a bloodpressure cuff around an arm. The cardioprotective effect of dialysat of plasma will be tested on Langendorff-perfused rabbit hearts and on

atrial strips from diabetic patients.
Dependent on the results of the outlined study further mechanistic studies will be planned.

P13.09 Michael Madsen CO-TREATMENT WITH PEGVISOMANT AND A SOMATOSTATIN ANALOGUE (SA) IN SA-RESPONSIVE ACROMEGALIC PATIENTS

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Acromegaly is a disease caused by excessive production of growth hormone (GH) from a pituitary adenoma. Active acromegaly is associated with increased morbidity and mortality. Surgery remains primary treatment, which provides "cure" in 50-60 % of patients. Retrospective surveys indicate that achievement of near-normal GH status is important in order to normalise mortality. Treatment with somatostatin analogs (SA) is able to control GH hypersecretion in 50-60 % of patients. A disadvantage with SA is the concomitant suppression of insulin secretion, which may cause glucose intolerance, and type 2 diabetes mellitus. Pegvisomant (Somavert®) is a specific GH receptor antagonist, which is able to normalise IGF-I levels in 97 % of acromegalic patients. Moreover, Pegvisomant improves glucose tolerance. The cost of the treatment is more expensive than that of SA. Co-treatment with a SA and Pegvisomant is theoretically attractive since it combines suppression of tumor activity with peripheral suppression of GH bioactivity and improved glucose tolerance. The main objective is to study if co-treatment will result in better disease control compared to SA mono therapy and if these effects can be obtained at a neutral cost. Methods: 18 acromegalic patients well-controlled on SA mono therapy were included in a non-blinded, parallel study over 24 weeks, randomised to either continue on SA-monotherapy or receive co-treatment with Pegvisomant and SA. They were examined at baseline and after 24 weeks of treatment with 1H-MRI spectroscopy, DEXA, a six hour metabolic study including a two hour hyperinsulinemic euglycemic clamp. 16 patients have completed the trial.

P13.10 Birgitte Kousholt CARDIAC NATRIURETIC PEPTIDE THERAPY IN A PORCINE MODEL OF ACUTE MYOCARDIAL INFARCTION

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Background: The heart produces natriuretic peptides (ANP and BNP) that regulate circulatory volume homeostasis through natriuresis, vasodilation, and vascular permeability. In addition, local effects within the heart musculature have been observed in experimental animal models, where both increased coronary blood flow and myocardial antifibrotic properties have been reported.
Hypothesis/Aims: To examine whether administration of exogenous BNP reduces infarct size during the first hours of acute myocardial infarction assessed by tetrazolium staining.
Materials and methods: Anaesthetized pigs (weight=25 kg) are subjected to coronary balloon artery occlusion of the distal LAD for 60 min followed by 180 min reperfusion. The experimental groups (n=8) will receive saline infusion (placebo) or exogenous BNP-32 (0.05 µg/kg/min respectively).
Results: Pending.
Conclusions: BNP treatment has been approved for acute heart failure but not for acute myocardial infarction. The results from the outlined project may thus contribute to the potential use of a BNP-related treatment strategy in acute coronary syndromes.

P14.01 Jette Ahrensberg CHILDHOOD MALIGNANCIES - SYMPTOMS AND DELAY IN DIAGNOSIS AND TREATMENT.

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Background: Timely diagnosis of childhood cancer is difficult because of the rarity of the disease and because of the nonspecific nature of its symptoms which mimick much more common conditions. Misinterpretation of ambiguous cancer symptoms by patients, parents and physicians may delay diagnosis and treatment.
Methods: As a first step in a larger study of delay in childhood cancer a review of the literature was performed.
Results:
Doctor delay is generally longer than patient delay. Mean delay times varied by cancer type from 2.5 weeks (Wilms tumors) to 29 weeks (brain tumor). The type of presenting symptom may account for some of the delay. Most studies report longer delay for older than for younger children. The influence of cancer type on delay still remains even after covariates like age have been taken into account. Socio-economic status has been reported to affect the distribution of delay. There are no previous Danish studies on the overall diagnostic delay in childhood cancer. Conclusions: Delay in childhood cancer seems to represent a particular problem in cancer delay. The symptom presentation in general practice remains uninvestigated. Research is needed to describe associations between the delay and symptoms, cancer type and patient characteristics and the newly introduced "fast track" for children. We propose a research design using the Danish Registry of Childhood Cancer and data obtained via questionnaires sent to parents and general practitioners.

P14.02 Merethe Kousgaard Andersen

THE OVERWEIGHT CHILD IN GENERAL PRACTICE - IDENTIFY, ASSESS, ADDRESS

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Background:The rapidly increasing prevalence of overweight among children is one of the most challenging dilemmas facing physicians involved in paediatric health care today. General Practitioners (GPs) seem ideally placed to take on this issue because in many countries they are the only source of primary health care accessible to families across most of the social spectrum. The family general practice is a potential setting for weight management in children as it provides both the opportunity and the potential for ongoing, frequent contact on a family-centred basis. Timely identification of overweight by GPs remains the crucial initial step in the prevention of child overweight. The annual routine health examination until age 5 may be a place to start. The use of basic assessment methods such as comparing the child's BMI with BMI-for-age and gender percentile charts is presumed helpful and prerequisite when correctly identifying and assessing overweight in children.

Objective: The aim of this study was to determine how GPs identify overweight, and to find out to what extend they assess causes and derived consequences of the overweight problem.

Design: A cross sectional survey of Danish general practitioners' self reported identification and assessment methods concerning child overweight.

Results: Data arriving.

Conclusions: As data have not been analyzed, no conclusions have been drawn.

P14.03 Lene Bastrup

IDENTIFICATION OF COPD PATIENTS' STRATEGIES FOR COPING WITH

Jørgensen

DYSPNOEA

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Introduction: COPD patients experience dyspnoea as the most exhausting symptom and develop coping strategies that may reduce important daily activites such as personal body care (PBC). We know that strategies are multidimensional but a more systematic characterization is needed

Aims: To identify typical strategies for coping with dyspnoea during PBC and to develop an instrument for identifying individual strategies, for intervention and advice

Methods: The study has two phases:1)A Grounded Theory design is used. 12-15 patients with severe to very severe COPD are recruited during hospitalization for an acute exacerbation of COPD. Data are collected through Video Based Narratives (VN) and combined with recordings of oxygen saturation (OS) and energy expenditure (EE) both during hospital stay and at home. VN contains videotaping patients 6 times during PBC and interviewed twice on the basis of video sequences. 2)Subsequently an instrument will be developed for identifying individual strategies and tested on COPD patients and health care professionals

Results: The study is in the 1. phase. Preliminary results based on 4 patients show, that patients on average during PBC desaturated respectively below 90% and 85% SaO2 in 54% and 37% of the time. The coping strategies seem to result in a certain level of activity during PBC. EE during PBC compared to EE during the day seem to support that the respons to PBC is a reflection of the individuals general coping strategy

Conclusion: Coping strategies, OS and EE are interrelated. Yet further characterization of the strategies is necessary to describe possibel correlation between the behavioral and physiological dimension of the strategies

P14.04 Jakob Kjeldgaard Jakobsen

TREATMENT OF FAECAL INCONTINENCE WITH SACRAL NERVE STIMULATION – IMPROVED FUNCTION WITH STIMULATION BILATERALLY

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Background: Faecal incontinence is a devastating condition causing psychological stress, affecting daily living and influencing quality of life. Faecal incontinence affects 0.8 to 6.2% of the adult population. The magnitude of the problem is underestimated, because most patients don't discuss this affliction with their general practitioner. Sacral Nerve Stimulation (SNS) has over the last decade given new hope to patients who don't benefit from conservative treatment. Unilateral SNS gives satisfactory continence results in 70% of patients offered permanent implantation of lead and an impulse generator (IPG). The remaining gets little or no improvement in continence.

Hypothesis: Bilateral SNS leads to improved continence and quality of life compared with standard unilateral stimulation.

Study: Prospectively study of forty patients with idiopathic faecal incontinence included consecutively. IPG's are implanted bilaterally. After 2-6 months of standard optimization, they are randomized to 3x1 month treatment with unilateral left/right or bilateral stimulation in a double blinded crossover design. In each period they fill in bowel diary cards and questionnaires including faecal incontinence severity scores and quality of life assessments. Anorectal physiology measurements are conducted at baseline and after each four week period. Bilateral SNS is compared with unilateral left/right SNS and baseline values.

Status: The study has been approved by The Central Denmark Region Committees on Biomedical Research Ethics, Danish Data Protection Agency the study is posted on ClinicalTrials.gov. The study is currently recruiting patients we don't have any

data to publish yet.

P14.05 Christina Malmose Stapelfeldt

THE DEVELOPMENT IN SICK-LEAVE AMONG YOUNG (<40 YEARS) NORWEGIAN AND DANISH ELDERCARE EMPLOYEES IN THE PUBLIC SECTOR BETWEEN 2000 AND 2010.

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Background: On average sick-leave days per full-time employee per year are twice the size in Norway (22 days) as compared to Denmark (10 days). This may partly be explained by structural differences. In a Norwegian study GP authorised sick-leave was replaced by self-administered sick-leave. Changing the structure, with which employees called in sick, effected young and older employees differently and led to an increase and decrease in sick-leave, respectively. The eldercare sector is challenged by high sickness absenteeism in both countries.

Objectives: 1) In a Norwegian and Danish national perspective to describe sickness absence and follow up changes between 2000 and 2010. 2) To study the consistency between sick-leave records of more than 14 days on workplace - and national register level. 3) To describe and analyse differences and similarities in patterns of sickness absence between employees from the eldercare sector in the municipalities of Kristiansand and Aarhus. 4) On an individual as well as on workplace level to study if the psychosocial working environment is associated to the number of sick-leave days or changes in patterns of sickness absence. 4a) Which pattern of sickness absence is predicting becoming a disability pensioner?

Materials and methods: Cross sectional and longitudinal study-design will be used. Data on public transfer payments from Norwegian (FD-Trygd) and Danish (DREAM) registers, work related information about the employees as well as the psychosocial working environment obtained by the Copenhagen Psychosocial Questionnaire (COPSOQ) constitute the materials. Statistical methods will be applied.

P14.06 Vibeke Bregnballe

FROM CHILD TO ADULT WITH CYSTIC FIBROSIS

V. Bregnballe

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Aim: To map out health care services that according to adolescents with cystic fibrosis and their parents can prevent decrease in essential disease-related physiological and quality of life parameters among adolescents.

Background: In adolescence many patients with cystic fibrosis experience declining lung function, stagnating growth, reduced compliance and quality of life as well as psycho-social and psychiatric problems, often irreversible continuing into adult life. Previous studies indicate that the adolescents are not prepared well enough for adulthood and that they need help concerning personal development in addition to help with coping with their disease. The parents might also need help to support their children.

Method: The study is descriptive and designed in two parts: a qualitative part with focus group interviews and a questionnaire-based quantitative part. Questionnaires are developed on the basis of focus group interviews.

Results: The qualitative findings will provide an estimate of which health care services can prevent a decline in disease-related parameters according to adolescents with cystic fibrosis and their parents. The hypotheses are tested using the questionnaires. The quantitative results are correlated to age, gender, disease severity, quality of life and the responses of the adolescents and parents, respectively.

Perspectives: Substantiated hypotheses for intervention studies can be generated from the results and illustrate the best use of resources. As the problems of this

study are probably also relevant for patients with other chronic diseases, the questionnaires can also be used for adolescents with other chronic diseases and their parents.

P14.07 Morten Søndergaard Jensen

IS PRENATAL EXPOSURE TO PARACETAMOL, ASPIRIN AND IBUPROFEN A RISK FACTOR FOR CRYPTORCHIDISM?

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BACKGROUND AND AIMS: Cryptorchidism (undescended testis) is a common malformation that affects 4-9 % of newborn boys in Denmark. Boys with cryptorchidism have markedly increased risk of testicular cancer and infertility in adulthood. Many Danish pregnant women occasionally use non-opioid analgesics, especially paracetamol (acetaminophen), which is considered safe to use during pregnancy. Animal studies show that arachidonic acid is important for the testosterone production in the testis' Leydig cells, and testosterone is considered necessary for normal testicular descent. By varying mechanisms paracetamol, aspirin and ibuprofen are capable of reducing the arachidonic acid synthesis, and it is hypothesized that the use of these drugs during pregnancy decreases testosterone production in the foetal testis and increases the risk of cryptorchidism.
METHODS: Data from 41 268 live born singleton boys of mothers enrolled in the Danish National Birth Cohort (DNBC) in 1996-2002 are used. During early childhood, 1598 cases of cryptorchidism were identified and 398 of these were orchiopexy verified. Information on cryptorchidism diagnoses (ICD10-codes: Q53, Q531, Q531A, Q532, Q532A and Q539) and corrective orchiopexy (codes KKFH00, KKFH01 and KKFH10 in the Nordic Classification of Surgical Procedures) was obtained from the Danish National Hospital Discharge Register. Maternal use of weak analgesics including the timing in pregnancy was assessed in one self administered questionnaire and 3 computer-assisted telephone interviews. Adjusted hazard ratios (HRs) of cryptorchidism are estimated by Cox regression.
RESULTS: Will be ready for presentation on PhD day 2010.

P14.08 Ann Dyreborg Larsen

RISK OF NEGATIVE BIRTH OUTCOME WHEN EXPOSED TO ADVERSE PSYCHOSOCIAL WORK ENVIRONMENT DURING PREGNANCY.

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Background: Studies in both animals and humans have shown that prenatal stress may interfere with development and behaviour of the offspring and increase the risk of congenital malformations, preterm birth, low birth weight and behavioural problems. Numerous studies have examined the effects of prenatal exposure to stress on birth outcomes but only few have included the impact from psychosocial work environment.
Objectives and hypothesis: The project aims to examine if exposure to adverse psychosocial workplace factors during pregnancy is associated with preterm birth, low birth weight and congenital malformations.
Material and methods: Population and data material is the Danish National Birth Cohort "Better health for mother and child". The cohort includes data from more than 100,000 pregnant women including interviews during pregnancy and after birth. Exposure data on psychosocial workplace factors is self-reported data from week 16 of pregnancy, which may allow assessment in relation to the dimensions of

the Karasek Job Strain Model. Data related to endpoints are obtained by from the interviews and from the Medical Birth Register and the National Hospital Discharge Register.
Data analysis: Statistical analysis using standard tools (logistic regression for prevalence data and survival analysis for follow-up data e.g. anomalies). Control for known potential risk factors such as mother's age, social class, smoking, alcohol intake, BMI, lactation, hereditary predisposition to allergies etc

P14.09 Mette Bach Larsen

DIAGNOSTIC DELAY IN CANCER IN PRIMARY HEALTH CARE -BEFORE AND AFTER THE INTRODUCTION OF FAST TRACK REFERRALS TO SECONDARY HEALTH CARE

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Introduction: On 1 April 2008 fast track referrals were introduced in Denmark for four types of cancer. Patients with specific symptoms of one of those cancers have the right to be referred urgently to secondary health care.
Aim: To analyze whether the introduction of fast track referrals to secondary health care influenced delay in primary health care.
Methods: 7,060 incident cancer patients were sampled from the patient administrative systems in two Danish regions six months before and after the introduction of fast track diagnosis. Questionnaires were sent to the patients' general practitioners providing information about the date of first contact with the GP and the date of first referral to secondary health care, enabling us to calculate diagnostic delay in primary care.
Results: No statistically significant difference in diagnostic delay in primary health care before and after introducing urgent referrals for suspected cancer neither for diagnoses with access to fast track ($p = 0.210$) nor for diagnoses without access to fast track ($p=0.069$).No statistically significant change in the percentage of patients with diagnostic delay in primary health care less than 30 days neither for diagnoses with access to fast track ($p=0.873$) nor for diagnoses without fast track ($p=0.138$).
Discussion/Conclusions: These preliminary results do not confirm the hypothesis that introducing fast track referrals for suspected cancer would influence diagnostic delay in primary health care. Further research is needed to uncover any difference between those referred to fast track and those who are not.

P14.10 Marianne Lisby

THE EFFECT OF SYSTEMATIC MEDICATION REVIEW IN ELDERLY PATIENTS ADMITTED TO AN ACUTE WARD OF INTERNAL MEDICINE

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Introduction: Elderly patients are vulnerable to medication errors and adverse drug events due to increased morbidity, poly-pharmacy and inappropriate interactions. The objective was to investigate if systematic medication review accomplished by a clinical pharmacist and clinical pharmacologist would reduce in-hospital length of stay (LOS) in elderly patients admitted to an acute ward of internal medicine.
Methods: A randomised controlled study of 100 patients aged 70 years or older was conducted on an acute ward of internal medicine in Denmark. Intervention: a clinical pharmacist conducted systematic medication reviews after an experienced medical physician had prescribed the patients medication. Information was collected from medical charts, interview with patients and database registrations of drug purchase. Subsequently, these informations were conferred with a clinical pharmacologist and recommendations for medication changes were completed. Physicians were not obliged to follow the recommendations. Control: medication was reviewed by usual routine in the ward. Primary end-point was in-hospital LOS. In addition, re-admission, mortality contact to primary healthcare and quality of life were measured

at 3-month follow-up.
Results: In the intervention arm the mean in-hospital LOS was 239,9 hrs (190,2-289,6) and in the control arm: 238,6 hrs (137,6-339,6), which was nor a statistical significant neither a clinical relevant difference. Moreover, no differences were observed for any of the secondary endpoints.
Conclusion: Systematic medication review and drug counselling did not show effect on LOS in elderly patients, when admitted to an acute ward of internal medicine.

P15.01 Julie Glavind

TIMING OF ELECTIVE CAESAREAN SECTION AND MORBIDITY OF THE NEWBORN

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Introduction: The caesarean section (CS) rate is rising globally. Studies have shown higher risk of respiratory disorders the earlier in pregnancy CS is performed. This has led some to recommend elective CS be performed after 39 weeks of gestation. The optimal gestational age at which to perform elective CS with respect to neonatal or maternal morbidity has never been studied in a randomized trial.
Aim of study: To compare neonatal and maternal morbidity after elective CS performed at 1) 38 weeks and 3 days of gestation with 2) 39 weeks and 3 days of gestation (both groups +/- 2 days).
Study design: Randomized controlled multicentre trial.
Population: 1010 women from 6 (8) Danish tertiary hospitals will participate. Recruiting period is estimated to 1.5 years.
Primary Outcome: Neonatal admission within 48 hours after elective CS.
Secondary Outcomes: 1) Neonatal. Umbilical arterial pH and sBE. Apgar score and if admission – duration, diagnoses, treatment. Breastfeeding 2 months post partum (p.p.)
2) Maternal. Intraoperative complications (haemorrhage, uterotonic agents, organ laceration). Duration of admission. Postoperative complications (bleeding, infection, reoperation, antibiotics). At 2 months p.p. wound pain, depression and satisfaction with timing of elective CS. 3) Logistics.
Inclusion: Elective CS. Gestational age verified by ultrasound. Singleton pregnancy.
Exclusion: Under 18 years of age. Need of an interpreter. Diabetes. Estimated high risk of having CS before 39+5 weeks.
Trial Status: 214 participants are included by August 2009, of these 116 women had a CS. Questionnaire respond rate is 94 %. Compliance with allocated treatment is 109/116 ~ 94%.

P15.02 Nellie Bering Zinther

ADHESION FORMATION, SHRINKAGE AND BIOMECHANICS OF PROSTHETIC MESHES AFTER LONG-TERM INTRA-ABDOMINAL IMPLANTATION IN A SHEEP MODEL.

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Background: Laparoscopic ventral hernia repair uses an intraperitoneal prosthetic mesh and fixation devices (IPOM-technique). Mesh adhesion, shrinkage, and ingrowths to the abdominal wall, may influence the long term results. This study aimed to compare extent of adhesions, shrinkage, and incorporation to the abdominal wall 3, 6 and 12 months after intra-abdominal placement of two different meshes, with two different fixation devices.
Methods: Twelve sheep each received laparoscopic placement of four (10x10 cm) meshes on intact peritoneum. Two meshes and fixation devices were investigated: DynaMesh, Parietex, ProTack, and AbsorbaTack. After 3, 6 and 12 mounts four

animals respectively, underwent a new laparoscopic procedure were the extent of intraabdominal adhesions were described. The animals were sacrificed and meshes were extracted. Prosthetic shrinkage and biomechanics were recorded. Groups were compared using Student´s t-test.
Results: There were significantly more adhesions to DynaMesh than to Parietex at all time points. Parietex underwent significant more shrinkage than DynaMesh after 3, 6 month, and 12 months ($p<0.01$). In the biomechanical testing, there were no significant difference in total energy between the different meshes and fixation devices.
Conclusion: Current literature reports short-term result after open anchoring of stamp-size meshes. This study is the first long-term animal study with laparoscopic anchoring of large meshes. This study is applicable in future studies on mesh and fixation devices. In the animal study we found significant difference between the different meshes with regards to both adhesion and shrinkage.

P15.03 Bjarne Otto Rittig-Rasmussen

NECK PAIN, NECK TRAINING AND CORTICAL PLASTICITY.

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By tradition musculoskeletal pain research has focused on peripheral tissues and biomechanical factors, but this pain should be looked upon in the light of new research. Research which demonstrates that pain can be accompanied by measurably cortical plastic changes.
Hence, the hypothesis of this study is to demonstrate a difference in transcranial magnetic stimulation (TMS) induced neuronal plasticity measured by motor evoked potentials (MEP) in patients with chronic neck pain versus healthy controls.
To answer this hypothesis we will perform the following experimental studies: 1. Measure MEP of defined neck muscles during TMS of the motor cortex. 2. The correlation of MEP and performance of preprogrammed movements in the NeckTech3000 © with and without experimental pain. 3. The correlation between changes in MEP amplitudes and chronic neck pain.
In the preliminary pilot study we have investigated the corticomotor excitability in seven healthy participants, before and after neck training. MEPs were measured from the unilateral trapezius muscle and from the thumb muscle which was used as a control. Using the related t-test we found an MEP amplitude increase after neck training equivalent to 213 µV ($t = 1.906$, $p=0.11$). Latencies in the neck MEPs were unchanged ($p=0.56$), MEPs and latencies from the thumb muscles were also unchanged ($p=0.85$ and $p=0.53$).
The results from these pilots do not show any statistically significant increase in neuronal plasticity or excitability following neck training. Despite the few changes in MEPs in these preliminary results, these changes seem to be clinical relevant. Accordingly we will pursue these studies.

P15.04 Dorte Rytter

MATERNAL INTAKE OF FISH OIL AND RISK FACTORS FOR THE METABOLIC SYNDROME IN THE 18 YEAR OLD OFFSPRING

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Background: A number of interconnected disorders constituting the metabolic syndrome together strongly predispose for the development of CVD and type II diabetes. It is well established that several of these risk factors exhibit strong tracking

from early childhood into adult life and an increasing body of evidence supports that cardiovascular diseases (CVD) have origins in the foetal or neonatal environment. Studies in both humans and experimental animals have suggested that changes in the peri- and early post-natal intake of n-3 polyunsaturated acids can affect the development of CVD risk factors in adult life. This leads to the hypothesis that n-3 fatty acid supplementation in the latter half of normal pregnancy will have a beneficial impact on offspring CVD risk.
Specific aims: To investigate the effect of fish oil supplementation during third trimester of uncomplicated pregnancies on blood pressure, autonomic function, and glucose and lipid metabolism in the 18 year old offspring.
Research design and methods: The study is based on long term follow-up of a randomised controlled trial from 1990, in which 533 pregnant women were randomised to fish oil, placebo with olive oil or no oil.
Briefly, all children will be invited in writing and those accepting to participate will be given a standard physical examination including blood sampling and measuring of mean arterial blood pressure, waist circumference, BMI and heart rate variability. A subgroup of children comprising the off-spring from women categorized as having a low basic fish-intake will undergo additional examination including 24 hour heart rate variability.

P15.05 Trine Guldberg

DEVELOPMENT AND EVALUATION OF ELECTRONIC FEEDBACK, A TOOL FOR QUALITY ASSURANCE OF THE DIABETIC CARE IN GENERAL PRACTICE.

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Objective: To evaluate the effect of an electronic feedback system (EFS) to general practitioners (GPs) on quality of care for people with type 2-diabetes (T2D).
Method: 86 general practices (158 GPs) in a Danish county caring for 2458 people with T2D were randomised to receive electronic feedback or not. People aged 40-70 years with prevalent T2D were identified from registers using a validated algorithm. A quantitative evaluation is performed on one year follow-up data of fulfilment of guidelines in relation to prescribed medication, measuring HbA1c and cholesterol, level of HbA1c and cholesterol and diabetes related visits to ophthalmologists. Additionally, a qualitative evaluation of the impact of the EFS, seen from the GPs' point of view, is performed. Ultimately, using a mixed method approach an attempt is made to explain the mechanisms behind the detected quantitative effects of the EFS, using qualitative data collected through interviews with the intervention participants.
Results: Significantly ($p<0,03$) more antidiabetic medication was prescribed in the intervention group compared to the control group: oral antidiabetic drugs (Δ: 21.4%), lipid lowering drugs (Δ: 19.7%), insulin (Δ: 27.4%) and blood pressure lowering drugs (Δ: 11.3%). New overview of patient populations, provided by the EFS, facilitated increased attention to patients previously poorer cared for as well as allocation of diabetes care to nurses. This could be a mechanism behind the observed improvement in quality of care
Conclusions: An EFS containing new overview of patient data could spawn increased attention to diabetes care and organisational changes, leading to improvement of process measures.

P15.06 Mette Trøllund Rask

DIAGNOSTIC CLASSIFICATION OF MEDICALLY UNEXPLAINED SYMPTOMS IN PRIMARY CARE

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INTRODUCTION: MUS or functional somatic symptoms are very frequent in general practice. MUS represent a spectrum of disorders ranging from mild symptoms to serious and persisting disorders. However, current diagnostic classifications of MUS only include single symptoms or chronic cases of somatoform disorders leaving many patients undiagnosed or misclassified.
AIMS: Development and test of diagnostic criteria for a new classification of mild to moderate MUS in general practice.
METHODS: A diagnosis 'Multiple symptoms' specified as 3 or more symptoms not verified as diseases/disorders during the last 6 months was tested using a short questionnaire. During 2 weeks 20 general practitioners (GPs) classified symptoms presented in about 2000 consecutive consultations according to the International Classification of Primary Care (ICPC) and the new category 'multiple symptoms'.
RESULTS: Prevalence of symptoms not attributable to any conventionally defined disease and the GPs' classification of these as: 1) Multiple symptoms, 2) Patient fear of having a disease, 3) Self-limiting or in need of further investigation, or 4) Somatoform disorder will be presented along with variation in GPs' MUS diagnostics.
PERSPECTIVES: This ongoing project includes a register study of GP diagnostics related to MUS, focus group discussions of the clinical utility of 'multiple symptoms', qualitative assessment of the validity of this diagnosis, and a controlled study of the precision of GPs' MUS diagnostics. Valid diagnostic classification of MUS in general practice is a prerequisite for high-quality clinical research, appropriate academic education, and for improved treatment of patients.

P15.07 Ioannis Basinas

EXPOSURE ASSESSMENT OF DUST AND PATHOGEN ASSOCIATED MOLECULAR PATTERNS (PAMPS) IN DANISH FARMS. THE SUS12 STUDY.

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Aim: To assess current and retrospective exposure to dust and PAMPs in the framework of a 15 year follow-up of a young Danish farmers cohort.
Methods: A questionnaire was used to identify the remaining active farming population of the initial cohort. Based on the results 26 cattle and 54 pig farms were selected, and visited summer and winter 2008-9. Additionally, 3 poultry and 4 mink farms were visited during 4 well defined production stages. Full-shift personal inhalable dust samples were collected from 323 farmers, who filled in activity diaries for 1 week during each visit. Information on technical parameters and farm characteristics with alleged influence on exposure was collected through interviews and walk through surveys. For cattle and pig farmers, linear mixed models will be used to model associations between parameters, farm characteristics, tasks and exposure. Assessment for poultry and mink farmers will be based on exposure matrices. The derived equations will be used to estimate exposure for all study participants.
Results: Overall dust concentrations ranged from 0.1 to 48 mg/m^3 with a Geometric mean (GM) of 2.5 mg/m^3. Exposure differed significantly between farm categories ($p<.0001$). The highest GM dust levels were found among poultry layer farmers (5.5 mg/m^3), followed by pig (3.3 mg/m^3), poultry broiler (3.1 mg/m^3), mink (1.3 mg/m^3) and cattle farmers (1.0 mg/m^3). A positive trend between dust exposure among broiler poultry farmers and chicken age was also observed.
Prospects: Our results are in concordance with the literature. Currently endotoxin, glucan and common allergen concentrations are determined. Subsequently, the modeling process will be initiated.

P15.08 Christian Wulff

THE EFFECT OF CASE MANAGEMENT IN COMPLEX CANCER PATHWAYS

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Introduction: Case management (CM) has been proposed as a method for optimizing the course of treatment for complicated cancer patients. However evidence of the effect of CM is limited and methodologically rigorous research is needed.
Aim: To analyze effects of Nurse CM in complicated cancer care.
Methods: Two-arm randomized controlled trial (RCT) including approximately 280 colorectal cancer patients.
Intervention group patients are offered usual medical treatment plus supportive intervention from a case manager. Control group patients receive usual medical and supportive treatment.
The intervention: Case managers are registered nurses and possess thorough knowledge of cancer treatment and pathways. Core intervention elements: Planned and ad hoc personal and telephone contacts, surveillance of care pathways, coordination and dissemination of care plan (including transfer of patient-specific information to other departments and general practice).
Results:
Primary outcomes: Patient evaluations of care pathways and "Quality of Life" (questionnaires).
Secondary outcomes: Use of health care services and care process measures (The National Health Insurance Service Registry and The National Patient Registry; and GPs' evaluations of continuity of care (questionnaire).
Schedule:
"Case management used to optimize cancer care pathways: A systematic Review" has been published in BMC Health Services Research.
A CM manual and questionnaires has been developed.
Two case managers were appointed 1. January 2009.
After training and pilot testing of the intervention the RCT began in March 2009.
Inclusion period is 14 months.

P15.09 Hjördis Osk Atladottir

THE ASSOCIATION OF MATERNAL INFECTION REQUIRING HOSPITALIZATION DURING PREGNANCY AND AUTISM SPECTRUM DISORDER: AN EXPLORATIVE DANISH COHORT STUDY

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Introduction: Maternal infection during pregnancy has been suggested to cause adverse fetal brain development. The present study investigates the effect of maternal infection requiring hospitalization during pregnancy on the subsequent development of Autism Spectrum Disorder (ASD) in the offspring, using a large scale epidemiological study design.
Methods: A population based cohort study, including all children born in Denmark from January 1, 1980, through December 31, 2005, a total of 1,583,520 children. Cases of ASDs were obtained from the Danish National Psychiatric Register using ICD-8 and ICD-10. Data on diagnoses of maternal infection were obtained from the Danish National Hospital Register. Possible associations were tested in Cox regression models. Results are not adjusted for multiple testing.
Results: A total of 10,005 children were diagnosed with ASD. No association was found between different maternal infections and a diagnosis of ASD in the child when looking at the total period of pregnancy. Admittance to hospital due to

maternal viral infection in the first trimester: adjusted HRR=2.90 (CI: 1.21;6.99) and maternal bacterial infection in the second trimester: adjusted HRR=1.48 (CI: 1.13;1.93) were found to be statistically significantly associated with the development of ASD in the offspring.
Conclusions: We observed no overall association between a variety of maternal infections requiring hospitalization during the total length of the pregnancy and development of ASD in the child, however the results support prior hypotheses concerning early prenatal viral infection increasing the risk for ASD.

P15.10 Kasper Grosen

PREDICTION OF THE CONSUMPTION OF OPIOID ANALGESICS FOLLOWING MINIMALLY INVASIVE CORRECTION OF PECTUS EXCAVATUM

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OBJECTIVES: Surgical correction of pectus excavatum is primarily performed to obtain cosmetic and psychological benefits for the patient. This study estimates the effect of the severity of pectus excavatum on the postoperative consumption of opioid analgesics following this procedure in order to optimize pain management.
METHODS: A retrospective study was conducted on 236 consecutive patients undergoing minimally invasive repair of pectus excavatum from 2005-2008. The collected data included among other things depth of preoperative pectus excavation and data on pain management. The consumption of opioid analgesics was registered after discontinuation of epidural analgesia and other types of opioid analgesics used during the study period were converted to morphine equivalents. Multiple linear regression analysis was performed to estimate the effect of the severity of pectus excavatum on the postoperative consumption of opioid analgesics and to adjust for potential confounding.
RESULTS: Multiple linear regression analysis explained approximately 30% of the variation in daily morphine consumption (R-squared=0.2957). There was a significant positive linear relationship between pectus severity and daily consumption of morphine. Thus, postoperative consumption of morphine increased by 6% (95% CI: 0.3 to 11%) when preoperative pectus excavatum depth deteriorated with 1 cm.
CONCLUSION: This study confirms that pectus severity has a significant impact on the consumption of opioid analgesics following minimally invasive repair of pectus excavatum. We conclude that knowledge of pectus severity might be useful in the prediction of the expected morphine consumption in future patients.

P16.01 Lise Juul

A PRACTICE-NURSE ADDRESSED INTERVENTION TO ENHANCE SELF-MANAGEMENT IN PEOPLE WITH TYPE 2 DIABETES. A RCT IN PRIMARY HEALTH CARE.

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Background: A huge challenge in type 2-diabetes care is how to motivate patients to health behaviour change. The majority of patients with type 2-diabetes are taking care of in general practice, and some of their consultations are provided by nurses. Observational studies with self-determination theory as the underlying theory found the perception, that ones behaviour is self-chosen and meaningful (autonomous self-regulation), and perceived competence as predictors of improved HbA1c- levels among patients with type 2 diabetes. Research is needed to develop and test interventions that support patients´ autonomous self-regulation and perceived competence.
Aim: To investigate the effect of a training course for practice nurses in autonomy support in patients with type 2 diabetes by

1. Describing the extent of implementation in daily practice, 2. Evaluating the effect of the intervention on patient outcomes, 3) Assessing the association between effect of the intervention and patients´ sex, age, and education-level.
Methods: The intervention was developed using a logic model approach. A logic model is a graphic representation of a program that describes the program's essential components and expected outcomes. The intervention will be evaluated in a cluster randomized controlled trial with 40 general practices and about 2500 patients with type 2 diabetes. The patients will be followed 15 months from nurse-participation in the course. Data will be collected from registers, and primary outcomes will be changes in HbA1c and total-cholesterol.
Status: The intervention will take place in the autumn of 2009. The follow up data will arrive in February 2011.

P16.02 Jens Christian Jensen

THE ODDER PROJECT: PREDICTORS OF MUSCULOSKELETAL PAIN, WITH EMPHASIS ON THOSE LEADING TO CONSULTATIONS IN PRIMARY CARE
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Musculoskeletal pain is a common condition with a multifactorial origin. It is unclear why some patients with musculoskeletal pain consult their GP, while others with the same pain level do not. Physical factors and psychological factors at the workplace a well as individual factors have been related to low back pain and pain in the upper limbs. This project attemps to describe such factors and their relation to care-seeking behaviour. The purpose is to identify factors predicting care-seeking in relation to an upcoming intervention programme.
8,517 men and women, between the ages 17 and 65 years, listed with eight General Practitioners (GPs) in the town of Odder, Denmark, were identified. A baseline questionnaire adressing issues related to musculoskeletal pain was sent to all participants and all diagnosis made by the GP in relation to these symptoms were registered. Patients cases given a diagnosis of musculoskeletal pain were recruited for the study. They were followed-up for eighteen months.
Analysis is ongoing. Of the 8,517 registered, 5,068 answered the questionnaire (59%). Among the respondents 56 % were women and 44 % were men. In a period of 4 weeks prior to the questionnaire, 68 % reported back pain, 43 % reported pain in the right upper limb, and 37 % reported pain in the left upper limb. 46 % of respondents had seen their General Practitioner due to musculoskeletal pain during the past 12 months.
Factors predicting care-seeking and frequent GP attendance will be analysed.

P16.03 Pia Kirkegaard

BY WHAT CRITERIA DO GENERAL PRACTITIONERS (FAMILY PHYSICIANS) ASSESS NEWLY DEVELOPED DECISION AIDS?
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Background
Decision aids have been developed during the last two decades, primarily in the English speaking countries. Before implementing decision aids in general practice in other countries, it is important to investigate in depth how GPs in specific countries practice decision making with patients. The aim in this study is to identify the criteria by which Danish GPs assess newly developed decision aids.

Design and Methods
12 GPs (6 female, 6 male) were interviewed in three groups, each interview lasting 2 hours.
They were presented with new tools: a published booklet about cholesterol, a one-page decision aid about cholesterol and cardiovascular disease, and a visual aid with

three different risk formats presenting the effect of lowering LDL-cholesterol.
The interviews and interview notes were transcribed, discussed, categorized and analyzed.
Results
Criteria by which GPs assess newly developed decision aids:
1) The decision aids should support and enhance the trusting relationship with the patient which is felt more important than information about risk numbers.
2) Decision aids should be low tech to be compatible with the personal and supportive interaction of the consultation. The published low tech material with only cholesterol as a variable was not deemed appropriate, as GPs wanted more variables, e.g. sex, age, smoking status, blood pressure and cholesterol.

Conclusions
Decision aids need to be adjusted when introduced to a new context. In this case, the GPs showed reluctance to use web-based/high tech tools, which goes against most current developments in decision aids that tend to be orientated to create extremely sensitive individualized profiles.

P16.04 Stine Yde Nielsen

Q-FEVER IN PREGNANCY AND FETAL CONSEQUENSES

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Q-fever is a bacterial zoonosis caused by Coxiella burnetii, with cows, goats, and sheep being the primary animal reservoirs. Earlier the infection was considered non-existing in Denmark, but recent serologic analysis of Danish cattle and people working with cattle has changed this perception.
Human infection occurs by inhalation of aerosols from animal birth products. Constituting a particular group at risk, pregnant women may, when infected, experience complications by way of spontaneous abortion, preterm delivery, oligohydramnion, growth retardation and intrauterine death. While the pregnant women are often asymptomatic, one of the few existing studies on this topic reports negative pregnancy outcome in more than 80% of infected cases lacking long-term antibiotic treatment.
Exploring the importance of Q-fever in relation to the completion of pregnancy among women exposed via risk occupation is the main objective of this study. The study will address specific hypotheses on heightened seroprevalence of Q-fever among women exposed to domestic animals; it will explore the association between serologic indications of Q-fever and adverse pregnancy outcome, and seek to establish if there is a correlation between exposure to domestic animals and adverse pregnancy outcome. Data will consist of questionnaire data and blood samples from the Danish National Birth Cohort.
This project will provide essential and specific knowledge on the prevalence and dissemination of clinical and sub clinical Q-fever infection among pregnant women, and it will thereby further our understanding of risk factors in order to develop guidelines regarding rational prevention and handling of risk.

P16.05 Lotte Ørneborg Rodkjær

SCREENING AND TREATMENT FOR DEPRESSION IS ASSOCIATED WITH A DECLINE IN DEPRESSION AMONG HIV-POSITIVES. A THREE-YEAR PROSPECTIVE FOLLOW-UP STUDY.

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Background: Studies suggest that between 20 to 37 per cent of HIV-positives have a diagnosable depression and depression is under-diagnosed and undertreated. Screening for depression is not conducted regularly to provide full evaluation and relevant psychiatric treatment. This study is a 3 year follow-up of a cohort of HIV-positives first evaluated for risk of depression in 2005.

Methods: HIV-positives were assessed at baseline and at a 3-year follow-up in a questionnaire-based study. The Beck Depression Inventory II (BDI-II) was used to assess the prevalence and severity of depressive symptoms. Patients with a BDI score of 20 or above were offered a clinical evaluation by a consultant psychiatrist.

Results: In 2005, 205 HIV-positives participated and symptoms of depression (BDI>14) were seen in 77 (38 per cent) and major depression (BDI ≥20) in 53 (26 per cent). In 2008, 148 participants were retested (72 per cent) and symptoms had decreased. Symptoms of depression (BDI>14) were seen in 38 (26 per cent), major depression (BDI ≥20) in 16 (16 per cent). Sixteen patients had a BDI ≥20 both in 2005 and 2008 due to periodic depression and 21 had a BDI ≥20 in 2005, but not in 2008. Among non-responders (57) 16 patients had a BDI ≥20 in 2005. In 2008, 3 patients got antidepressive treatment,10 patients were not depressed and for 3 patients there were no information (medical records).

Conclusion: Screening and treatment for depression minimize undiagnosed depression and improve clinical outcomes over a three year period. The study found a nearly two third decline in depression score due to screening and starting antidepressive treatment.

P16.06 Chunsen Wu

HEALTH OF CHILDREN BORN TO MOTHERS WITH PREECLAMPSIA – A POPULATION-BASED SIBLING-COHORT STUDY

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BACKGROUND: Children prenatally exposed to preeclampsia have an increased risk of a variety of diseases, especially in children born at term. This increased risk could be induced by pathologies activated by preeclampsia, or because these diseases and preeclampsia share genetic causes. A family study where affected siblings are compared with their unaffected siblings will better control for the influence of genetic factors and other factors shared by the same family.
METHODS:We linked the Danish Civil Registration System with the data from the Danish National Hospital Register and the Danish Medical Birth Registry. Children were followed from the day of birth until the first hospitalization of the disease, death, emigration, or December 31, 2006, whichever came first. Cox proportional hazard models were used to assess incidence rate ratios (IRR) for being hospitalized due to a variety of diseases for children exposed to preeclampsia compared to their unexposed siblings.
Among 64,103 siblings, 49% of them were exposed to maternal preeclampsia. Children born at term exposed to preeclampsia had similar hospitalizations for most of diseases compared to their unexposed siblings. We would further assess whether children whose mother had a history of preeclampsia but themselves were not directly exposed to preeclampsia still have an increase diseases compare to children whose mothers never had a history of preeclampsia.
CONCLUSIONS:The finding of this study may suggest that adverse long-term outcomes for children exposed to preeclampsia may, in part, be due to genetic factors shared with preeclampsia or common maternal intrauterine environment of siblings.

P16.07 Charlotte Gjørup Pedersen

QUALITY OF CARE AND CRIME RATES AMONG PATIENTS WITH SCHIZOPHRENIA: A NATIONWIDE POPULATION-BASED FOLLOW-UP STUDY

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Introduction:Denmark has seen a substantial increase in the number of forensic

patients since 1980 with annual growth rates reaching 7%. In the same period, the population of forensic patients with schizophrenia has increased from 50% to 75%. Evidence-based care for patients with schizophrenia is well-established in international and national guidelines. However, a possible association between quality of care and risk of crime among patients with schizophrenia has not previously been studied.
Aim:To study the association between quality of care and risk of crime among patients with schizophrenia.
Methods: This follow-up study is based on the Danish National Indictor Project (DNIP), a national clinical database for patients with schizophrenia, and the Danish Crime Register, a national register of criminal offences. We include all patients diagnosed with schizophrenia (ICD-10: F20.00-F20.99), Danish citizens, and older than 18 years. All patients have been admitted as inpatients at a psychiatric ward in the period 1 January 2004 to 31 December 2007 (approx 20,000 patients). In DNIP quality of care is assessed as fulfilment of a set of quality of care criteria related to the diagnostic process, contact with the health care system, use of antipsychotic medication, evaluation of side effects, family intervention, psycho education, planned outpatient treatment by discharge and suicide prevention. All patients will be followed up for 1-year after discharge. We identified all convictions for both violent and property crimes in the population. Separate analyses will be made for subtypes of crimes. Results: The study is in progress and will be completed and published in 2010.

P16.08 Gija Rackauskaite

ADD INSTITUTION CHANGE ORDER OF INSTITUTIONS VALIDATION OF DANISH GMFCS FAMILY REPORT QUESTIONNAIRE

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Background:
Gross Motor Function Classification System (GMFCS) is a validated method to evaluate severity of motor impairment of children with cerebrla palsy and available in danish. Family reported GMFCS questionnaire has been validated in an English version only.
Methods and materials:
We translated and validated Family Questionnaire by comparing parental report to physiotherapist report about GMFCS level among 54 danish children with cerebral palsy at age 8 to 12 years. The answers were analysed for agreement by kappa statistics.
Results:
Good agreement between parents and physiotherapist about GMFCS level (kappa = 0,62 for exactly agreement; kappa =0,75 for accepting 1 levels difference on weight 0,5).
Conclusion:
Danish GMFCS Family Report Questionnaire can be used to rate GMFCS level among danish 8 to 12 year old children with cerebral palsy in epidemiological studies.

P16.09 Grethe Elholm

THE EFFECT OF FARMING EXPOSURE ON CHANGES IN ATOPY OVER TIME

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Aim
Farmers are exposed to a wide range of allergens and run the potential risk of developing allergy and asthma. Research though implies that the prevalence of

atopic sensitization and atopic asthma is low in farmers. The SUS cohort consists of 1964 young farmers, and 52% were re-examined during the follow-up study. We aim to describe the changes in prevalence of sensitization in this farming cohort.
Methods
The participants were skin prick tested twice for sensitization to 15 different allergens, first during the SUS study (1992-1994) and subsequently during the follow-up SUS12 study (2006-2008).
Results
Preliminary analyses have been performed on 520 of the first participants. The overall low sensitization rate seen in SUS among farming students compared to controls was confirmed in SUS12, and the difference was even more pronounced in SUS12. The sensitization to cat, cow and grass was significantly lower in the male farmers compared to the controls. In contrast storage mite sensitization appears to increase for the farmers.
Conclusion
The preliminary analyses show that farmers maintain a low sensitization rate compared to the controls, with the exception of sensitization to storage mites, which appears to increase in farmers.

P16.10 Morten Charles

NEUROPATHY IN A POPULATION WITH SCREEN-DETECTED TYPE 2 DIABETES

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Aim: To investigate whether intensified multi-factorial treatment decreases the risk of development of peripheral/autonomic neuropathy in a screen detected diabetic population.
Design: A pragmatic cluster-randomised controlled trial of the effectiveness of intensified multi-factorial treatment on 5 year follow up in people with screen-detected type 2 diabetes.
Population:1533 people with screen-detected diabetes were recruited in 181 general practices to the Danish arm of the ADDITION study after a stepwise screening programme involving 28.031 people.
Methods: GP practices were randomized into Conventional Therapy Group or Intensified Therapy Group according to strict targets from a prespecified treatment algorithm. Neuropathy will be assessed based on: monofilament, Vibration detection threshold, cardiac autonomic neuropathy. The participants will also be described with measures similar to baseline (BMI, waist, Blood pressure, ECG, fundus-photo, blood- and urine samples.) The participants will fill out standard questionnaires regarding neuropathy, pain, sexual dysfunction and QoL.
Subjects: At baseline the ADDITION population was aged 59.7 years (SD: 6.8), 58% men, HbA1c 7.0% (SD: 1.6), BP 151/87 mmHg (SD: 23/12), total cholesterol 5.6mmol/l (SD: 1.1).
Conclusion: Knowing the prevalence of neuropathy in people with screen-detected diabetes will indicate whether GP efforts should be directed primarily at glycaemic management, general CVD risk factor management or also at the detection and tracking of initial stages of diabetic neuropathy. This study will also provide evidence on the benefits of early intensive intervention on the development of neuropathy.

P17.01 Annette Langager Høgh

TRENDS IN ACE-INHIBITOR TREATMENT 1996 – 2003, AMONG DANISH PERIPHERAL VASCULAR RECONSTRUCTED PATIENTS

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Introduction

Peripheral arterial disease (PAD) is a common manifestation of systemic arthrosclerosis associated with significant morbidity and mortality. The incident of PAD is 3 to 10 %, increasing to 15% to 20% in persons over 70 years. Symptomatic PAD patients have the same risk of cardiovascular events as patients with symptomatic ischemic heart disease, but are less likely to receive optimal secondary prevention and intensive risk factor modification than patients with coronary artery disease. We investigate trends in ACE-inhibitors consume from 1996 to 2003.

Materials and methods

We included all patients (>40 years) who had a primary vascular surgical reconstruction on atherosclerotic basis: 1996 to 2003. The Danish Vascular Registry was the main data source and was by civil registration number facilitated to the "Prescription Database registries" and "The National Hospital Discharge Registry".

Results

12847 patients was peripheral vascular reconstructed, 54.5% was males, mean age 68 (SD 10.7). Comorbidity: 13.2% MI, 15.6% stroke. 49.8% had ACE-inhibitors prescripted, there was no difference between gender (RR=1).Patients at age 60-80 had a RR=1.2, compared to age 40-60, + 80 RR=1. By increasing comorbidity-index, the prescription-rate also raised. We found geographic variation: 44.5% - 53.3%, and variation over time (1996: 44.3% to 2003: 54.0%).

Discussion

ACE-inhibitor prescription increased from 1996 – 2003, but geographic variation was present. The rate of prescription raised as comorbidity increased. We expect medical secondary prevention had increase in general, especially from 2003 up till today. We are processing data from 2003 to 2008 to follow up.

P17.02 Rikke Jørgensen

MEANINGFUL CHANGE WITH THE METHOD GUIDED SELF-DETERMINATION – A RANDOMISED CONTROLLED STUDY FOR PATIENTS DIAGNOSED WITH SCHIZOPHRENIA.

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Background: Rehospitalisation and discontinued treatment are common among patients with schizophrenia and is often associated with lack of insight into the illness. Improving patients' insight has been attempted through psychoeducation and standard treatment but without any considerable change. A newly developed method, Guided Self-Determination (GSD), originally developed and proved effective in difficult diabetes care has been adjusted to patients with schizophrenia.
Aim and hypotheses: The aim of the study is to evaluate the effects of the method GSD in the care of patients with schizophrenia compared to treatment as usual (TAU). The following hypotheses will be tested:The method GSD will improve: Cognitive and clinical insight in patients, various domains of self-management of schizophrenia, patients' self-esteem, psychopathology and social functioning. Primary outcome is cognitive insight measured by the self-rating scale Beck Cognitive Insight Scale (BCIS).
Material and method: The study design is a randomised controlled trial. The participants are diagnosed with schizophrenia, receiving treatment in 3 Assertive Outreach Teams (AOT) in Region North. Participants complete four self-rating questionnaires, a demographic data sheet, an interview concerning psychopathology and an assessment of social functioning at baseline, and after 3, 6, and 12 month. Inclusion of 50 participants in each group is sufficient to detect an effect of 3 BCIS scale points. Intervention with the method GSD will be conducted by the community

nurses but under supervision from the investigator.
Results: So far there are no preliminary results to be presented.

P17.03 Peter Agergaard

CAN 22Q11.2 DELETION BE DETECTED ON BEHALF OF A CLINICAL ASSESSMENT OF A PATIENT WITH CONGENITAL CARDIAC MALFORMATION?

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Introduction: 22q11 deletion syndrome is one of the most frequent syndromes with an estimated prevalence of 1:2,000-4,000. The genetic background is a deletion of 1.5-3 mega bases on chromosome 22q11.2 . The clinical phenotype is highly variable, and more than 180 manifestations are associated with it. No genotype-phenotype has yet been found. Congenital cardiac malformation (CCM) is seen among 49-86% of children with 22q11.2. This range reflects that diagnosis depends on clinical referral. Thus, patients with typical and/or several manifestations are easily found, but when manifestations are atypical or subclinical, diagnosis may be delayed or even missed.

Objective: The aim of the present study was to evaluate the validity of clinical assessment as a method of predicting 22q11.2 deletion in patients with CCM.

Materials and methods: We performed meta-analysis of 12 studies from the period 1995-2008 that met our inclusion criteria.

Results: Among 1,339 patients with CCM, 151 (11.3%) carried the 22q11.2 deletion. The clinicians correctly identified 108 (71.5%) of them, whereas 43 (28.5%) would have remained undiagnosed if screening had not been performed. Sensitivity, specificity, predictive value of positive and negative tests ranged from 0-100, 43-100, 7-100, and 83-100 %, respectively. 6/8 studies of patients with conotrunkal CCM showed modest sensitivities (0-86%). In contrast, 3/4 studies of patients with unselected CCM showed high sensitivities (99-100%).

Conclusion: Clinical assessment is not a valid method of detecting 22q11.2 deletions among patients with CCM. All children with conotrunkal malformations should be screened for 22q11.2 deletions.

P17.04 Anne Sophie Ågård

LONG-TERM IMPACT OF ACUTE CRITICAL ILLNESS AND ADMISSION TO INTENSIVE CARE UNIT. PATIENTS' AND RELATIVES' PERSPECTIVE

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Background
In Denmark every year 15-25.000 patients are admitted to ICU. The number is increasing and survival still improving. International literature gives reasons to believe that critical illness and admission to ICU radically affects both patients and their relatives during hospitalisation as well as convalescence after discharge. Thus, internationally there is an increasing focus on the long-term impact of critical illness on ICU-patients and their relatives.
Aim

To study the trajectories of patients and relatives during the first year after discharge in order to identify their use of healthcare and social services and long-term affiliation to labour market and develop a theoretical account of their coping strategies during convalescence.
Method and material
The design is explorative and qualitative using grounded theory as the methodological framework. Former intubated (>96 hrs) ICU-patients (n = 15-20) with no appreciable chronic conditions prior to admission struck with acute, critical illness aged 25-70 years and their partner or spouse are invited to participate. Data are collected through several semi-structured interviews with patients and relatives as well as from public registers.
Results
Results will be reported after February 2010. We expect the study findings about post-ICU trajectories to add valuable knowledge to the ongoing efforts to prevent complications during admission to ICU and to prepare patients and relatives for discharge and convalescence. The overall goal is to strengthen the joint efforts to support former ICU-patients and their relatives in their endeavour to retrieve a well-functioning everyday life participating in working- and social life.

P17.05 Lisa Gregersen Østergaard

THE EFFECT OF MODERN REHABILITATIONSTRATEGIES FOR LUMBAR SPINAL FUSION PATIENTS - TWO RANDOMIZED CLINICAL STUDIES

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Background
Each year around 1000 persons have a lumbar spinal fusion due to degenerative diseases. Some of these patients have a long absence from work, and risk exclusion from the work force.
Early rehabilitation after disc-surgery has proven to have a positive effect on the patients' daily activities. However, no studies have so far examined early initiation of rehabilitation for patients with lumbar spinal fusion.
Research on low back pain indicates, that focused return-to-work-interventions can reduce absence from work and prevent exclusion from the work force. No studies have examined similar interventions for lumbar spinal fusion patients.
The aim of the present Ph.D. study is to examine:
The effect and cost-effectiveness of early rehabilitation after lumbar spinal fusion
The effect and cost-effectiveness of a return-to-work-tutor for lumbar spinal fusion patients Methods
Two multi-center clinical randomized studies will be carried out.
Study 1: 80 patients are randomized to early start of rehabilitation (6 weeks post surgery) or a control group with start of rehabilitation 3 months post surgery. All patients receive the same rehabilitation just with different starting time. Inclusion period: Feb. 2008 – Oct. 2009.
Study 2: 80 patients will be randomized to either a group with a return-to-work-tutor or a control group (no return-to-work-tutor). Inclusion starts: Nov. 2009.
Primary outcome: Oswestery Disability Index and absence from work after the surgery. Secondary outcome: Dallas Pain Questionnaire, EuroQol, Low Back Pain Rating Scale and use of health care service. For study 1 also the physical tests "6 min walk test" and "Aastand's physical fitness".

P17.06 Bodil Bjørnshave

IS EVIDENCE-BASED EFFECT OF PULMONARY REHABILITATION (PR) – BASED ON SELECTED STUDYPOPULATIONS?

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Background

The effect of PR is documented in RCTs and PR is recommended for patients with Chronic Obstructive Pulmonary Disease (COPD). Prior to a widespread application of PR it is of interest to determine, whether an effect as documented in RCT can be achieved in a non-selected COPD population.

Aim

Are patients completing RCT studies testing PR a representative subset of the COPD population?

Material and Methods

A Cochrane Review, which have concluded positive effect of PR on the basis of 26 RCTs, was analysed to describe selection and dropout of patients in the studies (1).

Results

Selection of patients included in RCTs can be introduced at three levels 1) Sampling 2) Inclusion and exclusion and 3) Dropout

Only 3 (12%) out of RCTs described the selection of participants from number of patients contacted. Few RCTs were explicit about the characteristics of the population from which the study populations were drawn.

47% of the patients contacted were de-selected before they were screened.

Moreover a range from 6-64% of the patients were de-selected during screening due to exclusions criteria. Dropout ranged from 0-54%.

In all approximately ¾ of the patients relevant for PR did not complete PR. None of the studies discussed external validity.

Conclusion

Patients participating in RCTs on PR were not drawn from a representative subset of the target population and therefore the ability to generalize the results is affected.

(1) Lacasse Y et al. Meta-analysis of respiratory rehabilitation in chronic obstructive pulmonary disease. A Cochrane Systematic Review 2007 43(4):475-85.

P17.07 Leanne Langhorn

EARLY REHABILITATION OF PATIENTS WITH POSTTRAUMATIC AMNESIA IN THE INTENSIVE CARE UNIT

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Early rehabilitation of patients with posttraumatic amnesia (PTA) in the neurointensive care unit (ICU)

Introduction: About 70% of patients with traumatic brain injury (TBI) experience PTA. The outcome is depending of the severity of the initial computerized tomography (CCT) findings, the Glasgow coma score (GCS) and intracranial pressure (ICP). The duration of PTA is inversely correlated with the potential for full recovery. In the study we tested whether a reality orientation programme (RO) in the ICU could reduce the duration of PTA and improve outcome. We hypothesized that patients introduced to the RO had a shorter duration of PTA than the control group. This could not be correlated to the CCT or the GCS as the Galveston orientation and amnesia test (GOAT) was more precise to evaluate the status of the patient and improve outcome. METHOD: The design was quasieksperimentel. Two matched groups of patients diagnosed with TBI were selected from two university hospitals. In addition to conventional treatment, patients in one group were introduced to the RO consisting of systematic orientation, information, and systematic cooperation with the relatives. The control group received conventional treatment only. All patients had a CCT performed, ICP monitored, GCS and a daily GOAT test. RESULTS: We expected that TBI patients exposed to the RO would experience improved orientation, a more favourable prognosis and better recovery

compared with conventionally treated patients. We compared the patients overall function, daily activity, work status, the duration of PTA and length of stay (LOS). CONCLUSION: The preliminary results indicates a shorter PTA, LOS and improved outcome.

P17.08 Mai-Britt Guldin DEVELOPMENT OF A PROGNOSTIC CLINICAL TOOL FOR SCREENING FOR COMPLICATED GRIEF IN GENERAL PRACTICE

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Objective
The aim of the study was to identify specific items and scales that were prognostic for the development of complicated grief and to analyze different combinations of these in predicting complicated grief (CG). Finally to propose a model for a screening tool applicable among bereaved patients in general practice.
Methods
We examined the responses of 296 bereaved patients to a variety of questionnaire items concerning grief: Depression (BDI), PTSD (HTQ), Personality Inventory (NEO-PI-R), Coping Style Questionnaire (CSQ), The Crisis Support Scale (CSC) and a variety of single item, Likert-type questions on distress experienced in relation to the death. Inventory of Complicated Grief (ICG-R) was used as a golden standard. Receiver operating characteristic (ROC) curve analysis was performed for all scales and items on the data set and measured against the answers on ICG. Sensitivity, specificity and AUC were calculated for scales and items.
Results
Beck's Depression Inventory (BDI) was the scale with the highest AUC (0.83 at 6 months after bereavement). Due to a low positive predictive value, we added a single item about sense of purpose in life which resulted in a sensitivity of 80% and specificity of 75%. The positive and negative predictive values for this combination of questions were 70% and 85% respectively, with a final AUC of 0.81, suggesting a useable screening tool.
Conclusions
This study suggests that the BDI in combination with a single item can be used for clinical screening for CG. The prognostic tool is currently being used and tested in our ongoing study: Bereavement Management in the Danish health care system. A randomized controlled study.

P17.09 Anna Lamberg REGISTRATION IN THE REGIONAL NMSC DERMATOLOGY DATABASE: COMPLETENESS OF REGISTRATION OF NON MELANOMA SKIN CANCER (NMSC) AND POSITIVE PREDICTIVE VALUE OF KEY VARIABLES REGISTERED IN THE DATABASE.

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Objective: To validate a clinical database for non melanoma skin cancer (NMSC-database) - A database for monitoring and prediction of prognosis of NMSC, Mb. Bowen and keratoakanthoma treated by dermatology clinics in the Regions of Central and Northern Jutland.
Methods: We assessed the completeness of registrations of NMSC, Mb. Bowen and keratoacanthoma in the NMSC-database using the Danish Pathology Registry as gold-standard. Not all treated skin tumors are histologically verified. The completeness was therefore also assessed by review of medical records from all contacts on randomly selected days of work in two clinics registering in the database from January 1–June 30 2008. The PPV of diagnoses registered was assessed using the Pathology Registry as gold-standard and the PPV of other registered data was

assessed by review of medical records from samples of randomly selected patients registered in the NMSC database.
Results:The completeness assessed using the Pathology Registry was 58.6 %. Practice no. 1 had a completeness of 93.5 % and practice no. 2 a completeness of 40.1 %. Results from the review of medical records will be presented at PhD Day.
Conclusion:The completeness of the database is not satisfactory. However the result from practice no. 1 shows that it is possible to obtain high completeness. In future, practices registering in the database will receive lists every third month on missing registration using the Pathology Registry in order to obtain information on skin cancers diagnosed by dermatology clinics.

P17.10 Helle Svenningsen

DOES SEDATION INFLUENCE ON DELIRIUM AND POST-TRUMATIC STRESS DISORDER AS A RESULT OF HOSPITALIZATION IN INTENSIVE CARE - AN ONGOING PROJEKT

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Patients in intensive care that experience delirium have longer hospital stay, higher mortality and morbidity. Foreign studies indicate that post-traumatic stress disorder, dementia or depression emerge after discharge from hospital. There is a link between delirium and sedation. In Denmark sedation is used frequently.
Hypotheses:
1. that patients who are sedated minimal, remember staying in intensive care and experiences fewer episodes of delirium
2. that patients are more likely to develop post-traumatic stress syndrome after discharge if they have experienced delirium during hospital
3. that patients who have experienced delirium, have impaired health-related quality of life after discharge compared with patients without delirium
Methods: All adults admitted to Aarhus University Hospital intensive care ITA or 600 from September 2009 - September 2011. Patients hospitalized less than 48 hours in intensive care, with head injury or under 18 years is excluded.
Registration from medical- and nursing records of factors likely to affect the hypothesis. Approximately 1 week after discharge from ITA/600 the ICU memory tool is applied. Two and 6 months after discharge from the hospital the patient is contacted. Through a structured interview the ICU memory tool, and the Harvard Trauma Questionnaire for PTSD are applied. To screen for depression the Major Depression Inventory is used. State-Trait Anxiety Inventory is used to assess the degree of anxiety. Quality of life is assessed by Short-form 36.

P18.01 Asger Granfeldt

CARDIOPROTECTION BY POSTCONDITIONING IN VIVO INVOLVES LOCAL INHIBITION OF NEUTROPHILS

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Neutrophils(PMNs) contribute to ischemia-reperfusion(I-R) injury by generating superoxide radicals($\bullet O_2$). Postconditioning(PC) reduces infarct size(IS) and myocardial $\bullet O_2$ generation. It is unknown whether inhibition of PMNs is critical to postcon cardioprotection. We tested whether 1) IS reduction by PC is dependent on inhibition of PMNs, and 2) PC inhibits PMN $\bullet O_2$ generation. Rats were randomized after 30 min left coronary artery (LCA) occlusion and 3 h R to 1) Control: I-R (n=13) 2) PC: 3x10s R and 10s reocclusion at onset of R (n=13) 3) PMN depletion: rabbit anti-rat PMN antiserum injected 8 hr before ischemia (n=9) 4) PC in PMN-depleted rats (n=9). In PMN $\bullet O_2$ studies, blood was sampled at 2 and 24hr from the anterior interventricular vein(AIV) draining the area at risk(AAR) in dogs with 60 min LAD

occlusion and 24hr R ± PC (3x10s R and 10s reocclusion); blood was immediately analyzed for PMN-derived $\bullet O_2$ (chemiluminescence,CL). In rats, PMN antiserum reduced plasma PMNs by 84%. CD18+PMNs (% of total nuclei) in AAR were less in PC (21.2±0.3%*) and PMN-depleted (9.4±0.3%*) vs Control (30.5±1.2%), with a further decrease in PMN-depleted rats (5.4±0.6 %*). Both PC and PMN depletion reduced IS (necrosis/AAR, 42.6±2.1%* and 43.9±3.0%* resp) vs Control (58.8±0.9%). There was no further decrease in IS with PC in PMN depleted rats (37.2±2.9%). In AIV blood from Controls, PMN-derived $\bullet O_2$ increased at 2 and 24 hrs of R. PC reduced PMN-derived $\bullet O_2$ to baseline. Conclusions: PC or PMN depletion reduces PMN accumulation and IS, but PC did not further reduce IS in PMN-depleted rats. PC inhibits PMN $\bullet O_2$ generation. PC may reduce IS by inhibiting PMN $\bullet O_2$ generation.*P<0.05 vs Control

P18.02 Maria Bach Laursen

THE ROLE OF MIRNA AND AID IN B-CELL MALIGNANCIES

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miRNA deregulation is often associated with cancer, and given the importance of miRNA in developing and maintaining cellular fate, this is expected to play a profound role in cancer formation and progression. Deregulation of mature miRNA may take place at the level of biogenesis as a result of mutations in the miRNA transcript. In B-cell malignancies, such mutations could be caused by AID (Activation Induced cytidine Deaminase).

AID is a B-cell specific mutagenic factor and its expression is normally limited to GC B-cells, where it acts on Ig-genes. Constitutive expression of AID can lead to aberrant mutation of non-Ig target including oncogenes. Thus, AID may lead to miRNA transcript mutation that could impair miRNA biogenesis and result in deregulated miRNA expression. However, the effect of AID on miRNA transcripts has never been investigated.

The hypothesis of this project is that a specific miRNA signature is present in cases where AID is overexpressed and that the target genes of these deregulated miRNA are important in understanding cancer initiation and/or progression. This will be investigated by; 1) analysing miRNA array and GEP data from DLBCL and CLL patient samples in order to identify differentially expressed miRNA in samples with high AID level 2) performing siRNA knockdown of AID in DLBCL cell lines to validate differentially expressed miRNA 3) using affinity purification to identify the mRNA targets of these miRNAs 4) quantifying the amount of pri-, pre- and mature miRNA of the differentially expressed miRNA by Northern blot analysis.

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P18.03 Jette Lindorff Riis

CCL17 AND CCL27 ARE DIFFERENTIALLY EXPRESSED IN INFLAMMATORY SKIN DISEASES

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CCL17 is a Th2 type chemokine, which binds to the CC chemokine receptor 4. It is constitutively expressed in the thymus and is produced by dendritic cells, endothelial cells, keratinocytes, and fibroblasts. CCL27 is a skin-specific CC-chemokine continuously expressed by keratinocytes. CCL27 binds to the chemokine receptor CCR10 and mediates Th1 and Th2 lymphocyte migration into the skin. The purpose of our study was to review the differences in the expression of the chemokine CCL17 and CCL27 in the three inflammatory skin diseases: psoriasis, atopic dermatitis (AD) and allergic contact dermatitis (ACD). We determined the expression of both CCL17 and CCL27 in the skin at mRNA level using quantitative RT-PCR and at protein level by ELISA. Interestingly, a pronounced raise in CCL17 mRNA was found when comparing lesional ACD with non-lesional ACD affected skin. This result was also seen at CCL17 protein level. In lesional psoriatic skin only

a minor increase in CCL17 mRNA was measured when compared to non-lesional psoriatic skin. Surprisingly, our studies revealed that the expression of CCL27 mRNA and protein in psoriatic skin lesions was markedly decreased compared to non-lesional psoriatic skin. This fall in CCL27 mRNA and protein was also found in lesional skin from patients with ACD when compared to non-lesional skin although to a lesser degree. No alterations in either CCL17 or CCL27 were seen in AD skin. Overall, our principal findings were a marked upregulation of CCL17 in lesional ACD skin and a distinct decrease in CCL27 in lesional psoriatic skin. These findings may explain the different recruitment of T-cells into the skin in these inflammatory diseases.

P18.04 Trine Silkjær

VARIATIONS IN MITOCHONDRIAL DNA IN PATIENTS WITH ACUTE MYELOID LEUKEMIA

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BACKGROUND: In acute myeloid leukemia (AML), cytogenetic and molecular genetic abnormalities are known to play an essential role in the pathogenesis and are now accepted to be of paramount prognostic significance. However, mitochondrial dysfunction is also emerging as a major impact factor of importance in cancer. The mitochondrion has its own double-stranded circular 16.568 base pairs DNA (mtDNA) encoding 13 genes involved in oxidative phosphorylation and the respiratory chain, two rRNAs, and 22 tRNAs. As such, they are important in apoptosis and might thus, be crucial in response to chemotherapy and to disease progression. The purpose of this study was to determine if mtDNA variations are of importance to outcome of chemotherapy and to long-term survival in AML. METHODS AND MATERIAL: The whole mitochondrial genome was sequenced using a resequencing system from Applied Biosystems, Foster City, CA, performed on a Genetic Analyzer 3130 (Applied Biosystems). Diagnostic bone marrow from 55 patients with AML, treated with curative intent and bone marrow from 10 normal controls, was analyzed. RESULTS: We sequenced the entire mitochondrial genome in 55 patients with AML and 10 normal controls and compared our findings with clinical data and survival data. When analyzing data, variations found in normal controls, where subtracted from variations found in patients. Variations were scattered throughout the entire mitochondrial genome, and observed in all genes as well as in non-coding regions. Data from this study will be presented. CONCLUSION: This is, to our knowledge, the first demonstration of whole mitochondrial genome sequencing in a sizeable cohort of patients with AML.

P18.05 Rasmus Boye Kjellerup

CHARACTERIZATION OF THE MAPK PHOSPHATASES IN SKIN INFLAMMATION

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The MAPK phosphatases DUSP1, 2 and 10 seem to be important in the regulation of inflammation. The purpose of this study was to investigate and characterize the expression of DUSP1, 2 and 10 in skin inflammation. In a TPA mouse model of skin inflammation mice were treated with TPA on the ears, and punch biopsies were taken after six hours or three days. In patients, punch biopsies were taken from nonlesional and lesional plaque-type psoriatic skin (n=17), guttate psoriatic skin (n=6), and atopic dermatitis skin (n=6). The mRNA expression was analyzed by quantitative RT-PCR. In TPA-treated mice the mRNA expression levels of DUSP1 and DUSP2, but not DUSP10, were significantly ($p<0.05$) upregulated after six hours with 3.4 fold and 21 fold, respectively. In contrast, three days after the first TPA application DUSP1 and DUSP10 were significantly downregulated with 0.21 fold and 0.15 fold, respectively. No significant difference was seen for DUSP2. In lesional plaque-type psoriatic skin the DUSPs all displayed significantly ($p<0.05$) altered

expression as compared with nonlesional psoriatic skin. DUSP1 and DUSP10 were both downregulated with 0.74 fold and 0.63 fold, respectively, whereas DUSP2 was upregulated with 1.8 fold. In lesional guttate psoriatic elements the same trend was seen; however, only DUSP2 and DUSP10 mRNA levels showed a significant change with 1.8 fold upregulation and 0.70 fold downregulation, respectively. In atopic dermatitis we found no significant difference between nonlesional and lesional skin. In conclusion, our findings suggest that dysregulation of the DUSP1, 2 and 10 expression may contribute to the sustained inflammation seen in psoriasis.

P18.06 Emilia Wiechec

COMPARATIVE STUDY OF DIFFERENT DIAGNOSTIC TECHNIQUES (AI, MLPA, FISH) IN BREAST CANCER PATIENTS WITH 1Q25.3 ALTERATIONS.

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Breast cancer is the leading cause of cancer related death worldwide. Molecular genetic studies have revealed subgroups of breast cancer within which the genomic alterations affecting chromosome 1q are considered to be an early event in breast carcinogenesis, and are correlated with good prognosis for the patients. We have found a high percentage of concordance between Allelic Imbalance (AI) and Multiplex Ligation Probe Amplification (MLPA) assays pointing towards gain of the 1q25.3 region harbouring Regulators of G protein Signaling (RGS) genes in breast cancer.

Our main objective was to compare the sensitivity and specificity of AI and MLPA with other cytogenetic method (FISH) in breast cancer patients with or without previously confirmed alterations within 1q25.3.

FISH was performed on paraffin-embedded tumour material in order to verify previous findings and assess the level of genetic alterations of 1q25.3 in breast cancer. The 1q25.3 test and 1p32 reference probes labeled with different fluorochromes were used for analysis.

A total of 70 nuclei from each breast cancer case were examined and scored for the percentage of 1q25.3 alterations. The non-tumourigenic nuclei obtained from healthy individuals served as adequate cut-off for the 1q25.3-specific changes. The overall FISH results are consistent with results obtained from previous analysis in majority of analyzed cases. Furthermore, FISH resolved the level of 1q25.3 alterations in few cases that were uncertain by AI and MLPA analysis.

This study shows that both AI and MLPA assays are able to map regions of copy number changes in the cancer genome and proved to be an efficient tool for diagnosis of 1q25.3 alterations.

P18.07 Gao Hong

RIFAMPICIN-SOAKED SILVER-COATED DACRON VERSUS POLYTETRAFLOURETHYLENE GRAFTS FOR IN SITU REPLACEMENT OF EARLY DEEP STAPHYLOCOCCUS AUREUS GRAFT INFECTION IN A RANDOMIZED CONTROLLED TRIAL IN A PORCINE MODEL

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Objectives: To compare the efficacy of in situ replacement with rifampicin-soaked silver-coated polyester (RSSCP) or expanded polytetrafluoroethylene (ePTFE) grafts in a porcine model for early aortic prosthetic graft infection (PVGI).

Material and methods: Sixty pigs had 8 mm wide grafts implanted end-to-end in the infrarenal aorta, and the grafts were inoculated with 10^6 S. aureus directly. Two weeks later, all surviving pigs were reoperated. All developed PVGI, and were randomized 1:1 to undergo in situ graft replacement with either ePTFE grafts or RSSCP grafts. Postoperatively, each animal received orally administration of 300 mg

rifampicin and 750 mg ciprofloxacin twice a day for 3 weeks until euthanasia and autopsy. Perigraft swabs and graft material were taken initially at reoperation and at autopsy, and analysed for S. aureus quantitatively.
Results:. Only 1 out of 25 RSSCP grafts were infected with S. aureus, whereas 15 of 27 ePTFE grafts were still infected with S. aureus (OR=0.033, 95% C.I.: 0.004; 0.283, P<0.001).
Conclusions: RSSCP grafts are more efficient to clear S. aureus contamination after in situ replacement of S. aureus PVGI than ePTFE grafts.

P18.08 Bekka Anina Ozer Christensen

WOUND HEALING – A PROTEOMIC ANALYSIS OF ERYTHROPOIETIN'S EFFECT ON GRANULATION TISSUE ISOLATED FROM EPTFE IMPLANTS

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Erythropoietin is a multifunctional cytokine and recent studies indicate a positive effect on wound healing in models of incisional and burn wounds.
The purpose of this study was to investigate the changes in protein expression after daily injections of recombinant human erythropoietin in granulation tissue isolated from subcutaneous implants of expanded polytetrafluoroethylene (ePTFE-tube).
Materials and methods: ePTFE tubes were implanted subcutaneously in twelve C57bl6 mice. Six mice were treated with daily subcutaneous injection of recombinant human erythropoietin 1000 IU/kg. Six mice acting as controls were treated with saline 0.9%. The implants were removed on day 9 after implantation. The granulation tissue was isolated and analysed for protein expression by a proteomic approach including 2D PAGE, and MSS. The results were confirmed with Western Blotting.
Results: We identified 21 proteins that were downregulated in the rhEPO-treated group, three proteins, GAPDH, ENOA and TPIS, were confirmed to be involved in the effect of rhEPO on formation of granulation tissue.
Conclusion: Daily injection of recombinant human erythropoietin 1000 IU/kg alters the protein expression of GAPDH, ENOA and TPIS in granulation tissue from wounds on postoperative day 9.

P18.09 Jenny Blechingberg

REGULATION OF GENE EXPRESSION BY THE TET-PROTEIN FAMILY

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FUS, EWS and TAF15 are RNA and DNA binding proteins which together are called the TET-protein family. They are structurally and functionally related and are found in a variety of cancer-associated fusion genes. The TET-proteins are also involved in neuronal diseases such as familiar Amyotrophic Lateral Sclerosis, Huntingdon's disease and frontotemporal dementia.
The TET-proteins are expressed in the majority of human tissues. They localize mainly to the nucleus, but are also seen as a smaller amount in the cytoplasm. The wild-type TET-proteins associate with a number of factors involved in transcription and RNA processing, implying the TET-proteins are involved in transcriptional regulation. The functions of the RNA-binding capacities of the TET-proteins are largely unknown, but FUS and EWS localize in RNA-transporting granules in dendrites. Recent evidence also shows that FUS is recruited by non-coding RNAs to the cyclin D1 gene to inhibit its expression upon DNA-damage.
This project aims to elucidate the roles of the TET-proteins in regulation of gene expression. These functions are analyzed by siRNA mediated gene knock-down in human Hek293 cells, and subsequent expression array analysis. The functions of the TET-proteins during oxidative stress and DNA-damage are also analyzed by

immunofluorescent staining and protein-protein interaction analysis.

P18.10 Troels Schepler

GROWTH INHIBITORY MICRORNAS SUPPRESSED BY THE WNT PATHWAY IN COLORECTAL CANCER

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Colorectal cancer (CRC) is one of the most prevalent and deadly cancers worldwide. The onset and progression of the disease is intimately linked to hyper-activation of the Wnt pathway. Here, we investigated whether microRNAs (miRNAs) might be part of the Wnt signaling network in CRC. MiRNAs are small non-coding RNAs that serve as important post-transcriptional regulators of protein expression, and widespread changes of miRNA abundancy are known to occur in CRC. To identify miRNAs controlled by the Wnt pathway, we inactivated Wnt signaling in cultured CRC cells and profiled changes in miRNA levels using microarray technology. The abundancy of several miRNAs increased upon inhibition of Wnt signaling activity, and these changes were confirmed using quantitative real-time PCR. In clinical specimens from CRC patients, we observed a pronounced down-regulation of these miRNAs relative to healthy tissue in agreement with the Wnt pathway commonly being highly activated in CRC. By artificially up-regulating these miRNAs individually in cultured CRC cells, independent of changes in Wnt signaling activity, we noticed a marked inhibition of cell growth. In addition, by transfecting cells with different combinations of miRNAs, we could demonstrate an additive reduction of cell growth. In conclusion, the aberrant activation of the Wnt pathway, commonly observed in CRC, may suppress a network of growth suppressive miRNAs thereby fueling uncontrolled cell proliferation of cancer cells. Ongoing investigations are aimed at identifying specific transcripts that are targeted by these miRNAs.

P19.01 Christopher Nordentoft Vejgaard

ARRAY BASED CHARACTERIZATION OF LEUKEMIC MODEL SYSTEMS

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Background: Cell lines systems are extensively used in research, as they provide uniform and practically unlimited sample material. However, concerns have been raised regarding the significance of scientific conclusions obtained from cell line experiments, as most cell lines have undergone substantial alterations during transformation. Therefore, it is becoming increasingly important that experiments involving cell line based models use material where the genomic composition has been thoroughly investigated.
Aim: To characterize genomic aberrations and microRNA expression in five common leukemic cell lines in order to establish insight into the genetic alterations during transformation.
Materials and Methods: The genomic compositions of the five leukemic cell lines, REH, BV-173, U-937, Kasumi-1 and ME-1, were investigated by G-banding, Spectral Karyotyping, FISH and array-CGH while microRNA expression was analyzed with expression arrays and qPCR.
Results: Our analyses suggest that the investigated cell lines have highly complex genomic alterations as a result of multiple events, including deletions, amplification, translocations and inversions. MicroRNA expression data indicates that although the cell lines have similar expression profiles as expected for cells from the same tissue system, the expression of some microRNAs distinguish the different systems.
Conclusions: Future research based on cell line models should use well characterized cell lines enabling a thorough evaluation of biological pertinence.

P19.02 Tomasz Kazimierz Wojdacz

METHYLATION SENSITIVE HIGH RESOLUTION MELTING (MS-HRM) FOR ASSESSMENT OF METHYLATION IN CLINICAL SAMPLES

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Methylation biomarkers have been shown be highly useful in non-invasive diagnostic and treatment of cancer and other disorders. However until now no methylation marker screening method has been described that would meet rigorous diagnostic criteria. We have developed the High Resolution Melting Technology (HRM) for the methylation screening in clinical samples. The new Methylation Sensitive HRM protocol requires amplification of bisulfite-modified template DNA. Proportional amplification of methylated and unmethylated alleles is hard to achieve due to the PCR bias favouring amplification of unmethylated alleles of the locus and therefore leading to significantly deceased sensitivity of marker detection [1]. As sensitivity of the protocol is critical for diagnostic application of the method, we have addressed the issue of PCR bias in methylation studies. We have developed a new primer design system which allows to eliminate PCR bias from the amplification [2] and combined it with the HRM technology. The new protocol (MS-HRM) allowed us to detect methylated biomarkers with the sensitivity of 1-0,1% and furthermore to estimate the methylation level in the screened material [3,4]. We have shown that MS-HRM is a highly sensitive, specific and robust method for methylation detection with a power for diagnostic application[5,6].

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P19.03 Lone Schmidt Sørensen

ABSTRAC INCORPORATION OF OMEGA-3 FATTY ACIDS INTO GRANULOCYTE CELL MEMBRANES WITHIN ONE WEEK OF ORAL SUPPLEMENTATIONT TITLE

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Several studies indicate that perioperative supplementation with omega-3 fatty acids may reduce the risk of postoperative complications after major surgery through an immune modulating effect. Omega-3 fatty acids, are incorporated into cell membranesThe purpose of this pilot study was to discover whether an omega-3 fatty acid enriched oral nutritional supplement (ONS)given for 7 days before surgery would be sufficient to incorporate omega-3 fatty acids into neutrofile granulocyte cell membranes. 5 patients, were given an omega-3 fatty acid enriched ONS for 7 days before surgery. Blood samples were taken at day 0 and day 8 and the samples were analysed for incorporation of omega-3 fatty acid into neutrofile granulocyte cell membranes.We found that 4 of the 5 patients that participated in the study incorporated EPA 7 days after intake of an omega-3 enriched sip feed (paired t test p=0.0015 sign test p=0.0625) One patient did not incorporate EPA due to non compliance. There was no significant incorporation of DHA after 7 days. EPA was incorporated into cell membranes within one week. A large randomized placebo controlled trial is now under way in patients scheduled for colorectal cancer surgery in order to examine possible beneficial effects on postoperative infectious complications.

P19.04 Anders Jensen

PHYLOGENETIC AND TAXONOMIC ANALYSIS OF GROUP C STREPTOCOCCI

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Unlike group A and group B streptococci, group C streptococci (GCS) are a very inhomogeneous group consisting of several pathogen and non-pathogen species. Studies have shown, that pathogenic GCS resemble the pathogenesis of group A streptococci and hence may lead to severe invasive infections as well as localized infections like tonsillitis. However, due to the fact that a thorough taxonomic description and phylogenetic analysis of the group as a whole is missing, GCS are almost never identified to species level in the clinical microbiology laboratory. This may lead to serious clinical misinterpretations. Aim: To study the taxonomy and phylogeny relationships of GCS leading to a more precise description of coherent and distinct clusters within GCS. M&M: A total 212 strains is being studied, including both β-haemolytic and non-haemolytic human invasive and non-invasive strains and animal strains of all known species belonging to GCS. Several molecular approaches will be used including Multi Locus Sequence Analysis (MLSA), analysis of 16S rRNA gene sequences, and sequencing of virulence genes. Finally, a biochemical scheme for a quick identification and differentiation between the taxonomic and phylogenetic clusters found by the phylogenetic analysis will be developed. Results: preliminary results will follow at the PhD day. Conclusion and perspectives: Thorough phylogenetic and taxonomic analysis of GCS may help in the species identification of GCS in the clinical microbial laboratory resulting in improved insight into the role GCS in human infections as well as better epidemiologic surveillance of GCS. Ultimately this should lead to improved treatment of GCS infections.

P19.05 Tine Gregersen

GASTROINTESTINAL FUNCTION IN PATIENTS WITH CARCINOID SYNDROME

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Background: Diarrhea is the most common symptom in patients with neuroendocrine tumor (NET). Somatostatin analogues reduce stool frequency and may increase gastrointestinal transit time (GITT). Motility tracking system® MTS-1 (MTS) is a novel, safe, minimal invasive and easy-to-perform method for description of gastrointestinal motility.
Aim: To compare GITT and motility patterns in NET patients before and after treatment with Sandostatin® LAR with those of healthy subjects.
Methods: For MTS a small magnetic pill (6x15 mm) was ingested and a matrix of magnetic sensors (4x4) tracked the position of the magnet defined by 5 coordinates (position: x, y, z, angle: θ, φ). Nine NET patients (5 men, age 39-73 years, median 60) were investigated and compared to 10 healthy subjects. Patients were studied before and during treatment with Sandostatin® LAR.
Results: The basic contractile frequency was similar in healthy subjects and in patients with NET. Before treatment median gastric emptying in patients with NET was 16 min (4-200) versus 57 min (1-172) in healthy subjects (p=0,97) and median intestinal transit time was 186 min (74-326) versus 308 min (131-435) ($p<0.05$). Treatment with Sandostatin® LAR increased non significantly median intestinal transit time to 259 minutes (145-344) (p=0.11) and median gastric emptying time to 16 minutes (range: 5-380) (p=0.16).
Conclusion: In spite of normal basic contractile frequency, NET patients with diarrhea have faster than normal transit times of the small intestine (p=0,019). After treatment with Sandostatin® LAR 30 mg there was a trend towards increased small intestinal transit time (p=0,108) without change in basic contractile frequency.

P19.06 Simon Lønbro Jensen

RESISTANCE TRAINING AND DIETARY SUPPLEMENTS AS INTERVENTION FOR REGAINING MUSCLE MASS FOLLOWING RADIOTHERAPY IN HEAD AND NECK CANCER PATIENTS.

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Introduction: Head and neck cancer (HNC) patients experience a considerable decrease in muscle mass due to cachexia and dysphagia following radiation therapy. This decrease in muscle mass is associated with a lower survival rate and a decrease in muscle strength and functional capacity. Resistance training (RT) has been shown to be effective for regaining muscle mass, muscle strength and functional capacity among healthy individuals and various groups of patients and HNC patients may benefit from this as well. In addition, a dietary supplement of protein and creatine could enhance the positive effects induced by RT. Purpose: The aims of the study are to 1) investigate whether RT with or without dietary supplement is tolerable among HNC cancer patients, 2) determine the effects on body mass, muscle mass and functional capacity. Methods: Post radiation treatment, 30 patients will be randomly assigned into two groups. In the following twelve weeks, group 1 completes an RT protocol combined with a protein and creatine supplement, whereas group 2 completes the same protocol with placebo supplement. Before and after 12 weeks of training, body mass, muscle mass, maximal muscle strength and functional capacity (e.g. walking test) are evaluated. Hypotheses: We hypothesize that RT is tolerable among HNC patients and that combination of RT with dietary supplement has a significant positive effect on muscle mass that is larger than the effect of RT alone. Results: Not available

P19.07 Malene Krag Kjeldsen

THE ROLE OF SOX4 IN MAILGNANT LYMPHOPOIESIS

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The stem cell derived transcription factor SOX4 was observed to have deregulated expression in some human diffuse large B-cell lymphoma (DLBCL). SOX4 is a single exon gene important in the differentiation of early B-cells. The oncogenic impact of SOX4 is not fully elucidated but enhanced expression has been reported in several cancer types but so far not in human B-cell lymphomas. The oncogenic potential of SOX4 in hematopoietic cells is supported by murine studies on retroviral insertional mutagenesis where the gene loci encoding the SOX4 transcription factor is a common integration site in B-cell lymphomas in general.
In 53 cases of DLBCL, we demonstrated deregulated expression of SOX4 by global gene expression analysis and subsequently validated these findings by quantitative real time RT-PCR on 14 cases. Pathway analysis based on GEP combined with class comparison of patient samples with the highest and lowest expression of SOX4 indicates that multiple genes are differentially expressed between the two groups, including genes involved in apoptosis and proliferation suggesting SOX4 to be an important determinant in these processes. Protein expression and subcellular localisation by Western blotting is ongoing. We hypothesise that SOX4 regulates genes with important impact on oncogenesis in DLBCL. To determine SOX4 target genes chromatin immunoprecipitation will be performed. Identification of genes that are regulated by SOX4, in both normal and malignant B-cells, will contribute to our knowledge about the potential role of SOX4 in the oncogenesis of DLBCL. A part of the scientific programme CHEPRE supported by The Danish Agency for Science, Technology and Innovation.

P19.08 Johan Grankvist

METASTASES IN BREAST CANCER MRI OR PET/CT A CLINICAL

COMPARISON

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Can metastases be detected without using ionizing x-ray irradiation?
MRI-scanning uses strong magnetic-fields and radio-waves to produce diagnostic images. It has no-known side-effects and doesn't use X-rays.
But, can it replace imaging methods using ionizing radiation?
Cancer cells consume more sugar than normal cells, as they grow and multiply faster. Radioactive marked sugar injected into the blood is metabolized in all cells, and radioactive hot-spots can be detected on a scan one hour after injection; thus indicating the physiologically most active cells in this one-hour-period. This type of scan, positron emission tomography, combined with a standard computed tomography, is called a PET/CT-scan. Because of the high diagnostic value, PET/CT is chosen as the gold standard in this project.
My project compares MRI including diffusion imaging with PET/CT in breast-cancer-patients with metastases to the spine and pelvis. If the MR-scan detects bone-metastases comparable to the PET/CT-scan, these patients may be subjected to less ionizing radiation, during their long series of follow-up scans necessary for treatment monitoring.
In our study, the T1 weighted sequence was the the most important one for detecting metastases. Furthermore, when it is combined with the STIR and the diffusion weighted sequence the MRI-scan is sensitive enough compared to PET/CT for the evaluation of breast cancer metastases to the spine and pelvis.
My poster will provide these results, which may allow the use of an imaging method with less side effects for the patients, without loosing diagnostic accuracy.

P19.09 Maria Luise Salskov-Iversen

CASPASE-5 IS UPREGULATED IN PSORIASIS

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Inflammatory caspases are believed to play a pivotal role in innate immune responses and may link innate immunity to auto-inflammatory diseases like psoriasis. The purpose of this study was to characterise caspase-5 in psoriatic skin including stable psoriatic plaques and acute guttate elements. Finally, we studied the induction of caspase-5 mRNA. Paired biopsies were taken from nonlesional psoriatic skin, stable plaques and guttate elements from 6 patients with moderate to severe psoriasis. Caspase-5 mRNA and protein was analysed using quantitative RT-PCR and Western blotting techniques. Cultured normal human keratinocytes were stimulated in 3-24 hours with IFN-g, 10ng/µl before caspase-5 mRNA was measured in RNA extracts by RT-PCR. We found a 23-fold upregulation ($p<0.05$) of caspase-5 mRNA in stable plaque psoriasis compared with nonlesional psoriatic skin. Guttate elements revealed 36-fold increase ($p<0.05$) compared with nonlesional psoriatic skin. We found no statistically significant difference in caspase-5 mRNA between plaques and guttate elements in these 6 patients. Protein studies revealed a 1.4 fold increase ($p<0.05$) in caspase-5 in lesional psoriatic skin compared with nonlesional skin. RT-PCR analysis on IFN-g stimulated human keratinocytes showed a significant and time dependent upregulation of caspase-5 mRNA during 3-24 hours stimulation. In conclusion, we found significant upregulation of both caspase-5 mRNA and protein expressions in lesional psoriatic skin compared with nonlesional psoriatic skin. Furthermore, in vitro studies in keratinocyte cultures suggest an important role of IFN-g in the regulation of caspase-5.

P19.10 Simon Rasmussen

THE ROLE AND MECHANISM OF AUTOPHAGY IN TOLL LIKE RECEPTOR 9 MEDIATED VIRAL RECOGNITION

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During herpes simplex virus (HSV) infection, detection is, among others, conducted by the germline-encoded toll like receptor (TLR)9, located in the endosomes where it detects DNA. Upon binding to DNA, TLR9 initiates downstream signalling cascades resulting in induction of interferon (IFN)α/β and other antiviral cytokines. The exact route of HSV to the endosomes and thus TLR9 recognition is not clear-cut. Recently the role of autophagy in TLR mediated viral recognition has been drawn into focus. In this project we have found that TLR9 mediated HSV-1 IFNβ induction is independent of viral replication. Instead we found a dependency on viral entry, since entry defect glycoprotein (g)L and gH HSV-1 were unable to initiate IFNβ/α induction. In addition, inhibition by 3-methyladenine of PI3 kinase Class III, which is crucial in autophagosome formation, abrogates IFNβ induction. Immunoblotting against LC3 showed that the functional form, called LC3 II, becomes up-regulated during HSV-1 infection. Furthermore, we found a role for dsRNA-dependent protein kinase (PKR), which is well established as an inducer of autophagy, in HSV-1 induced IFNβ expression. By use of the macrophage-like cell line RAW264.7 expressing dn PKR, it was established that a constitutive level of LC3 II was partially dependent on PKR. Collectively, these findings indicate that autophagosomes have a role in translocation of HSV, or part of it, from the cytosol to the endosomes, thus making TLR9 recognition possible. Our findings seats PKR upstream of TLR9 mediated recognition. The precise mechanism, in which HSV mediated LC3 II up regulation, and thus autophagosome formation, has still not been established.

P20.01 Pernille Bach Jørgensen

TELOMERE DYNAMICS IN SPERMATOGENESIS

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Telomere dynamics in spermatogenesis is important for reproduction, development and human ageing. The DNA protecting Telomeres, located at the ends of chromosomes, shorten progressively with each somatic cell-division. When the telomeres reach a critical length, they will induce senescence or apoptosis. The telomere length (TL) may consequently be an indicator of the cell-replicative capacity. In germ cells, cancer cells and stem cells, telomerase elongate the telomere. Until now a complete telomere profile during spermatogenesis has only been studied in mouse and rat. We have measured human TL in spermatogonia, primary and secondary spermatocytes, and spermatids. This was done with quantitative fluorescent staining using FISH with a telomere-specific PNA-probe, where fluorescent signal-intensity represents the relative telomere length.
Human telomere dynamics resemble that seen in mouse and rat, where telomere length shortens and telomerase activity decrease from spermatogonia to round spermatids. In elongated spermatids the telomerase activity is restored and the telomeres elongate, resulting in long telomeres in the spermatozoa.
We show that TL in humans shortens from spermatogonia to round spermatids. Currently we are doing experiments on decondenced spermatozoa, to investigate telomere dynamics during the development from round spermatids to spermatozoa. Furthermore we examine whether TL is inherited from parents to offspring. If short telomeres are inherited from the parents, it could lead to inheritance of short lifespan in the offspring. Investigating this will give an overall knowledge on telomeres, which play important roles in ageing, reproduction, cancer etc.

P20.02 Jakob Stegger

ANTHROPOMETRY AND RISK OF ACUTE CORONARY SYNDROME

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The incidence of cardiovascular disease has declined in developed countries in recent years, but this may change as obesity increases in epidemic proportions. It is now known that not only does adipose tissue secrete abundantly amounts of active proteins, but also that the quality and quantity of these proteins varies extensively according to the type of adipose tissue. The visceral adipose tissue secretes a relative greater amount of pro-inflammatory and pro-thrombotic proteins than does subcutaneous adipose tissue. Cytokines secreted by adipose tissue are supposed to augment the inflammatory processes in the artery wall leading to increased atherosclerosis.
The objective of this PhD study is to investigate the associations between anthropometric measures and risk of acute coronary syndrome. Furthermore we will explore interactions between intake of non-steroid anti-inflammatory drugs or polymorphisms in inflammatory related genes (PPAR-gamma and COX) and obesity on risk of acute coronary syndrome. The PhD study is based on data from the Diet, Cancer and Health study. The interaction studies also include data from the Nurses' Health Study and the Health Professionals Follow-up Study. The total number of participants exceeds 340.000.
The raw data will be transformed into a complete dataset for statistical analyses. The associations will bee analysed using Cox regression analysis with extensive control of confounding. Exposure variables include classic anthropometric indices such as body mass index, waist- and hip-circumferences as well as indices derived from bio-impedance measures. The latter has not previously been investigated in such large-scale cohorts.

P20.03 Lene Sundahl Mortensen

DIFFERENTIAL EFFECTS OF PROTEIN QUALITY ON POSTPRANDIAL LIPEMIA IN RESPONSE TO A FAT-RICH MEAL IN TYPE 2 DIABETES: COMPARISION OF WHEY, CASEIN, GLUTEN AND COD PROTEIN.

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Background: Enhanced and prolonged postprandial triglyceride responses involve increased cardiovascular risk in type 2 diabetes (T2DM). Dietary fat and carbohydrates profoundly influence postprandial hypertriglyceridemia whereas little information exists about the effect of proteins.
Objective: To compare the effects of the proteins casein, whey, cod, and gluten on postprandial lipid and incretin responses to a high-fat meal in T2DM.
Design: Cross-over study of twelve type 2 diabetics. Blood samples were collected over 8 h after ingestion of a test meal containing 100g butter and 45g carbohydrate in combination with 45g of either casein (Cas-meal); whey (Whe-meal); cod (Cod-meal); or gluten (Glu-meal). We measured plasma levels of triglyceride, retinyl palmitate (RP), free fatty acids (FFA), insulin, glucose, glucagon, GLP-1, and GIP.
Results: The incremental area under the curve for triglyceride was significantly lower after the Whe-meal than after the other meals. The RP response was lower after Whe-meal than after Cas- and Cod-meal in the chylomicron-rich fraction and higher after Whe-meal than after Cod- and Glu-meal in the chylomicron-poor fraction. FFA was most pronouncedly suppressed after whey. The glucose response was lower after the Whe-meal than after the other meals, whereas no significant differences were found in insulin, glucagon, GLP-1, and GIP responses.
Conclusions: The data suggest that as a supplement to a fat-rich meal in T2DM

subjects, whey protein seems to outperform other proteins in terms of postprandial lipemia improvement possibly owing to formation of fewer chylomicrons or increased clearance of chylomicrons.

P20.04 Jens Ølholm

ANTI-INFLAMMATORY EFFECTS OF RESVERATROL ON MCP-1 EXPRESSION AND SECRETION IN HUMAN ADIPOSE TISSUE EXPLANTS

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Human obesity is closely associated with a state of chronic low grade inflammation which involves enhanced production of bioactive substances (adipokines) in adipocytes. Proinflammatory adipokines establish a link between obesity and the reduced insulin sensitivity and atherosclerosis in obese subjects. Monocyte chemoattractant protein (MCP)-1 attracts macrophages to sites of inflammation. Obese subjects are characterized by increased adipose tissue macrophage infiltration and MCP-1 play an essential role this process.Calorie restriction reduces adipokine production and improves metabolic profile. These effects depend upon Sirt1 enzyme activation, and can be mimicked by a natural phytoalexin, resveratrol (RSV), a potent Sirt1 activator. Sirt1 has recently been found in human adipose tissue and we surmise that the beneficial role of RSV in improving metabolic profile are at least in part due to altering MCP-1 expression and secretion through Sirt1 dependent pathways. The effect of RSV on IL1β induced change of MCP-1 mRNA gene expression and secretion were measured in human adipose tissue explants and in 3T3-L1 adipocytes. Exposure to IL1β for 24 hours increased secretion of MCP-1 ($p<0.05$) and increased mRNA expression ($p<0.05$) accordingly.Concomitant incubations with RSV reversed the IL1β-stimulated secretion and gene expression.Sirtinol (inhibitor of SIRT-1 activity) reduced the anti-inflammatory effect of RSV ($p<0.05$) in 3T3-L1 adipocytes, indicating that the anti-inflammatory effects of RSV are mediated through the SIRT-1 enzyme.Inhibition of MCP-1 expression in human adipose tissue may represent a novel mechanism of resveratrol in preventing obesity-related pathologies

P20.05 Thomas Svava Nielsen

REGULATION OF LIPOLYSIS IN HUMAN MUSCLE AND ADIPOSE TISSUE

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Lipolysis is the process of triglyceride (TAG) breakdown to free fatty acids (FFA) and glycerol. FFA as well as certain intermediates in lipolysis (DAG, ceramides) can induce insulin resistance and are believed to be important molecular mediators in the pathogenesis of type 2 diabetes (T2D). However, the underlying mechanisms have yet to be clarified. Previous studies have shown a close interplay between the enzymes (lipases) involved in the lipolysis. Small changes in the amount and/or activity of a single lipase can have great implications regarding the balance between complete and partial breakdown of TAG.
The aim of this project is to study the regulation of lipolysis in human skeletal muscle and adipose tissue. This will be done after exercise, fasting, and stimulation with growth hormone - conditions known to affect both insulin sensitivity and the regulation of lipolysis. The main focus will be on the two central lipases Adipose Triglyceride Lipase and Hormone Sensitive Lipase. The analyses will include well established methods such as western blotting, mRNA quantifications and HPLC as well as a newly developed lipase activity assay. Thus, it will be possible to determine if an imbalance in the regulation of the individual lipases can lead to an accumulation of lipolytic intermediates, which could negatively affect the insulin

sensitivity.

P20.06 Kristin Rós Kjartansdóttir

IN VITRO DERIVATION OF SPERMATOGENIC CELLS FROM HUMAN EMBRYONIC STEM CELLS

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Background: The main human embryonic stem cell (hESC) characteristics are their ability to renew themselves and that they can differentiate into various cell types. This dual property makes hESCs promising candidates as therapeutic cells in treating disorders involving loss of specific cell types, such as germ cells (GCs) in infertility. Infertility is the inability of a person to contribute to conception and it affects 10-15% of all couples. In half of the cases the problem is linked to the male partner, due to diminished sperm formation and abnormal sperm functional ability. Fertile men produce millions of sperm cells every day by a process called spermatogenesis.
Aim: This study aims at elucidating the human spermatogenesis process. This study fills a gap in a poorly elucidated area and gives an exceptional opportunity to clarify the human spermatogenesis process, which we know so little about.
Methods: First, we want to generate male GCs from hESCs by adding different hormones, vitamins and growth factors. Second, we would like to develop the GCs into mature sperm cells in a co-culture with supporter cells called Sertoli cells.
Results: Preliminary results show that when adding Retinoic acid (RA) to hESC culture it induces differentiation into GCs. Addition of RA is positively correlated with the expression of specific markers for GC differentiation. Elevated levels of the germ cell specific marker VASA have been detected in the differentiating hESCs by using RT-PCR and Q-PCR. Further more the optimal amount of RA added to the hESC culture, for induction of GC differentiation, has been established.
Conclusion: RA can induce differentiation of hESCs into GCs.

P20.07 Jeppe Grøndahl Rasmussen

HYPOXIA INCREASES EXPRESSION OF ANGIOGENIC AND ANTIAPOPTOTIC CYTOKINES IN HUMAN ADIPOSE TISSUE-DERIVED STEM CELLS

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Background: Heart failure following acute myocardial infarction is a major cause of mortality and morbidity worldwide. Transplantation of mesenchymal stem cells (MSCs) shows promising results reducing the deleterious effects of myocardial infarction in animal models. A significant proportion of the ameliorating effect of stem cell transplantation is believed to be caused by their secretion of cytokines that exert antiapoptotic and angiogenic effects, particularly IGF-1, VEGF, and Secreted frizzled-related protein-2 (Sfrp2) are promising. Short term (24-72 hours) reduction of the oxygen tension during MSCs culture increases VEGF gene expression. The aim of this study was to examine the effects of a more prolonged hypoxic culture using adipose tissue-derived stem cells (ASCs) to test whether IGF-1, VEGF and Sfrp2 expression would be further augmented.
Materials and methods: ASCs from three healthy donors were cultured at 1%, 5%, and 21% oxygen. During a 13 day period, IGF-1, VEGF, and Sfrp2 gene transcription was measured by using real time qPCR.
Results: ASCs cultured at 1% oxygen markedly upregulated the IGF-1 ($p=0.001$), VEGF ($p=0.0001$), and Sfrp2 ($p=0.0001$) genes at day 13. Comparing ASCs cultured at 1% oxygen at day 1 and day 13 the VEGF gene was found to be significantly more upregulated at day 13 ($p=0.03$).
Conclusions: Culture of ASCs at 1% oxygen for 13 days compared to 1 day significantly upregulates the expression of the VEGF gene. These results implicate that prolonged hypoxic culture of ASCs could lead to an augmented angiogenic

stimulation, and support that an ameliorating effect of stem cell transplantation can be caused by their secretion of cytokines.

P20.08 Ruta Tuckuviene

PREDICTIVE VALUE OF PAEDIATRIC THROMBOSIS DIAGNOSES IN A NATIONWIDE HOSPITAL DISCHARGE REGISTRY

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Data on validity of paediatric thrombosis diagnoses are missing. We aimed to examine the predictive value of venous and arterial thrombosis diagnoses for individuals in Denmark aged 0-18 years in the nationwide hospital discharge registry.

Methods: We identified all first-time diagnoses among children and adolescents between 1994 and 2006 in the Danish National Patient Registry. Medical records were reviewed and the positive predictive value (PPV) was computed.

Results: In total, 1138 potential cases of thrombosis were identified among which the medical records could be retrieved for 1111 (97.6 %). Overall, the thrombosis diagnosis was verified in 600 of the 1111 possible cases, corresponding to a PPV of 54.0 % (95% CI 51.0-57.0). Two-third of the non-confirmed cases had not been examined with imaging tests or the tests did not confirm the presence of a thrombosis. The predictive value of thrombosis diagnoses depended on age, with a higher PPV (77.4 %, 95 % CI: 68.7-84.7) in neonates than in children aged 28 days-15years (46.8 %, 95% CI: 41.9-51.7) and adolescents aged below 18 years (54.6 %, 95% CI: 50.4- 58.7). The predictive value of thrombosis diagnoses could be improved by restricting to diagnoses from wards, patients with primary diagnoses and admissions with a length of stay of more than three days.

Conclusions: The interpretation of non-validated data hospital discharge data of paediatric thromboembolic diseases in Danish National Patient Registry should be done with caution.

P20.09 Kristian Havmand

DILATION OF THE ASCENDING AORTA IN TURNER SYNDROME DURING SHORT-TERM FOLLOW-UP

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Background: Aortic dissection causes excess mortality in Turner syndrome (TS) but little is known of the natural course of the dilatory aortopathy beyond cross-sectional studies. Aim: To study aortic dimensions over time as well as the predictors of a possible progressive dilatory aortopathy. Methods: Prospective magnetic resonance imaging follow-up study of aortic dimensions in TS (N=102) compared with healthy age-matched females (N=65). Echocardiography assessed aortic valve morphology, and ambulatory blood pressures were performed. Results: Successful repeat magnetic resonance imaging was performed in 80 of 102 TS patients (11 were lost to follow-up, whereof one had undetected chronic aortic dissection). Aortic dilation was more common in TS, where bicuspid aortic valve, aortic coarctation, and elongated transverse aortic arch were seen in 28%, 11%, and 38%. 45,X karyotype was seen in 61%. Blood pressures and heart rates were elevated in TS. The mean follow-up time was 2.4 (range: 1.4 to 3.5 years). The sinutubular (P=0.02) and mid-ascending (P=0.009) aortic diameters increased with 0.16 and 0.23 mm/year,

respectively. The remaining thorax aortic diameters were unchanged. Overall, 22 of 80 (30%) TS patients had an aortic diameter increment above the limits of agreement (derrived from Bland-Altman variability analysis). No congenital anomaly or karyotype predicted increasing aortic size, except from heart rate that was higher in associatin with more progressive dilatation (P=0.03). Conclusion: An ascending aortopathy was indicated in adult TS, where the currently used indices of risk of aortic dissection did not clearly predict the increase in aortic size.

P20.10 Emil Toft Brøndum

EDHF RESPONSE IN RESISTANCE ARTERIES FROM GASTRIC BYPASS PATIENTS

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EDHF response in resistance arteries from gastric bypass patients

Background and purpose:
This study investigates the EDHF-type relaxation in abdominal subcutaneous resistance arteries from patients undergoing gastric bypass or gastric banding surgery. Patients with a BMI >35. The purpose is to investigate the effect of NS309 (6,7-dichloro-1H-indole-2,3-dione 3-oxime), a potent activator of small- and intermediate-conductance calcium activated potassium channels (SK_{Ca} and IK_{Ca}) in human tissue.

Experimental approach:
Biopsies are collected during surgery and endothelium-dependent ACh relaxation is investigated under isometric conditions. The EDHF type relaxation is investigated in the presence of 3 μM indomethacin, an inhibitor of cyclooxygenase, and 100 μM l-NAME (N(omega)-nitro-L-arginine methyl ester), an inhibitor of nitric oxide (NO) synthase before and after addition of 1 μM NS309.
The levels mRNA for SK_{Ca} and IK_{Ca} will be evaluated using qPCR technique and intracellular calcium will visualized using confocal microscopy.

Key results:
Surprisingly both ACh and the EDHF-type relaxation seem unaltered when compared to control arteries. The effect of NS309 on human arteries seems to be an increase in the relaxing response to ACh, as previously described in a rat model of obesity and diabetes.

P21.01 Charlotte Rotbøl Bøje

THE IMPORTANCE OF COMORBIDITY IN HEAD AND NECK CANCER

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Background: The aetiology of head and neck squamous cell carcinoma (HNSCC) is predominantly cigarette smoking and/or alcohol abuse and HNSCC pts may therefore experience a high rate of comorbidities compared with other cancers. HNSCC is treated with primary radiotherapy but even though local control is good the overall survival is poor. Comorbidity is a coexisting disease not related to the index disease and it has shown increasing importance as prognostic factor for survival and other treatment related outcomes for HNSCC pts.
Aim:
•Estimate the prevalence and type of comorbidity in HNSCC patients.
•Study the prognostic role of comorbidity for the outcome of radiotherapy in head and neck cancer.
•Justify the assessment of comorbidity in prognostic staging for HNSCC patients.
Material and methods: Through the DAHANCA (Danish Head and Neck Cancer group) database and the Danish Cancer Registry we will identify patients with HNSCC treated with radiotherapy from 1992 – 2006. The cohort will consist of

appr.10.000 patients. Through cross linking with the CPR Registry and "Landspatientregisteret" the comorbidities will be obtained and adapted to Charlson Comorbidity Index. Survival will be analysed according to level of comorbidity stratifying for other known prognostic factors and the end points will be locoregional control, disease specific survival, and overall survival.
Perspectives: To improve survival after HNSCC we need to investigate prognostic factors, as co-morbidity, with the aim of developing targeted interventions. Addition of co-morbidity to the current TNM staging will probably provide a more accurate way of individualise and optimise the treatment for HNSCC pts.

P21.02 Claus Tvedesøe

THE INFLUENCE OF HEAT ON EXTRAVASATION OF USPIO PARTICLES

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INTRODUCTION
In this study we have investigated the effect of various lengths of localized mild hyperthermia (41,5 degrees Celcius) on the extravasation of i.v injected USPIO particles in a murine tumor model to determine the optimal heating length.

METHODS:
C3H tumors were grown in the rear right foot female CDF1 mice.
Heat treatment was performed locally by submerging the tumor bearing foot in a circulating water bath, the water temperature was 41.5 °C.
MRI was performed using a 1.5 T MR scanner (Philips Healthcare Systems).
Animals were randomized into four groups receiving either 1, USPIO particles only; 2, USPIO particles and 5 min of hyperthermia; 3, USPIO particles and 30 min of hyperthermia and 4, USPIO particles and 60 min of hyperthermia. N=9 in each group. Animals were MR scanned prior to injections and again after 90-, 390- and 1140 min.

RESULTS SECTION:
Change in T2* in response to heating length shows a significant difference between animals heated for 30- and 60 minutes compared to animals heated for only 5 minutes and controls having received only USPIO particles and no heat ($p<0.05$). T2* decreases rapidly by the time of the first scan (90min) and incline slightly on scans 390, 1140 min. After 1140 min (24h) the T2* value in the control group, is 39.5 +/-4.3 compared to 27 +/-3.2 in the group receiving heat for 60 minutes and after 90 min the values are 31+/- 5.6 and 10 +/-2.1. There is a fine relationship between heating length and T2* value throughout the data.

DISCUSSION:
The optimal heating length seems to be 30 minutes, with very little benefit of going up to 60 minutes.

P21.03 Tanja Eiersted Molzen

IDENTIFICATION OF ESSENTIAL GENES IN STREPTOCOCCUS PNEUMONIAE MENINGITIS

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Background
S. pneumoniae meningitis is a serious infectious disease causing death in app. 25% of cases and severe sequels in half of survivors in spite of relevant treatment.

Vaccination with capsular polysaccharides prevents invasive pneumococcal disease only from included serotypes.
In this study we applied Genetic Array Foot printing (GAF) in the search for genes essential for S. pneumoniae in experimental meningitis, hoping to identify targets for future vaccination and adjuvant treatment of meningitis.
Methods
Pneumococcal mutants were screened for survival in rabbit meningitis. Mutant pools were injected into Cisterna magna and CSF was collected after 3, 9 and 15 hours. Attenuated mutants were identified by Microarray-analyses comparing infecting inocula to sampled CSF.
GAF-results were validated for a subset of mutants by testing their growth properties in co-infection with the wild-type strain in rat meningitis.
The pathogenic properties of mutants confirmed to be attenuated in co-infection were tested in mono-infection in rats.
Results
81 pneumococcal genes were identified as essential in rabbit meningitis. Essential genes were mainly components of metabolic or nutrient uptake pathways and capsule polysaccharide biosynthesis genes.
Attenuation of 8 of 15 mutants was confirmed in co-infection.
Mutant strains Δ purA, Δ livJ and Δ fld were significantly impaired in rat meningitis.
Conclusions
In spinal fluid, the pneumococcus relies on genes that enable access to and utilization of nutrients. The genes purA, livJ and fld are critical for pneumococcal survival in meningitis and could be potential targets for future treatment of meningitis.

P21.04 Lykke Grubach EPIGENETIC INHIBITION OF CBF-MUTATED LEUKEMIA - AN ONGOING STUDY

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Background: In acute myeloid leukemia (AML) a subtype with genetic aberrations in the core binding factor (CBF) is defined. In the experiments these aberrations are represented by the cell lines ME-1 (inv16) and Kasumi-1 (t(8,21)). Given that the hallmark of AML is lack of myeloid end differentiation, we focused on the Hox genes, which are involved in differentiation and leukemogenic progression.
Epigenetic modifications affect the structure of chromatin. Thus, being dominated by repressive modifications, the chromatin coils up very tightly leading to a conformation that impairs binding of the transcription complex to the promoter region. By inhibiting specific epigenetic modifications, I am analysing whether chromatin becomes more or less accessible to gen transcription. Furthermore as the modifications cooperate I will determine whether inhibition of one mark affects the presence of the others.
Setup: ME-1 and Kasumi-1 are exposed to treatment with inhibitors towards DNA methylation (5-aza), histone deacetylation (TSA) and histone phosphorylation (Staurosporine). Cells will be harvested at specific timepoints up to ten days after exposure and analysed. Data analysis includes testing DNA methylation state, chromatin immunoprecipitation and RQ-PCR for Hox gene expression analysis.
Results: I expect to find increasing Hox gene expression as a result of treatment with TSA and 5-Aza. Exposure to Staurosporine will most probably lead to enhanced apoptosis and histone methylation. I presume that inhibiting the DNA methylation will increase histone acetylations and phosphorylations. The data will be raised during the next 2 months.

P21.05 Hanne Østergård Larsen COMPARISON OF TRANSFECTION METHODS FOR SIRNA DELIVERY IN HEMATOPOIETIC SUSPENSION CELLS

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Background: RNA interference is a powerful tool for identifying gene function in biological processes but one of the prerequisites to this analysis is to find a method that can achieve high efficiency gene transfer of siRNA into the cells and at the same time leave the cells with a high viability. Previous studies have shown that working with suspension cells and other hard to transfect cells the transfection method of choice would be nucleofection. In this study, we tested the transfection efficiencies using the nucleofection technology and a newly developed chemically technology called Accell siRNA delivery. Materials: For transfection the AML cell line HL-60 and the CML cell line K562 was used. Nucleofection was performed using the Amaxa nucleofector. For determining transfection efficiency eGFP plasmid was used. Accell delivery media and Accell FITC labelled siRNA was used for measurement of transfection efficiency using the Accell method. Apoptosis and viability post transfection was determined by flow cytometry using annexin V and 7-AAD. Results: Best result for HL-60 was obtained 72 hours post transfection by the Accell technology (efficiency 100% viability of 90%). Nucleofection of HL-60 showed best 48 hours post transfection (efficiency 35% viability 40%). Regarding the K562 cell line the best result was obtained 24 hours post transfection by the Accell technology (efficiency 100% viability 75%). Nucleofection of K562 showed best 48 hours post transfection (efficiency 50% viability 60%). Conclusion: We have proven delivery of siRNA by the Accell method to be more efficient and more gently to the cells compared to the generally accepted nucleofection technology.

P21.06 Ole Schmeltz Søgaard

IMPROVING THE IMMUNOGENICITY OF PNEUMOCOCCAL CONJUGATE VACCINE IN HIV-INFECTED ADULTS WITH A TLR9 AGONIST-ADJUVANT. A RANDOMIZED TRIAL

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Background: People infected with HIV are often hypo-responsive to immunization, including pneumococcal vaccines. We hypothesized that adding CPG 7909, a TLR9-agonist and novel vaccine-adjuvant, to 7-valent pneumococcal conjugate vaccine (PCV-7) would increase its immunogenicity in HIV-infected adults.

Methods: A double-blind, placebo-controlled phase Ib/IIa trial randomizing persons with HIV to immunization with double doses of PCV-7 (Prevnar®, Wyeth) ±1 mg CPG 7909 at 0 and 3 months followed by single dose 23-valent pneumococcal polysaccharide vaccine (PPV-23, Pneumo Novum®, Sanofi-Pasteur MSD) ±1 mg CPG 7909 at 9 months. Immunogenicity and safety were evaluated at 0, 3, 4, 9, and 10 months. The primary endpoint was the proportion of vaccine high-responders at 9 months, defined as 2-fold increase in IgG levels to ≥1 µg/mL for at least 5 of 7 PCV-7 serotypes.

Results: 97 participants were included, 48 in the experimental group and 49 in the control group. The proportion of vaccine high-responders was higher in the experimental group than among controls (48.8% vs. 25.0%, P=0.02). Greater proportions of high-responders were also observed at 3 (51.1% vs. 39.6%, P=0.26), 4 (77.3% vs. 56.3%, P=0.03), and 10 months (87.8% vs. 51.1%, P<0.001). Mild systemic and injection-site reactions to PCV-7 were more common in the experimental group than the control group (100% vs. 81.3%, P=0.002). CPG 7909 did not increase non-PCV-7 IgG levels after PPV-23 immunization. No adverse effects on CD4+ cell count or organ functions occurred in either group.

Conclusions: The addition of a TLR9-agonist to PCV-7 significantly enhanced the proportion of vaccine high-responders.

P21.07 Torben Stamm Mikkelsen

SHORTENING THE INFUSION TIME OF HIGH DOSE METHOTREXATE REDUCES THE ACCUMULATION OF ACTIVE METHOTREXATE POLYGLUTAMATES IN LEUKEMIA CELLS AND THE ANTILEUKEMIC EFFECTS

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Cure rates for childhood acute lymphoblastic leukemia (ALL), the most common cancer in children, are approaching 90%, thus a natural aim of future protocols will be to reduce the treatment related toxicity. Infusions with high-dose methotrexate have for more than two decades been an integral part of essentially all ALL treatment protocols worldwide. Most protocols use 24 hour infusions of methotrexat but a reduction in infusion time could be a strategy to decrease drug related toxicity and at the same time shortening hospitalization time and workload. However, it is not clear whether a reduction in infusion time alters the accumulation of methotrexate polyglutamates (MTXPG) in leukemia cells or reduces the antileukemic effects. In a prospectively randomized trail, from St Jude Children's Research Hospital, 358 children with newly diagnosed ALL were randomized to receive methotrexate 1 g/m^2 as either a 4 hour infusion or a 24 hour infusion at the first day of treatment. The accumulation of MTXPG was determined in leukemia cell obtained by a bone marrow biopsy 42 hours after start of the methotrexate infusion and the antileukemic effect was measured a inhibition of de novo purine synthesis and change in circulating leukemic cells. We found that the 24 hour infusion produced a statistically significant higher concentration of MTXPG in leukemia cells and that this was related to a stronger antileukemic effect. However the there were differences amongst the major ALL subtypes indicating that 4 hour infusions with high-dose methotrexate could be used for patients with TEL-AML1 without changing the excellent survival rate related to this ALL subtype.

P21.08 Vanda Turcanova

HERPESVIRUS-INDUCED EXPRESSION OF A HUMAN ENDOGENOUS SUPERANTIGEN

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The K18-Env, an envelope protein of human endogenous retrovirus (HERV)-K18, displays superantigen (SAg)-like properties. As such, it may play a role in the development of autoimmune diseases by antigen non-specific activation of autoagressive T cells. HERV-K18 mRNA levels are known to be upregulated during an EBV infection, or following IFN-α treatment in B cells. This upregulation is coupled with a functional SAg-like activity. Our study shows that the K18 env mRNA is upregulated in the peripheral blood mononuclear cells during infection with a number of herpesviruses, namely herpes simplex virus type I, varicella zoster virus, human cytomegalovirus, Epstein-Barr virus, and human herpesvirus (HHV) types 6A and -6B. We characterized the mechanisms behind this upregulation in closer detail for HHV-6B, a virus causing the childhood disease exanthem subitum and associated with certain neuropathologies. The K18 env induction appeared to need viral entry into the cell and ongoing protein synthesis, but was independent of HHV-6B replication or expression of viral genes. This, and the fact that other viruses are capable of inducing K18 env, suggests involvement of pattern recognition receptors (PRRs). This was true for TLR9, although other PRRs may also be involved. These results suggest existence of a common mechanism for viral induction of K18 Sag. It seems possible that PRRs triggered by a virus infection induce expression of a

SAg, which may have consequences for development of autoimmune reactions, as well as for general shaping of immune responses.

P21.09 Anders Kirch Dige

ETHYLENE-DIAMINE-TETRA-ACETATE (EDTA) MIMICS THE EFFECT OF REGULATORY T CELLS IN SUPPRESSION ASSAYS: A POTENTIAL PITFALL WHEN USING AUTOMACS-SEPARATED CELLS

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Background: CD4+CD25+ regulatory T cells (Tregs) mediate tolerance towards self antigens and prevent the development of autoimmunity. Treg function is typically evaluated by the ability to suppress proliferation and cytokine production of co-cultured CD4+CD25- T cells in Treg suppression assays.

Methods: Purified Tregs were obtained using the "Regulatory T Cell isolation kit" from Miltenyi Biotech. Separation was performed automated using the AutoMACS Cell Separator.

Results: We discovered a potential pitfall in Treg suppression assays evaluating magnetically separated CD4+CD25+ T cells obtained by the "Regulatory T Cell isolation kit" and AutoMACS Cell Separator. The AutoMACS Running Buffer recommended by the manufacturer for separation contains Ethylene-Diamine-Tetra-Acetate (EDTA). We show that even minute traces of EDTA in the CD4+CD25+ T cell fraction mediate significant suppression of CD4+CD25- T cell proliferation. The suppressive effect of EDTA is dose-dependent and mimics Treg mediated suppression of CD4+CD25- T cell proliferation. The influence of EDTA can be eliminated by thoroughly washing of the CD4+CD25+ T cell fraction following the separation.

Conclusion: Care has to be exercised when concluding on results based on Treg suppression assays evaluating magnetically separated Tregs obtained by the "The regulatory Cell isolation kit" and AutoMACS Cell Separator.

P21.10 Britta Weber

TREATMENT WITH ERLOTINIB SHOW A DRAMATIC EFFECT AND BRAIN ACCUMULATION IN A PATIENT WITH METASTATIC NON-SMALL CELL LUNG CANCER HARBOURING A MUTATION IN THE EGF-RECEPTOR

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A 32 year-old woman with non-small cell lung cancer (NSCLC) and multiple brain metastases was referred to the department of Oncology in a poor clinical condition, suffering from severe nausea and vomiting. She was treated with the epidermal growth factor receptor (EGFR) targeting drug erlotinib as a first line treatment and had a remarkable intra- and extra-cranial response.

We demonstrated that the tumor harboured a mutation (15 bp deletion in exon 19) of the EGFR gene. Interestingly, this EGFR mutation has recently been shown to enhance erlotinib sensitivity. After 9 months of progression free survival, the patient was readmitted to hospital in a poor clinical condition due to hydrocephalus. The treatment was discontinued for 2 weeks and a ventriculo-peritoneal shunt was implanted.

To explore a possible accumulation of erlotinib in brain metastasis, the patient was recruited for a PET scanning with a new tracer ^{11}C-labbeled-erlotinib, developed by our group (Memon et al, Cancer Research, 2009). We demonstrate that cerebral metastases can be visualized by PET scan with ^{11}C-labelled-erlotinib, showing for the first time that erlotinib enters the brain tumours. This is in accordance with the remarkable clinical response during the first period of erlotinib treatment in this patient.

In conclusion, we report a remarkable response to erlotinib in a lung cancer patient with a mutated EGF receptor. Furthermore we demonstrate for the first time that

erlotinib is capable of crossing the blood brain barrier. However further studies are needed to confirm these results.

P22.01 Stefan W. Harders

HIGH RESOLUTION SPIRAL CT OF SOLITARY PULMONARY NODULES. MORPHOLOGIC ASSESSMENT, DIAGNOSTIC ACCURACY AND INTER-RATER AGREEMENT.

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Introduction: A Solitary Pulmonary Nodule (SPN) may represent early stage lung cancer. We applied High Resolution spiral CT (HRCT) to SPNs to test whether morphological characteristics are associated with lung cancer, assessed the diagnostic accuracy of HRCT in the characterization of SPNs, and addressed reproducibility of all measures.

Materials and Methods: A retrospective follow-up with 215 participants. Blinded HRCT images were assessed with regard to Margin Risk Categories (MRCs), calcification patterns and other characteristics, and an overall Disease State Rating (DSR) was given. Multiple likelihood ratios were calculated, morphological characteristics were tested and ROC-methodology was applied to assess diagnostic accuracy. Reproducibility was measured with Kappa statistics and 95% CIs were computed for all results. Pathology (89%) and CT follow-up (11%) was used as reference standard.

Results: MRCs [P<0.001; κ: 0.66 (0.58; 0.74)], calcification patterns [P=0.003; κ: 0.74 (0.43; 0.93)], and pleural retraction [P<0.001; κ: 0.55 (0.44; 0.66)] were statistically significantly associated to lung cancer. The sensitivity, specificity and overall diagnostic accuracy of HRCT was 98% (94%; 100%), 23% (15%; 33%) and 88% (83%; 92%) respectively [κ: 0.77 (0.71; 0.83)].

Discussion: We established statistically significant associations between SPN MRCs, calcification patterns, pleural retraction and disease state. Reproducibility of these measures was moderate to substantial. We also established that HRCT yielded a very high sensitivity and a somewhat more fair specificity for lung cancer. Overall diagnostic accuracy was high, and reproducibility was substantial.

P22.02 Thomas Reinert

WHOLE GENOME METHYLATION ANALYSIS IN BLADDER CANCER

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In bladder cancer epigenetic DNA changes have been reported for a limited number of genes, e.g. TNFRSF25 and BCL2, and aberrant methylation may silence expression of genes in cancers. This study aims to vastly improve the current knowledge level; thus a whole genome methylation analysis was performed. The technology reveals the extent of methylation of 14.475 genes in bladder cancer and using this new information we propose candidates for earlier bladder cancer detection and aim to enhance the diagnoses by improving the quality of molecular risk scores.
This study included 51 bladder tumors from 27 patients with no prior history of tumors and 6 samples from healthy individuals. Samples with at least 75% tumor cells were analyzed by the Infinium methylation array.
We identified genes with a highly significant difference in methylation between normal urothelium and tumors (e.g. MMP26 (p= 0.00007) and CNOT6 (p=0.0001)). Additionally, we have found genes being differently methylated in low risk and

high risk superficial tumors with the most predominant being Cathepsin E (p= 0.0043) and Interleukin 1 receptor antagonist (p= 0.0005). In a similar convincing manner methylation can distinguish between non-invasive and invasive tumors. The most prevalent difference in methylation was found between urothelium from healthy donors and patients with bladder tumors, but methylation may also distinguish between superficial tumors with low and high malignant potential; thus, aberrant methylation was found to be a frequent and early process in the development of bladder cancer and methylation markers may be used both prognostic and diagnostic to improve treatment of bladder cancer patients.

P22.03 Anne-Cathrine Bareid Østby

COMMUNITY RESPIRATORY VIRUSES CAUSING ACUTE RESPIRATORY DISEASE IN PATIENTS ADMITTED AT INTENSIVE CARE UNITS AND DEPARTMENTS OF HEMATOLOGY

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Several hundreds of viruses can cause respiratory symptoms. Especially children, elderly and immunocompromised patients are susceptible to severe disease, and each year, 1500 deaths are attributed to influenza alone. Still, respiratory viruses are underestimated causes of acute respiratory infections in hospital patients, probably due to former insensitive methods and lack of interest, as only a few anti-viral drugs are available. Molecular techniques are now developed that make rapid and sensitive diagnostics possible.
Aims: Study of epidemiology of respiratory viruses in critically ill patients.
Method: Throat swabs from patients admitted with symptoms of acute respiratory infection at two Intensive care units and two departments of Hematology from 01-12-08 until 01-12-10, aiming at approx. 800 samples. Samples are analyzed using real time multiplex PCR-method on Influenza A and B, parainfluenza 1, 2 and 3, respiratory syncytialvirus, human metapneumovirus, rhinovirus and coronavirus NL63, -OC43 and -229E. The prevalence and significance of bacterial findings are illustrated for each patient with data from dept. of Clinical Microbiology. Patient records provide epidemiological data.
Perspective: The project will describe the role of respiratory viruses in critically ill patients. Despite that only anti viral drugs are available, it is of great importance to know the magnitude of the problem, as well as to clarify whether virus alone causes the clinical symptoms, or double infections with bacteria is more common or more severe. Possibly, a more nuanced diagnostics could contribute to reducing the use of antibiotics, thus reducing problems with drug resistance.

P22.04 Lasse Sommer Kristensen

MAKING THE MOST OF METHYLATION SPECIFIC PCR EXPERIMENTS: HOW TO OBTAIN ALLELE-SPECIFIC INFORMATION

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Methylation and silencing of tumor suppressor genes play an important role in the development and progression of cancer, and many of these genes are considered promising DNA methylation biomarkers for early cancer diagnostics, prognostics, and for predicting response to therapy. The predictive value of DNA methylation biomarkers may be depending on the allele-specific methylation status of the biomarker, as the inactivation of tumor suppressor genes usually require two hits. Methylation specific PCR (MSP) is the most widely used methodology for the detection of single locus methylation due to its high sensitivity and simplicity. Conventional MSP, however, does not resolve the methylation status of individual alleles, thus potentially loosing important information. We hypothesized that allele-specific methylation information can be obtained by designing MSP amplicons that include a single nucleotide polymorphism (SNP), as post-PCR analysis of the SNP then may determine which of the two alleles that was amplified and thus

methylated. We designed an assay that targets the rs16906252 SNP found in the MGMT promoter CpG island. We have shown that direct sequencing and high-resolution melting (HRM) can be used independently as post-PCR platforms for the detection of allele-specific methylation. Standards of known allele-specific MGMT methylation status and 10 NSCLC samples heterozygous for the rs16906252 SNP were successfully analyzed using both platforms and identical results were obtained. This new approach to allele-specific methylation detection may have wide implications for future research and may also become important for diagnostic and therapeutic purposes.

P22.05 Anders Petersen NODAL AND EXTRANODAL MANIFESTATIONS OF DIFFUSE LARGE B-CELL LYMPHOMA DIFFER IN EXPRESSION OF SPECIFIC MICRORNAS

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Diffuse Large B-Cell Lymphoma (DLBCL) is a cancer originating from the B-lymphocytes. DLBCL is a heterogenic disease that has an incidence of approximately 2.9 per 100,000. DLBCL can be located in lymph nodes (nodal manifestation) or other tissues, e.g. mamma, liver or brain (extranodal manifestation). MicroRNAs are short non-protein coding RNAs about 21-23 nucleotides. MicroRNAs have been demonstrated to direct the binding of the RISC (RNA-inducing silencing complex) primarily to the 3´UTR of specific mRNAs containing target sequences complementary to the microRNA. Thereby the RISC post transcriptional regulates the expression of this mRNA. To understand what facilitates the tumour to spread from nodal to extranodal tissue, we study miRNA expression. MiRNAs are estimated to regulate at least 30% of all genes in humans, the hypothesis of this project was: microRNA profiles differ among biopsies from nodal and extranodal manifestations of DLBCL resulting in differential targeting of mRNA pathways in nodal versus extranodal tissue. We analysed 50 snap frozen biopsies, carefully collected in patients either from a nodal or an extranodal localisation at time of diagnosis. MicroRNA array and QPCR were used to show that mir-130a, mir-143, mir-145 and mir-195 differ significantly between nodal and extranodal manifestations. The findings are further being validated on 83 new FFPE samples to test the expression pattern in extranodal manifestations from an individual tissue type.
These data indicate that microRNAs might be involved in the process of generating metastasis.
A part of the scientific program CHEPRE supported by The Danish Agency for Science, Technology and Innovation

P22.06 Maria Bro Kloster THE ROLE OF PAX5, BCL6, AND PRDM1 PROMOTERS AND ISOFORMS IN B CELL DIFFERENTIATION AND MALIGNANCIES

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Alternative promoters may direct the production of alternative transcripts; directly through different transcription start sites, indirectly by promoter-directed exon inclusion, or by promoter selection. The promoter regulation may be essential for accurate gene function and accordingly, aberrant promoter usage has been associated with various diseases, including cancer. Deregulation of the transcription factors, paired box protein 5 (PAX5), B cell lymphoma 6 (BCL6), and the positive regulator zinc finger domain 1 (PRDM1), has been observed in B cell lymphomas. However, the role of PAX5, BCL6, and PRDM1 alternative promoters and resulting protein isoforms remains to be fully elucidated.

To assess the role of PAX5, BCL6, and PRDM1 isoforms in normal and malignant human B cells, mechanisms that regulate the use of alternative promoters will be studied by determination of gene copy number variation and promoter methylation status. Furthermore, mRNA and protein levels will be determined by qPCR and Western blot, respectively. Finally, the interaction between the PAX5, BCL6, and PRDM1 isoforms and their target genes will be determined by chromatin immunoprecipitation (ChIP) combined with serial analysis of gene expression (SAGE). Knowledge of the role of PAX5, BCL6, and PRDM1 isoforms should elucidate biological regulation and disease mechanisms. Thus, these isoforms may interfere with the functional transcription factors and thereby disrupt molecular pathways that regulate B cell differentiation, proliferation, and apoptosis.
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P22.07 Hans Linde Nielsen

CLINICAL EPIDEMIOLOGY AND MANIFESTATIONS OF *CAMPYLOBACTER CONCISUS* AND *CAMPYLOBACTER UPSALIENSIS*

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Campylobacter jejuni/coli (95/5%) are currently the major causes of bacterial diarrhea throughout the western world. After the acute gastroenteritis some patients have sequelae like irritable bowel syndrome, reactive arthritis, inflammatory bowel disease and Guillain Barré syndrome. For emerging Campylobacter spp. the frequency and the ability to cause diarrhea in humans is unknown. C. concisus and C. upsaliensis can be isolated from the stool with use of a filter methods but it is not clear whether they are equally pathogenic and give the same illnesses as C. jejuni/coli. In this study we will clarify the epidemiology of C. concisus and C. upsaliensis and describe the differences and similarities of the clinical manifestations inclusive sequelae caused by C. jejuni/coli, C. concisus and C. upsaliensis respectively. Patients with C. jejuni/coli, C. concisus, C. upsaliensis in the fecal sample are included in the study. Two questionnaires are given to the patients. The first covers general health information and disease symptoms during the acute diarrhea episode with daily observations for 7 days. The second questionnaire concerns other symptoms for the following 6 months. Patients over 18 years will be asked to give blood samples used to describe an antibody response. The total study period will be two and a half years. Around 8000 fecal samples from an equivalent numbers of patients will be included. The study is expected to include 400 patients with C. jejuni/coli and 75 patients with C. concisus and C. upsaliensis. A minimum of 1000 fecal samples all from healthy individuals will also be cultivated for Campylobacter spp. to identify any healthy carriers.

P22.08 Niels Fristrup

RISK STRATIFICATION OF BLADDER CANCER PATIENTS USING A PANEL OF 6 PROGNOSTIC PROTEIN MARKERS

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Background: The majority of patients with bladder cancer are initially diagnosed with noninvasive or superficially invasive urothelial tumors. These tumors form a heterogeneous group, spanning from low grade Ta tumors that rarely progress to high grade T1 tumors with concomitant CIS that progress in up to 60% of cases. The

aim of the study was to identify a panel of prognostic markers that can predict the outcome for each individual patient and thereby guide treatment regimens. Six proteins were chosen for investigation of prognostic potential: Cathepsin E, Maspin, p53, TRIM29, Plk1 and Survivin. These were previously included in gene expression signatures for predicting disease progression in non-muscle invasive bladder cancer.
Materials & Methods: A tissue microarray was constructed from 289 primary non-muscle invasive urothelial tumors (182 pTa, 101 pT1 and 6 CIS) with long-term follow-up. Protein expression was investigated using immunohistochemistry.
Results: The expression of Survivin, Plk1 and p53 identified patients with an increased risk of progression to muscle invasive bladder cancer; (HR=2.47 (1.57-3.87), P<0.001), (HR=1.52 (1.00-2.29), P=0.048), (HR=2.03 (1.03-4.03), P=0.042), respectively. The expression of Cathepsin E, Maspin and TRIM29 identified patients with a lowered risk of progression; (HR=0.60 (0.39-0.93), P=0.02), (HR=0.58 (0.38-0.89), P=0.01), (HR=0.38 (0.20-0.73), P=0.003), respectively.
Conclusions: We found all six proteins to be independent prognostic variables for predicting disease progression to muscle invasive disease. This marker panel should now be tested in a prospective study of risk stratification in the management of bladder cancer.

P22.09 Martin Skøtt

THE ANTI-INFLAMMATORY EFFECTS OF ALFA-MELATONIN STIMULATING HORMONE (ALFA-MSH) ON MULTIPLE ORGAN FAILURE IN RATS WITH OR WITHOUT CHRONIC KIDNEY DISEASE

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Introduction: In the last decades the prevalence of chronic kidney disease (CKD) and the progression to end-stage renal disease has increased rapidly. Mainly because of people are getting older and the exponential growth of diabetic nephropathy and cardio-vascular disease. Many attempts have been made to prevent the progression of CKD. Still the population, who require renal replacement therapy, is increasing annual. It is known that impaired renal function per see is associated with an inferior prognosis after acute illness of any kind who requires hospitalization.
Emerging evidence show that inflammation has a strong impact on morbidity and mortality in chronic, as well as acute kidney disease. Various inflammatory mediators, such as pro-inflammatory cytokines, has been ascribed as the key regulator of inflammation. Because they act in both a paracrine and an autocrine fashion and are therefore able to induce a mixture of reactions involving not only the initiatory cell but also its neighbours. Inhibition of these inflammatory mediators is therefore of therapeutic interest.
a-MSH is a tridecapeptide known to inhibit inflammation thought blocking of NF-kB, which is one of the regulatory pathways for synthesis of pro-inflammatory cytokines.
Aim: To investigate the anti-inflammatory effects of a-MSH in rats exposed to multiple organ failure with and without chronic renal failure.
Methods: Two rodent models; 1) 5/6 nephrectomy, remnant kidney model, 2) intestinal ischemia & reperfusion, where multiple organ failure develops.
Outcome measurements: Mortality. Pro-inflammatory cytokines and histomorphology will be measured in lung, kidney, intestine, spleen and liver.

P22.10 Thomas Greve

A CASE OF SEVERE SUBDURAL EMPYEMA CAUSED BY STREPTOCOCCUS INTERMEDIUS AND STREPTOCOCCUS PNEUMONIAE DETECTED BY LYTA PCR AND BINAX NOW, ONLY.

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Objectives

To describe a unique case of a subdural empyema (SDE) implicating supra- and infratentoriel structures co-infected with Streptococcus intermedius and Streptococcus pneumoniae detected only by the combined use of Binax NOW S. pneumoniae antigen detection and S. pneumoniae specific lytA real-time PCR.

Methods

DNA extraction and amplification. DNA was extracted by the use of two different commerciel kits. Universal amplification of bacterial 16S rDNA and sequencing of the amplicon was performed. Specific autolysin (lytA) PCR was performed on every sample fraction.

Pneumococcal antigen detection. Sample fractions were tested using the immunochromatographic membrane assay, Binax NOW S. pneumoniae.

Results

The severity of the clinical presentation elicited the use non conventional and molecular microbiological methods to comprehend the aggressive and rapid development of the symptoms.

The lytA specific PCR set up for my PhD was positive in material from the negative blood culture taken on the third day and in the empyema material taken during surgery on the eighth day.

An antigen detection kit was positive in the same two samples and also in the orbital abscess material.

Only, these two tests detected the pneumococci, whereas the other tests detected S. intermedius.

Conclusion

Only by the combination of several diagnostic methods the synergistic infection with S. pneumoniae and S. intermedius in the SDE was detected.

Antigen detection in pus has the ability to supplement the detection of S. pneumoniae.

S. pneumoniae lytA specific real-time PCR may be a usefull method in polymicrobial infections with a suspicion of S. pneumoniae.

P23.01 Maja Døvling Kaspersen

IDENTIFICATION OF MULTIPLE TYPES OF HUMAN PAPILLOMAVIRUSES AND HERPESVIRUSES IN SEMEN FROM SPERM DONORS

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BACKGROUND: Human papillomaviruses (HPV) and herpesviruses (HHV) may cause sexually transmitted diseases. Neverthelesss, European regulations do not require donor semen to be tested for viruses.

HYPOTHESIS: We postulate that the presence of virus on sperm cells constitutes a serious risk of viral transmission during intercourse and by intrauterine insemination with donor sperm. Virus in semen might compromise the ability of sperm to fertilize the egg or reduce embryo survival.

METHODS: The presence of 35 types of HPV and 8 HHV was examined on DNA from semen of sperm donors using sensitive HPV and HHV arrays. To examine

whether HPV was associated with sperm cells, in situ hybridization was performed with HPV-16 and -6-specific probes.
FINDINGS: The prevalence of HHV-positive sperm donors was 16.1%, and in 18.5% of these cases the virus was identified as cytomegalovirus (CMV), which may be harmful to the foetus. The prevalence of HPV-positive sperm donors was 15.9%, and 2/3 had high-risk types. In situ hybridization experiments identified HPV genomes at the equatorial segment of the sperm cells.
INTERPRETATION: Sperm cells may be a vehicle for transmitting virus to the cervix and uterus. The high prevalence of oncogenic HPV types and CMV in sperm suggests that donor semen should be tested for the presence of virus. Moreover, vaccines protecting against HPV should include additional high-risk types and be considered for all children in order to interfere with transmission of oncogenic HPV. It remains to be determined whether or not HPV and HHV have effects on sperm DNA integrity, female endometrial receptivity, fertilization, and embryo development.

P23.02 Mette Møller Handrup

PLACING OF TUNNELED CENTRAL VENOUS CATHETERS PRIOR TO INDUCTION CHEMOTHERAPY IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA.

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The increasing use of intensive chemotherapy in children with acute lymphoid leukemia (ALL) makes use of tunneled central venous catheters (CVCs) inevitable. The aim of this study was to evaluate the risk of CVC-related complications in children with ALL in relation to timing of catheter placement and type of catheter. All children hospitalized from January 2000 to March 2008 with newly diagnosed ALL and with double-lumen total implantable devices (TIDs) or tunneled external catheters (TEs) were included. We only used data related to the patient´s first catheters.
A total of 102 children were found. We identified a total number of 29,690 catheter days and 93 catheter-associated blood stream infections (CABSI). We found a CABSI rate of 3.1/1000 catheter days (5.4/1000 catheter days for TEs and 1.4/1000 catheter days for TIDs, $p<0.0001$). We found no difference in CABSI between early versus later placed catheters when stratifying for catheter type. We found TEs to be removed non-electively more frequently than TIDs (relative risk 4.2 (2.0 to 8.9) $p<0.0001$). We did not find any difference in non-elective removal regarding time of catheter placement (relative risk 0.9 (0.7 to 1.1) $p=0.34$). Ten (16%) TEs and 19(54%) TIDs remained in place until the end of treatment ($p<0.001$). TIDs were removed after a median of 543 days (range 15-894) whereas TEs were removed after a median of 155 days (range 12-734, $p<0.001$).
Conclusions: Children with ALL and TEs experienced more CABSIs than children with TIDs and they had a higher risk of non-elective catheter removal. Early placement of tunneled CVC does not enhance the risk CABSI or non-elective catheter removal.

P23.03 Peder Fode

DETERMINATION OF COPY NUMBER VARIATIONS OF THE HUMAN β-DEFENSIN 3 GENE USING THREE INDEPENDENT METHODS

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Background
Recent work has demonstrated a high prevalence of copy number variation in the human genome. It is believed that this variation may play a role in predisposition to diseases. Some genes including human beta defensin 3 (DEFB103) are shown to vary in copy number over a high range. Typing of the exact copy number has posed a technical challenge, and today no simple, cheap, high-throughput approaches are suitable for large-scale screening.
Methods
In this study we have determined the copy number for DEFB103 in 155 English control samples (ECACC) using three different methods: Quantitative real time PCR (QPCR), Paralogue Ratio Test (PRT) and Pyrosequencing-Based Paralogue Ratio Test (PPRT). Using linear regression we calculated the copy number for each sample and compared the copy number between each method.
Results
The copy number for DEFB103 varied from 2-11 copies in the PPRT and from 2-9 copies in both the PRT and the QPCR setup. The average copy number for PPRT was 4.3, for PRT 4.4 and for QPCR 4.4. To validate the accuracy of the methods we compared the calculated copy number for each sample between the three methods. For 106 samples (68%) a single PPRT assay gave the same integer copy number as PRT. For PRT vs. QPCR this ratio was 75 % and for QPCR vs. PPRT the ratio was 70 %. Comparing all three methods the same integer copy number was obtained in 97 samples (63%).
Conclusions
In this study we have shown that it is still a major challenge to determine the exact copy number for DEFB103 and that further improvements are needed to be able to distinguish between high copy numbers (e.g. 4 and 5).

P23.04 Mette Bak Nielsen

EVALUATION OF PATIENTS OPERATED FOR LOCALLY RECURRENT RECTAL CANCER

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Objective
To evaluate patients operated for locally recurrent rectal cancer (LRRC) at department of surgery between January 2001 and January 2009.
Methods and material
From 2001 to 2009 167 consecutive patients were referred to department of surgery P, Aarhus University Hospital for LRRC. All patients were evaluated for the purpose of surgery with curative intent. For all patients' data on age, sex, time for referral, results of preoperative evaluation etc were registered prospectively in an on-line clinical database. Data of treatment of primary rectal cancer was retrieved from the Danish Colorectal Cancer Group (DCCG) database. This included data on patients referred to neo-adjuvant treatment, tumor level and stage, type of operation, perioperative and postoperative complications.
The majority of the patients were subsequently seen in our out-patients' clinic. The group of patients who were diagnosed with an inoperable re-recurrence of local disease or metastasis were most often terminated and referred to department of Oncology.
Results
All data is now collected in the database and will be analysed. Among the group of patients found operable some will develop metastasis during radio- and chemo therapy. All patients found operable will be characterized according to the type of recurrence. The operation will be described according to number of organs removed, duration of operation, possible brachytherapy, R-classification. Outcome in terms of postoperative mortality, morbidity and survival will also be analysed.

Conclusion

This study is a part of quality assessment of patients operated for primary advanced rectal cancer and locally recurrent rectal cancer.

P23.05 Thomas Damgaard Sandahl

A NATIONWIDE STUDY OF THE INCIDENCE AND SHORT-TERM MORTALITY RATE OF ALCOHOLIC HEPATITIS IN DENMARK FROM 1999–2008

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Abstract
Background: Alcoholic hepatitis is a life-and health-threatening disease with a wide clinical spectre. Accurate data on incidence and prognosis are important, but scarce and sought after in the existing literature.
Aim: To examine the incidence, 28 and 84 -day mortality rate and their changes over time in patients with alcoholic hepatitis.
Methods: Using nationwide administrative registers, we identified all patients diagnosed with alcoholic hepatitis in Denmark, 1999–2008, and their dates of death. We computed annual standardized incidence, 28 and 84-day mortality rates.
Results: We identified 1952 patients with alcoholic hepatitis, of whom 63% were men. Between 1999 and 2008, the incidence rate increased from 37 to 46 per 1 000 000 for men and from 24 to 34 per 1 000 000 for women. The total 28-day mortality rate rose from 12% in 1999 (12% for men ; 11% for women) to 15% in 2008 (16% for men ; 14% for women).84-day mortality rate rose from 14% in 1999 (15%men; 14% women) to 24% in 2008 (21% men ; 28% women).
Conclusions: Using the comprehensive Danish patient registers this large nationwide study spanning 10 years, describes increasing incidence rate and short-term mortality in patients with alcoholic hepatitis.

P23.06 Lene Mølgård Hansen

EARLY DEATHS AND TREATMENT-RELATED MORTALITY IN CHILDHOOD ACUTE MYELOID LEUKAEMIA (AML) IN THE NORDIC COUNTRIES: 1984-2003

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The prognosis for children with AML has improved considerably the last decades with intensive chemotherapy and better supportive care. However, the survival rate has reached a plateau at 60%. Most deaths are due to progressive disease but 5-15% dies from toxic effects of treatment. To further improve current AML survival rates, a more individualized therapy is probably needed using targeted and much more leukaemia-specific drugs combined with improved supportive care to reduce the number of early (before treatment) and treatment-related deaths.
AIM: to identify the incidence, the clinical features and the risk factors for early deaths and deaths during treatment for childhood AML in the Nordic countries.
METHODS: a historical prospective cohort study including children treated for AML or who died before starting treatment at the Nordic paediatric cancer centres from 1984 to 2003. Patients with isolated myelosarcoma, secondary AML, myelodysplastic syndrome, Down's syndrome and patients dying from resistant disease or relapse are excluded from the study. Leukaemia-related data is collected from the Nordic database. 128 early and treatment-related deaths have been registered and supplementary clinical data are collected from each of these patient files. Possible risk factors will be identified by comparing with the AML population database.
RESULTS: 99 files have been reviewed (1-10-2009). The early death rate was 4% and

the rate of treatment-related deaths 4%. Preliminary analyses showed that 65% of these patients died from infection, 15% from bleeding and 7% from transplant-related complications. The final results of the study will be presented at the PhD day 2010.

P23.07 Diem Bentzon

HEREDITARY PROSTATE CANCER IN MIDTJYLLAND: A STUDY OF GENETIC VARIANTS IN PROSTATE CANCER

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Prostate cancer (PC) in men is the second commonest lethal disease in Denmark with same rank of mortality. Scientists state five important observations: first, age increases risk for PC. Secondly, familiar disposition increases PC risk. Thirdly, elderly men die with PC, while younger men die from PC. Fourthly, early onset PC is diagnosed six to eight years earlier than sporadic PC. Fifthly, hereditary factors play a greater role in PC than in any other cancers.
A Swedish group shows that five specific genes (SNP = Single Nucleotide Polymorphism) and family history of PC are correlated with risk for PC; the correlation increases PC risk 10-fold. We now wish to investigate if these five SNPs are similarly present in Danish men.
Patients & Methods: Eight hundred PC patients from PC Database[1] fill out questionnaires about PC, and other cancers among first degree relatives, and their birth dates. All information about first degree relatives was verified in Central Personal Registry and Danish Cancer Registry. The patients are divided into two groups according to their family history of PC, the hereditary PC group and the sporadic PC group. First degree relatives, who are dead before 1968 or born before 1950s, were found in church books in the parish, where their parents were born. Alternatively, they could be identified through the four National Archives. Blood of the PC patients were analyzed for the five SNPs.
Results: still ongoing study. We will eventually apply logistic regression model to find any association/correlation between the 5 SNPs, family history, and clinical observations.

[1] PC Database in Skejby Hospital contains all PC patients in Jutland.

P23.08 Carina Agerbo Rosenberg

CHARACTERISATION OF AGE-SPECIFIC T CELL RESPONSES FOLLOWING VACCINATION AGAINST HEPATITIS B VIRUS INFECTIONS

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Virus infections are a major source of morbidity. Although many viral vaccines, including those protecting against hepatitis virus, have been successfull in reducing the incident of disease it is nevertheless the case that as many as 10% of the vaccine recipients do not respond to the vaccine and consequently are left unprotected. Here, we propose to study the molecular mechanisms involved in the immune response to vaccination against hepatitis B infection. The study cohort contains samples from 28 healthy vaccine recipients younger than 35 and 28 healthy vaccine recipients older than 55. Preliminary data collected so far indicated a differential immune response towards the HBV vaccine in young and elderly donors. Evaluation of the antibody titer showed a significantly higher prevalence of non-responders (HBsAg specific antibodies < 10 IU/L) among elderly donors and a significantly higher proportion of high responders (HBsAg specific antibodies > 1000 IU/L) among younger donors ($p < 0.0361$). We suggest that an analysis of the vaccine response in elderly recipients may throw new light on the more general issue of non-responding vaccine recipients. By comparison of donor-derived samples we aim at identifying the mechanism that support protection against the infection and hence may play a role

in differential response to vaccination. A comprehensive analysis using flow cytometry is applied to characterise the role of T cells in the regulation of antibody formation following in vitro re-stimulation assay. Markers such as cytokine synthesis and immunosenescence indicators will be tested in parallel.

P23.09 Sine Nygaard Langerhuus

EFFECT OF FISH OIL SUPPLEMENTATION IN A PORCINE MODEL OF AORTIC VASCULAR PROSTHETIC GRAFT INFECTION

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Aortic vascular prosthetic graft infection (AVPGI) caursed by Staphylococcus aureus (Staph. aureus) is a feared postoperative complication. Polyunsaturated n-3 fatty acids in fish oil are potentially anti-inflammatory, and may benefit patients at risk of developing sepsis. A porcine model of AVPGI was developed to study nutritional and surgical strategies against graft infection. This study was conducted to investigate effects of fish oil supplementation on erythrocyte fatty acid composition and plasma PGE_2 metabolite concentration.

60 pigs were randomised to three diets containing 10% fat; fish oil, sunflower oil or animal fat. The pigs were fed the diets for 35 days. On day 21 they all had AVPGI. During anaesthesia an aortic vascular prosthetic graft was inserted in the abdominal part of the aorta, and the grafts were infected with Staph. aureus (strain ATCC29213). Blood samples were drawn on day 0, day 21 (prior to AVPGI) and day 35. Ratios of aracidonic acid (AA) and eicosappentanoic acid (EPA) in erythrocytes were analysed by gas chromatography. A commercial Elisa kit (Caymann Chemical Company, Ann Arbor, USA) was used to determine plasma PGE_2 metabolite concentration (13,14-dihydro-15-keto-metabolite).

Fish oil supplementation decreased AA ratio, and increased EPA ratio in pig erythrocytes. A more pronounced decrease in plasma PGE_2 metabolite concentration ($1.1(-1.4;-0.8) pg*ml^{-1}*day^{-1}$) was observed in the fish oil supplemented group compared to the two other supplemented groups.

Due to this result, Fish oil may very well have an immune modulating effect in this porcine model and further analyses of inflammatory mediators are necessary to address this effect.

P23.10 Lise Saksø Mortensen

4 D BIOLOGICAL IMAGING OF HYPOXIA IN HUMAN TUMOURS

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Background:

Solid tumours contain varying degrees of hypoxia. Hypoxia is associated with poor local control and survival, and the development of a more aggressive tumour. Previous attempts to measure hypoxia have been biased and difficult to apply on a routine basis. Measuring hypoxia in tumours could lead to individualized hypoxia-modifying therapy and prediction of treatment response. Knowledge of change in hypoxia over time is limited, but of great interest as individualised treatment is emerging.

^{18}F-FAZA, a new hypoxic marker, appears promising. It is a nitroimidazole, which can be detected by a PET scan. Compared to other nitroimidazoles, ^{18}F-FAZA is believed to provide a faster and clearer image of hypoxia.

Materials and methods:

A correlation study; patients with operable SCC will receive an ^{18}F-FAZA PET/CT scan prior to surgery. Following staining with pimonidazole (a well established hypoxia marker) the surgical specimen will be correlated to the scan and ^{18}F-FAZA autoradiography. The objective is to examine ^{18}F-FAZA PET/CT scan as a marker of hypoxia A prognostic and a time study: patients with SCC requiring radiation will receive ^{18}F-FAZA PET/CT scans prior to treatment and the scan will be correlated

with outcome. Some patients will also receive scans during their treatment and once following radiation. The objective is to examine the change of hypoxia over time during radiation.
Perspectives:
Establishing ^{18}F-FAZA PET/CT scan as a superior hypoxia marker is essential as this could lead to integrating biological information in radiotherapy treatment planning with the aim of targeting resistant regions.

P24.01 Jimmi Søndergaard

THE ACUTE MORBIDITY DURING RADIOTHERAPY OF BLADDER CANCER IN RELATION TO THE TREATMENT TECHNIQUE

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Purpose: Intensity modulated radiation therapy (IMRT) reduces normal tissue irradiation compared to conformal radiotherapy (CRT) in the treatment of bladder cancer. Whether these improvements translate into reduced acute and late morbidity is unclear. We have retrospectively compared the acute toxicity and dose volume histograms (DVH) of the present IMRT technique to the previous CRT technique.
Materials: 87 patients recieved RT for urinary bladder cancer. 56 patients received CRT and 31 patients have received IMRT. Peak gastrointestinal (GI) and genitourinary (GU) toxicity was scored from patient charts according to the RTOG acute radiation morbidity scoring criteria. DVH data for 55 patients (30 received IMRT and 25 CRT) were retrieved for the current DVH/EUD analysis. DVH parameters and the generalised Effective Uniform Dose (gEUD) for the bowel and the rectum were calculated. Chi2 test and the student t-test were used to test for significance.
Results: IMRT resulted in a significant risk reduction of 26%(5-47%) compared to the CRT group. For the bowel, a significant volume reduction was obtained at all dose levels between 30 and 50 Gy ($p<0.05$), while the gEUD was reduced from 59 Gy (56-61 Gy) to 54 Gy (51-56 Gy) ($p<0.05$). No difference in gEUD or DVH characteristics for the rectum. Mean bowel gEUD was reduced from 57 Gy(54-60 Gy) to 55 Gy(52-58 Gy) (not significant) for patients with vs. without GI toxicity >=2, respectively.
Conclusions: IMRT resulted in reduced GI morbidity and volume sparing of the bowel and rectum compared to CRT. We did not find that the gEUD or DVH for the bowel were significantly different between the high or low GI morbidity (GI>=2) groups.

P24.02 Pauliina Wright

A METHOD TO INDIVIDUALIZE ADAPTIVE PLANNING TARGET VOLUMES FOR DEFORMABLE TARGETS

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Background: Traditionally planning target volumes (PTVs) in radiotherapy is based on a computer tomography (CT) snapshot of the patient anatomy, where population specific margins are added to the clinical target volume (CTV). To account for patient specific shape variations of the target, we have investigated a method to individualize PTVs based on patient specific deformation patterns.

Materials and methods: All combinations of the CT and up to five CBCTs were considered. The clinical target volumes (CTVs) in the CBCTs were matched to the CTV in the CT. PTVs investigated were the unions, the intersections, and all other structures defined by a volume with a constant CTV location frequency. The method was evaluated on three bladder cancer patients with a CT and 20-27 CBCTs.

Results: Reliable alternatives to a standard PTV required use of at least 4 scans for

planning. Considering volumetric coverage of the remaining repeat scan CTVs to minimum 99%, the CTV unions of 4 or 5 scans gave similar results. For patient 1 64% and for patient 2, 86% of the repeat scan CTVs were covered. Further, the PTVs defined by the volume occupied by the CTV in all except one of the 4 or 5 planning scans were feasible. On average 52% of the repeat CBCT CTVs for patient 1 and 64% for patient 2 were covered to minimum 99% by these PTVs. For patient 3 the method failed due to poor volume control of the bladder.

Conclusions: By incorporating CBCTs acquired during setup into planning; the suggested method leads to improved conformity for deformable targets in radiotherapy, without compromising coverage. For successful implementation volume control of the CTV is crucial.

P24.03 Lars Toft Nielsen

TLR SIGNALING INCREASES IMMUNOGENICITY OF RETROVIRAL HIV-1 VACCINE CANDIDATE

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Toll-like receptors (TLRs) recognize unspecific conserved microbial patterns and initiate adaptive immune responses by activating dendritic cells (DCs). Plasmacytoid dendritic cells (pDCs) have intracellular TLR7/8 and TLR9 receptors recognizing viral and bacterial nucleic acids, such as single stranded RNA and CpG DNA motifs, respectively. It has been reported that pDCs are most efficiently activated when simultaneously co-stimulated by both TLR7/8 and TLR9. Upon TLR stimulation, pDCs secrete interferon-α (IFN-α) that up regulates MHC-1 expression, leading to enhanced presentation of peptides derived from cytosolic proteins. We have studied effects of using the TLR9 agonist CpG ODN 1826 as vaccine adjuvant in a setting where Balb/c mice were vaccinated with non-replicating retroviral particles encoding an HIV-1 derived antigen. We show that TLR9 signaling increases cell-mediated immune responses against the HIV epitope. Another subset of dendritic cells, myeloid dendritic cells (mDCs) have TLR3, TLR4 and TLR7/8 receptors, recognizing double-stranded RNA, LPS and single stranded RNA. Upon TLR stimulation, mDCs secrete IL-12, a T cell stimulating factor. A beneficial effect of combining different TLR-agonists as vaccine adjuvants has been reported. We are currently investigating the effects of activating both pDCs and mDCs with combinations of TLR3-, TLR7/8- and TLR9-agonists when vaccinating Balb/c mice with retroviral particles.

P24.04 Magdalena Julia Dabrowska

IMPACT OF GROWTH FACTOR INDEPENDENCE 1 IN HUMAN T-CELL LYMPHOMAS; PATHOGENIC POTENTIAL IDENTIFIED BY INSERTIONAL MUTAGENESIS IN A MURINE T-CELL LYMPHOMA MODEL

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Growth factor independence 1 (Gfi1) has a major oncogenic potential and is aberrantly expressed in murine lymphomas and human cancers. The genomic locus encoding the murine Gfi1 is a frequent integration locus activated in lymphomas induced by the SL3-3 MLV as well as other MLVs,indicating that Gfi1 is essential in development of these tumors. Gfi1 protein expression has been observed in some human cancers, but no knowledge exists on how Gfi1 contributes to development of human T-cell lymphomas. Here,we have determined Gfi1 gene and protein expression patterns in precursor and mature human T-cell lymphomas by real time PCR and Western blot analysis. Localization and expression patterns of the Gfi1 protein was determined in human T-cell lymphomas by IHC staining and compared to similar staining of MLV induced tumors. Our results demonstrated that Gfi1

mRNA and protein expression varies significantly among the human T-cell lymphomas, and does not always show a direct proportional pattern. IHC staining demonstrated varying Gfi1 protein expression in both nucleus and cytoplasm in the T-cell lymphomas and different distributions of the protein within the tumors and tumor cells were observed among samples. Staining of normal human tonsil demonstrated Gfi1 protein to be localized in the cytoplasm.We hypothesise that regulation of Gfi1 includes shuttling between cytoplasm and nucleus and that lymphomagenesis enables unlimited nuclear access. Our data shows that deregulated Gfi1 expression plays a major role in MLV induced lymphomagenesis and indicates that insertional mutagenesis in murine models of human NHLs can be used to identify new genes involved in lymphoma development.

P24.05 Trine Tramm

PROGNOSIS IN PATIENTS WITH UNTREATED, NODE-NEGATIVE EARLY BREAST CANCER: - USING AN ALGORITHM DEVELOPED FROM AND APPLIED TO FORMALIN FIXED, PARAFFIN EMBEDDED TISSUE (FFPE).

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Background: The majority of gene-profiling studies on breast carcinoma (BC) have been performed on fresh frozen tissue (FFT). Tumours represented in cryo-banks are, however, biased in size, and follow-up time often insufficient. Archival FFPE constitutes a biobank of malignant tumours of all sizes; often linked to clinical studies of great statistical power, e.g. DBCG protocols. BC has a tendency for late distant metastasis, with 15% recurring 15-20 years after debut. FFPE is an invaluable source when conducting retrospective studies with long follow-up time.

Material and methods: 1049 FFPE tumour samples have been collected from untreated patients diagnosed with BC (Jan. 1983- Apr. 2001), and enrolled in the DBCG82a/89a protocols. 501 FFPE samples will provide basis for constructing an algorithm from genes considered of prognostic relevance. The algorithm will be tested in the remaining 548 independent FFPE samples, and compared to clinical data. RNA will be extracted from FFPE sections using a proprietary silica bead based method, and genes examined by RT-PCR. Selected genes will be determined by immunohistochemistry (IHC).

Results: RNA has been successfully extracted from 501 samples, and processing of the validation cohort (548) is pending. We have previously shown that isolation and quantification of selected genes is feasible and reproducible from 15 year old FFPE using this method. IHC for ER, PGR and HER2 is being correlated to RNA level. An algorithm will be constructed, and clinical data updated.

Discussion and conclusion:

Isolation of mRNA is feasible from < 25 year old FFPE. mRNA level and IHC seems to correlate nicely. Further conclusions await results.

P24.06 Anders Christian Larsen

INCIDENCE OF VENOUS THROMBOEMBOLIC DISORDERS IN UPPER GASTROINTESTINAL CANCER

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Background

Cancer is a well known risk factor for deep venous thromboembolism (DVT) and pulmonary embolism (PE). In fact PE is the second most common cause of death in cancer patients . The mechanism by which cancer induce venous thromboembolism

(VTE) is still unknown. The aim of the present study is to estimate the incidence of VTE in these patients.
Material and methods
Clinical cross-sectional observational study. Patients admitted to our department with a tentative diagnose of upper GI cancer including pancreatic cancer is offered a Flow-doppler ultrasonography (US) of both legs for the diagnosis of DVT. Further the CT or PET-CT scan included in the routine evaluation of the patient is modified to diagnose PE also. The US examinations are compared with bloodsamples collected at the time of US examination.
Results
Interim analysis, of the first 158 patients included from February 2008 to September 2009 indicates that patients with pancreas cancer is at a particular risk of VTE complications, since 8 out of 53 (frequency 13.2%) pancreas cancer patients had either DVT or LE at time of cancer diagnosis. Overall there was 19 VTE in total (i.e another 11 cases after inclusion) between 135 upper GI cancer patients. As control, 23 patients is enrolled . 3 out of 4 patients with VTE after radical surgery (gastrectomi and thoracic-abdominal cardia resection) had no sign of recurrence of the malignancy until now.
Conclusion
The results confirm our hypothesis. At time of cancer diagnosis these patients are at risk and VTE should be taken into consideration. The data also indicates, that the risk do not decline after radical surgery.

P24.07 Kåre Gotschalck Sunesen

IMMUNOSUPPRESSIVE DISORDERS AND RISK OF ANAL SQUAMOUS CELL CARCINOMA: A NATIONWIDE COHORT STUDY IN DENMARK, 1978-2006
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Compromised immune function may increase the risk of anal squamous cell carcinoma (SCC). We examined the risk of anal SCC in patients with HIV infection and other chronic disorders associated with immunosuppression. A population-based cohort study was conducted using Danish nationwide medical databases. We identified patients with a first-time diagnosis of HIV infection, solid organ transplantation, haematologic malignancy, or autoimmune disease in Denmark, 1978-2005, and followed these for a subsequent anal SCC, starting follow-up one year after diagnosis of the index disease. Standardised incidence ratios (SIRs) were computed as the ratio of observed to expected numbers of anal SCCs, based on national age-, sex- and period-specific rates. Among 4,488 patients with HIV, we observed 21 anal SCCs with 0.3 expected (SIR: 81.1 (95% confidence interval (CI): 51.6-121.9)). Risk of anal SCC was also markedly increased among 5,113 solid organ recipients (SIR: 14.4 (CI: 7.0-26.4)) and 30,165 patients with haematologic malignancies (SIR: 2.3 (CI: 1.1-4.2)) but only moderately increased among 242,114 patients with autoimmune diseases (SIR: 1.3 (CI: 1.0-1.6)). SIRs varied according to type of autoimmune disease and were high in patients with Crohn's disease (SIR: 3.1 (CI: 1.2 - 6.4)), psoriasis (SIR: 3.1 (CI: 1.8-5.1)), polyarteritis nodosa (SIR: 8.8 (CI: 1.5-29.0)), and Wegner's granulomatosis (SIR: 12.4 (CI: 2.1-40.8)). In conclusion, we found HIV infection, solid organ transplantation, haematologic malignancies, and a range of specific autoimmune diseases strongly associated with increased risk of anal SCC.

P24.08 Emil Kofod-Olsen

HUMAN HERPESVIRUS-6B PROTEIN U19 STABILIZE AND INACTIVATE P53.
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Objectives: Activation of the protein p53 is an essential process in response to

cellular stress. During viral infection, it is of utmost importance for the virus to prevent p53 activity, and human herpesvirus-6B (HHV-6B) accomplishes this by stabilizing p53 in an inactive state in the cytoplasm of the cell. We wanted to uncover the mechanisms by which p53 is inactivated and stabilized during HHV-6B infection. Methods: To study the level, localization, and activity of p53 and viral proteins we used Western blot, confocal microscopy, a p21 promoter driven luciferase reporter assay, cell cycle analysis, flowcytometry, homologous recombination to generate stably expressing cell lines, siRNA knock-down during infection, and lenti-viral transduction assays. Results: Expression of the HHV-6B early gene U19 stabilized and inactivated p53. Overexpression of U19 led to a massive accumulation of cytoplasmic p53 and a cell cycle profile similar to that from p53 knock-out cells. Knock-down of U19 during infection led to a decreased stabilization of p53. At ND10-like foci in the nucleus, U19 co-localized with MDM2, a ubiquitin-ligase primarily responsible for the degradation of p53. A likely MDM2-binding sequence was identified in U19 and shown to bind MDM2 in ELISA. Conclution: The U19 protein upregulates the level of p53, stabilizes it, and sequesters it in the cytoplasm. U19 did not lead to cell cycle arrest or apoptosis despite the elevated levels of p53. HHV-6B may therefore, in part via U19, play a role as a cofactor in certain hematological lymphomas.

P24.09 Søren Beck

THE INNATE IMMUNE SYSTEM RECOGNIZES CYTOPLASMIC DNA IN A SEQUENCE DEPENDENT MANNER

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Pathogen recognition receptors (PRR) of the innate immune system detect pathogen infections and activate the immune system. Detection of aberrantly placed nucleic acids by PRRs lead to production of type I interferon (IFN-I) which is essential for mounting an anti-viral immune response. An unidentified PRR recognizes double-stranded (ds)DNA in the cytoplasm and initiates to IFN-I production. It is believed that IFN-I induction by cytoplasmic DNA is independent of the DNA sequence recognized. However, only little effort has been put into identification of DNA-motifs that possess strong stimulatory potential. In the present study transfection of chemically synthesized double-stranded DNA-sequences, derived from the herpes simplex virus genome, into mouse embryonic fibroblasts has lead to the identification of a DNA-motif which can induces potent IFN-I production. Hence, induction of IFN-I by cytoplasmic DNA receptors happens in a sequence dependent manner.

P25.01 Karen Louise Thomsen

TUMOR NECROSIS FACTOR-ALPHA ACUTELY UP-REGULATES UREA SYNTHESIS *IN VIVO* IN RATS - A HEPATIC ELEMENT OF INFLAMMATORY CATABOLISM

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TUMOR NECROSIS FACTOR-ALPHA ACUTELY UP-REGULATES UREA SYNTHESIS IN VIVO IN RATS – A HEPATIC ELEMENT OF INFLAMMATORY CATABOLISM

Background: Catabolism is a serious clinical problem during active inflammation. The tissue nitrogen (N) depletion is related to increased hepatic capacity for N-elimination by conversion of amino-N into urea-N. This is caused by the inflammatory process, but the mediators responsible are unknown. Tumor necrosis factor α (TNF-α) plays a key role in inflammation, and we hypothesized that TNF-α up-regulates urea synthesis.
Methods: We examined the in vivo capacity of urea-N synthesis (CUNS) 3 and 24 hours after TNF-α injection and 3 hours after interleukin-6 (IL-6) injection in rats.

Circulating concentrations of cytokines, glucagon, corticosterone, insulin, glucose, and acute phase proteins were measured.
Results: TNF-α acutely increased CUNS by 40% ($P<0.05$) and IL-6 ($P<0.05$). After 24 h TNF-α induced an acute phase response, but had no effect on CUNS. Likewise IL-6 had no effect on CUNS 3 h after injection. After 3 and 24 h TNF-α significantly increased glucagon, whereas corticosterone, insulin and glucose levels and the HOMA-index were unchanged.
Conclusion: Injection of TNF-α acutely up-regulated the in vivo capacity of urea synthesis which favours loss of nitrogen from the body. TNF-α also increased IL-6 and glucagon, however, we found no acute effect of IL-6 injection on urea synthesis. After 24 h TNF-α induced acute phase response. These results indicate that TNF-α, in addition to its key function in inflammation as well as effects on proteolysis, has an effect on urea synthesis regulation independent of the acute phase protein synthesis.

P25.02 Charlotte Christie Petersen

REACTIVATION VERSUS PRIMARY CYTOMEGALOVIRUS INFECTION IN CHRONIC LYMPHOCYTIC LEUKEMIA PATIENTS

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Human cytomegalovirus (HCMV) is a highly prevalent β-herpesvirus, which usually results in a sub-clinical infection. However, primary infection or reactivation of latent HCMV can be fatal for immunocompromised individuals, thus, particularly dangerous for leukaemia patients, who often receive immunosuppressive treatment.

Using multi-parametric flow cytometry, we analysed peripheral blood samples from a group of six patients with chronic lymphocytic leukaemia undergoing treatment with alemtuzumab by five weekly blood samples. One patient had a primary HCMV infection while another patient reactivated HCMV during that period. Common for both patients was a very low CD4:CD8 ratio in the T cell population. Moreover, the early activation marker, CD69, was substantially increased for both the CD4+ and the CD8+ T cell subset.

At the onset of primary HCMV infection, most of the patients CD8+ T cells shifted immediately from an effector memory phenotype (CD3+CD8+CD45RA+CD62L-) towards an effector cell phenotype (CD3+CD8+CD45RA-CD62L-). These cells have the potential of killing virus infected cells.

During all five weeks the patient who reactivated HCMV was observed, 67-87% of his CD8+ T cells were of the effector memory phenotype, whereas only 10-25% were of the effector phenotype. Additionally, IL-10 was found in plasma samples. At the time of reactivation the patient's number of regulatory T cells (CD3+CD4+CD25+CD127+) completely vanished, whereas the control patients numbers of regulatory T cells was constant over the time period observed.

The viral load will be measured by quantitative PCR and correlated to the immunologic observations and the clinic.

P25.03 Caroline Winther Tørring

HOW EPSTEIN-BARR VIRUS MAY INITIATE MULTIPLE SCLEROSIS

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Background:

Multiple sclerosis (MS) is a chronic inflammatory disease of the central nervous system (CNS). Epstein-Barr virus (EBV) shows a strong association with MS on the basis of epidemiological and serological evidence, but it is not clear how EBV may initiate MS that is normally considered an autoimmune disease.
Hypothesis:
We hypothesize that EBV-infected B cells, producing antibodies directed against antigens in CNS, is a trigger of MS. A defective immune control of EBV-infected B cells in genetic susceptible individuals may increase EBV-load, thereby increasing the risk of MS.
Aim:
We will test our hypothesis by answering the following three questions:
1. Is EBV-load increased in MS patients compared to healthy EBV carriers?
2. Do MS patients have a defective immune control of EBV-infected B cells?
3. Are antibodies produced by EBV-infected B cells in MS patients directed against autoantigens in CNS?
Methods:
1. We will determine the frequencies of EBV-infected B cells in MS patients and controls using limiting dilution and PCR with primers for EBER.
2. We will determine the frequencies of spontaneous lymphocyte transformation in MS patients and controls, after depletion of NK cells and $CD8^+$ T cells. Lymphocyte cultures are examined for 13 weeks. The lymphoblastoide cell lines (LCL) are confirmed by immunofluorescence analysis.
3. We will purify antibodies from LCL. We will identify the antigens/epitopes first by testing commercially available myelin components (MBP, PLP, MAG, MOG and others). Linear epitopes will be identified on brain material by Western blotting. Non-linear epitopes will be selected using a phage display of CNS proteins.

P25.04 Line Reinert

TOLL LIKE RECEPTORS (TLR2/9) INDUCED ANTIVIRAL ACTIVITY AGAINST HSV-2

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The herpes simplex virus (HSV) is a common sexually transmitted virus causing genital ulcers, cold sores, infection of cornea, and encephalitis. HSV encephalitis is rare, nevertheless it is the most common fatal sporadic encephalitis in humans. Around 80% of adults in industrialized countries are seropositive to one of the two types of HSV, HSV-1 or HSV-2.

In order to eliminate viral infections, the host immune response initiates with a rapid and less specific innate response. The virus is recognized by its pathogen-associated molecular patterns (PAMPs), which interacts with receptors on cells of the innate immune system, called pattern recognition receptors (PRRs). Toll-like receptors (TLRs) constitute a class of membrane-bound PRRS, where TLR 2 and TLR 9 are involved in initial detection of HSV. The virus recognition activates the cells of the innate immune system to produce interferons and chemokines, which recruits leucocytes to the infected area. Previous studies have shown that synergistic activation of antiviral activity by TLR2 and TLR9 during HSV infection in the brain.

In this study we focus on the mechanisms behind this TLR2/9 induced antiviral activity against vaginal HSV infection in C57bl/6 mice. We are examining a subset of interferons and chemokines produced in the vagina and the CNS of the TLR2/9 knock out mice. We also want explore the viral infections route to the brain by investigating the amount of virus and which cells are recruited to the vagina and the CNS.

P25.05 Christoffer Sølling

ERYTHROPOIETIN (EPO) ATTENUATES ACUTE RENAL DYSFUNCTION IN A PORCINE MODEL OF ISCHEMIA-REPERFUSION INJURY.

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Background:
Erythropoietin (EPO) has recently been shown to be a potent protector of renal ischemic-reperfusion injury (IRI) in rodent models. Multiple protective effects of EPO have been demonstrated; however the anti-inflammatory effects are not well characterized. The aims were to evaluate the EPO effect on renal IRI in a porcine model and to characterize the immunomodulatory effects.

Methods:
Twenty-four pigs were anesthetized and mechanically ventilated. The pigs were randomized to receive: EPO n=9; or placebo n=9 before 45 min. of ischemia. A group, n=6; served as controls. Renal blood flow was continuously measured. The glomerular filtration rate (GFR) and plasma cytokines (TNF-α, IL-6, IL-8 and IL-10) were analyzed hourly. Renal biopsies were analyzed for cytokine content and apoptosis was evaluated by immunohistochemistry for caspase-3.

Results:
EPO markedly attenuated the renal dysfunction induced by IRI within the first hours of reperfusion. The GFR in the EPO treated group was significantly higher during reperfusion compared to the placebo group ($p < 0.01$). There were no hemodynamic, renal blood flow differences between the IRI-groups. IRI did induced apoptosis, but with no effect of EPO. Both TNF-α and IL-10 were significantly reduced in the cortex of the EPO group compared to the placebo and sham groups ($p<0.05$), however contrary to our hypothesis IRI did not induce an inflammatory response.

Conclusion:
This study demonstrates that EPO attenuates renal IRI in a larger animal model. The effect was observed within the first hours of reperfusion. The mechanism was not related to changes in renal blood flow, hemodynamics or apoptosis.

P25.06 Ditte Andreasen Søborg

OCCURRENCE AND CHARACTERIZATION OF VIRULENCE GENES AMONGST NATURALLY OCCURRING ENVIRONMENTAL BACTERIA

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There is an increased occurrence of infections caused by naturally occurring environmental bacteria which given the right opportunities may cause infections. The mechanisms by which pathogenic bacteria cause disease are relatively well understood. Little, however, is known about the origin of many emerging human pathogens. It has long been believed that the complex interactions between pathogens and their hosts are the main driving force for development of mechanisms to counter host defence strategies by pathogens. However, new evidence suggests that non-host environments may also play a role in the evolution of pathogens, and that acquisition of virulence traits through horizontal gene transfer occurs at a high frequency. The concept that environmental pressures can select for traits conferring virulence, leads to the possibility that soil or other environments could be a source of new pathogens.
In this project, four environments (beech wood mulch soil, organic soil fertilized with manure, PAH-contaminated soil, biofilm from a stream) will be investigated for the presence of genes of selected toxins, adhesins, secretion systems etc. It is hypothesized that the occurrence of virulence genes differs between the environments due to selective pressures derived from e.g. land management

practices, contaminant levels, and interactions with invertebrates. Experimentally, the hypothesis will be tested by analyzing the occurrence of virulence genes by PCR using ~20 primer sets derived from the literature which target conserved genes of the selected virulence factors, and relating the occurrence of these genes to background measurements of the environments.

P25.07 Louise Brøndt Hartlev

UNBIASED STEREOLOGICAL ESTIMATION OF CARTILAGE AND SUBCHONDRAL BONE IN HUMAN OSTEOARTHRITIC FEMORAL HEADS

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Background: Osteoarthritis involves changes in the articular cartilage and juxtaarticular bone (subchondral sclerosis, cyst- and osteophyte formation). The interplay between these tissues has been discussed for several years, but there is still a need for studies quantifying the morphological changes seen in both the articular cartilage and the subchondral bone.

Most research studies use semiquantitative scoring systems. However, unbiased stereological methods enable accurate quantification of absolute volumes and surfaces of articular cartilage and subchondral bone.

Objectives: To develop and test an unbiased stereological method on human primary osteoarthritis of the hip, allowing for estimation of structural and remodelling changes in both subchondral bone and cartilage.

Methods: 5 Danish patients allocated for hip joint replacement due to severe primary osteoarthritis. Excised femoral heads were fixed in ethanol, and were sawn into 7-mm-thick slices a.m. Cavalieri. Every slice was cut into two halves and embedded in methylmethacrylate, cut into 7-mm-thick slices, and stained with Masson Goldner trichome. In order to quantify bone and cartilage volumen, cartilage and cancellous bone surfaces, we used a microscope equipped with a motorized specimen stage and controlled by the stereological software package NewCAST.

Results: The advantage of this new unbiased stereological technique will be presented. Further, preliminary data on cartilage and subchondral bone changes in human osteoarthritis will be shown.

Conclusion: We have applied an unbiased stereological method in order to quantify the articular cartilage and subchondral bone in human osteoarthritis femoral heads

P25.08 Susie Mikkelsen

RIG-I-MEDIATED ACTIVATION OF P38 MAPK PROCEEDS THROUGH A PATHWAY DEPENDENT ON TRAF2, TAK1, AND P38 KINASE ACTIVITY: IMPACT ON TYPE I IFN PRODUCTION AND ACTIVATION OF DENDRITIC CELLS

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The innate immune system is essential for control of viral infections and contributes to the development of the adaptive immune system. One primary aspect of the innate response is the secretion of type I interferons (IFN), which induce resistance to the cytopathic effect of the virus and activate host responses. Dendritic cells (DCs) are natural IFN-producers as well as important antigen-presenting cells responsible for priming of the adaptive immune.

Here we have investigated the role and mechanisms of activation of the MAPK

pathway in innate immune responses induced by Sendai virus (SeV), a negative sense single-stranded RNA virus. Both p38 and JNK were activated in fibroblasts and DCs after infection with SeV in a manner dependent on virus replication and RIG-I. Virus replication was also required for stimulation of interferon production in both cell types and interleukin-12 production in DCs. Blocking of p38 MAPK activation by the specific inhibitor SB202190 abolished the expression of these cytokines. p38 MAPK exerted its function independent of the MAPK-activated protein kinases MK2, MNK, and MSK1/2. We also observed that TRAF2 and TAK1 were essential for RIG-I-mediated activation of p38 MAPK. Interestingly, the kinase activity of p38 MAPK was required for its own phosphorylation, which was kinetically associated with TAB1 interaction. By contrast, the canonical p38 upstream kinase MKK3 was not involved in the p38-dependent response. Thus, activation of p38 MAPK by RIG-I proceeds via a TRAF2-TAK1-dependent pathway, where the enzymatic activity of the kinase plays an essential role. The p38 MAPK in turn stimulates important processes in the innate antiviral response.

P25.09 Ulrik Vindelev Elstrøm

CONE-BEAM CT AND DEFORMABLE REGISTRATION FOR MONITORING ANATOMIC CHANGES AND EXPLORATION OF ADAPTIVE STRATEGIES IN RADIOTHERAPY OF HEAD AND NECK CANCER

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Purpose: The aim of this study was to explore the workflow and feasibility of using the volumetric images from cone-beam CT (CBCT) acquired on a daily basis to obtain information on the actually delivered dose in radiotherapy (RT) of head and neck cancer (HNC) patients utilizing a commercially available deformable registration algorithm.

Methods and Materials: More than 70 consecutive HNC patients have undergone CBCT-guided treatment and this group formed the patient material for the investigation. The initial step was an export from the treatment planning system (TPS) of the daily CBCTs and the planning CT (pCT). After import in Velocity Advanced Imaging (VAI) a non-rigid image registration using an intensity-based method was used to deform the anatomy of the pCT into that of each CBCT. The final deformation map was applied to propagate all contours from pCT to CBCT. A re-sampled export and subsequent import in the TPS yielded an automatic connection between each CBCT plus deformed pCT and the original pCT via the daily online registrations. This enabled re-calculation of the dose to the "daily" anatomy and thereby dose accumulation during the RT course.

Results: For the cases studied the dosimetric effect of weight loss and/or tumour shrinkage were clearly observed. The potential for dose reduction in normal-tissue structures such as the parotid glands by adaptation of the treatment plan was disclosed.

Conclusion: A proof-of-principle method to quantitatively monitor changes in anatomy and delivered dose during the course of fractionated RT for HNC has been demonstrated. Using daily CBCT and deformable registration offline adaptive strategies are feasible.

P25.10 Søren Egedal Degn

A QUANTITATIVE ASSAY FOR MAP19, THE ALTERNATIVE SPLICE PRODUCT OF THE MASP-2 GENE

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The lectin complement pathway may be initiated by four pattern recognition molecules, mannan-binding lectin (MBL), H-, L-, and M-ficolin. All are found in complexes with three MBL-associated serine proteases (MASP-1, -2 and -3) and the MBL-associated protein of 19 kDa (MAp19), a truncated non-enzymatic form of MASP-2. MASP-2 and MAp19 are differential splice products of the MASP2 gene.

MAp19 shares its first 4 exons with MASP-2, encoding the two N-terminal domains: CUB-EGF. A 5th MAp19-specific exon encodes the C-terminal 4 unique aa (EQSL). Activated MASP-2 is known to cleave C4, while the role of MAp19 is unclear. To facilitate further studies, MAp19-specific antibodies were developed. Wistar rats were immunized with a peptide encompassing the 4 unique aa of MAp19, coupled to PPD. Following immunizations spleens were harvested and fused with myeloma cells. The resulting hybridomas were subcloned 4 times. High affinity IgM isotype antibody that did not cross-react with MASP-2 was obtained. A time-resolved immunofluorometric sandwich assay for MAp19 was made, using MASP-2/MAp19 specific antibody for capture of MAp19 from human serum samples under dissociating conditions (high salt, EDTA). Bound MAp19 was measured using biotinylated MAp19-specific antibody, followed by Eu^{3+}-streptavidin and fluorescence reading. The mean MAp19 level in 350 serum samples was 391 ng/ml whereas a mean level of 153 ng/ml was found in urine samples. The distribution of MAp19 in serum was analyzed by gel permeation chromatography under native conditions, revealing that 95% of MAp19 was not in complex with MBL or ficolins. Furthermore MAp19 was found not to compete with MASP-2 for binding to MBL.

P26.01 Vagn Erik Lisbjerg Johnsen

3D-MOTION CAPTURE OF GAIT IN PARKINSON'S DISEASE TREATED WITH DEEP BRAIN STIMULATION

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Deep brain stimulation (DBS) of the subthalamic nucleus (STN) is effective in alleviating Parkinson's disease (PD) symptoms (tremor, rigidity and bradykinesia) and may improve gait and postural impairment associated with the disease. However, improvement of gait is not always as predictable as the clinical outcome. This may relate to the type of gait impairment or localization of the active DBS contact.
The active contact was visualized on peroperative MRI in 22 patients with PD, consecutively treated with bilateral STN DBS. Stimulation site was grouped according to dorsal/ventral STN or medial/lateral borders and anterior/posterior STN or medial/lateral borders. The localization was compared with relative improvement of clinical outcome (UPDRS-III). Furthermore, in ten patients, quantitative gait analyses were performed with 3D-motion capture, and the improvement in gait performance was compared with stimulation site in the STN. Of 44 active contacts, 77% were inside the nucleus, 23% were medial hereof. Stimulation of the dorsal half improved UPDRS-III significantly more than ventral STN DBS ($p=0.02$). Step velocity and length improved significantly more with dorsal stimulation compared with ventral stimulation ($p=0.03$ and $p=0.02$). Balance during gait was also more improved with dorsal stimulation compared with ventral stimulation.
DBS of the dorsal STN is superior to stimulation of the ventral STN. Possible different effects of stimulation inside the nucleus underline the need for exact knowledge of the active stimulation site position in order to target the most effective area.

P26.02 Nina Dyrberg Lorenzen

A COMPARISON OF TWO DIFFERENT SURGICAL RESURFACING TECHNIQUES

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BACKGROUND/AIM
Osteonecrosis in the femoral head and femoral neck fracture are major complications in hip resurfacing arthroplasty (RHA), causing implant failure. Concern has been

raised regarding the influence of surgical procedure on the vascularity of the femoral head. The aim of this study was to compare two different surgical techniques in RHA, a posterior approach versus an anterolateral approach. Using the posterior approach an artery will be cut, that may lead to a decrease in blood flow in the femoral head and neck. Using the anterolateral approach the artery is left intact. We hypothesized that the anterolateral approach will preserve the blood flow in the femoral head and improve implant longevity.
METHOD/FACILITIES
The study design is a randomised clinical trial. Fifty patients, age 30 to 60 years, suffering from osteoarthritis in the hip will be randomised to a RHA implant inserted either through an anterolateral or a posterior surgical approach. Primary point of evaluation is the blood supply to the femoral head and neck measured by Laser Doppler Flowmetry during surgery. Secondary point of evaluation is the bone tissue metabolism measured by micro dialysis established during surgery and monitored during the first three postoperative days. Primary metabolites are glucose, lactate, pyruvate and glycerol.
RESULTS
Inclusion is currently ongoing. Preliminary data and results will be presented.
PERSPECTIVES
A randomised clinical trial comparing two different surgical techniques in RHA surgery, regarding blood supply and implant survival has never been published before.

P26.03 Anders Dohn

THE NEURAL FOUNDATION OF ABSOLUTE PITCH ABILITY

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Absolute pitch (AP), the rare ability to instantly and effortlessly identify and produce any musical pitch without aid from external references, is a very unique cognitive trait that is often regarded by musicians to be the ultimate in musical endowment. AP has been surveyed in numerous behavioral studies; however, the neural basis and coherent brain function have only sparsely been examined, and the etiology of AP remains unclear.
We aim to investigate (1) the neuro anatomical basis of AP using DBM, (2) the functional disadvantage of AP (i.e. the auditory Stroop interference) using EEG, and (3) the heritability of AP using genome scan of blood samples.
Methods: 20 AP possessors and a matched control group will all have a structural MRI scan to perform DBM, an Affymetrix SNP6 genome scan of AP blood samples to search for genetic components of AP, and EEG recordings in two different paradigms of transposition. The paradigms involve video stimuli presenting visually a playing keyboard and auditorily congruent and incongruent piano tones in transposed and non-transposed conditions with auditory masking in between. The tasks are (1) to look for deviant sounds and keys (semi-attentive MMN study) and (2) to determine whether visual and audio are congruent or not.
We hypothesize that the AP group will exhibit a strong Stroop effect in the transposed conditions, whereas the non-AP group will show no (or little) effect of the reference transposition since they do not hear the difference.
Perspectives: AP provides an excellent model for understanding how cognitive functions in general emerge from the interplay of genes, brain structure, brain function, development and environment.

P26.04 Kasper Severinsen

THE TRIGGER TRIFECTA AND CONFORMATIONAL TRANSITIONS IN THE HUMAN SEROTONIN TRANSPORTER

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The serotonergic system utilizes serotonin as a neurotransmitter and is involved in the regulation of mood, aggression, anxiety, sleep, appetite and body temperature. A key player in this system is the human serotonin transporter (hSERT) which is also the principal target for antidepressants. In recent years the structure of a evolutionarily distant bacterial homologue, LeuT, has advanced the structural understanding of hSERT and related proteins but several functional findings in LeuT are contradicting the findings from mammalian neurotransmitter transporters. In this study we used homologymodels of hSERT to guide the way of rational mutagenesis. The resulting constructs was examined in regards to their effect on substrate and inhibitor binding and the appertaining conformational changes of the protein. teh results provided valuable insight in a "trigger trifecta" that seems to govern the conformational transitions of the human serotonin transporter and the molecular dynamics involved in ligand binding.

P26.05 Louise Munk Rydtoft

MR STUDIES AT 16.4 T OF NEURITE DENSITY AND PLAQUE DEPOSITION IN A MOUSE MODEL OF ALZHEIMER'S DISEASE

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Alzheimer's disease (AD) is a progessive, irreversible neurodegenerative disorder. The prevalence of AD increases with age. Because of the increased life expectancy of the population, AD is therefore likely to become a major public health problem. The degeneration of neurites in relation to the formation of amyloid plaques is a central feature in the neuropathology of AD and is believed to closely correlate with the progressive cognitive impairment. I aim to develop and apply MR methods for non-invasive assessment of neurite density and detection of individual plaques.
Studies of plaque detection in a mouse model in vivo and ex vivo have been initiated and I have indeed detected individual plaques ex vivo within a reasonable scanning time at 16.4 T. A part of the project will be focused on further optimization and refinement of the methods towards plaque detection in vivo. Novel detection methods, e.g., ^{19} F-MRI based on ^{19}F-containing amyloid-binding organic compounds is also being implemented to achieve confident plaque detection in vivo.
The objective is to obtain a novel method for plaque detection in vivo and to correlate plaque deposition with neurite density in an AD mouse model. The results will be documented by correlation of in vivo MRI, ex vivo MRI, and histological measurements.
MRI of individual neuritic plaques has great potential as a non-invasive biological marker of disease progression and for evaluation of potential therapeutic agents as well as providing interesting new insight into the AD mechanism when correlated with the neuritic density.

P26.06 Dan Sonne Pedersen

METALLIC GOLD TREATMENT INDUCES NEUROPROTECTIVE ASTROCYTOSIS AND EVOKES STEM CELL RESPONSE IN A RODENT MODEL OF MULTIPLE SCLEROSIS

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Multiple sclerosis (MS) is the most common neurodegenerative disease in the Western world. MS mainly affects younger, healthy individuals and no curative

treatment against the disease exists. Recurring attacks of demyelination and the underlying neuroinflamation, ultimately leads to loss of neurons and focus is thus given to treatments slowing down the course of the disease. Recent research has revealed that localized bio-liberation of gold ions from metallic gold implants ameliorate inflammation, reduce apoptosis and promote proliferation of neural stem cells in a mouse model of focal brain injury. Based on these findings, the present study is the first to investigate whether metallic gold implants induce a neuroprotective response, in Experimental Autoimmune Encephalomyelitis (EAE), a rodent model of MS. Metallic gold particles 20-45 μm suspended in hyaluronic acid were injected bilaterally in the lateral ventricles (LV) of young Lewis rats prior to EAE induction. Gold-treated animals were compared to sham-operated (vehicle). A statistically significant upregulation of GFAP positive reactive astrocytes were seen in periventricular areas, both next to the lateral fourth ventricle. Selective immuno staining for NSC proliferation was performed using frizzeled-9 and nestin showing a statistically significant upregulation of the number of NSCs migrating from the subventricular zone into the surrounding area. Furthermore an upregulation of MT1+2 was seen in corpus callosum. In conclusion: Gold-implants induce astrogliosis throughout the brain and elicit a NSC response in an animal model of MS. Such implants could thus prove beneficial in future treatments against MS.

P26.07 Rune Thomsen OTIMIZING THE BOYDEN CHAMBER ASSAY FOR ASTROCYTIC CELLS.

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Localization of mRNA to the processes of polarized cells is a well described phenomenon, where for example in neurons beta-Actin mRNA localize to the growth cones of neurites. Astrocytes are the most abundant cell type in the central nervous system (CNS), which among many functions serves as supporting cells for neurons. Only very few studies have demonstrated mRNA localization in astrocytes, where for example the mRNA of the intermediary filament protein GFAP, localize to the processes of cortical astrocytes isolated from a neonatal rat.
The two chamber assay also known as the Boyden Chamber Assay, has been developed for various cell types, to investigate the content of cell processes. The Boyden Chamber Assay, is designed in such way that it allows only parts of a cell to grow through a porous membrane, thereby separating the cell soma from the cell processes. The cell processes can subsequently be purified and their content be analysed by various biochemical methods. This method provides a picture of which components (i.e. mRNAs) that are localized to the cell processes of a cell.
To study the localization of mRNA molecules in the processes of astrocytes, the development of new methods have been essential for this PhD project. I have optimized the Boyden Chamber Assay, to allow growth of processes of the mouse astrocyte cell line C8-S. This is the first example that the Boyden Chamber method also can be applied for cells of astrocytic origin.

P26.08 Henriette Thisted PREAMISSION ANTIDIABETIC TREATMENTS AND MORTALITY AFTER ISCHEMIC STROKE IN PATIENTS WITH DIABETES MELLITUS: A NATIONWIDE POPULATION-BASED FOLLOW-UP STUDY

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Background and aims. It remains uncertain whether antidiabetic drugs have adverse effect on the cardiovascular system.
We examined the impact of different antidiabetic treatments on mortality in patients with type 2 diabetes hospitalized with ischemic stroke.
Methods. We conducted a nationwide population-based follow-up study among all Danish patients hospitalized with first-time ischemic stroke from 2003-2006 and

registered in The Danish National Indicator Project. We obtained data on diabetes, type of antidiabetic treatment, patient characteristics, use of other mediciations, comorbidities, socioeconomic status, quality of in-hospital care, and mortality from medical databases. We computed 30-day and 1-year mortality rates according to type of antidiabetic treatment and used Cox's proportional hazards regression analysis to compute hazard ratios (HRs) as estimates of relative risk controlling for differences in prognostic covariates.
Results: We identified 4,816 stroke patients with type 2 diabetes. We found lower 30-day mortality rates among users of metformin (adj. HR: 0.32 (95% CI: 0.15-0.67)), insulin (adj. HR: 0.50 (95% CI: 0.29-0.84)) and among patients not receiving antidiabetic pharmacotherapy (adj. HR: 0.57 (95% CI: 0.36-0.91)) compared with users of sulfonylureas. Users of any combination also had decreased mortality rate, but it did not reach statistical significance (adj. HR: 0.63 (% CI: 0.33-1.20). After 1-year, we found no significant differences between the antidiabetic treatments.
Conclusion. Sulfonylureas may be associated with increased mortality after ischemic stroke, however the deleterious effect seems restricted to the acute phase following the stroke.

P26.09 Fabia Febbraro

STUDY OF THE RELATION OF IRON AND α-SYNUCLEIN AT TRANSLATIONAL AND POST-TRANSLATIONAL LEVEL: IMPLICATIONS FOR PARKINSON'S DISEASE

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Parkinson's disease (PD) is a neurodegenerative disease characterized by the neuronal death in substantia nigra (SN) and the presence of cellular inclusions termed Lewy bodies (LB). The main component of LB is the protein α-synuclein (α-syn), which plays a central role in the neurodegenerative process. In addition, iron has been also be related to PD and other synucleinopathies. The presence of iron in LB, the iron accumulation found in dopaminergic neurons in the SN, suggest that iron may be involved in the disease process. The aim of this study is to explore the relation (at translational and post-translational levels) between iron and α-syn in order to elucidate whether iron chelation therapy could be meaningful in Parkinson' s disease. It has been recently suggested a possible translational control of α-syn by iron. We will therefore address if α−syn expression is regulated at the translational level by iron using cell cultures.
In addition, it is widely documented that in vitro iron interacts directly or indirectly with α-syn at post-translational level by inducing changes in solubility, thus compromising cell integrity. Therefore we postulate that the chelation of iron would decrease or delayed the α-syn induced cell death. To explore the possible neuroprotection exerted by iron chelator deferoxamine in vivo, the viral vector based model of PD will be used.

P27.01 Marie Bagger Bohn

MECHANICAL STABILITY OF ACL RECONSTRUCTION IN AN EXPERIMENTAL PORCINE MODEL

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Introduction
ACL reconstruction is traditionally performed using Single Bundle technique with grafts/drill holes in femur of 8-10mm in diameter. As anatomical double-bundle ACL reconstruction is gaining influence, using two grafts/drill holes in femur of smaller diameters, a mechanical study were fixation devices with a smaller diameter (6mm) was tested up against 9mm fixation devices, was needed. Material & Methods
ACL reconstructions were performed using two different fixation techniques in porcine femora: CL endobutton (EB) and Hexalon interference screw (IS). Each

technique was performed in diameters 6 and 9mm. The specimens were tested cyclically for 1000 cycles between 50 and 250N (MTS 858 Mini Bionix testing machine) and subsequently the sample was tested to failure. Following parameters were determined; displacements at 50, 100, 500 and 1000 cycles, the stiffness over the first 0.5mm of the failure test, the force to failure, displacement to failure and the energy to failure.
Results
All groups displayed a significantly different load to failure, which could be ranked in the following order: EB-9mm (947N), IS-9mm (708N), EB-6mm (569N), IS-6mm (433N). The stiffness of the IS-9mm group (364N/mm) was found to be significantly higher than the EB-9mm (266N/mm) and IS-6mm (289N/mm) groups. No significant differences were found between the displacements of the various groups during cyclic testing
Conclusion
Fixation of the 9mm graft is superior to fixation of the 6mm graft concerning maximum load to failure. This was expected. The IS offered a better stiffness of the femur/graft complex than the EB. There were no difference between EB and IS concerning elongation.

P27.02 Kristina Dupont Hougaard

REMOTE ISCHEMIC PERCONDITIONERING IN ACUTE STROKE: AN ENDOGENEOUS MODEL TO GENERATE NEUROPROTECTION.

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Background: Stroke is leading cause of death and a frequent cause of adult disability in developed countries. 80 % of all strokes are due to blockage of a cerebral artery caused by tromboembolism. Intravenous trombolyses with atleptase (rtPa) is the only approved treatment for acute ischemic stroke. During ongoing ischemia, the neuronal death can be delayed or even prevented, a process called neuroprotection. Animal studies have proven these methods effective and smaller brain infarcts are seen in these studies. Experimental animal studies shows that infarct reduction in the heart and the brain can be induced by stopping the blood flow to an extremity temporarily after occlusion of a coranararteria or cerebral arteria. This is called remote perconditionering.
Aim: To describe method of remote perconditioning in clinical practice regarding feasibility. Pros and cons and potential limitations.
To estimate the size of the effect of remote perconditioning in combination with rtPa treatment within four and a half hours of onset of symptoms.
Methods: A blinded randomized study. 120 patients are needed. Randomization for treatment/not treatment with remote preconditioning and the potential treatment takes place during transportation to the hospital. As the size of the effect is unknown, we will use multiple MRI scans to determine the size of a potential neuroprotective effect.
Results: None, still including.

P27.03 Line Bie Mertz

ANGELMAN SYNDROME IN DENMARK. GENOTYPE COMPARED WITH PHENOTYPE

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Background:
Angelman syndrome (AS) is a neuro-genetic disorder due to an abnormality on chromosome 15. Characteristics of Angelman syndrome include intellectual

disability, lack of speech, happy behaviour, ataxia, autistic behaviour and epilepsy. The incidence of AS is unknown, but estimated to be 1:10.000- 1:20.000. The genetic cause of AS is a maternel deletion of chromosome 15q11-13 (70%), UBE3A mutations (5-10%), uniparental disomy (5%) and imprinting defects (5%) and in 10% unknown. The genes responsible for AS are expressed only from the maternal chromosome 15. This is called parental imprinting, which is known to have impact on growth and behaviour. Some genes in the deleted 15q11-13 region code for three of the GABA subunits. The GABA receptor plays an important role in epilepsy and autism.
Objective:
1)The incidence of AS in Denmark.
2)The exact genetic cause of AS in each child.
3)Comparison of genotype and antropometrical meassures.
4)Comparison of genotype and autistic behaviour.
5)Comparisom of genotype and epilepsy
6)Comparison of genotype and eating behaviour
Methods:
Genotype analysis:These will be done in cooporation with Clinical Genetic Department, Århus and we will use Multiplex Ligation dependent Probe Amplification and OligoarrayCGH.
Antropometrical meassures:we will collect all meassures from the family doctor, the health visitor and the childrens department.
Epilepsy:The parents will fill out a questionaire about the severity and treatment of epilepsy.
Autism:ADOS and Mullen.
Eating behaviour:The parents will fill out a questionaire of eating behaviour.

P27.04 Hans Gjørup

THE MORPHOLOGY OF THE NEUROCRANIUM, SPLANCHNOCRANIUM AND CERVICAL COLUMN IN PATIENTS WITH HYPOPHOSPHATAEMIC RICKETS.

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Hypophosphataemic rickets is a rare, inherited disease characterized by deficient mineralisation of the bones due to lack of renal reabsorption of phosphate. The most common form is X-linked hypophophataemic rickets (XHR). Malformation of the bony structures, primarily the lower extremities, is a consequence of XHR.
Hypothesis: the morphology of cranium and cervical column in patients with XHR is abnormal compared to healthy individuals, and the abnormal morphology can be related to the type of ossification (chondral vs. desmal ossification)
The aim of the study is to analyse the osseous morphology of the cranium and cervical column in patients with XHR, and as part of the analysis to focus on the different types of ossification.
Material. 53 XHR-patients (17 males, 36 females) aged 3-74 yr. Control group: 70 healthy individuals with normal occlusion, or only minor malocclusion, and no signs of craniofacial abnormalities. Data concerning morphology of cranium and cervical column are collected from standardized profile radiographs.
The Regional Committee on Biomedical Research Ethics, Region Southern Denmark, has approved the study.
Methods. The radiographs are used for 1) cephalometric analysis and for 2) visual assessment of osseous structures. 1) Cephalometric analysis includes angular and linear measurements of neurocranium, craniofacial skeleton, cervical vertebrae and sinus frontalis. The cephalometric analyses are performed using the software Pordios®. 2) Visual assessments of the morphology of sella turcica, os nasale and the cervical column. This part of the study requires development of morphometric methods to describe these structures.

P27.05 Kari Konstantin

MULTIPLE SCLEROSIS AND THE IMPACT OF A SPECIFIC ENDOGENOUS

Nissen

RETROVIRUS ON HUMAN CHROMOSOME X

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Multiple sclerosis (MS) is an autoimmune disease attacking the central nervous system. Twin-studies suggest a strong heredity of MS, with estimated three genes involved. So far, only involvement of the MHC locus has been firmly established. However, human endogenous retroviruses (HERVs) seem to influence MS, since different virus factors and antibodies are more common in MS patients compared to the general population.

Since HERVs are part of the human genome and therefore ubiquitous in all persons, it is hard to establish the pathogenic effect of such an agent. Instead, we will treat HERVs as mendelian loci and study their association with and potential involvement in MS.

Resent analysis of all HERVs with a potential for protein expression have revealed a specific HERV on chromosome X to show exceptional association with MS. This HERV (here HERV-X) has a complete Env gene, and therefore a potential to express viral envelope proteins.

The other two retroviral proteins of HERV-X (Gag and Pol, expressed as a polyprotein), is interrupted by mutations and frameshifts. We will correct these to obtain sequences for expression in vector systems. We expect expression of Gag and Pol to result in formation of virion particles, which can be used as antigens for antibody production.

To study the amplification potential of HERV-X, we will look for additional integrations of the virus on other chromosomal sites than the common X position. This is especially interesting in relation to the primary progressive form of MS, where no HERV-X association is found. In addition, other HERV families will be investigated for so far unknown integrations, segregating in smaller parts of the population.

P27.06 Dariusz Orlowski

AUTOMETALLOGRAPHIC (AMG) ENHANCEMENT OF THE GOLGI-COX STAINING AND ITS USE FOR HIGH RESOLUTION VISUALIZATION OF DENDRITES AND SPINES

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We present a method for autometallographic (AMG) enhancement of the Golgi-Cox staining enabling high resolution visualization of dendrites and spines. The method is cheaper and more flexible than conventional enhancement procedures performed with commercial photographic developers. The staining procedure is thoroughly described and we demonstrate with qualitative and quantitative data how histological tissue sectioning, Golgi-Cox immersion time and different AMG enhancement length may influence the staining of dendrites and spines in the rat hippocampus. The described method will be of value for future behavioural-anatomical studies examining changes in dendrite branching and spine density caused by brain diseases and their subsequent treatment.

P27.07 Stephen Austin

REMISSION, METACOGNITIVE PROCESSES AND QUALITY OF LIFE-OUTCOMES FROM OPUS TRIAL. A 10 YEAR FOLLOW-UP OF A RANDOMIZED MULTI-CENTRE TRIAL OF INTENSIVE EARLY INTERVENTION VERSUS STANDARD TREATMENT FOR PATIENTS WITH FIRST EPISODE SCHIZOPHRENIA SPECTRUM DISORDER

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Background: The OPUS trial is the largest randomized clinical trial comparing

intensive early intervention versus standard treatment in people with first episode schizophrenia spectrum disorder. Results collected post intervention revealed that the intensive intervention participants showed significantly lower psychopathology, rates of hospitalization and improved functioning compared to those patients that received standard treatment, The following study will examine outcomes within the OPUS cohort (intensive early intervention versus standard treatment), eight years after the trial was completed.
Objectives: The study will examine three areas relating to outcome: Rates of remission/recovery and predictive validity of remission criteria for functioning, the role of meta-cognitive beliefs in the maintenance of psychopathology and factors contributing to subjective and objective quality of life over the course of illness.
Methods and materials: A sample of 547 patients included in the original OPUS trial conducted between 1998-2000 will be invited to participate in the study. The study is a randomized control trial with multiple follow up assessments Participants will complete a series of measures to evaluate psychopathology, quality of life, social/vocational functioning, meta-cognitive beliefs and cognitive functioning.
Perspectives: The OPUS trial is the worlds' largest randomized control trial comparing early intensive intervention vs standard treatment within schizophrenia spectrum disorder. Data gathered from this 10 year follow up will help identify factors for better treatment outcomes and the long term prognosis for schizophrenia spectrum disorders.

P27.08 Vibeke Fuglsang Bliksted

SOCIAL COGNITION IN FIRST-EPISODE SCHIZOPHRENIA: THEORY OF MIND AND SOCIAL PERCEPTION

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Patients with schizophrenia have more comprehensive deficits in social cognition compared to patients with other mental disorders. There is growing evidence that aspects of social cognition, primarily social perception , may serve as a mediator between neurocognition and functional outcome in schizophrenia
This project will focus on theory of mind (the ability to represent human mental states and/or make inferences about other's intentions) and social perception (the ability to process nonverbal, paraverbal, and/or verbal cues to make inferences about complex or ambiguous social situations). There will be use a new way of measuring social cognition based on small filmclips (the TASIT test) showing scenes from everyday life in either a sincere or a sarcastic version. TASIT is thought to be a more ecologically valid and realistic reflection of the complexity of everyday social cognition than formerly used tests.
Social cognition will be measured by psychological testing of social cognition and in an fMRI study. Healthy controls will be matched 1:1 to the schizophrenia patients regarding age, gender, race/ethnicity, handedness, education level (based on the quality of the last commenced educational level + parental educational level), and community of residence.
All the patients in this PhD-study have just received a diagnosis of first-episode schizophrenia and will be included from OPUS, Clinic for young people with schizophrenia, Aarhus University Hospital Risskov.

P27.09 Kåre Sanden Ettrup

A PORCINE MODEL OF HYPOTHALAMIC DEEP BRAIN STIMULATION FOR THE TREATMENT OF MORBID OBESITY.

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Background: Obesity is the cause of several lifestyle diseases, resulting in escalating health care costs and premature mortality. Achieving and maintaining long-term weight loss through the use of food restriction, exercise and medications is difficult and surgery is the only treatment which has proven to achieve long-term weight

loss. The safety and efficacy of deep brain stimulation (DBS) surgery is now being widely accepted and several hypothalamic areas involved in the central regulation of energy homeostasis have been identified as potential targets for DBS. Hypothesis: We hypothesize that DBS of chemoarchitectonic distinct cell populations involved in the central regulation of energy homeostasis in the minipig hypothalamus will lead to a reduction in body weight. Materials and methods: Two female Göttingen minipigs is used in this pilot study approved by the Danish National Council of Animal Research Ethics. DBS-electrodes is stereotactically inserted bilaterally in the ventromedial hypothalamus and connected to a pulse-generator implanted in a subcutaneous pocket in the lower neck region. In order to conduct a crossover study the pulse generator is switched on and off for periods of 1-3 months while the weight and food consumption of the pigs is monitored on a daily basis. Perspectives: The aim of this pilot study is to provide a porcine large animal model of hypothalamic-DBS for the treatment of obesity. If we establish that hypothalamic-DBS indeed is safe and efficient, it could become one of the standard treatments offered to patients with morbid obesity.

P27.10 Kathrine Just Andersen

CHARACTERIZATION OF BASAL GANGLIA DYSFUNCTION IN A RODENT MODEL OF PARKINSON'S DISEASE

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Parkinson's disease (PD) is a progressive illness characterized by the neurodegeneration of dopaminergic neurons in the substantia nigra (SN). The lack of dopamine release in the brain leads to the dysfunction of the circuitry of the basal ganglia (BG). The BG includes several areas in the brain that are interconnected and play an essential role in the movement coordination. The malfunction of the BG results in the typical motoric symptoms found in PD. Another hallmark of PD is the presence in the brain of intracellular Lewy Bodies, which primarily consist of insoluble α-synuclein (α-syn). Our lab is working with a rat PD model based on the local overexpression of α-syn in SN by means of viral vector injections in the adult brain. The overexpression of α-syn in dopaminergic neurons results in progressive cell loss and pathological accumulation of the protein resembling what is found in PD patients. The purpose of this project is to characterize the progression of the induced changes with respect to functional read-outs and dysfunction in the BG circuitry. To do so the following will be conducted: characterization of the motor/behavioral profile; in vivo measurements of relevant neurotransmitters by microdialysis; immuno chemistry of proteins relevant in PD; analysis of pertinent receptors or transporters in the BG by binding analysis; electrophysiology in relevant nuclei of the BG. The characterization of the model will bring a better understanding of the process occurring in the disease. In addition the changes characterized in this project can be used in the future as markers for evaluation of novel therapeutic strategies for PD.

P28.01 Lene Vammen Søndergaard

CLONED GöTTINGEN MINIPIGS SHOW REDUCED INTER-INDIVIDUAL VARIATION IN BEHAVIORAL TESTS

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In a porcine model of Alzheimer's disease cloned healthy minipigs are compared with non-cloned controls to explore the possible effects of genetic identity on two behavioral tests of memory and olfaction.
We tested 6 cloned Göttingen minipigs, transgenic for the APPsw gene, and 14 (olfaction) and 6 (memory) unrelated minipigs. In the olfaction test each pig is

subjected to a go/no-go task (pressing of lever in case of odor reinforced by food and non-pressing in case of no odor). At a low odor concentration detection threshold is reached and the pig performs at chance. Olfactory function is measured as number of correct presses. Memory is assessed using an object recognition test. Each pig is exposed to two identical objects and allowed to explore freely for 10 min. After a 10 min pause one object is exchanged with a novel one, available for 10 min exploration. Because of novelty preference, pigs explore the novel object the most. Memory is measured as time spend exploring the novel object compared to the familiar one.
Olfactory threshold in cloned pigs varied from 10^{-7}-10^{-8}% (v/v) and from 10^{-3}-10^{-7}% in controls. In the memory test exploration range (Q1-Q3) for cloned pigs was 18-33 sec and 3-118 for controls.
Our results indicate that genetic homogeneity reduces inter-individual behavioral variation. This suggests that the complex behavioral patterns, assessed in the two tests, are under substantial genetic control.

P28.02 Thomas Maribo

LOW BACK PAIN PATIENTS EXPERIENCE LOWER PAIN INTENSITY AFTER EXTENSIVE PHYSICAL TESTING

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Background: Low back pain (LBP) is the most common and costly musculoskeletal complaint with a lifetime prevalence of 70-80 %. No studies have analysed how LBP patients tolerate physical testing.
Objectives: To evaluate intensity of pain before and after physical testing in patients with recurrent LBP.
Methods: The study population was 223 LBP patients of both gender and 18-63 years of age advised to exercise after physical examination. The physical test battery included postural balance, core muscle endurance, and physical fitness. Every test session lasted 45 minutes. Pain was recorded just before and 10 minutes after completion of the test battery using a 0-10 numeric rating scale (NRS). The Mann-Whitney test was used to test for changes in pain.
Results: Pain was recorded on all 223 patients. Mean initial pain was rated as 2.23 (CI95 1.99; 2.48) and after test as 1.76 (CI95 1.50; 2.02) ($p<0.001$). Of all the patients 100 (44.8 %) reported decreased pain, 88 patients (39.5 %) reported unchanged pain and 35 patients (15.7 %) reported increased pain.
176 patients (74.8 %) reported none or mild initial pain (NRS ≤ 3). Initial mean pain was 1.37 (CI95 1.19; 1.54) and after test this was reduced to 1.00 (CI95 0.81; 1.19) ($p<0.001$).
55 patients (24.6 %) reported moderate initial pain (NRS ≥ 4). Initial mean pain was 4.82 (CI95 4.54; 5.10) and after test this was reduced to 4.04 (CI95 3.50; 4.58) ($p=0.001$).
The presence of patients with severe initial pain (NRS ≥ 8) was negligible.
Conclusion: Physical testing was safe in patients with recurrent LBP. Most patients reported the same or less pain after physical testing. Only 15.7 % reported an increase in pain.

P28.03 Torben Albert Devantier

ASSOCIATIONS BETWEEN DEPRESSION AND CARDIOVASCULAR DISEASE IN PATIENTS WITH LATE ONSET SINGLE EPISODE MAJOR DEPRESSIVE DISORDER

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OBJECTIVE

Depression is a risk factor for the development of cardiovascular disease, and there is an increased occurrence of depression in patients with ischemic heart disease (IHD). Furthermore, patients with IHD and depression have a higher rate of major adverse cardiac events, including cardiac death, when compared to non-depressed patients with IHD. Among other mechanisms atherosclerosis is believed to play an important role regarding these notable associations between depression and cardiovascular disease. Patients with late onset major depression have an increased number of small lesions found in the white matter of the brain, commonly named white matter lesions. The main objective of this study is to determine whether these white matter lesions are associated to atherosclerotic disease of the coronary arteries.

METHODS
30 patients, 50-70 years of age with single episode major depressive disorder as defined by ICD-10 and DSM-IV and 30 healthy controls will undergo magnetic resonance imaging of the brain and a coronary artery calcium scan of the coronary arteries of the heart. Data will be analyzed for correlations between coronary artery calcium score and the number and the total volume of white matter lesions.

RESULTS
Recruitment of patients has recently commenced, hence data analyses is not possible at this point.

CONCLUSION
No conclusion can be made at this stage.

P28.04 René Ernst Nielsen

COMPARISON OF THE EFFECTS OF SERTINDOLE AND OLANZAPINES ON COGNITION (SEROLA)

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Cognitive deficits are considered as the core symptoms of schizophrenia, and these symptoms are correlated to functional outcome, partly independent of positive and negative symptoms.
The effect of antipsychotics and cognitive deficits are not sufficiently examined, but side effects of antipsychotics can worsen cognitive function, e.g. extra pyramidal side effects (EPS), sedation and anticholinergic side effects.
This poster will present study design for the SEROLA study, which compares sertindole and olanzapine in a population of patients with schizophrenia, with cognition as primary outcome.

Sertindole is an effective and well tolerated atypical antipsychotic with a better metabolic profile than olanzapine. Sertindole has low or no affinity for the muscarinergic and histaminergic receptors and EPS is present at placebo level.

The antipsychotic effect of olanzapine has been documented in several studies. Olanzapine has affinity for both the histaminergic and muscarinergic receptors, which can diminish cognition. An open-label study comparing olanzapine versus aripiprazole did not show any differences on cognition, except for an improvement on verbal learning in the aripiprazole group. However, the drop-out rate was significantly higher in the aripiprazole group.
Theoretically, sertindole has a better receptor profile than olanzapine in regards to cognition. No double-blinded randomized head-to-head studies comparing sertindole with another atypical antipsychotic, with cognition as primary outcome measure has been conducted so far.

P28.05 Annette Ingeman

QUALITY OF CARE AND MEDICAL COMPLICATIONS AMONG PATIENTS

WITH STROKE: A FOLLOW-UP STUDY

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Introduction: Medical complications (e.g., pneumonia, decubitus, falls venous thromboembolism) appear to be associated with poor clinical outcomes among patients with stroke. The relationship between quality of care and the risk of medical complications is unclear. Objective: To examine the association between quality of care and complications among patients with stroke in a population-based follow-up study.

Methods: Using data from The Danish National Indicator Project, we identified all admissions for stroke to specialized stroke units from the former Copenhagen Hospital Corporation (H:S) and Aarhus County between January 13, 2003 to December 31, 2008 (n = 11.557). Quality of care was measured in terms of nine specific criteria: early admission to a stroke unit, early initiation of antiplatelet or oral anticoagulant therapy, early examination with computed tomography/magnetic resonance imaging scan, and early assessment by a physiotherapist, an occupational therapist, of nutritional risk and of swallowing function and early mobilization.

Results: The final results will be ready for presentation at the Ph.D.–day 2010. The preliminary results indicate that early assessment of nutritional risk and early mobilization are associated with lower risks of complications and that there is an inverse dose-response relationship between the number of quality of care criteria met and the risk of complications; the lowest complications rate was found among patients whose care met all criteria compared to patients whose care failed to meet any criteria.

Conclusions: Higher quality of care was associated with lower risk of complications.

P28.06 Jannik Jakobsen

GENERATION OF EGFP PIGS REVEALED A NOVEL TWO FACED FUNCTION OF THE SLEEPING BEAUTY TRANSPOSASE.

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We used the transposase, Sleeping Beauty (SB), to test its ability to mediate transgene insertion in the pig genome. A plasmid carrying an eGFP transposon was co-transfected into primary porcine fibroblast together with a plasmid expressing a variant of SB (HSB3). A significant number of neomycin selected cell colonies were obtained when the HSB3 plasmid was used in contrast to a control plasmid (pUC 19 plasmid), demonstrating SB´s ability to increase transgenesis in primary porcine fibroblasts. The selected cells were used for handmade cloning (HMC) to create eGFP expressing pigs. Three transgenic cloned pigs were born carrying multiple copies of the eGFP transposon plasmid. Surprisingly, the majority of these transgene copies were randomly integrated into the pigs genome and not, as expected, transposed by SB. We investigated this random integration capacity of SB using several variants of SB including a variant with an inactive integrase activity, designated (m-SB). To our surprise, in primary pig fibroblasts m-SB was more efficient than HSB3 for transgenesis in an assay where the number of neomycin selected colonies is visualized. Thus, it appears that SB, besides being able to make the expected transposition in primary cells, also dramatically increases random integration of plasmid DNA. In conclusion, SB can be used as an efficient tool to develop eGFP expressing pigs. However, transposition in the porcine genome is greatly diminished compared to random integration. The presented findings could have important implications for the use of SB in gene therapy as SB besides integrating the gene of interest accordingly also integrate prokaryotic plasmid-DNA.

P28.07 Kaare Meier

SPINAL CORD STIMULATION, A 3-YEAR EXPERIENCE

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Spinal Cord Stimulation is a minimally invasive neurosurgical treatment for chronic neuropathic pain resistant to conventional therapy. The treatment consists of a sophisticated electrode placed in the epidural space and connected to an implanted impulse generator. Weak electrical impulses create a tingling sensation in the affected area, often with remarkable effect on the chronic pain.
Spinal cord stimulation was first described in 1967 and is based theoretically on the gate control theory of pain (as suggested in 1965 by Melzack & Wall). The precise mechanism of action is, however, not clear.
The treatment was introduced at the Department of Neurosurgery, Aarhus University Hospital, in 2006, and 27 patients have been treated to date.
Patients are managed in close collaboration with the Danish Pain Research Center / Neuropathic Pain Clinic, Aarhus University Hospital, and most patients are thoroughly examined pre-operatively and at 3-6 months post-operatively. Examinations include quantitative sensory testing (QST), recording of pain on conventional NRS scale, and quality of life questionnaire (SF-36).
Preliminary analysis of the data from our patients will be presented.

P28.08 John Brincks

OVERGROUND GAIT TRAINING OR ROBOTIC GAIT PRACTISE? NO SUPERIOR GAIT INTERVENTION WAS DETERMINED FOR SUBACUTE PATIENTS WITH STROKE. A PILOT STUDY

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Repetitive task-specific gait interventions have shown promising results for hemiparetic patients. Still, the effect of the Lokomat Gait Orthosis (LGO) are not established for restoration of subacute ambulatory patients abnormal gait patterns compared to overground gait training (GT).
Thirteen patients with stroke located in the middle cerebral artery were bloc randomised into intervention module A-B (n=7) or B-A (n=6) in this cross-over study. Phase A consisted of three weeks of LGO and phase B consisted of three weeks of GT conducted by a physiotherapist. Primary outcome measures were self-selected walking speed (SWS) and single support stance time (SSS) and secondary outcome measures were power variables on impaired side; A2-S, H1-S, H3-S, H3-F and K3-S. Outcomes were recorded with the Vicon V612 3D movement analysis system including one force plate. The level of significance was $p<0.025$ for primary outcomes.
Primary outcomes showed significantly median improvements within patients practising LGO (SWS: 0.12 m/s (range: 0.02 to 0.28), p=0.018; SSS: 4.5 % (2.1 to 17.9), p=0.018), but were not observed within patients practising GT (SWS: 0.27 m/s (0.04 to 0.53), p=0.028; SSS: 9.1 % (4.1 to 10.6), p=0.028) after the first three weeks.
Secondary outcomes showed significantly median improvements within LGO (A2-S: 0.15 W/kg, K3-S: -0.08 W/kg; $p<0.05$), within GT (A2-S: 0.76 W/kg, H1-S 0.04 W/kg, K3-S: -0.04 W/kg, $p<0.05$) and improvement in A2-S was significantly larger in GT compared to LGO ($p<0.046$) after the first three weeks.
No superior gait training was determined in this pilot study, but GT might improve plantarflexion power more than LGO.

P28.09 Faramarz Jadidi

EFFECT OF STIMULUS LOCATION ON INHIBITORY RESPONSES IN HUMAN JAW-CLOSING MUSCLES

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Objective: Examine the inhibitory responses in bilateral masseter and temporalis muscle activity when six different orofacial locations were electrically stimulated. In addition, (1) the influence of a maintained voluntary contraction versus a voluntary relaxation on the inhibitory responses and (2) the reproducibility of the inhibitory responses were tested.
Design: The exteroceptive suppression period (ES2) and inhibitory responses were recorded in the surface electromyogram (EMG) of masseter and temporalis muscles in 16 healthy subjects. Two stimulus durations (1 ms single and 450 ms square-wave pulse train) adjusted to a perceived intensity of 7 (distinct painful) on a 0-10 verbal rating scale were applied to the following six orofacial locations while the subject was biting at 50% of the maximal voluntary contraction level (MVC): right masseter muscle, right temporalis muscle, right temporomandibular joint, infraorbitalis nerve, supraorbitalis nerve and right mental nerve.
Results: There were no significant main effects in the magnitude of ES2 suppression between the six orofacial locations ($P > 0.876$) evoked by 1 ms stimuli. No significant session effect on the magnitude of ES2 suppression was found ($P > 0.500$). There were no significant main effects of maintaining or relaxing the contraction level at 50% MVC ($P > 0.829$). There were significant decreases evoked by the 450 ms stimuli in RMS-EMG values in the 400-500 ms post-stimulus epoch compared with the pre-stimulus interval ($P < 0.023$).
Conclusions: We have shown that short and long-lasting electrical stimulation of various orofacial locations produces similar bilateral inhibitory effects in the jaw-closing muscles.

P28.10 Simon Hjerrild

CEREBRAL INVOLVMENT IN CHRONIC HEPATITIS C VIRUS INFECTION ASSESSED BY MRI

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Objectives:
Globally, 170 mio. are infected with hepatitis C virus (HCV). Patients with chronic HCV infection have a high prevalence of depressive disorders, cognitive disturbances, reduced quality of life and chronic fatigue. The majority of HCV patients in Europe have a history of drug abuse and psychosocial stress, making the causal relationship between HCV infection and psychiatric symptoms complex. HCV have been isolated in brain tissue and cerebral magnetic resonance spectroscopy revealed metabolic abnormalities indicating chronic inflammation. Furthermore, 1/3 of patients develop major depression during antiviral interferon treatment.
Aim:
To correlate neuropsychological performance and psychiatric symptoms with viral characteristics (HCV genomic sequencing from peripheral blood and cerebrospinal fluid) and magnetic resonance imaging (MRI). First, we wish to elucidate the causal relationship between chronic HCV infection, cognitive disturbances and psychiatric symptoms using MRI. Second, we would like to identify MRI markers for the development of interferon-induced depression.
Methods:
A 3T MRI protocol including DTI with possibility of fiber tracking, magnetization transfer sequences, regional cerebral blood flow, FLAIR, hippocampal volumetry and MR Spectroscopy performed before and after antiviral treatment of 60 HCV patients. 40 HCV patients without pending antiviral treatment and 30 healthy

subjects will serve as controls. HCV patients receiving antiviral therapy will be examined for the development of depression after 8 weeks of treatment. Neuropsychological testing, psychiatric assessment will be performed concomitant to the MRI in another study.

P29.01 Sanna Lemming Kjær

CONTEXTUAL NEGATIVE CUES APPEAR IMPORTANT FOR INDUCTION OF INCREASED STATE OF ANXIETY IN PRENATALLY STRESSED RATS

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The startle reflex is highly sensitive to fear and anxiety in humans and animals. In humans, elevated startle magnitude is a marker for anxiety disorders. We have recently established an animal model for development of anxiety: Female rats are exposed to 2 stressful life events; prenatally (daily Dexamethasone injections from gestational day 14-21) and postnatally in young adults (stressful blood sampling). Here, the blood sampling procedure three months prior to testing increased the basal startle, but only in prenatally stressed rats. In the present study, we investigated whether the increase in startle after a stress exposure was induced by a context or a general experience of stress, by exchanging the blood sampling with another stressful but dissimilar event, i.e. the Forced Swim Test.

The prenatally stressed rats exposed to the highest dose of prenatal dexamethasone (DEX 150 µg) were statistically significantly more immobile in the forced swim test than both the low prenatal dexamethasone group (DEX 50 µg); Fischers LSD: LoDEX – HiDEX, p=0.012, and controls (Fischers LSD: CON - HiDEX p=0.021), which indicates reduced escape behavior in these animals. But exposure to the forced swim test was unassociated with increased startle. That the Forced Swim Test did not trigger the same startle response as the blood sampling, suggest importance of contextual similarity in the test and stress situation, highlighting that lacking a contextual warning, prenatally stressed animals cope equally to controls with novel stressful exposures with regard to anxiety related behaviour.

P29.02 Marianne Toft Vestermark

STRONTIUM SUBSTITUTED BIOACTIVE GLASS AS COATING FOR ORTHOPAEDIC IMPLANTS.

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The purpose of this canine experimental study was to evaluate early fixation and osseointegration of strontium (Sr) substituted bioactive silica-glass, SiO_2-Na_2O-CaO-SrO-K_2O-MgO-ZnO-P_2O_5, coating (BG) on grit blasted Ti alloy implants.

Ten american hounds dogs each received 4 experimental implants in the humerus: BG w 0% Strontium substitution, BG w 10% Strontium substitution, BG w 50% Strontium substitution, and plasma sprayed HA as control. The implants were surrounded by 1.0 mm concentric gap and were inserted into the trabecular bone in the epiphysis of humerus. Mechanical implant fixation was evaluated by push-out test, and osseointegration was evaluated by quantitative histomorphometry.

Results of the push-out test:

One of the four groups was statistically significant different from the others within the parameters strength ($p<0.002$), and total energy absorption ($p<0.002$) (Friedman). The HA coated implants were statistically significant better compared with all three intervention groups in terms of mechanical implant fixation on both strength and total energy absorption ($p<0.006$, Wilcoxon signed rank test).

Results of the histomorphometric analysis:
No ongrowth of bone or implant-bone contact was detected on BG coatings, whereas the HA coating had 40% ongrowth of bone ($p<0.005$). The ingrowth of bone or volumen of new bone in gap of BG coated implants were statistically significant, very sparse compared to the HA coated implants ($p<0.013$ for 0% and 50% Sr, and $p<0.007$ for 10% Sr).
Conclusion: The bioactive glass coatings did neither improve the fixation nor the osseointegration of the Ti implant.

P29.03 Sabrina Maria Gade Sundbye

P25α EXPRESSION IN MODELS OF EXCITOTOXICITY

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P25α is a protein primarily expressed in the oligodendroglial cells of the brain. The physiological function of this protein is yet to be characterized, however it is linked to myelin production and microtubuli dynamics. In this study we show that p25α expression is upregulated upon excitotoxic insult. We use both organotypic rat brain tissue slices and an in vivo rat model for ischemia to induce excitotoxic insult. Treatment of organotypic rat brain tissue with the excitotoxin NMDA induces an upregulation of p25α immunoreactivity . Using specific cell type markers, the upregulation of p25α was demonstrated to be in oligodendroglial cells. Using an in vivo model for ischemia in rats, we are inducing excitotoxicity by performing middle cerebral artery occlusion. We subsequently observe an upregulation of p25α immunoreactivity in oligodendroglial cells around the injury site. Experiments are being performed to determine the relation between p25a expression and oligodendroglial differentiation and the consequence of having an enriched environment during the rescue period following injury. A conditional p25α transgenic mouse strain is also being developed to further investigate the role of increased oligodendroglial p25α expression in the susceptibility to stroke.

P29.04 Jennifer Heather Christensen

POST-OPERATIVE COURSE AFTER REMOVAL OF LOWER THIRD MOLARS: EFFECT OF LONG-DURATION ANAESTHETIC AND ANTI-INFLAMMATORY TREATMENT ON PAIN AND SWELLING

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Background: After removal of lower third molars complications can occur, such as pain, swelling, and infection. As pain intensity has been shown to be worst during the first 4-8 hours post surgery, use of a local anaesthetic (LA) with long duration might reduce post-operative pain. Likewise, the use of an anti-inflammatory (AI) treatment might reduce postoperative swelling and inflammation.
Aim: To compare postoperative complications after removal of lower third molars using two types of LA (bupivacaine and lidocaine) and two AI treatments (methylprednisolone and placebo). The hypothesis is that a combination of a long-duration anaesthetic combined with methylprednisolone will result in significantly less post-operative pain and inflammation.
Methods: The study is conducted as a double-blind, split-mouth crossover trial, where each patient has both lower third molars removed at two occasions with at least one month between the operations. 148 patients are randomised to receive one type of LA and AI/placebo treatment at the first operation and the other at the second. An objective assessment of post-operative swelling and inflammation is performed by means of thermographic imaging after the operation and at 2 and 7

days post-surgery. Complications are assessed objectively and recorded at the post-surgery visits.
Patients record their perception of pain and swelling post-operatively on 100mm visual analogue scales and also record other post-operative complications.
Present: 118 patients have been screened for the trial, 71 patients have been included, 28 patients have completed the study, 9 patients have been excluded and 36 patients are underway.

P29.05 Hanna Järnum

GENDER AND AGE DEPENDENCE OF CINGULUM AND CORPUS CALLOSUM IN HEALTHY VOLUNTEERS ASSESSED BY DIFFUSION TENSOR IMAGING: A VIRTUAL DISSECTION STUDY

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Introduction: Diffusion Tensor Imaging presents an important tool for understanding the complexity of cerebral white matter microstructure. However, the published results concerning FA and ADC in limbic tracts are divergent, demonstrating a need for a re-evaluation of these findings with a robust DTI postprocessing technique.

Purpose: To perform virtual dissections of the limbic tract cingulum comparing with corpus callosum in healthy volunteers using Catani's tractography approach (1) and to study intra-observer repeatability.

Material & Methods: 31 healthy volunteers. Axial 2D DTI SE-EPI, 32 directions, b-value 1300, scan time 5:42min. DTI data were analyzed using Diffusion Toolkit and TrackVis software with a track turning angle ≤ 60° and FA ≥0.2. Intra-observer repeatability was assessed on five data sets.

Results: In contrast to ADC, FA in cingulum exhibited gender dependency. Neither FA nor ADC in cingulum was age dependent. Corpus callosum showed no gender - or age dependence for FA and ADC. Our intra-observer reliability for FA had a repeatability coefficient between $0.3x10^{-3}$ and $1.6x10^{-2}$ in the three tracts. The repeatability coefficient for ADC was less than $1.0x10^{-12}$ m^2/s in all tracts.

Conclusion: To our knowledge, no previous study has demonstrated a statistically significant different FA for cingulum between healthy females and males. Absence of age dependence concerning FA and ADC in cingulum is in agreement with previous studies. The repeatability coefficient suggests potentials for comparative DTI studies.

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P29.06 Eduardo Garza

SONATA ANALGESICA: IS MUSIC-INDUCED ANALGESIA JUST A CONSEQUENCE OF THE PLACEBO EFFECT?

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Music was recognized as a type of therapy by the Greek philosopher Pythagoras more than 2000 years ago. To this time, it is still used as a concomitant treatment of different illnesses like schizophrenia and Parkinson's, or to relieve pain. The literature about the analgesic effects of music is contradicting, however the majority of the studies suggest that music relieves pain in humans. It has been suggested that the mechanisms behind the analgesic effect are merely distraction and placebo effect, but there could be an emotional component elicited by the pleasure of listening music that has not been taken into account.
To study the mechanisms behind music-induced analgesia, we will divide the population into two groups, emotional and non-emotional, and then induce acute pain in healthy participants while they listen to different auditory conditions (control, sounds, speech, and music). We will also induce placebo effect with suggestion. To measure the pain we will use the visual analog scale (VAS) and physiological data (heart rate, blood pressure, etc).
With this study we expect to determine if there is another mechanism besides distraction and placebo effect inducing pain relief while listening to music, and if there is a personality type that could benefit more from it.

P29.07 Kristian Sandberg

LOCALIZATION OF CORTICAL AREAS INVOLVED IN CONSCIOUS PROCESSING DURING BINOCULAR RIVALRY USING MEG

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In the present experiment we use source localization employing a beamformer technique on MEG data recorded while subjects were experiencing binocular rivalry (BR). BR occurs when a different image is presented to each of a subject's eyes. This causes the subject to perceive only one of the images at a time. After every few seconds, the perceived image switches. BR is often used to study the neural correlates of consciousness as it allows alternations in conscious content while keeping the physical stimulus constant. In our experiment, a face and a grating were used as stimuli. Stimuli were presented at different flicker frequencies.
Extrastriate areas of the ventral visual pathway, and spatial attention related parietal and frontal regions have previously been found to be involved in perceptual switches during BR. Additionally, activity increases in FFA when a subject reports seeing a face, and competition between eye signals occurs primarily in V1 while competition between colors takes place in V3. We use a beamformer technique to look at regions of cortex which exhibit changes in the tagged frequencies consistent with the subject's report and compare our results to previous findings. Initial results suggest that activity in the ventral visual pathway covary with the subjects' conscious perception.

P29.08 Christopher Joseph Bailey

CONCURRENT MEASUREMENT IN THE RAT OF THE EPIDURAL ELECTROENCEPHALOGRAM AND BRAIN GLUCOSE CONSUMPTION USING µPET: DEVELOPMENT OF METHODS

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The relationship between brain information processing and energy consumption remains uncertain. Local changes in blood flow and/or oxygenation are routinely used as indicators of brain work, though extensive research indicates that these variations are considerably larger than changes in actual energy turnover. Only few methods are today available for the study of brain energy consumption in vivo, one of these being positron emission tomography (PET) of radioactively labeled glucose

analogs. No imaging method exists, however, that is capable of measuring the electrical signature of neuronal information processing. In experimental animals such as rats, the electroencephalogram (EEG) can be recorded directly on the dural surface, offering a reasonable spatial resolution (the signal is a distance-weighted average of synchronous transmembrane currents in a volume of ca. 10 mm^3). In the present study we investigate the feasibility of and methodology for obtaining high-quality cortical field potentials in rats whilst simultaneously acquiring metabolic imaging data using a small animal μPET scanner. First, we use phantom measurements of the glucose analogue FDG to quantify the effect on the PET measurement of the miniature stainless steel screws used to measure the epidural EEG. We then record simultaneous FDG-PET and EEG in a group of animals to ascertain optimal acquisition parameters for subsequent kinetic modeling of the PET data. We discuss the motivation for applying concurrent electrical and metabolic recordings in the context of flash-stimulation of the rat visual system.

P29.09 Trine Christensen

GENE EXPRESSION PROFILING OF VENTRAL HIPPOCAMPAL GRANULAR CELL LAYER IN RATS EXPOSED TO CHRONIC MILD STRESS

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Depression is a complex and heterogeneous disease and treatment strategies include antidepressant medication. Only 50-60% of depressive patients respond to the first line of treatment and onset of drug action is often delayed for several weeks.
The purpose of the present study is to quantitatively investigate global gene expression differences independent of any hypothesis describing depression etiology, recovery and resistance to treatment. Furthermore we want to investigate differences in stress reactivity comparing stress susceptibility and stress resiliency.
For this purpose we use the validated rat chronic mild stress model of depression followed by gene expression studies in the granular cell layer (GCL) of the rat dentate gyrus. This specific area was chosen due to its predominant involvement in adult neurogenesis , stress response and antidepressant treatment.
Homogeneous isolation of GCL was performed by laser capture microdissection (LCM). Illumina microarray chips were used to identify differentially expressed genes and selected genes were confirmed by quantitative polymerase chain reaction (qPCR) analyses.
Several genes were found to be changed due to the stress response, however only 8 genes with implication in recovery was detected. Likewise, we detected 8 genes involved in treatment resistance and 13 genes involved in resiliency.

P30.01 Leslie Foldager

USING LOGIC REGRESSION TO IDENTIFY SNP INTERACTIONS BASED ON INDIVIDUALLY TIME-MATCHED CASE-CONTROL DATA

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Gene-gene and gene-environment interactions are likely to be involved in the disease aetiology of schizophrenia (SZ). In an individually time-matched (nested) case-control candidate-gene study of SZ on subjects obtained from the Danish Newborn Screening Biobank[1], genetic markers from susceptible DNA regions were genotyped using whole genome amplified DNA from neonatal dried blood spot samples[2]. A number of environmental factors were also included.
Logic regression has been proposed as a classification method for prediction of a response by use of Boolean combinations of binary covariates[3]. A subset-based logic regression approach was recently proposed for identifying and quantifying

importance of single nucleotide polymorphism (SNP) interactions in case-control studies[4]. Identification of gene-environment interactions is possible too as long as the environmental measure can be formulated as a Boolean combination of binary variables. We aim at extending logic regression to individually time-matched case-control studies which we will term "conditional logic regression".
Logic regression has been implemented as libraries in R (www.R-project.org): LogicReg and logicFS. These implementations do not allow for missing genotypes and imputation is thus needed as a pre-processing step[5]. The documentation of LogicReg gives conditional logistic regression as an example of how to implement new models. Thus, implementation of conditional logic regression is expected to be fairly straight forward.

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P30.02 Ivana Konvalinka

SYNCHRONIZATION IN JOINT ACTION: FROM TAPPING TO FIRE-WALKING

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Synchronization of actions, goals, and intentions among people is an essential phenomenon in successful social interactions. It has been observed in coordination tasks requiring mutual information exchange between individuals, as well as scenarios of unidirectional coupling whereby one individual aligns with another through mimicking or simulation. In order to explore the dynamics and mechanisms involved in entrainment, a finger tapping experiment was carried out. Pairs of subjects were asked to tap on their respective keyboards following an 8-beat stimulus. They were instructed to keep the given beat as well as synchronize with the 'other', while they received auditory feedback of themselves tapping, the other, or the computer metronome. Analysis of their inter-tap intervals showed that dyads were unable to achieve full synchrony but rather in the attempt to lock in phase with each other, they corrected their tapping onsets in opposite directions. Windowed cross-correlations revealed high correlation in both lag +1 and -1 in the interactive condition, suggesting a shared continuous adaptation to the other's output. Unintentional synchronization was also considered through a second study, looking at heart rates of spectators and participants during a fire-walking ritual. Preliminary analysis revealed high synchronization among family members. Dynamical systems analysis showed that both types of interactions may be represented through varying degrees of coupling strengths between people, possibly correlated with their affinity to one another; however, even through indirect contact with each other, people do not adopt leader/follower roles.

P30.03 Malene Hørnø Schmidt

ASSESSMENT OF A NEW COMPOSITE DENTAL RESTORATIVE MATERIAL

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Introduction
In the process of improving composite restorative materials, special attention has been paid to polymerization shrinkage. Shrinkage of the material induces forces that tend to pull the restoration away from the cavity walls. These forces may cause microleakage, marginal staining, gap formation, and increase the risk of postoperative pain. The most frequently reported reasons for replacement of composite restorations are secondary caries and fractures. In particular, gap

formation may be an important factor in the development of secondary caries, because a gap acts as a retention groove for bacteria. A new composite material (Filtek Silorane), that has shown reduced polymerization shrinkage in laboratory studies, has been introduced.
Aim
To study the clinical performance and biocompatibility of Filtek Silorane compared with another composite material (Ceram X)
Methods
The project includes:
1. A randomized clinical trial to investigate the clinical performance of the materials.
2. A scanning electron microscopic examination of the marginal adaptation.
3. An analysis of substances released from the polymerized material.
72 patients participated in the clinical trial. 158 restorations were placed in 80 premolars, and in 78 molars. The restorations were evaluated at baseline and after one year according to marginal adaptation, cavo surface marginal discoloration, approximal contact, fractures, caries associated with restorations, and postoperative hypersensitivity.
Results from the study of biocompatibility have been submitted for publication. Data from the two other studies are collected and now analysed statistically.

P30.04 Kaare Dyre Palnum

USE OF MEDICAL PROPHYLAXIS AND CLINICAL OUTCOME IN PATIENTS WITH ISCHEMIC STROKE: A NATIONWIDE FOLLOW-UP STUDY

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Background- Patients with ischemic stroke have an increased risk of new cardiovascular events and death. However, a series of large randomized controlled trials report that medical prophylaxis, including antiplatelet, antihypertensive and lipid lowering treatment reduces the risk of new cardiovascular events. Nevertheless, uncertainty remains whether this effect can be transferred to real-life patients and whether it applies to all regardless of age and sex. Therefore we aim to examine the association between use of medical prophylaxis and clinical outcome in patients with ischemic stroke, including the risk of new stroke, myocardial infarction and death.
Methods and design- A nationwide follow-up study including approximately 29.000 patients with ischemic stroke registered by the Danish National Indicator Project (DNIP). Data on use of medical prophylaxis after hospital discharge are obtained by linkage to the Danish Medicines Agency Register. All patients surviving at least 30 days will be followed up until the date of first outcome. Data on outcomes will be obtained from the DNIP, the National Registry of Patients and the Danish Civil Registration System. The association between cardiovascular drugs and the clinical outcome will be assessed using Cox proportional hazards regression, stratified according to age and sex and adjusted for potential confounders.
Results- Will be presented at the PhD day.
Conclusions- Danish registers provide unique opportunities for monitoring and assessing the impact of implementing evidence-based interventions in the health care system and may be a useful tool for bridging the gap between clinical research and real-life clinical settings.

P30.05 Jan Hendrik Rölfing

ERYTHROPOIETIN'S OSTEOGENIC POTENCY IN POSTEROLATERAL FUSION

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INTRODUCTION Erythropoietin (EPO) has recently been shown to improve fracture healing. Hypothesis: EPO is beneficial in uninstrumented posterolateral spondylodesis (PLF).

MATERIAL AND METHODS Two groups consisting of 11 mature rabbits (4 kg) underwent PLF (L5-L6). Autograft was applied (2g/side). NeoRecormon (Roche; 250 IU/kg/day) or saline were injected s.c. for 20 days starting 2 days preoperatively. Blood samples were taken before the first injection and 2, 4 and 6 weeks postoperatively. CT scan at 6 weeks was used to evaluate fusion rate and fusion volume. After CT the animals were killed and the lumbar spine removed. Manual flexion was used to evaluate motion. Post mortem x-rays were taken. Histological and mCT results are pending. All analyses were blinded. T-test was used for statistics.
RESULTS Three animals died due to anesthetic complications. No motion at the fused segment was present in 67% vs. 40% in EPO and control group estimated by manual palpation (mp). X-ray and CT overestimated the fusion rate compared to mp: 100% vs. 80% and 89% vs. 80% respectively. The fusion volume of the EPO group was significantly higher than that of the control group (3,382±0,273 ccm versus 3,022±0,235 ccm; p=0.007). Hemoglobin and hematocrit were elevated and thrombocytes were decreased in the EPO as compared to the control group at all timepoints (p

P30.06 Jesper Ougaard Schønnemann

RASCH-ANALYSIS OF THE DANISH VERSION OF THE DISABILITIES OF ARM, SHOULDER AND HAND QUESTIONNAIRE.

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Introduction:
Disabilities of Arm, Shoulder and Hand (DASH) questionnaire is widely used as a patient reported outcome in patients with wrist disorders. All though intensivley validated in other languages, using classical test theory, no studies have been published demonstrating the psychometric properties of the questionnaire. Rasch-analysis is a way to investigate properties of individual items in a questionnaire testing unidimensionality and constructions of repsonses of individual items.
Material and Methods:
60 patients with wrist disorders were included during ambulatory treatment and answered the DASH twice during their treatment, resulting in a total of 120 questionnaires. These are to be analyzed using the RUMM2020 software.
Results:
Analysis is currently ongoing, and will be reported when finished.
Discussion:
Analysis is currently ongoing.

P30.07 Bjørn Petersen

MUSICAL EAR TRAINING WITH COCHLEAR IMPLANTS

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Cochlear Implants (CIs) in most cases provide impressive speech perception for adults and children with severe or profound hearing loss, owing to the incredible cortical plasticity of the brain. However, due to the highly impoverished input from the implant, CI-recipients often fail in perceiving speech prosody and music. Improved perception of musical pitch, rhythm and timbre may not only provide a greater joy of music but very well generalize to lingual abilities. In the present study we evaluate the behavioral and neurologic effects of musical ear training on CI users' perception of music and speech. Advancements in discrimination skills and brain activity, measured by PET- scanning in two groups of "naïve" adult CI-users over a 6 month period, are correlated and analyzed (music training vs control). Preliminary results indicate a general training benefit particularly in musical discrimination skills, which correlates well with the observed progress in brain areas activated by

language stimuli during scanning. The study shows that musical ear training may be a valuable supplementary rehabilitation strategy for CI-recipients, while they are adapting to their implant. The methods created and used in the study combine personally and computer assisted training and can, when administered professionally, provide an efficient and rewarding strategy for improving speech understanding for both adults and children with CIs.

P30.08 Louise Buur Lund

IDENTIFICATION/ CHARACTERISATION OF SIGNALLING PATHWAYS INVOLVED IN P25α INDUCED α-SYNUCLEIN DEPENDENT DEGENERATION

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α-synuclein is implicated as a critical factor in several neurodegenerative diseases including multiple system atrophy and Parkinson's disease.
We present a cellular model of oligodendroglial degeneration that shows a fast morphological reorganisation of the microtubules from the cellular processes to the perinuclear region followed by a slowly progressing apoptosis with development of apoptotic markers such as: Activated caspase-3, phosphatidylserine externalisation, and nuclear condensation and fragmentation. The process is triggered by coexpression of α-synuclein and the brain specific protein p25/Tppp. P25/Tppp is an oligodendroglial protein that potently stimulates α-synuclein aggregation in vitro and which is found in glial cytoplasmic inclusions in MSA and also in Lewy bodies of PD along with α-synuclein.
The observed cellular response was dependent on α-synuclein phosphorylation at Ser-129, demonstrated by site-directed mutagenesis as well as inhibition of two kinases proposed to be responsible for the α-synuclein phosphorylation, casein kinase 2 and polo-like kinase 2. Also, a specific inhibitor of α-synuclein aggregation, El Agnaf peptide ASI1D as well as nonselective inhibitors of aggregation Congo Red and Baicalein showed to have protective effects.
Recently a selection of small molecule kinase inhibitors with known mechanism of action also showed to have a potential inhibitory effect on the cellular degeneration observed in the model. By further investigation these findings may add to the knowledge of the degenerative pathway and potentially be a target for therapeutic intervention or early biomarkers.

P30.09 Joel Fredrik Astrup Aanerud

SEROTONIN RECEPTORS IN THE HUMAN BRAIN

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Background: Serotonin is a neurotransmitter that regulates mood, sleep cycles and other aspects of our behavior. When serotonin's function in the brain is faulty conditions such as depression, and anxiety, eating and sleep disorders occur. Several of these disorders are associated with aging [1]. Our aim is to compare binding of an agonist to the serotonin$_{1A}$ receptor (5-HT$_{1A}$R) in young and old healthy controls to better understand the changes observed during aging.
Methods: So far, seven subjects have been scanned with [^{11}C]-100365-WAY, a tracer that binds to the 5-HT$_{1A}$R. Subjects are divided into young (4 subj. 21-26 years) and old (3 subj. 64-72 years). Brain images were acquired with an HRRT positron emission tomograph (PET). All subjects had T1-weighted 3T MR images that were coregistered with the PET-scans. The frontal cortex was used as region of interest and cerebellar white matter was used as reference region. Time-activity curves for region of interest and reference region were fitted with a simplified reference tissue model [2].
Results: The mean binding potentials (standard deviation) for young 4.3 (± .3) and old 5.7 (± 1.3) were not significantly different (p=0.29) from each other.
Discussion:Earlier work [2] have shown a decline in binding of [^{11}C]-100365-WAY in aging. Our material is not yet sufficiently large to detect a trend. The study is ongoing.

References:
1. Meltzer CC et al. "Gender-specific aging effects on the serotonin 1A receptor" Brain Research 2001
2. Tauscher J. et al. "Serotonin 5-HT_{1A} Receptor Binding Potential Declines with Age as Measured by [^{11}C]WAY-100635 and PET" Neuropsychopharmacology 2001

P31.01 Sanne Kragh Kjær

IS TREATMENT OUTCOME ASSOCIATED WITH COGNITIVE DYSFUNCTIONS IN OCD?

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Obsessive-compulsive disorder (OCD) is a complex psychiatric anxiety disorder characterized by involuntary and returning obsessions and compulsions. It is well documented that patients with OCD have mild cognitive dysfunctions, primarily in visuo-spatial memory and executive functions. First choice treatment for OCD is Cognitive Behavioural Therapy (CBT) and Selective Serotonin Reuptake Inhibitors (SSRI). Up to 50% of OCD patients do not have significant treatment outcome when dropout rates are taken into account. One main object of the present study is to investigate whether cognitive dysfunctions are associated with treatment outcome. 40 adult patients with OCD will be assessed with neuropsychological tests to estimate cognitive (dys)functions and a semi-structured interview to rate severity of symptoms (treatment outcome) pre- and post standard treatment at an outpatient clinic for OCD at Aarhus University Hospital Risskov, Denmark. As comparison group 40 healthy controls will be assessed with neuropsychological tests and re-assessed after 20 weeks. If cognitive dysfunctions are associated with poor treatment outcome, future treatments may need to take this aspects into account, either by compensating for or by focusing treatment directly at cognitive dysfunctions.

P31.02 Kasra Zainali

THE EFFECT OF GOLD PARTICLES IN SHEEP ALLOGRAFT

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INTRODUCTION

The use of allograft in arthroplasty causes a foreign body immune response. We hypothesized that an allograft containing gold particles would reduce fibrous tissue production by suppressing inflammation and modulate graft resorption and hence improve biocompatibility and entail better osseous integration.

MATERIAL AND METHODS

The study was performed as a paired animal design with 10 mature sheep. Spherical 45-63-mm gold particles were used. Cylindrical plasma-sprayed porous titanium implants (L 10 mm/Ø 6 mm) with endcaps and top screws (Ø 11 mm) were inserted, leaving a 2.5-mm circumferential defect around each implant. Each sheep received two implants in the proximal humerus surrounded by impacted allograft +/- gold particles (129 mg). Biomechanical push-out tests and histomorphometrical analysis were performed 12 weeks later.

RESULTS

Biomechanical results:
Max Shear Strength (MPa) gold/control = 1.27(0.94; 1.71) p=0.098
Total energy absorption (kJ/m^2) gold/control = 1.47(0.85; 2.53) p=0.134
Histomorphometrical analysis: No statistically significant differences were found in new bone formation, graft resorption or amount of fibrous tissue.

CONCLUSION
We failed to demonstrate any statistically significantly improvement in osseous integration. The power of the study may have been insufficient, and it was further reduced with the loss of three out of ten included animals. However, the consistent (but statistically non-significant) trend that the gold particles improve biomechanical strength and stability is noticeable and warrants further experiments.

P31.03 Kristine Rømer Thomsen

ELUCIDATING THE FUNCTIONAL NEUROANATOMY OF SOCIAL PLEASURE

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AIM: The aim of my project is to help elucidate the functional neuroanatomy of social pleasure using magnetoencephalography (MEG) and deep brain stimulation (DBS) techniques. BACKGROUND: Pleasure is a central part of human life and in many ways pleasure is what makes life worth living. Unfortunately a vast amount of people suffer from anhedonia, a lowered or missing ability to experience pleasure, which is a key symptom in many psychiatric disorders. Knowledge of the brain mechanisms responsible for the generation of pleasure can sub-serve our currently limited knowledge of anhedonia, and potentially aid treatments of anhedonia. METHODS: I have developed 4 behavioural tasks that tap into different components of social pleasure: (a) a priming task looking at specific responses to infant faces, (b) a priming task looking at the effect of valence on consciousness, (c) a probabilistic social reward task looking at how we use faces to learn who is happy and who is sad, and (d) a social reversal task looking at how we learn to change behaviour based on changes in social stimuli, and whether we can affect this explicit learning using subliminal priming. The tasks are used in MEG experiments, and we are now ready to look at the first data. In addition, we have recorded activity directly from the anterior cingulate cortex in 3 DBS patients treated for chronic pain, while doing the tasks. The behavioural data has shown interesting findings, and we are now ready to analyse the local field potential (LFP) data.

P31.04 Martin Gottliebsen

REVERSIBEL EPIPHYSIODESE - STAPLING VERSUS TENSION BAND PLATING TECHNIQUE

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Background: Correcting angulating deformities of the lower limb is a subject of major interest in paediatric orthopaedics. Using reversible techniques to obtain hemiepiphysiodesis it is possible to correct deformities in the growing child. The tension band plating technique is believed to reduce the risk of premature closure of the growth plate compared to stapling. Two experimental studies are carried out on an animal model.

Aims: To compare the histopathological effects (A) and reversibility (B) of stapling versus tension band plating.

Material and Methods: In both studies we use 10 weeks old domestic pigs in a paired randomised design with animals being their own control. Right proximal tibia is randomised to medial epiphysiodesis by either stapling or tension band plating. The left proximal tibia receives the opposite treatment. In study A we harvest and prepare the epiphyseal plate after the planned treatment period. In study B the implants are removed after treatment and the animals are kept alive for an additional period before harvesting of the epiphyseal plates. The parameters we use

in the analysis are 1) Descriptive analysis of the microscopically appearance of the growth plate, 2) Histomorphometric analysis, 3) Bone volume, 4) Bone surface to volume ratio and 5) Mineral appositional rate.

Time schedule: Experimental surgery; June 2009 – October 2009. Analysis; November 2009 – June 2010. Preparation of manuscripts; June 2010 – November 2010.

P31.05 Caspar Skau Madsen

EXPERIMENTAL PAIN MODEL WITH TOPICAL CAPSAICIN AND CONTACT HEAT EVOKED POTENTIALS

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Capsaicin activates receptors located on small- to medium- sized nociceptors. The activation causes an erythematous response, intense ongoing pain and hyperalgesia to heat stimuli. It is unsettled whether capsaicin mainly activates C fibers or also activates A delta fibers. Since capsaicin-evoked sensory symptoms mimic the symptoms seen in neuropathic pain, the capsaicin model is commonly used as a surrogate model of positive symptoms and signs in human neuropathic pain. We wanted to examine the capsaicin-induced hyperalgesia towards heat stimuli. We hypothesized that capsaicin would cause a facilitated response to contact heat with a shorter latency and a larger amplitude of the evoked potentials compared with the contralateral and non-sensitized skin. To elicit a C-fiber response, the superficial radial nerve was blocked by pressure. The progress of the conduction blockade was continuously monitored with touch, pinprick, cold and warm detection. Heat hyperalgesia was induced by topical application of 200 µl (50 mg/ml in 70% ethanol solution) capsaicin on the dorsum of the hand. We used a contact heat evoked potential stimulator (CHEPS) to active the small fibers. Pain was evaluated on a numeric rating scale (NRS 0-10) and with a validated Danish pain questionnaire. A descriptive analysis on preliminary data from 14 subjects showed an A-delta response in a time window of 300-500 ms recorded from the vertex position which diminished with a complete A delta fiber blockade, and further, in some subjects, a C-fiber response was elicited (1000-1500 ms). Our findings suggest that capsaicin application enhances pain perception and shows a facilitated evoked response.

P31.06 Anne Hansen

SPASTICITY AND PAIN FOLLOWING STROKE: A PROSPECTIVE STUDY

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Background: Post-stroke pain, such as shoulder pain and central pain, is a known consequence of stroke. The relation between spasticity, spasms and pain is not clear.
Aims: The objectives of this study were to determine the incidence of spasticity, spasms and pain after stroke and the relation between these phenomena.
Methods: All consecutively eligible patients admitted to the Stroke Unit, F2, Aarhus University Hospital from 1 February to 1 August 2008 were asked about pain, spasms and spasticity prior to and at stroke onset and subjected to a brief examination of sensory abnormalities, reflex activities and muscle tone and strength. The patients were contacted and interviewed by phone or mail after three and six months and asked about pain status, spasms and spasticity.
Results: Of 164 acute stroke patients, 157 and 152 patients completed three and six months follow-up respectively. After six months, 15.2% (24/152) reported spasticity or spasms; 33.3% (8/24) of them reported pain due to their spasticity or spasms and 20.8% (5/24) reported discomfort. Central pain was reported by 6.6 % (10/152) and was more common in those with spasticity and spasms while shoulder pain was not related to spasticity and spasms (Fisher's exact test, P= 0.001).
Conclusion: Spasticity, spasms and central pain may be associated.

P31.07 Juozas Petruskevicius

CEMENTATION OF FEMORAL COMPONENT WITH PROXIMAL CENTRALIZER. *ANALYSIS OF CEMENT PENETRATION IN CANCELLOUS BONE*

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INTRODUCTION: Previous studies have shown that higher intramedullary pressure yields deeper cement penetration into cancellous bone during cementation of the femoral stem. The use of a proximal stem centralizer may prevent cement-outflow during stem cementation and increase cement penetration into the bone, particularly in the metaphysical region of the femur.

MATERIAL AND METHODS: We used eight pairs of embalmed cadaveric femora for cementation of the femoral prostheses (Bi-Metric, Biomet) with or without proximal stem centralizer. The femora were prepared by a standard procedure, and the cementation was performed according to a 3rd generation cementing technique. CAT scans of the specimens were performed after the operation, and the proximal part of each femur was transversely sectioned into nine samples. Cement penetration and the thickness of the cement mantle were both measured at eight ROIs using a stereological technique.

RESULTS: Cement penetration in the proximal femur did not differ significantly between the groups (mean value of the difference between the groups was 121.85 µm; 95% CI, from -117 to 361; P = 0.3, paired t-test). The same findings were observed for the thickness of the cement mantle (mean diff. between the groups 147.16 µm, 95% CI from -215.4 to 509.72, P=0.42, paried t-test) .

CONCLUSION: In this setup using cadaveric femurs, we were not able to show significantly positive effects on either cement penetration or thickness of the cement mantle during cementation of femur prosthesis with a proximal centralizer. We could not confirm the same positive findings observed when a proximal centralizer was used with other designs of the femoral stem.

P31.08 Kåre Eg Severinsen

LONG TERM EFFECTS OF PROGRESSIVE RESISTANCE TRAINING VS. HIGH INTENSITY ENDURANCE TRAINING ON REHABILITATION OF WALKING IMPAIRMENT AFTER STROKE: A ONE YEAR FOLLOW-UP

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Objective: To evaluate the long term effect of progressive resistance training of the lower extremities vs. high intensity endurance training on walking impairment in chronic hemiplegia after stroke one year after 12 weeks of physical training.

Design: One year follow-up.

Setting: University clinic with evaluations of outpatient subjects.

Subjects: Forty-two chronic stroke patients with an age between 50-80 years and with independent walking ability participated in a follow-up one year after completion of a randomized controlled clinical trial. The clinical trial investigated the effect of either progressive resistance training of the lower extremities (RT-group, n=13), high intensity endurance training (ET-group, n=13) or control intervention (CT-group, n=16) on walking capacity after stroke.

Main outcome measures: One year test values of Aerobic capacity (VO_2-$peak_{rel}$), Isometric paretic knee extensor strength ($ParKnee_{rel}$) , six minutes walk test distance ($6MWT_{rel}$), and 10 meter walk test speed ($10mWT_{rel}$). Furthermore, Physical Activity Score (PAS) at baseline, 12 weeks, during the follow up, and at one year follow-up as well as Multiple Fatigue Inventory 20 (MFI-20) at baseline 12 weeks and one year follow-up.

Results: The one year period has not yet ended (October), but data will be reported.

Conclusion: It is expected that pt´s will have preserved at least part of their initial improvements in muscle strength, aerobic capacity and walking function and that

pt´s are less fatigued than before participation.

P31.09 Mette Buhl Callesen

DOPAMINE AGONIST INDUCED PATHOLOGICAL GAMBLING IN PARKINSON'S DISEASE

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Parkinson's Disease (PD) is a neurodegenrative disorder caused by progressive loss of dopamine-producing cells in the midbrain. One type of treatment for PD symptoms is dopamine agonists (Siegel, 2006). Unfortunately, for a subgroup of PD patients, this kind of treatment seems to induce Pathological Gambling (PG). PG is an Impulse Control Disorder characterized by recurrent maladaptive gambling behavior (DSM-IV-TR). Since 2000, numerous reports have described PG in PD and it has been shown that 6-8% of PD patients develop PG. This seems to occur within 3 months after onset of treatment with dopamine agonists or increases in dosages. After discontinuing the treatment the majority of patients stop the gambling behavior (Seedat, 2000;Driver-Dunckley, 2003;Avanzi, 2004, 2006;Dodd, 2005;Grosset, 2006;Wong, 2007). A recent PET study found that PD patients with secondary PG released significantly more dopamine in the ventral striatum during gambling, compared to PD patients without PG. Furthermore, PD patients with PG had a significantly lower baseline binding potential for [11C]raclopride than PD patients without PG (Steeves, 2009). The objective of the present PET study is to contribute to explaining the pathogenesis of PG in PD, and it is driven by the main hypothesis that PD patients, who develop PG secondary to treatment with dopamine agonists, have a decreased sensitivity towards dopamine, and hence, an increased dopamine demand.

P32.01 Tue Hartmann

PRETREATMENT MR-SCANNING IN OCD

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Although the understanding of the neurophysiological background of OCD has improved considerably, many questions remain unanswered. To further approach the understanding of the function of the cortico-basal ganglia circuit in OCD, important aspects await clarification:
Functional studies (Cognitive tasks, provocation and rest), which includes
a. Comparison between areas of cortico-basal ganglia circuit on different cognitive tests to clarify the significance of the circuit
b. Symptom provocation using visual stimuli to differentiate between anxiety related reactions in OCD and controls
c. Correlation in BOLD-signal between areas in the cortico-basal ganglia circuit in a resting condition
These are investigated before and after cognitive behavioural treatment to clarify the influence of the short-term effects of treatment.

Methods: Both Structural and functional MR-imaging will be combined to investigate the
Functional magnetic resonance imaging (FMRI)-scans and clinical measures are gathered as soon as possible after the inclusion in the clinic before the first cognitive behavioural sessions as well as on completion of the treatment approximately 20 weeks later. Clinical measures are gathered in the clinic.

Results: Preliminary results from the functional studies will be presented at the phd-day.

Conclusions: These are investigated before and after cognitive behavioural treatment

to clarify the influence of the short-term effects of treatment.
Opposite most studies the focus will be on neuronal circuits rather than simple anatomical localisation.

P32.02 Andreas Schröder

SPECIALISED TREATMENT FOR PEOPLE WITH SYNDROMES OF SEVERE BODILY DISTRESS: A RANDOMISED CONTROLLED TRIAL

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Background
Syndromes of severe and chronic bodily distress – functional somatic syndromes and somatoform disorders – are highly prevalent, costly, and disabling. We aimed to compare the effectiveness of a specialised treatment, based on a cognitive behavioural approach, with enhanced standard care on perceived physical health in patients with severe bodily distress syndromes.
Methods
In a randomised, controlled, non-blinded trial, we enrolled 120 patients aged 20-45 years with severe bodily distress syndromes, who were consecutively referred from primary and secondary care. We randomly assigned 66 of the participants to enhanced standard treatment with their primary care doctor, and 54 to specialised treatment delivered by liaison-psychiatrists at a general University Hospital. The primary outcome was improvement in physical health at 16 months after baseline, assessed with SF-36 Perceived Physical Health score. Analysis was by intention to treat. This trial is registered with ClinicalTrials.gov, number NCT00132197.
Findings
At the trial endpoint, data on the primary outcome were available for 94 participants. Patients allocated to specialised treatment reported better physical health at 4, 10 and 16-months after randomisation compared to those allocated to enhanced standard treatment ($p<0.0001$). The adjusted mean difference at 16-months was 4.2 (95 % CI 2.1 – 6.2), the corresponding effect size was 0.52 (95 % CI 0.27-0.77). NNT was 5.
Interpretation
The intervention – Specialised Treatment for Severe Bodily Distress Syndromes (STreSS) – provides a promising model for an effective management of patients with disabling functional somatic syndromes in secondary care.

P32.03 Linda Locht

METALLIC SILVER INDUCES INFLAMMATORY RESPONSES IN THE MOUSE BRAIN

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Silver is a popular coating agent on medical devices like various catheters and prostheses primarily because of its anti-bacteriel effects, but little are known about the impact of silver on brain tissue.
Micro-sized silver particles (<20 μm) were injected into the cortical part of the mouse-brain and in situ histochemical analysis of silver up-take and immunological responses to the silver implants were performed.
Using the highly sensitive Autometallography (AMG) method we found a vast spreading of silver ions to the ipsilateral cortex and hippocampus, with traces seen also in the contralateral cortex and hippocampus. Immunohistochemistry was applied on brain sections in order to examine the area surrounding the silver

implant. Two-way ANOVA analysis showed that compared to controls the micro-silver exposed animals had a statistically significant higher number of macrophages/microglia (41 [95%-CI: 20 – 62]; p=0.001) and a significant decrease of macrophages from 7 to 14 days of exposure was found (29 [95%-CI: 8 – 50]; p=0.009). GFAP positive astroglial cells was statistically significant higher in silver exposed mice compared to those of controls (60 [95%-CI: 47 – 72]; p<0.0001) and a significant decrease of GFAP positive cells from 7 to 14 days of exposure (21 [95%-CI: 8 – 34]; p=0.003). The metallothionein-1 and -2 (MT-1 and MT-2) load was statistical significantly increased in the silver exposed mice compared to that of controls (40 [95%-CI: 28 – 52]; p<0.0001), but no significant effect of the exposure time was found (p=0.60).
The study shows a widespread release of silver ions from silver implants in brain tissue followed by a marked tissue reaction.

P32.04 Birgitte Fuglsang Kjølby

CONTRAST AGENT CONCENTRATION MEASUREMENTS IN MAGNETIC RESONANCE PERFUSION WEIGHTED IMAGING

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Introduction: Perfusion weighted imaging can be used to measure the cerebral blood flow (CBF) in diseases such as stroke, cancer and dementia. Unfortunately, the method currently does not provide absolute quantification of the CBF because the method requires an accurate measurement of the passage of a tracer in the tissue and in the corresponding feeding artery (blood). This measurement is compromised by the limited spatial resolution of the MR images and a complicated signal response of the concentration of tracer in both tissue and blood. Method: We investigated the impact of these effects on the estimated CBF using mathematical models. Results: The limited spatial resolution both leads to underestimation and distortion of the tracer concentration curve describing the passage of the tracer in blood. The complicated relationship between signal and concentration of tracer in tissue and blood leads to a three-fold overestimation of the CBF. Discussion: Before quantification of CBF can be achieved we need to correct for the distortion and underestimation caused by the limited spatial resolution as well as for the difference in signal response of the tracer of blood and tissue.

P32.05 Henriette Klit

CHARACTERIZATION OF CENTRAL POST-STROKE PAIN (CPSP)

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Background
CPSP is a central neuropathic pain condition arising as a direct consequence of a cerebrovascular lesion of the CNS. It is characterized by pain within an area of sensory abnormality and has an incidence of 8%.

Aim
The aim of the study was to characterize patients with CPSP in a population based sample.

Methods
Patients suspected of CPSP were identified through a postal questionnaire and subsequently contacted (N=79). 65 patients underwent a clinical examination including a pain and medical history, a pain drawing, and bedside quantitative

sensory testing. Copies of medical records and results of CT or MR scans were obtained. All available information was anonymized and reviewed independently by two neuropathic pain experts. Patients were categorized as having definite CPSP, probable CPSP (i.e. other causes of pain could not be ruled out), CPSP-like dysesthesia, and not CPSP.

Results
A total of 65 patients (M=30, F=35) were examined, 43 in their private home and 22 at the Danish Pain Research Center. The mean age was 67.2 years. Patients were categorized as follows: 28 with definite CPSP, 16 with probable CPSP, 7 CPSP-like dysesthesia, and 14 not CPSP.

Patients with definite CPSP reported a mean pain intensity of 5 (on a scale from 0-10). 61% reported other types of concomitant post-stroke pain (i.e. shoulder-pain, pain from spasticity, or headache). Findings of allodynia ($p<0.001$) and hyperalgesia ($p=0.001$) was significantly more common in patients with definite CPSP.

Conclusion
Patients with CPSP often report moderate pain intensity and other concomitant pain conditions, and they are often found to have hypersensitivity.

P32.06 Jasna Furtula

MUNIX PERFORMED ON BRACHIAL BICEPS MUSCLE WITH QUANTITATIVE AND QUALITATIVE ASSESSMENT OF FORCE

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Objectives: To evaluate a novel MUNE technique MUNIX (Motor Unit Number IndeX) use in quantitative assessment of number of MUs in a proximal muscle.
Methods: 15 untrained healthy subjects (7 males, 8 females) - age 27-53 yrs - volunteered to participate in the study. MUNIX was performed with subjective assessment of force. The examiner was blinded for the result in the following test which was planned on a different day. Here the subjects were positioned with 90° flexion at the elbow in dynamometer LIDO Active Multijoint IIa. Surface interference pattern (SIP) was obtained in 9 recordings with gradually increasing voluntary isometric force in the brachial biceps muscle (BB) from slight to maximum activity with force increments of 10% maximal voluntary contraction (MVC) (KeyPoint Classic).
Results: There was linear relation between SIP area and force level throughout the test. The relation between index values and force level was similar to that between index values and SIP area. Correlation between index values in BB and CMAP amplitude was high ($p<0.01$). No relation was found between MUNIX and MVC.
Discussion: The demonstrated linear relation between SIP area and force performance supports the hypothesis proposed for MUNIX in which force is substituted by SIP area. In ALS the superimposition among MUPs decreases as number of MU decreases, thereby theoretically making MUNIX more sensitive for detecting the number of actual MUs.
Conclusions: MUNIX has a potential in following the pathophysiological changes in the lower motor system in ALS patients and a prospective study is ongoing to define more clearly the sensitivity and specificity of MUNE in patients with ALS.

P32.07 Signe Groth Renvillard

NEUROPSYCHOLOGICAL IMPAIRMENT AND HIGH PREVALENCE OF DEPRESSION IN PATIENTS WITH CHRONIC HEPATITIS C VIRUS.

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Objectives: WHO estimates that globally 170 million people are infected with chronic hepatitis C virus (HCV). Approximately 75% of these people have contracted the

disease by intravenous substance abuse. Impaired cognitive function is commonly found in patients infected with HCV. The cognitive deficits appear in the pre-cirrhotic stage of the disease and impair in combination with a high prevalence of depression, chronic fatigue and reduced quality of life the patient's level of functioning. Furthermore, the antiviral treatment with interferon induces depression in approximately 30% of the patients. Still very little is known about the causal relationship of HCV infection, psychiatric disorders and neuropsychological deficits, but evidence has shown that these symptoms cannot solely be accounted for by a history of substance abuse. In the present study we wish to thoroughly examine cognitive impairment and psychiatric symptomatology in HCV patients in order to understand the causal relationship.

Methods: 60 HCV patients about to commence antiviral treatment will be examined with a neuropsychological assessment battery and diagnosed according to the diagnostic interview SCAN. NEO-P-IR measuring personality traits will also be administered. In the 8th treatment week the patients will again undergo SCAN. 40 HCV patients not about to commence treatment and 30 healthy participants will serve as controls.

Results: Preliminary results will be presented delineating the cognitive function and psychiatric symptomatology of HCV patients.

P32.08 Thomas Urban

PATIENT DISCOMFORT IN IMMEDIATE IMPLANT PLACEMENT IN MOLAR REGIONS IN ASSOCIATION WITH THREE REGENERATIVE TECHNIQUES

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Objectives: To assess patient discomfort in terms of pain, swelling and bleeding following immediate implant placement in molar regions using three regenerative techniques.

Methods: Ninety-two patients (44 women and 48 men; mean age 50 years [range 23-77], 35 smokers and 57 non-smokers) in need of a single implant to replace a molar were included. The postoperative course was recorded on 100mm visual analogue scales (VAS) with extreme end points for the level of pain on the day of surgery, 1, 2 and 3 days postoperatively (no/extreme pain); swelling on the day of surgery, 1, 2 and 3 days postoperatively (no/severe swelling); bleeding from the wound on the day of surgery, 1, 2 and 3 days postoperatively (no/severe bleeding).

Results: Pain peaked 5-6 hours postoperatively (mean VAS=25). Swelling (mean VAS=62) and oozing from the wound (mean VAS=13) peaked 1 day postoperatively. There were no significant differences in the perception of pain, swelling or oozing from the wound between the three regenerative groups. VAS score for pain was higher for smokers than for non-smokers at all times; a significant difference was found 3 days postoperatively ($P<0.01$). All pain scores were significantly higher in younger (<50 yrs) than in older patients (≥50 yrs)($0.006 \leq P \leq 0.042$).

Conclusions: Patients experienced little to moderate pain in combination with slightly severe swelling and mild oozing after immediate implant placement in molar regions involving regenerative techniques. Being a smoker was associated with more pain in contrast to being >50 years, which was associated with less pain.

P32.09 Jimmi Nielsen

10-YEAR TRENDS IN THE TREATMENT AND OUTCOMES OF PATIENTS WITH FIRST-EPISODE SCHIZOPHRENIA

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Background: The first episode of schizophrenia is a critical period for illness course and outcomes. During the last ten years several new trends in treatment has been

issued, e.g. atypical antipsycotics and specielized inter-disciplinary treatment teams. We aim to assess trends in treatments and outcomes during the first year after a diagnosis of schizophrenia during the years fro 1996 to 2005.
Method: Pharmacopidemiologic inception cohort study of all patients diagnosed with schizophrenia for the first time in Denmark between 1996 and 2005.
Results: 13,600 individuals was diagnosed for the first time with schizophrenia in the years from 1996 to 2005. A significant decrease in the mean age of first diagnosis (29.2 to 26.1 years), and less patients resided in an institution, lived alone, or received early retirement pension (all p-values<.001). The number of psychiatric hospitalizations (1.6 (CI:1.6-1.7) to 1.4 (CI:1.3-1.5), p<.0001) and bed-days (89.9 days (CI:81.8-98.8) to 71.8 days, CI:63.7-80.8, p<.0001) decreased, whereas outpatient contacts (10.2 (CI:9.5-11.0) to 21.4 (CI:19.9-21.0), p<.0001) doubled. More patients received antipsychotics (67.2% to 80.7%, annual OR=1.07, CI:1.06-1.09, p<0.001), atypical antipsychotics (15.3% to 89.2%, annual OR=1.51, CI:1.48-1.43, p<0.001), and antipsychotic polypharmacy for >4 months (16.7% to 37.1%, OR=1.14, CI:1.12-1.57 p<0.001).
Conclusions: The decade between 1996 and 2005 is characterized by an earlier recognition of schizophrenia, intensification of outpatient treatment, increased use and dosing of antipsychotics and antidepressants, as well as by indicators of improved functional outcomes.

P33.01 Mette Sørensen

EFFECTS OF STATINS ON ORTHOPAEDIC IMPLANT FIXATION

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Background
In the western world about 2% of the population >60 years has a total hip replacement. Loosening of the prosthesis is a serious and painful complication that causes severe disability. Within the first ten years after receiving a total hip prosthesis 10% will have suffered from this condition and need revision surgery. Statins, cholesterol lowering drugs, affects the melvalonate synthesis by inhibiting the 3-hydroxy-3-methylglutrayl coenzyme A reductase and by increasing the expression of bone morphogenic protein 2 which stimulates osteoblast differentiation. The effects on bone metabolism were first reported by Mundy who found that statins were potent stimulators of bone formation in vitro. Skoglund published a study which suggests a positive effect of statins on healing fractures in rats. In vitro studies have shown that statins exert an anti-resorptive effect on bone; others indicate an anabolic effect on bone formation. By these mechanisms we think statins are able to augment early implant fixation and thereby reduce implant loosening long term.
Methods
Ten dogs will each receive four experimental implants, two inserted into the trabecular bone in the metaphysis of each humerus. The four groups tested are: implant, implant+coating, implant+coating+statin (low dosage), implant+coating+statin (high dosage). The implants will be surrounded by 1.0mm gap. After four weeks of observation mechanical implant fixation will be evaluated by push-out test and osseointegration by quantitative histomorphometry.
Hypothesis
Statins will augment early biomechanical implant fixation, inhibit periimplant bone resorption and induce increased bone formation.

P33.02 Esben Laugesen

PULSE PRESSURE AND AMBULATORY ARTERIAL STIFFNESS INDEX PREDICT CARDIOVASCULAR DISEASE IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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Objective: Patients with type 2 diabetes mellitus have an increased risk of cardiovascular disease (CVD). We examined the ability of ambulatory blood pressure monitoring (ABPM) parameters to predict fatal and non-fatal CVD in patients with type 2 diabetes mellitus.

Methods: 108 patients with type 2 diabetes mellitus (mean duration 6.6 years) were followed for 9.5 years (range 0.5-14.5) until death or until 1 April 2008. All patients underwent 24-h ABPM at baseline. Diagnosis of CV endpoints was performed by the hospital specialists treating the patients without knowledge of ABPM data. Follow-up data was analyzed by Cox regression analysis.

Results: 45 patients had at least one CV event of which 35 were non-fatal and 10 fatal. During follow-up CV events were encountered in 56.6 % of patients with 24-hour pulse pressure (24-h PP) above or equal to the median (57 mmHg) vs 27.8 % of patients with 24-h PP below the median ($p<0.01$), and in 48.1 % of patients with ambulatory arterial stiffness index (AASI) above or equal to the median (0.403) vs 35.2 % in patients with AASI below the median ($p<0.05$). In Cox regression analyses adjusting for well-established risk factors and mean arterial blood pressure (MAP), a 1 mmHg increase in PP and a 1% increase in AASI yielded an increased hazard ratio for CVD of 1.04 and 1.03, respectively ($p<0.05$ for both).

Conclusions: Ambulatory PP and AASI independently predict fatal and non-fatal CV events in patients with type 2 diabetes mellitus after adjustment for well-established risk markers.

P33.03 Frederik Hvid-Jensen

17 YEAR FOLLOW-UP OF 4706 GASTROESOPHAGEAL REFLUX PATIENTS; MORTALITY AND COMPLICATIONS.

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Introduction
Gastroesophageal reflux affects in Denmark alone approximately 400.000 people. 42% experience monthly and 17% have weekly symptoms. 10-20% develop mucosal damage (esophagitis) which can cause strictures and adenocarcinoma. Quality of life rating is on level with patients with angina pectoris or resent myocardial infarction.
Methods & Hypothesis
Because of known poor compliance with initiated PPI-treatment, we believe that present trials documenting the effects merely show the potential of the drugs in strict controlled trials – "real life" medication has a higher risk of complications and poorer effects.
We conducted a 17 year case-control follow-up of 4706 dyspeptic patients examined with endoscopy in 1992-93 at Århus University Hospital and 47060 population controls. Via the Danish Civil Registration System we looked at complications, mortality and medication.
Results
A total of 776 patients (16,5%) were found to have oesophagitis with an overweight of men (61,2%). During our 17 year follow-up 21 (2,7%) developed a stricture. 16 patients (2,1%) needed one or more dilatations and 0,6% developed esophageal cancer. Despite an average age of 53,3 (men) and 59,8 (women) we found a total mortality of 54,1% compared to matched population controls of 37,4%.
Discussion
We found that reflux disease is associated with higher morbidity and mortality than background population. Patients with esophagitis have in this large follow-up study 63% higher risk of strictures as described before in smaller studies and twice as high

incidence of esophageal cancer as matched controls. The correlation of poor medical compliance and complications will be assessed in a later paper.

P33.04 Sidse Kringelholt

VASOACTIVE EFFECTS OF PROSTAGLANDIN RECEPTOR AGONISTS IN ISOLATED INTRAOCULAR PORCINE CILIARY ARTERIES.

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Purpose: Prostaglandin analogues are used to reduce intraocular pressure in glaucoma. These drugs affect aqueous humor dynamics, probably involving effects on the tone of arteries supplying the ciliary body. These effects can be assumed to be mediated by prostaglandin receptors previously identified in ocular tissue.
Methods: The intraocular part of porcine ciliary arteries was isolated and mounted in a myograph system for isometric recording. The vascular tone was recorded during concentration-response experiments with PGD_2, PGE_2, two $PGF_{2\alpha}$ agonists and PGI_2 in the concentration range 10^{-9} M-10^{-5} M with and without precontraction with noradrenaline (NA) 10^{-6} M.
Results: In noradrenaline contracted arteries, $PGF_{2\alpha}$ agonists and PGD_2 increased the vascular tone dose-dependently, PGE_2 induced a dose-dependent vasorelaxation, whereas PGI_2 had no effect on the vascular tone.
Conclusions: Prostaglandins with affinity for receptors previously identified in ocular tissue have vasoactive effects on intraocular porcine ciliary vessels in vitro. The findings may be translated to clinical trials with the purpose of reducing the intraocular pressure in glaucoma.

P33.05 Line Mayland Kolstrup

HEMODYNAMIC EFFECTS OF THREE INOTROPIC STRATEGIES IN THE IMMATURE HEART

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INTRODUCTION Low cardiac output syndrome affects up to 25% of newborn children after surgery for congenital heart disease. The condition is a serious matter associated with high mortality. Traditionally, catecholamines have been used to reduce these postoperative problems, in the recent years often in combination with an inodilator (i.e. milrinone). Today, most centers for congenital heart disease use one of three strategies: (a) milrinone + adrenaline, (b) milrinone + dopamine, and (c) dobutamine alone. Whether any hemodynamic differences exist between these strategies regarding effects on the newborn heart has, however, never been investigated. AIM To compare and evaluate the hemodynamic effects of these three inotropic strategies on the immature myocardium. METHODS The study was conducted as an animal experimental study with 24 newborn piglets randomized into three intervention groups according to the three mentioned inotropic strategies. Ventricular function was assessed with real-time left and right pressure-volume loops measured with conductance catheters and by measuring cardiac output. Hemodynamic parameters were obtained with preload reduction at baseline and subsequently every hour throughout the 3-hour experiment. PERSPECTIVES At the time of submission, the study was still ongoing. Catecholamines are expected to induce a more potent increase in systolic function (primary endpoint). This study addresses the question of whether important differences are seen between the inotropes used after surgery for congenital heart disease. The knowledge will support clinicians to design inotropic therapies to match the need of each patient.

P33.06 Anne Roslev Bukh

BACTERIAL TRANSLOCATION AND IMMUNE ACTIVATION IN HIV- AND NON-HIV-INFECTED PERSONS

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Introduction

HIV-infection causes chronic immune activation. Recently, it has been suggested that bacterial translocation may contribute to the sustained immune activity. Highly active antiretroviral therapy (HAART) partially restores immune function but it is unknown if markers of inflammation and bacterial translocation return to the levels observed in non-HIV-infected individuals. We compare markers of immune activation and bacterial translocation among HIV patients (+/- HAART) and HIV-negative controls.
Materials and methods
Serum samples from HIV-infected persons, 76 on HAART and 20 HAART-naïve persons, were available, and from 50 HIV negative controls through the blood bank at Aarhus University Hospital. Markers of interest: soluble CD14 (sCD14), and lipopolyssacharides (LPS) (bacterial translocation), interleukin-1 receptor antagonist (IL-1Ra), soluble tumor necrosis factor receptor II (sTNF-rII), high sensitivity C-reactive protein (hs-CRP), and interleukin 6 (IL-6) (immune activation). We will compare group-differences using student's t-test, and correlate the markers of interest, analyzed by Spearman's rank test.
Results
As of now the results for sCD14, sTNF-rII, IL-1Ra, and hs-CRP are available. HIV-infected persons (HIV+) versus control (HIV-): For sCD14 HIV+ mean: 7,58 mg/ml (SD 3,54 mg/ml), and HIV- mean: 3,18 mg/ml (SD 0,79 mg/ml), p< 0,0001. sTNF-rII HIV+ mean: 5,56 ng/ml (SD 2,67 ng/ml), and HIV- mean: 4,25 ng/ml (SD 0,89 ng/ml), p<0,001.
Discussion
If bacterial translocation is associated with activation of the immune system, will this lead to an earlier initiation of HAART, which have shown to have a positive effect on the mucosal immune system?

P33.07 Trine Dalsgaard GENE THERAPY OF PKU

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Background: Phenylketonuria (PKU) is an inherited disease resulting in elevated levels of phenylalanine. In most patients this is due to defects in the enzyme phenylalanine hydroxylase (PAH). PAH catalyses the conversion of phenylalanine (phe) into tyrosine (tyr). Untreated PKU lead to growth failure, seizures and intellectual impairment. PKU positive children are treated with a lifelong diet with low concentrations of phenylalanine preventing the development of neurological and psychological changes.
Hypothesis: We hypothesize that patients would benefit from having a functional PAH gene inserted in the hepatocytes of the liver. Earlier studies have shown that 10% of the hepatocytes should contain the functional PAH enzyme for the PKU mouse to recover.
Aim and methods: The main goal of the project is to improve the current techniques in gene therapy and to target the PKU-disease.
Our strategy is to improve delivery and expression of PAH by several means: (1) Map the limiting step in the pathway of converting phe to tyr in cell culture and thereby improve the outcome of the PAH transduced cells. (2) Create lentiviral vectors containing the PAH gene and a reporter gene. (3) Transduce mice with the lentivirus and detect the efficiency by blood samples (4) treat the mice with a tyrosine free diet. (5) Treat the mice with CCl_4 leading to hepatocyte regeneration. This increase the frequency of cells expressing the lentivirus (5) Use site specific artificial zincfinger proteins to target the mutational region of the PAH gene, make double stranded breaks and supply the cell with the functional gene for homologue recombination.

P33.08 Kim Henningsen BEHAVIORAL AND MOLECULAR CORRELATIONS IN THE RAT CHRONIC MILD STRESS MODEL OF DEPRESSION.

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Purpose: Chronic mild stress (CMS) is a valid rat model of depression. Chronic exposure to mild and unpredictable stressors induces an anhedonia-like state, which is monitored as a reduced intake of a sucrose solution. Anhedonia-like behavior can be reversed by chronic treatment with antidepressant drugs. In our hands, the CMS model has additional features that enhances its validity. Thus a substantial fraction of animals submitted to stress are resilient and do not become anhedonia-like, but do possess other stress/depression related symptoms. Furthermore the antidepressant reversal of stress induced anhedonia only holds for about 50% of the treated animals, which closely mirrors clinical observations regarding treatment resistance. This phenomenon is highly reproducible across different classes and doses of antidepressant drugs. The purpose of the present study is to pinpoint molecular correlates to observed behavioral depression related symptoms in the CMS model. Methods: ITRAQ LC/MS was used for proteomic analysis. Behavior was addressed by sucrose intake, fear conditioning, spontaneous alternation behavior, tail flick and operant escape. Summary: We found a correlation between the anhedonia-like state and alterations in hippocampal-dependent memory (2) and thermosensitivity. Conclusion: On the basis of our investigations we conclude that the CMS model established in our laboratory has a substantial validity as a model for anhedonia, working memory deficits and increased pain sensitivity. Our findings on the behavioral level will be underpinned by proteomic investigations which are currently analysed.

P33.09 Line Andersen

ASSESSMENT OF PRESYMPTOMATIC CHANGES IN CEREBRAL TISSUE PERFUSION IN MUTATION CARRIERS OF FAMILIAL FRONTOTEMPORAL DEMENTIA, MEASURED WITH MRI

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Background/aims:
Frontotemporal dementia linked to chromosome 3 (FTD-3) is an autosomal dominant inherited neurodegenerative disease caused by a mutation in the CHMP2B gene related to endosomal trafficking.
The disease is characterized by insidious and progressive changes in personality, behavior, and cognition.
Preliminary studies in presymptomatic CHMP2B mutation-carriers have shown localized cortical brain atrophy. The purpose of this study is to assess possible functional change in the presymptomatic stage of the disease as indicated by local changes in brain tissue perfusion.
Methods:
Subjects were MR scanned twice with an interval of 15 months. The MRI-sequences Gradient Echo and Spin Echo were used to assess perfusion in all arteries and in arterioles, respectively. Perfusion images were co registered to structural T1-images in order to align the perfusion measurements to specific brain regions. Perfusion data were extracted from each region-of-interest, and statistically compared between carriers and non-carriers and over time.

Results:
The study included 16 family members. Nine were mutation carriers and 7 were first-degree-related non-carriers. None of the carriers showed any symptoms or clinical signs of the disease at the time of inclusion. Two scans have been obtained for each of the participants. Images are presently spatially aligned and data are extracted, ready for further statistical analysis.

Conclusion
Based on previous analysis of structural MRI data showing preclinical structural cortical changes in CHMP2B mutation carriers, functional MRI data are now being analysed for preclinical functional changes in cortical perfusion.

P33.10 Merete Ipsen

HOW MUCH DO MEDICAL SPECIALISTS TEACH IN THE HOSPITALS? INDICATORS OF EDUCATIONAL EFFORT IN THE DANISH SPECIALIST TRAINING.

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The medical specialist training in hospitals is provided by medical specialists, and this educational effort is central in optimal specialist training. However, in association to productivity measurements of research and patient service, the educational effort is less measured and thus less visible. Our aim in this project was to identify indicators of the educational effort, in order to measure and to make the effort visible and recognised.
Three qualitative methods were applied: (1) Semi-structured interviews with 12 medical leaders in county and university hospitals, transcribed verbatim and with saturation reached with 8 informants; and (2) Nominal Group Processes involving 24 medical specialists representing 18 specialties (medical, surgical, psychiatric and paraclinical). Both sets of data were analysed inductively in a modified grounded theory. (3) The emerging two sets of indicators were applied in a content analysis performed by the first author and validated by the co-authors. Twelve indicators were identified and used in an implementation study in two clinical departments (medical and surgical).
The identification of indicators shows that it is possible to measure educational effort. The twelve indicators of educational effort related to issues of: quantity, quality, and departmental resources for educational effort. The diversity in issues reveals that medical specialist training in hospitals involves many aspects, and hereby illustrate that medical education in a hospital is social learning in a work place. The implementation study in the departments supported this understanding and emphasised the need for visibility and recognition of the educational effort.

P34.01 Pia Damgaard Colding

EFFECTS OF THREE INOTROPIC STRATEGIES ON THE METABOLISM IN THE IMMATURE MYOCARDIUM

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INTRODUCTION: Neonates undergoing congenital heart surgery often need postoperative inotropic therapy, to prevent decompensated heart failure. Today at international centers of congenital heart disease the inotropic therapy used most frequently are: (1) dobutamine alone, (2) milrinone combined with adrenaline, or (3) milrinone combined with dopamine. The choice of inotropic therapy is based mostly on evidence from studies of adult patients. There is, however, reason to believe that similar to the age-dependent effects on hemodynamics, the effect of inotropes on metabolism may be different in the immature heart. Aim: To evaluate and compare the influence of the three inotropic strategies on the myocardial metabolism in the immature heart in newborn piglets. METHODS: Twenty-four neonatal piglets were randomized to receive dobutamine, milrinone and adrenaline, or milrinone and dopamine. For each intervention we gave an infusion resulting in a 25% increase in contractility, judged by dP/dT. The inotropes were infused for 3 hours. Metabolic parameters were sampled with microdialysis probes placed in the myocardium of both ventricles. The metabolism was measured in terms of: glycerol, glucose, lactate, and puruvate in the microdialysis fluid. Ultimately the hearts were excised, and

biopsies from both ventricles were taken, to determine the concentration of intracellular glycogen. PERSPECTIVES: The study is conducted at this moment. Results will help elucidating the interaction between hemodynamic effects and the concurrent underlying metabolism during inotropic therapies in the newborn heart.

P34.02 Julie Mackenhauer

PREVALENCE AND CHARACTERISTICS OF NON-LACTATE AND LACTATE EXPRESSORS IN SEPTIC SHOCK

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Although elevated lactate levels are associated with increased mortality in sepsis, not all patients with septic shock express lactic acidosis (LA). The objective was to determine the proportion of patients in vasopressor-dependent septic shock who presented with and without LA. Hypothesis:Patients in septic shock often do not have an elevated lactate, and still face significant mortality. Methods:Retrospective review of patients presenting between 01/08 and 09/08 to an urban tertiary care ED (50,000 patients per year). Patients with a presumed diagnosis of septic shock requiring vasopressors were divided to low (0-2.4), intermediate (2.5–3.9) and high (>4.0) lactate groups. Results:A total of 109 patients were enrolled. Of these, 49/109 (45%) were non-lactate expressors, and 55% were lactate expressors. The 28-day mortality trended with increasing lactate with 20% (10/49), 32% (8/25), and 40% (14/35) mortality within the low, intermediate and high lactate group respectively (p = 0.14). Acute liver failure statistically correlated with higher lactate levels with 4% (2/49), 16% (4/25), and 34% (12/35) prevalence as the lactate group increased from low, intermediate to high (p=0.001). Bacteremia increased significantly between lactate groups with 12% (6/49) in the low, 20% (5/25) in the intermediate, and 40% (14/35) in the high lactate group having positive blood cultures (p = 0.01). Conclusions:Almost one-half of patients with vasopressor-dependent septic shock do not express LA on presentation, though a high mortality rate remains in this population. The use of LA as the only indication of perfusion status or endpoint of resuscitation in septic shock may be inadequate

P34.03 Jesper Damsgaard

VIRAL MENINGITIS – A STUDY OF POST-INFECTIOUS COGNITIVE DYSFUNCTION AND ASSOCIATED NEUROPATHOLOGY

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Objective:
We aimed to study the neuropsychological outcome in adult patients with viral meningitis (VM) by a prognostic comparison of clinical, neuroradiological and biochemical parameters.
Background:
VM is a common infection in the central nervous system (CNS). Generally, the disease is considered self-limiting with a mild clinical course. However, studies have indicated that patients with VM may develop persisting cognitive impairment. Our hypothesis is that VM, which should be properly named as viral meningo-encephalitis, results not only in meningeal irritation, but also in parenchymal lesions leading to adverse cognitive dysfunction. Patients with CNS infections are commonly hospitalized in a department of general internal medicine where therapy is primarily focused on the initial acute phase of the disease. Cognitive dysfunction may thus be overlooked.
Methods:

We conducted a prospective follow-up study of patients with possible VM (n=35) based on clinical evaluation during a period of six months. Cognitive tests were carried out in order to study the cognitive function of the patients over time as well as to make a systematic assessment of depression and the Health-related Quality of Life. The computerized cognitive testing system, CogState, was used five times from disease unset until follow-up (at three months). MRI was performed within the 72 hours of admission. The cerebrospinal fluid was tested for levels of neurobiochemical markers.
Results:
Results are pending. We hope that the study will provide new insight into the prevalence and extent of neuropsychological adverse manifestations and associated prognostic indicators in patients with VM.

P34.04 Astrid Hjelholt Nielsen

IMMUNE CELLS IN HUMAN SALPINX INFECTED WITH *CHLAMYDIA TRACHOMATIS* SEROVAR D COMPARED TO UNINFECTED SALPINX.

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BACKGROUND: Chlamydia trachomatis is a major cause of bacterial sexually transmitted disease in the Western World. It is a intracellular bacteria infecting the epithelial cells in the salpinx. Untreated it can lead to scarring and occlusion of the fallopian tubes, causing ectopic pregnancy and infertility. It is believed that much of the damage is due to the immune response following the infection. To better understand the immune response, we will characterize the immune cells in the human salpinx using immunofluorescence microscopy to mark the membrane surface proteins expressed by the immune cells.
METODES: In sections of paraffin embedded human salpinx tissue (uninfected and infected with C. trachomatis serovar D), we use immunofluorescence microscopy to examine which surface markers there is found in infected tissue compared to uninfected tissue. We have used antibodies against CD3, CD8, CD20, CD68, CD163, CD205, HLA-DR, -DQ, -DP and against the outer membrane in C. trachomatis (MOMP), all conjugated with FITC.
EXPECTED RESULTS: We expect to find T-cells, dendritic cells and macrophages in the salpinx tissue. In the infected salpinx we expect the macrophages to be activated (express the CD molecule 163) compared to the inactivated macrophages in the uninfected tissue. Furthermore we might find the immune cells in different places in the infected salpinx.
DISCUSSION: Based on the results from this experiment, we will go further and investigate the cytokines in the infected tissue, and the pathway used to secrete the cytokines, by analyzing if the infected epithelial cells contain the NALP3 inflammasome.

P34.05 Anne Leegaard

PRESSURE PAIN TRESHOLD IN CHILDREN WITH JUVENILE IDIOPATHIC ARTHRITIS

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BACKGROUND: Pain is one of the primary symptoms in juvenile idiopathic arthritis (JIA) and occurs daily in many cases. This leads to lower quality of life and less participation in social activities. Some children with JIA report severe pain despite low disease activity. Dealing with this group of patients is a big challenge for the health care system. More knowledge in this area and an easily accessible, accurate method of measuring pain is needed to improve the treatment of these children.
AIM: To evaluate the pain threshold in children with juvenile idiopathic arthritis compared with healthy children by using a simple pressure algometer.

METHODS: The study includes 60 children born between 1995 and 2000 with JIA under care of the paediatric rheumatology clinics in Aarhus (Skejby) and Odense. 60 age- and sex-matched healthy school children serve as a control group. Pain threshold measurement is performed using a simple pressure algometer on 17 symmetric anatomically defined areas of the body. The pressure algometer is calibrated in kg/cm^2 and pain threshold is defined as the minimum force used to elicit pain. In addition, the children complete a children's health assessment questionnaire (CHAQ) and a visual analogue scale (VAS) of pain.
Correlation analyses are performed after data have been collected.
RESULTS: Preliminary results are expected to be ready in spring 2010.

P34.06 Adjmal Nahimi

SEROTONERGIC MODULATION OF EXOGENOUS L-DOPA-DERIVED DOPAMINE RELEASE IN RATS WITH UNILATERAL 6-OHDA LESIONS REVEALED WITH MICRO-PET IMAGING.

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Introduction: L-DOPA induced dyskinesias, a severe complication of parkinsonian therapy, occur in response to administration of therapeutic doses of L-DOPA and is modulated by rapid changes in extracellular and synaptic DA. Recently, the use of 5-HT agonists and antagonists as potential adjuncts to L-DOPA to modulate extracellular DA without loss of therapeutic benefits, has started to be actively investigated. We used raclopride, a tracer of the D_2/D_3 receptors which can be used as a surrogate marker of DA-release to evaluate the effect in-vivo of 8-OH-DPAT, a 5-HT agonist, on the L-DOPA induced release of DA and L-dopa induced dyskinesia in 6-OHDA lesioned rats.
Methods: In an animal model of Parkinson´s disease, a [^{11}C] raclopride baseline scan and then two pharmacological challenge PET scans were performed. For the challenge scans, the rats were pretreated with either L-DOPA+Benzeraside (50/25 mg/kg S.C.) or L-DOPA+Benzeraside+8-OH-DPAT (0,6mg/kg/i.p.) 30-45 minutes prior to the raclopride injection.
Results: In the parkinsonian striata, our results showed a decrease in raclopride binding after L-DOPA administration suggesting increased release of DA and that concurrent administration of 8-OH-DPAT reduced the L-DOPA induced release of DA in the lesioned striata compared to L-DOPA alone.
Conclusion: This study supports the continued evaluation of drugs that modulate the serotonin system as possible therapeutic agents in PD and L-DOPA induced dyskinesia

P34.07 Katrine Hygum

IN MICE TRANSCOBALAMIN STANDS IN FOR HAPTOCORRIN

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Vitamin B12 (cobalamin) is an essential vitamin and transportation of the vitamin in the blood stream is important to prevent vitamin deficiency. In humans two circulating proteins transcobalamin (TC) and haptocorrin (HC) bind cobalamin. HC is present also in exocrine secretions but the function of HC is unclear. We found that mice lack the gene coding for HC (BLAST analysis) and here we explore whether TC in mice "stands in" for HC in terms of localization, function, and structure of the protein.
Various tissues and blood were analyzed for the level of cobalamin binding capacity by an assay based on labelled cobalamin and precipitation of excess label with charcoal. TC mRNA was detected and quantified in a selection of tissues using quantitative real time PCR. Salivary glands from more than 300 mice were used for

purification of the cobalamin binding protein by affinity chromatography, subsequent protein sequencing, and further characterization in terms of glycosylation status (Concanavalin A sepharose) and binding specificity to the cobalamin analogue cobinamide (competitive assay).
A high cobalamin binding capacity was found in all tissues where either TC or HC is found in humans. Surprisingly we found TC in salivary glands and a high expression of TC in mammary glands. Mouse TC is non-glycosylated like human TC but has a higher binding affinity for cobinamide than does human TC.
In conclusion, we show that mouse TC stands in for HC in terms of localization, binds cobalamin and cobinamide but is non-glycosylated. The results suggest the importance of a cobalamin binding protein in exocrine secretions but that the type of binding protein present varies amongst species.

P34.08 Stine Maria Lund Andersen

TOPICAL APPLICATION OF VALRUBICIN HAS A BENEFICIAL EFFECT ON DEVELOPING SKIN TUMORS.

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Anthracyclines are effective and widely used cytostatic drugs, however not considered for topical use since their effect is associated to skin toxicity. Valrubicin, a second generation anthracycline, is characterized by an excellent safety profile, and does not induce skin toxicity and necrosis.
The aim was to investigate the effect of applying valrubicin, in a new topical formulation, on development of skin cancer, and to investigate how valrubicin affects cellular proliferation and apoptosis “in vivo” and “in vitro”. We used the “in vivo” two stage DMBA/TPA carcinogenesis mouse model where tumors as papillomas develop; tumor formation was observed in the presence or absence of applied topical valrubicin. In cultures of squamous cell carcinoma cell lines HSC-1 and DJM-1, we studied the effect of valrubicin on cell proliferation and on apoptosis by measure of caspases 3 and 7 activity. Western blot analysis was used to measure the pro- and anti-apoptotic markers Bax and Bcl-2, and the proliferation marker PCNA from both “in vivo” and “in vitro” studies.
Valrubicin significantly inhibited tumor formation “in vivo” as also shown by decreased PCNA expression. Moreover, valrubicin significantly decreased cell proliferation of squamous skin cancer cell lines “in vitro” as measured by cell viability and PCNA expression. Apoptosis was increased as shown by elevated levels of caspases 3 and 7 “in vitro”. However, Bax and Bcl-2 were not found to be regulated by valrubicin neither in mouse skin nor in squamous skin cancer cell lines.
In conclusion valrubicin, in a new topical formulation, was found to be very effective in the treatment of skin cancer in this model.

P34.09 Bjørn Borsøe Christensen

STRUCTURALLY GRADED POLYCAPROLACTONE HYBRID SCAFFOLDS FOR HYALINE CARTILAGE REPAIR

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Introduction
Articular cartilage defects have a limited potential to heal, which can lead to pain, swelling and early osteoarthritis. The common treatments such as microfracture, autologous chondrocyte implantation (ACI) and osteochondral autograft transfer, all show promising results, but no method has been established as a gold standard.
In this study we will be using a structurally graded polycaprolactone scaffold to improve the ACI method. The SG-PCL scaffold will successively degrade in line with the formation of new tissue. The aim of this study is to develop a new scaffold for articular cartilage regeneration.
Materials and methods

Fourteen New Zealand White Rabbits will be used in the study. The animals will receive a bi-lateral osteochondral drill hole defect (4mm diameter, 2mm depth) in the femoral part of each knee joint. One knee is treated with a clinically used Chondro-Gide® scaffold, while the other knee will be implanted with the SG-PCL scaffold. After 12 weeks the animals will be MRI-scanned, after which they will be euthanized. For further analyses of tissue regeneraton, confocal microscopy, histology and scanning electron microscopy will be used.
Perspectives
The production method of this new scaffold holds the ability of plotting the structure from an MRI or CT scan, thus creating a scaffold of the right shape for the individual defect for each patient. Moreover, the nano-structure has the ability of future embedding of proteins such as growth and differentiation factors that also facilitates the cartilage repair potential. These proteins could be embedded in a profile that is specific to the individual patient.

P34.10 Tue Asger Kruse Rasmussen

INCREASED LEVELS OF IL-21 AND IL-23 CORRELATE TO DISEASE ACTIVITY AND IL-23 ALSO TO RADIOGRAPHIC PROGRESSION IN RHEUMATOID ARTHRITIS

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Objective: The aim of this study was to investigate the presence of the T_H17 related cytokines IL-17A, IL-21 and IL-23 and their connection with disease activity and progression in rheumatoid arthritis (RA).
Methods: In a longitudinal sample set from early RA patients (n=40) we measured plasma cytokine levels of IL-17A, IL-21, and IL-23 and investigated these for correlation with DAS28, HAQ, VAS, CRP, ESR, and Sharp van der Heide score. In a transverse sample set of chronic RA patients with paired peripheral blood mononuclear cells and synovial fluid mononuclear cells we investigated cellular expression of IL-17A, IL-21, and IL-23R.
Results: We demonstrate that early RA patients have significantly increased plasma levels of IL-21 and IL-23, but not of IL-17A compared to both chronic RA patients and normal healthy volunteers. Plasma levels of IL-21 and IL-23 correlated with disease activity by DAS28 and to CRP and ESR but not with disease progression. However, changes in IL-23 plasma levels from time of diagnosis to 12 months after treatment initiation correlated to both DAS28, CRP, ESR at 12 months and to SvdH score at 2 years after treatment initiation. Further, numbers of IL-21 producing CD4+ T cells were significantly increased in the synovial fluid in comparison to peripheral blood of chronic RA patients. Finally we observed only a marginal co-expression of IL-21 and IL-17A.
Conclusion: Our results support a key role for IL-21 and IL-23 via an IL-23/IL-21 axis in RA and indicate a possible role for these cytokines in the pathogenesis of this disease. Furthermore, our data demonstrate that in RA IL-17A and IL-21 are not expressed by the same CD4+ T cell subset.

P35.01 Katrine Nielsen

ALDEHYDE DEHYDROGENASE ACTIVITY AS A MARKER FOR GRAFT QUALITY IN AUTOLOGOUS HEMATOPOIETIC STEM CELL TRANSPLANTATION FOR HEMATOLOGICAL MALIGNANCIES

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Background:

Autologous stem cell transplantation in combination with high dose chemotherapy is an important modality of treatment of hematological malignacies.
Autologous transplants consist of enriched $CD34^+$ leukocytes. The graft is collected from mobilized peripheral blood by leukapheresis. The human CD34 antigen is widely used to characterize hematopoietic stem cells, but only approximately 5% of $CD34^+$ cells are true stem cells with bone marrow regenerating capacity.
Although patients receive weight-correlated amounts of $CD34^+$ hematopoietic stem cells, some patients experience prolonged time to regeneration and ensuing chronic cytopenia. A supplementary marker for graft quality that could help predict the outcome of the treatment would therefore be of great value. Recent studies have suggested ALDH as a stem cell marker.

Aim of the study:
To validate ALDH as a marker for the regeneration potential of stem cells. To compare the graft quality of $ALDH^+$ stem cells to $CD34^+$ stem cells.
Materials and methods:
Cell material will be obtained from the biobank at the Laboratory of Immunohematology. Initially 30 patient samples with lymphoma, 30 with multiple myeloma and 15 with acute myeloid leukemia will be enrolled in the study.
ALDH activity will be determined using flow cytometry. CFU-GM cultures will be performed to demonstrate the growth potential of the stem cells reinfused to patients.
Perspectives
This study will contribute to the understanding of stem cell biology in the transplantation setting in patients with hematological malignancies. It will also give information about the quality of autologous grafts and thereby improve the outcome of autologous transplantation.

P35.02 Ole Møller Hansen

THE EFFECT OF CELL SEEDING DENSITY ON CARTILAGE REGENERATION IN MATRIX-ASSISTED CHONDROCYTE IMPLANTATION IN A RABBIT MODEL

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Introduction
We have in recent years seen a tendency towards either an increase in body weight or sports activities. Both of these tendencies have the potential to cause knee injuries. Among knee injuries 60 % include damage to the cartilage structures. As little natural regeneration is seen in cartilage, these injuries may lead to early development of osteoarthritis. A 3rd generation repair technique, matrix-assisted chondrocyte implantation, is widely accepted as the gold standard in treatment of cartilage defects. However almost no literature regarding the biological response of cell seeding density on the implanted scaffold exists. Hence the size of the cartialge biopsies and cultering time relies on insufficient evidence. The aim of this study is to determine the biological response to different cell seeding densities.
Materials and Methods
An examination of the current literature will be used to determine prior used cell seeding densities. 4 groups of 8 articular defects will be formed, 1: Methoxy-polyethyleneglycol-polylactic-co-glycolic acid(MPEG-PLGA) scaffold without cells, 2-4: MPEG-PLGA saffolds with 3 different cell-seeding densities based on the findings of the examination. 16 New Zealand White rabbits will be used for this experiment. The rabbits will be sacrificed 12 weeks postoperatively. The speciments will be evaluated and graded on a validated semi-quantitive score.
Perspectives
By establishing the optimal range of cell seeding density for the MACI procedure the chances of a succesful outcome of the operation increases. An increase in operational successes while become a step towards a better treatment of the patient and a

decreased risk of osteoarthritis.

P35.03 Katrine Schou

BACTERIAL AND VIRAL MENINGITIS - CLINICAL MANIFESTATIONS, COURSE AND SEQUELAE

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Background:
Survivors of bacterial meningitis have a substantial risk of sequelae – including cognitive deficits. Patients with viral meningitis may only have subtle cognitive deficits or none at all. However, little is known about long-term outcome of viral meningitis on cognitive function. The follow-up of patients with CNS infections is normally conducted with a main focus on the parameters of infectious diseases, whereas the neuro-psychological domain is seldom systematically evaluated. After discharge, our knowledge of the long term effects on quality of life, including depression, fatigue and the patients working disabilities, is limited.

Objectives:
To assess self reported health, quality of life and working disabilities in adults up to ten years after an episode of bacterial or viral meningitis. Furthermore, to compare the outcome of these patients (viral vs. bacterial) regarding the clinical manifestations, neurological status, and the course of the disease. Finally, to evaluate administration and effects of additional treatment with dexamethasone in patients with bacterial meningitis.

Method:
Patients with meningitis admitted at Aarhus University Hospital 1999-2008 received a questionnaire that included the following validated score-systems: SF-36 (self evaluated health), SCL-92 (emotional state), the Major Depression Inventory and the Fatigue Severity Scale Socio-demographic and clinical data were extracted from the patients' medical files for further in-depth analysis. Patients with bacterial and viral meningitis were age- and sex matched and the results from the questionnaire were compared with the clinical data.

Results:
Our results are pending.

P35.04 Morten Würtz

PATIENTS WITH PREVIOUS DEFINITE STENT THROMBOSIS HAVE A LARGER FRACTION OF IMMATURE PLATELETS AND A REDUCED ANTIPLATELET EFFECT OF ASPIRIN

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To evaluate the immature platelet fraction and the platelet response to aspirin in patients with previous ST.
Stent thrombosis (ST) is a potentially fatal complication of coronary stenting. A reduced platelet response to aspirin may increase the risk of cardiovascular events. We included 117 patients previously undergoing percutaneous coronary intervention, 39 of whom suffered ST within two years of stenting. 78 patients served as controls matched with respect to age, gender, stent type, diabetes and PCI

indication. Platelet function was assessed by Multiplate® whole blood aggregometry in citrated and hirudinized blood and by the VerifyNow® Aspirin Assay. Flow cytometric determination of the immature platelet fraction was performed to evaluate platelet turnover. Platelet activation was evaluated by soluble serum P-selectin. Compliance was confirmed by measurements of serum thromboxane B_2. All patients were compliant according to serum thromboxane B_2 levels. Platelet aggregation assessed by Multiplate® aggregometry was significantly higher in cases when induced by arachidonic acid ($p_{citrated\ blood} = 0.04$; $p_{hirudinized\ blood} = 0.02$) and by collagen ($p_{citrated\ blood} = 0.0002$; $p_{hirudinized\ blood} < 0.0001$). Similarly, platelet aggregation was increased in cases when assessed by VerifyNow® ($p = 0.09$). Soluble serum P-selectin levels did not differ between groups ($p = 0.92$), whereas the immature platelet fraction was significantly larger in cases ($p = 0.04$).
Patients with previous ST had an increased residual platelet aggregation compared to matched controls. This might be explained by a higher fraction of immature platelets reflecting an increased platelet turnover.

P35.05 Mette Julsgaard Nielsen

MEDICAL TREATMENT OF CROHN'S DISEASE PATIENTS PRIOR TO AND DURING PREGNANCY

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Introduction: Crohns disease (CD) affects patients in their fertile age. Limited data on CD regarding medical treatment prior and during pregnancy exist. The purpose of this study was to determine the type of drugs used to treat CD patients in the two periods of investigation and to detect any change in types of drugs taken during pregnancy.
Methods: Women with CD who had been pregnant within a 6 year period among a population of 1.6 million. Diagnoses were confirmed by the county hospital discharge registry. Medical treatments 6 months prior and during pregnancy were investigated by questionnaires. We assessed the validity of self-reported use of medication by comparing the data with data from the prescription database.
Results: Of 127 women, 83% fulfilled the questionnaire. Overall 58 (54%) women stated to be in medical treatment prior and/or during pregnancy. 50 patients had fulfilled a prescription on relevant medication according to the prescription database yielding a PPV on 86.2% (74,6-93,9). The PPV did not differ between the period 6 months prior or during pregnancy (85.2% (72,9-93,4) and 87.3% (75,5-97,4), respectively). Fifty-three percent were taking 5-ASA drugs prior and during pregnancy, respectively. The prevalence of patients taking immunosuppressants was higher prior to pregnancy (38%) than during pregnancy (30%). The prevalence of patients being treated with systemic glucocorticoid was lower prior (9%) than during pregnancy (15%).
Conclusion: More than half of the patients were in medical treatment prior and during pregnancy. 5-ASA was the most frequently used drug. Overall a third of the patients were treated with immunosuppressants.

P35.06 Kristina Bennet Emdal

THE ROLE OF HER4 IN ESTROGEN-RESPONSIVE AND ANTIESTROGEN-RESISTANT HUMAN BREAST CANCER

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Resistance to endocrine therapy, e.g. antiestrogens (AEs) and aromatase inhibitors, is one of the main challenges to overcome in the treatment of hormone-sensitive breast cancer (BC). The human epidermal growth factor receptor (HER) family comprises four closely related receptor tyrosine kinases with essential roles in tumorigenic processes including BC. However, the role of HER4 is controversial and the

biological processes regulated by HER4 are poorly understood.
In order to study AE resistance in vitro, we have developed several AE-resistant BC cell lines. HER4 expression is reduced in several of these cell lines compared to parental AE-sensitive MCF-7 cells, making loss of HER4 expression a potential marker for AE resistance. The aim of this study is to disclose the role of HER4 in estrogen-responsive and AE-resistant human BC cells through a combination of cell culture based studies and clinical studies. HER4 expression will be downregulated in AE-sensitive MCF-7 cells to analyze the consequences for estrogen-stimulated as well as AE-inhibited cell growth. HER4 exists in four isoforms and each of these will be re-expressed in AE-resistant cell lines to examine whether AE-sensitivity can be regained and whether a specific HER4 isoform is responsible. In tumor samples from BC patients receiving adjuvant endocrine therapy, HER4 expression and localization of a cleavable HER4 fragment will be examined to evaluate the association with disease-free and overall survival. Finally, HER4 isoform expression will be analyzed in tumor biopsies from BC patients receiving neoadjuvant endocrine therapy in order to evaluate the association with tumor response.

P35.07 June Anita Ejlersen

THE DIAGNOSTIC VALUE OF 2D-STRAIN STRESS ECHOCARDIOGRAPHY IN CHEST PAIN PATIENTS WITH SUSPECTED CORONARY ARTERY DISEASE

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Background: Chest pain in patients without known heart disease is a common clinical problem. Only 20 % of these patients suffer from significant ischemic heart disease (CAD).Coronary angiography (CA) is the gold standard when CAD is suspected but the procedure should be reserved to the patient group with a high prevalence of CAD. Adenosine stress-echocardiography is a non-invasive method with low economic and patient related costs. Two dimensional (2D) strain is mechanical deformation of the myocardium analysed in software based on 2D echocardiography images. This project will evaluate if 2D strain analysis performed on rest and stress echocardiography recordings can identify chest pain patients with CAD.
Hypothesis: In patients with chest pain but no documented heart disease: 1) Adenosine-stress induces a change in 2D-strain in myocardial segments supplied by a significantly narrowed coronary artery. 2) The diagnostic value of 2D strain is as good as, or better, as the diagnostic value of myocardial perfusion imaging and 3) improves when pretest variables and information from exercise test is added.
Method: 200 chest pain patients referred for a CA will be included. All undergo symptom limited exercise test including stress myocardial perfusion imaging (day 1), adenosine stress-echocardiography and myocardial perfusion imaging at rest (day 7) and CA (day 14).
Results:By September 2009 30 patients have been included. Preliminary results will be available during 2010.
Perspectives:If the diagnostic value of 2D-strain is high this method might be used to identify CAD patients non-invasively and potentially result in fewer patients without CAD undergoing invasive CA procedures.

P35.08 Louise Jensen

PLASMA CALPROTECTIN PREDICTS MORTALITY IN PATIENTS WITH ST-SEGMENT ELEVATION MYOCARDIAL INFARCTION TREATED WITH PRIMARY PERCUTANEOUS CORONARY INTERVENTION

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Abstract:
Background: We investigated the predictive value of plasma calprotectin levels for mortality in patients with ST-segment elevation myocardial infarction (STEMI) successfully treated with primary percutaneous coronary intervention (pPCI).
Methods and results: Plasma calprotectin levels were measured in 141 STEMI patients with acute occlusion of the left anterior descending artery and treated with pPCI at admission to the hospital. The plasma calprotectin levels were significantly higher in the STEMI patients compared with the 42 healthy controls (P<0.001). Furthermore, plasma calprotectin levels were higher in the 13 STEMI patients who died after a median follow-up period of 10 months compared to the STEMI patients who survived: 209 μg/L vs.174 μg/L (P<0.001). After adjustment for age and sex in a multivariate Cox proportional hazards regression analysis, the relative risk of mortality was 1.25 (95% CI: 1.1-1.4) per 10 μg/L increase in calprotectin (P=0.002). Furthermore, for patients with plasma calprotectin > 177 μg/L the relative risk of mortality was 6.24 (95% CI: 1.4-28.3) (P=0.018).
Conclusion: Plasma calprotectin levels, determined at admission in STEMI patients successfully treated with pPCI, predict mortality over a period of 10 months, indicating that plasma calprotectin may be a new important prognostic biomarker in acute ischemic heart disease.

P35.09 Lotte Abbildgaard

WILM'S TUMOR GENE 1 (WT1) AS A TUMOR-MARKER IN CHILDHOOD ACUTE MYELOID LEUKEMIA (AML) - DETERMINATION OF THE NORMAL VALUES OF WT1 IN CHILDREN.

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Background
There have been major improvements in the treatment of childhood AML during the last decades. Survival rates have risen dramatically and are now about 65% with intensive chemotherapy. Despite high-dose chemotherapy regimens many children still suffers from relapse and treatment toxicity is high. This is one of the reasons for the growing interest on molecular biologic monitoring of minimal residual disease (MRD) with tumor-markers which will make it possible with more individual risk-adapted treatment regiments with less toxicity and an earlier detection of pending relapse.
WT1 is over-expressed in about 70% of AML cases which makes it a potential tumor-marker. We do not have sufficient material on the normal values of WT1 in healthy children and whether these values are affected by infections or chemotherapy.

Aims
Determine the normal values of WT1 in peripheral blood and bone marrow of healthy children.
Examine whether these values are affected by infections or chemotherapy.

Materials and methods
We will include two patient categories in a prospective study.
1. Children with congenital heart anomaly which needs open surgery with splitting of the sternum whereby bone marrow can be extracted.
2. Children with fever seen in the children's ward who due to their clinical state have blood samples drawn.
Retrospectively we will analyze stored blood and bone marrow samples from
3. Children with ALL.
Samples will be collected at Aarhus University Hospital, Skejby and will be analyzed with RQ-PCR at the Laboratory of Immunohematology, Aarhus University Hospital, Aarhus.

P36.01 Chen Muwan

FREE RADICALS GENERATED BY 3-D TANTALUM SCAFFOLD ANTAGONIZE THE CYTOTOXIC EFFECT OF DOXORUBICIN

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INTRODUCTION: Both tantalum (Ta) and titanium have been widely used as orthopedic implants in joint replacement, tumor reconstructive surgery and spine. However, titanium dioxide could generate reactive oxygen specie (ROS). We aimed to investigate if the presence of 3-D porous Ta scaffold can undermine the cytotoxic effect of DOX, a widely used antineoplastic drug, by oxidative degradation.

METHODS: Rabbit rectal tumor cells were cultured with DOX (2, 5, 10 mg/ml in 10%FBS-DMEM). Prior to incubation, the Ta scaffold was immersed in the DOX solution with either UV irradiation, or 10 µg/ml Dithiothreitol (DTT), or both. Inhibition of cell growth was determined by MTT assay. Fluorescence spectra of DOX under different treatments were recorded by spectrofluorometer. ROS was detected by Tempo-9-acmolecular and flow cytometry.

RESULTS: The cytotoxicity of DOX was significantly reduced in the presence of Ta scaffold. This effect was more pronounced with UV irradiation. However, in the presence of a reducing agent, DTT, the cytotoxic effect of DOX can be recovered to some extents. A direct relationship between fluorescence intensity of DOX and its cytotoxic effect was observed. DOX solution with Ta scaffold, UV irradiated for 1 min had 96.9% reduced fluorescence intensity and 65% reduced cytotoxic effect, compared to those in the original drug.

CONCLUSION: The 3-D porous Ta scaffold generated hydroxyl radicals. This event was more pronounced in the presence of UV exposure. Thus Ta can potentially undermine the cytotoxic effect of DOX. Based on these findings, precautions should be taken when Ta is used as a bone void filler after tumor resection with ongoing chemotherapy.

P36.02 Søren Schou Olesen

EVIDENCE OF ALTERED CEREBRAL PAIN PROCESSING IN CHRONIC PANCREATITIS - A PILOT STUDY

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Altered pain thresholds and changes in cerebral pain processing to electrical stimulation of the upper gut have previously been demonstrated in painful chronic pancreatitis. We hypothesised that these changes would be widespread throughout the gastrointestinal tract and evident in a gut segment remote to the pancreas. The aims of the study were (1) to evaluate the psychophysical response to electrical stimulation of the sigmoid-colon and (2) to evaluate the event-related brain potentials (EPs) obtained following stimulation. Fifteen healthy volunteers and 22 patients suffering from painful chronic pancreatitis were included. The sigmoid-colon was stimulated electrically using a special designed probe. The electroencephalogram was recorded from 64 surface electrodes and EPs were obtained following stimulation at the pain threshold. The patient group showed decreased thresholds to electrical stimulation of the sigmoid colon ($P = 0.04$). An increased latency of the early P1 component of the EP was found in the patient group ($P=0.02$), whereas no difference in the latencies for the other components or amplitudes were found. The findings indicate that patients suffering from painful chronic pancreatitis have hyperalgesia to electrical stimulation of the sigmoid colon, possibly due to generalised hyperexcitability of the central nervous system. Also, evidence of changes in the cerebral pain processing was found, mirrored by the increased latency of the P1 component in the patient group. This may reflect reorganization of the brain centres encoding visceral pain as also seen in patients with neuropathic pain.

P36.03 Nis Borbye Pedersen

VASOPRESSIN-MEDIATED SIGNALING IN THE DISTAL CONVOLUTED TUBULE REGULATES PHOSPHORYLATION OF THE THIAZIDE-SENSITIVE NA^+-CL^- COTRANSPORTER (NCC) AT TWO CONSERVED THREONINE RESIDUES

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The thiazide-sensitive Na^+-Cl^- cotransporter (NCC) is important for renal electrolyte balance. N-terminal phosphorylation of NCC has been proposed to play a major role in its transport activity and cellular localization. We generated novel phospho-specific antibodies against two conserved N-terminal phosphorylation sites (Thr53, Thr58 and Thr53/Thr58 together) and used them to assess the role of vasopressin (AVP) in regulating NCC in vivo. Immunohistochemistry showed distinct staining of the apical plasma membrane domain of distal convoluted tubule (DCT) cells. Immunogold electron microscopy demonstrated that, unlike total NCC, pNCC was localized only in the apical plasma membrane and was not observed within the cell. In AVP-deficient Brattleboro rats, acute dDAVP exposure for 15 min significantly increased pNCC abundance at the apical plasma membrane 300%. Acute dDAVP did not alter the abundance of the STE20/SPS1-related proline/alanine-rich kinase (SPAK) previously implicated in NCC phosphorylation, suggesting an alternative signalling pathway for AVP. Freshly isolated early and late DCTs increased their intracellular Ca^{2+} levels in response to 1 min of superfusion of dDAVP (2x10(-10) M), confirming that the DCT is an AVP responsive segment. In rats fed a high salt diet alongside AT_1-R blockade by candesartan, similar increases in pNCC abundance were observed following chronic or acute dDAVP, indicating that the effects of AVP are independent of ANGII. Candesartan treatment reduced the abundances of total SPAK and pSPAK, suggesting that this kinase can be regulated via the AT_1-R in vivo. Taken together our results indicate that AVP is a potent regulator of NCC activity.

P36.04 Ayfer Topcu

EFFECT OF REFLEXOLOGY, HOMEOPATHY, AND TRADITIONAL MEDICAL TREATMENT IN ASTHMA: A RANDOMIZED CONTROLLED, PARALLEL-GROUP TRIAL

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Background: Asthma is one of the most common chronic diseases worldwide, with an estimated 300 million affected individuals. Although the symptoms can be controlled by drug treatment, many patients with asthma wish to improve asthma control and quality of life, and to reduce medication dosage. Therefore, there is increasing interest and awareness of complementary and alternative (CAM) among patients with allergic diseases, including asthma and rhinitis.
Aim: Even though CAM is widely used as adjunctive treatment, there is little evidence to confirm of efficacy of most alternative therapies in asthma patients. The aim of this study is to obtain reliable information about the effectiveness of the reflexology and homeopathy in asthma treatment.
Material and methods: This study is a 12- month, randomised, controlled parallel group trial. The primary efficacy objective of this study is to evaluate quality of life by using AQLQ.A total of 98 patients with asthma were recruited according to inclusion criteria.At visit 1, we assessed patients` quality of life by using Asthma Quality of Life Questionnaire (AQLQ) and performed spirometry and nitric oxide measurements. Furthermore, blood samples were collected for measurement of eosinophils and eosinophil cationic protein. After the run-in period, patients were randomly allocated to one of the three treatment groups (Conventional treatment + Homeopathy, Conventional treatment + Reflexology, Conventional treatment). Patients returned to clinic after 6 and 12 months for evaluation and completion of questionnaires. This study will be terminated in November and statistical analysis

will be performed immediately.

P36.05 Nicklas Heine Staunstrup

TRANSGENIC PIG MODELS

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The project consists of two legs, i) generating a phenotypic psoriasis model based on over-expression of human integrin alpha2 and beta1 (hITGA2 and hITGB1, respectively) ii) production of a pig model harboring a sensitive sensor-receptor system allowing for evaluation of skin penetration by topical applied formulations and their potency.

Psoriasis is a complex auto-immune disorder affecting 2-5% of the Danish population. The disease is hereditary, however certain environmental inducers such as trauma and stress are believed pivotal in disease outbreak. On a biological level psoriasis involves dysregulation of keratinocyte proliferation and differentiation and inflammation caused by increased invasion of immune-cells and there cytokine release. In the epidermis hITGA2 and hITGB1 expression is normally confined to the basal layer, however in psoriatic skin ascending keratinocytes also express these integrins thereby restraining differentiation but promoting proliferation. We have constructed Sleeping Beauty (SB) transposons holding expression-cassettes with one or both integrins under control of the human skin-specific involucrin promoter and the first pig-cloning attempt is in progress.

The sensor-receptor model potentially has a broad application potential, allowing for efficacy assessments of topical applied treatments interesting to the pharmaceutical industry. The system is based on the S. cerevisiae derived Gal4-UAS system. In the current context Gal4 is fused to the human vitamin D receptor under control of the human skin-specific K14 promoter. A SB transposon with the system in cis which is highly functional has been generated and is pending for cloning.

P36.06 Hanne Bjerregaard Møller

PHOSPHORYLATION REGULATED ENDOCYTOSIS OF THE WATER CHANNEL AQUAPORIN-2

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The water channel Aquaporin-2 (AQP2) is essential for urine concentration. Vasopressin regulates phosphorylation of AQP2 at four conserved serine residues at the COOH terminal tail (S256, S261, S264 and S269). In this study, we used stably-transfected MDCK cell models, replacing serine residues with either alanine (A), preventing phosphorylation, or aspartic acid (D), mimicking the charge state of phosphorylated AQP2, to address whether phosphorylation is involved in regulation of; 1) apical plasma membrane abundance of AQP2, 2) internalization of AQP2, 3) AQP2 protein-protein interactions, and 4) degradation of AQP2. S256D- and 269D-AQP2 mutants had greater apical plasma membrane expression compared to wildtype(WT)-AQP2 under control conditions. Activation of adenylate cyclase significantly increased apical plasma membrane abundance of all S-A or S-D AQP2 mutants with the exception of 256D-AQP2, although 256A-, 261A- and 269A-AQP2 mutants increased to a lesser extent than WT-AQP2. Biotin internalization assays demonstrated that the internalization of 256D- and 269D-AQP2 from the plasma membrane was slower than WT-AQP2. The slower internalization corresponded with reduced interaction of S256D- and 269D-AQP2 with several proteins involved in endocytosis, including Hsp70, Hsc70, dynamin, and clathrin heavy chain. The mutants with the slowest rate of internalization had a greater protein half live compared to WT-AQP2. Our results suggest that vasopressin-mediated membrane accumulation of AQP2 can be controlled via regulated exocytosis and endocytosis in a process that is dependent on COOH terminal phosphorylation and subsequent protein-protein interactions.

P36.07 Christian Fynbo Christiansen

COMORBIDITY AND MORTALITY IN INTENSIVE CARE UNIT PATIENTS – A POPULATION-BASED COHORT STUDY

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Objective: We examined the impact of comorbidity on 30-day and one-year mortality following intensive care unit admission in a population-based cohort study.
Methods: We identified all first-time ICU admissions (n= 28,172) among adults in Northern Denmark (population 1.8 million) from 2005 through 2007 using the National Registry of Patients. Data on comorbidity, surgery, and mortality were obtained through medical databases. For each ICU patient we computed the Charlson Comorbidity Index (CCI) score including 19 chronic disease categories. We computed 30-day and one-year mortality for ICU patients with no (CCI=0), mild (CCI=1-2), and severe comorbidity (CCI=3+). We used Cox regression to estimate mortality rate ratios (MRRs) controlling for age, gender and surgical/medical ICU admission.
Results: Among 28,172 adult ICU patients, 56.8% were men and median age was 63 years (IQR 48-74 years). Severe comorbidity was present in 5,669 (20.1%) patients, mild comorbidity in 10,369 (36.8%), while 12,134 patients (43.1%) had no comorbidities.
The 30-day mortality was 9.5% for patients no comorbidity, 17.5% for patients with mild, and 24.9% for patients with severe comorbidity, corresponding to adjusted MRRs of 1.3 (95%CI:1.2-1.4) for mild , and 1.8 (95%CI:1.6-1.9) for severe comorbidity compared with no comorbidity.
The one-year mortality was 14.4% for patients without comorbidity, 29.1% for patients with mild, and 44.5% for patients with severe comorbidity, corresponding to adjusted ORs of 1.7 (95%CI:1.6-1.8) for mild, and 3.6 (95%CI:3.3-4.0) for severe comorbidity.
Conclusion: Comorbidity is associated with substantially increased 30-day and one-year mortality among ICU patients.

P36.08 Elise Røge Nielsen

EFFECT OF HYPOXIA ON THE FUNCTION AND REGEULATION OF THE ADENOSINE A_{2A} RECEPTOR

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Coronary artery dilatation to hypoxia is a protective response that increases flow to endangered myocardium. Several studies of myocardial metabolism support that adenosine could be a central mediator between metabolic demands and coronary blood flow. Moreover, previous experiments showed that adenosine-induced dilatation is more pronounced during hypoxia than during normoxia. By blocking the adenosine A_{2A} receptor, hypoxia-induced dilatation was reduced suggesting that the A_{2A} receptor plays a role in the increased sensitivity for adenosine during hypoxia (Frøbert et al. J. Physiol. 2006). Adenosine A_{2A} receptors are coupled to a G_s protein and formation of cAMP, but at present it is unknown how hypoxia interacts with the pathway. Thus, the aim of the present study was to investigate the mechanisms underlying the increased sensitivity to adenosine during hypoxic vasodilatation. Smooth muscle cells were isolated from the porcine coronary artery and exposed to normoxia or hypoxia (1% O_2) for 1h. Expression of adenosine A_{2A} receptors and cAMP levels were measured. The amount of A_{2A} receptors expressed on the cell surface was larger in cells exposed to hypoxia than cells grown at normoxic conditions. Moreover, both adenosine and hypoxia increased cellular cAMP levels. The present study suggests that an increase in adenosine A_{2A} receptors at the cell surface leads to increased cAMP. This mechanism may explain the increased sensitivity to and vasodilation induced by adenosine during hypoxia.

P36.09 Kaspar René Nielsen

POLYMORPHISMS IN INFLAMMATORY MEDIATORS - RELATION TO DISEASE ACTIVITY AND SURVIVAL IN B-CELL DISEASES

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Background and present status: Normal and malignant B-cells are regulated by a complex network of growth factors, inflammatory mediators and cell surface molecules. Genetic polymorphisms in inflammatory response genes, affects gene expression and function, which can affect the tumor/host interaction, facilitating proliferation of the malignantly transformed clone. Hypothesis and aims: We hypothesize, that genetic polymorphisms in selected inflammatory mediators can influence the inflammatory response. The altered inflammatory host response may result in a microenviroment that facilitate the growth of malignantly transformed B-lymphocytes. The objective is to investigate the relationship between 28 polymorphisms in inflammatory genes with disease activity and overall survival in B-cell-non-Hodgkin's lymphoma (B-NHL), Hodgkin's Disease and Multiple Myeloma. Material and methods: A pilot study including 60 B-NHL patients were used to validate genotyping methods. The present study includes 1000 B-NHL patients, 500 patients with Hodgkin's disease and 280 Myeloma patients. DNA is extracted from whole blood or archival formalin-fixed, paraffin wax-embedded tissue taken at biopsy. 28 SNP's in selected inflammatory mediators are tested using TaqMan genotyping assays. Single-gene, haplotype and genetic load data will be used in multivariate survival analysis. Deliverables: The main goal is to investigate genetic polymorphism in the inflammatory system as prognostic biomarkers in B-cell diseases.

Session number	Presenter	Session number	Presenter
P34.06	Adjmal Nahimi	P24.06	Anders Christian Larsen
P26.03	Anders Dohn	O01.02	Anders Etzerodt
P19.04	Anders Jensen	P21.09	Anders Kirch Dige
O02.03	Anders Knudsen	P12.10	Anders Koustrup Niemann
O03.06	Anders Lindelof	P03.07	Anders Peter Søndergaard
P22.05	Anders Petersen	P32.02	Andreas Schröder
O03.03	Ane Bærent Fisker	P09.02	Anette Luther Christensen
P04.03	Anette Werner	P11.01	Ania Pietraszek
P14.08	Ann Dyreborg Larsen	FN	Anna Krarup Keller
P17.09	Anna Lamberg	P31.06	Anne Hansen
P34.05	Anne Leegaard	FN	Anne Nyholm Holdensen
P06.03	Anne Petas Swane Lund Krarup	P33.06	Anne Roslev Bukh
P06.05	Anne Skakkebæk Jensen	P17.04	Anne Sophie Ågård
O04.04	Anne Stidsholt Roug	P22.03	Anne-Cathrine Bareid Østby
P01.03	Anne-Mette Bay Bjørn	P28.05	Annette Ingeman
P17.01	Annette Langager Høgh	P18.01	Asger Granfeldt
P34.04	Astrid Hjelholt Nielsen	P36.04	Ayfer Topcu
P08.09	Aygen Øzbay	P19	Bekka Anina Ozer Christensen
P04.02	Berit Hvass Christensen	P32.04	Birgitte Fuglsang Kjølby
P13.10	Birgitte Kousholt	P15.03	Bjarne Otto Rittig-Rasmussen
P34.09	Bjørn Borsøe Christensen	P30.07	Bjørn Petersen
P11.10	Bo Løfgren	P17.06	Bodil Bjørnshave
P21.10	Britta Weber	P23.08	Carina Agerbo Rosenberg
P07.01	Carina Henriksen	P25.03	Caroline Winther Tørring
P31.05	Caspar Skau Madsen	FN	Casper Foldager
P06.07	Casper Nielsen	O01.06	Cathrine Søndergaard Baastrup
P10.04	Charlotte Amalie Ihlo	P25.02	Charlotte Christie Petersen
P16.07	Charlotte Gjørup Pedersen	P21.01	Charlotte Rotbøl Bøje
P12.09	Charlotte Strandhave	P36.01	Chen Muwan
P08.01	Christel Krøigaard	P09.08	Christian Daugaard Peters
P36.07	Christian Fynbo Christiansen	P11.09	Christian Høst
P12.01	Christian Møller Pedersen	P07.06	Christian Overgaard Steensen
P15.08	Christian Wulff	P14.05	Christina Malmose Stapelfeldt
P25.05	Christoffer Sølling	P29.08	Christopher Joseph Bailey
P19.01	Christopher Nordentoft Vejgaard	P16.06	Chunsen Wu
P21.02	Claus Tvedesøe	P26.06	Dan Sonne Pedersen
P05.04	Dang Quang Svend Le	P27.06	Dariusz Orlowski
P23.07	Diem Bentzon	P25.06	Ditte Andreasen Søborg
P12.02	Dorte Guldbrand Nielsen	P15.04	Dorte Rytter

P06.09	Dorthe Mørck Mortensen	P02.03	Ebbe Bødtkjer
P29.06	Eduardo Garza	P11.04	Eigil Husted Nielsen
P36.08	Elise Røge Nielsen	P24.08	Emil Kofod-Olsen
P20.10	Emil Toft Brøndum	P18.06	Emilia Wiechec
P01.07	Emma Tina Bisgaard Olesen	P12.03	Erik Grove
P33.02	Esben Laugesen	P09.01	Esben Søndergaard
P07.09	Eva Greibe	P26.09	Fabia Febbraro
P28.09	Faramarz Jadidi	P33.03	Frederik Hvid-Jensen
P18.07	Gao Hong	P16.08	Gija Rackauskaite
P06.01	Gitte Aarøe Dam	P11.02	Grazina Urbonaviciene
P16.09	Grethe Elholm	P29.05	Hanna Järnum
P36.06	Hanne Bjerregaard Møller	P02.05	Hanne Vebert Olesen
P21.05	Hanne Østergård Larsen	P04.12	Hanne-Lise Falgreen Eriksen
P27.04	Hans Gjørup	P09.06	Hans Henrik Møller Nielsen
P22.07	Hans Linde Nielsen	O03.05	Helene Kvistgaard
P10.03	Helle Damgaard Zacho	P03.04	Helle Damkier
P02.09	Helle Rosenberg	P17.10	Helle Svenningsen
P32.05	Henriette Klit	P26.08	Henriette Thisted
P15.09	Hjördis Osk Atladottir	P10.09	Hua Chen
P06.02	Iben Blaabjerg Sundtoft	O04.05	Iben Møller Jønsson
P02.08	Ida Sejersdahl Kirkegaard	O02.02	Ingunn Skogstad Riddervold
P15.07	Ioannis Basinas	P02.06	Irina Kruglikova
P30.02	Ivana Konvalinka	P10.07	Jacob Thorsted Sørensen
P14.04	Jakob Kjeldgaard Jakobsen	P20.02	Jakob Stegger
P08.04	Jakob Østergaard	P30.05	Jan Hendrik Rölfing
P11.03	Jane Byriel Knudsen	P02.02	Janne Lebeck
P28.06	Jannik Jakobsen	P32.06	Jasna Furtula
P29.04	Jennifer Heather Christensen	P18.09	Jenny Blechingberg
P16.02	Jens Christian Jensen	P09.04	Jens Holmer-Jensen
P20.04	Jens Ølholm	P20.07	Jeppe Grøndahl Rasmussen
P08.10	Jesper Brink Askov	P34.03	Jesper Damsgaard
P13.06	Jesper Fleischer	P08.07	Jesper Langhoff Hønge
P30.06	Jesper Ougaard Schønnemann	P14.01	Jette Ahrensberg
P18.03	Jette Lindorff Riis	P32.09	Jimmi Nielsen
P24.01	Jimmi Søndergaard	P30.09	Joel Fredrik Astrup Aanerud
P19.08	Johan Grankvist	P28.08	John Brincks
P07.03	Jonas Jensen	P15.01	Julie Glavind
P34.02	Julie Mackenhauer	P35.07	June Anita Ejlersen
P31.07	Juozas Petruskevicius	P30.04	Kaare Dyre Palnum
P28.07	Kaare Meier	P08.06	Karen Lorentzen
P25.01	Karen Louise Thomsen	P27.05	Kari Konstantin Nissen
P10.05	Karina Bech Cullberg	P36.09	Kaspar René Nielsen

P15.10	Kasper Grosen	P05.01	Kasper Lynghøj Christensen
P26.04	Kasper Severinsen	O04.01	Kasper Toustrup
P31.02	Kasra Zainali	P27.10	Kathrine Just Andersen
P01.08	Kathrine Kleis Tilma	P07.07	Katrine Emmertsen
P34.07	Katrine Hygum	P35.01	Katrine Nielsen
P35.03	Katrine Schou	P33.08	Kim Henningsen
P11.07	Kim Munk	P13.02	Krista Kjærgaard
O02.06	Kristian Altern Øvrehus	P20.09	Kristian Havmand
P29.07	Kristian Sandberg	P20.06	Kristin Rós Kjartansdóttir
P35.06	Kristina Bennet Emdal	P27.02	Kristina Dupont Hougaard
P31.03	Kristine Rømer Thomsen	P31.08	Kåre Eg Severinsen
P24.07	Kåre Gotschalck Sunesen	P27.09	Kåre Sanden Ettrup
O03.04	Lars Erik Bartels	P09.03	Lars Jakobsen
P01.04	Lars Peter Sørensen	P08.03	Lars Rolighed
P24.03	Lars Toft Nielsen	P22.04	Lasse Sommer Kristensen
P08.05	Lau Brix	P10.02	Lea Brader
P17.07	Leanne Langhorn	P04.05	Lena Aadal
P14.03	Lene Bastrup Jørgensen	P23.06	Lene Mølgård Hansen
P20.03	Lene Sundahl Mortensen	P28.01	Lene Vammen Søndergaard
P30.01	Leslie Foldager	P32.03	Linda Locht
P33.09	Line Andersen	P27.03	Line Bie Mertz
P33.05	Line Mayland Kolstrup	P25.04	Line Reinert
P17.05	Lisa Gregersen Østergaard	P05.03	Lisbeth Venø Kruse
P16.01	Lise Juul	P23.10	Lise Saksø Mortensen
P19.03	Lone Schmidt Sørensen	P35.09	Lotte Abbildgaard
P16.05	Lotte Ørneborg Rodkjær	P25.07	Louise Brøndt Hartlev
P30.08	Louise Buur Lund	P35.08	Louise Jensen
P26.05	Louise Munk Rydtoft	O03.01	Louise Wamberg
P21.04	Lykke Grubach	P10.08	Mads Brix Kronborg
P13.01	Mads Kjølby	P24.04	Magdalena Julia Dabrowska
P17.08	Mai-Britt Guldin	P11.08	Maiken Glud Dalager
P07.05	Maiken Kudahl Larsen	P08.02	Maj Lesbo
P23.01	Maja Døvling Kaspersen	P01.02	Majbritt Hauge Kyneb
O04.03	Malene Hvid Larsen	P30.03	Malene Hørnø Schmidt
P19.07	Malene Krag Kjeldsen	P04.01	Margrethe Smidth
P18.02	Maria Bach Laursen	P22.06	Maria Bro Kloster
P02.07	Maria Jakobsen	P19.09	Maria Luise Salskov-Iversen
P13.03	Maria Mærsk Nielsen	P10.01	Marianne Bennetzen
P01.09	Marianne Cathrine Rohde	P14.10	Marianne Lisby
P29.02	Marianne Toft Vestermark	P27.01	Marie Bagger Bohn
P04.09	Marie Louise Svendsen	P04.08	Marie Louise Tørring
O01.05	Marion Delenclos	P10.10	Marta Bauerek

O02.01	Martin Broch-Lips	P31.04	Martin Gottliebsen
P13.05	Martin Majlund Mikkelsen	P22.09	Martin Skøtt
P33.10	Merete Ipsen	P14.02	Merethe Kousgaard Andersen
P14.09	Mette Bach Larsen	P23.04	Mette Bak Nielsen
P31.09	Mette Buhl Callesen	P35.05	Mette Julsgaard Nielsen
O01.03	Mette Juul Koefoed	O01.01	Mette Laursen
P23.02	Mette Møller Handrup	P33.01	Mette Sørensen
P15.06	Mette Trøllund Rask	P13.09	Michael Madsen
P01.06	Michael Winterdahl	P06.06	Mie Hessellund Samson
P12.08	Mikkel Misfeldt	P04.04	Morsi Abdallah
P16.10	Morten Charles	O02.04	Morten Olsen
P14.07	Morten Søndergaard Jensen	P04.11	Morten Willert
P35.04	Morten Würtz	P15.02	Nellie Bering Zinther
P36.05	Nicklas Heine Staunstrup	P22.08	Niels Fristrup
P13.07	Niklas Johan Alexander Telinius	P26.02	Nina Dyrberg Lorenzen
P36.03	Nis Borbye Pedersen	P03.08	Nynne Sharma
P07.02	Ole Halfdan Larsen	P35.02	Ole Møller Hansen
P21.06	Ole Schmeltz Søgaard	P24.02	Pauliina Wright
P23.03	Peder Fode	P20.01	Pernille Bach Jørgensen
P03.01	Pernille Kure Vandborg	P02.04	Pernille Munk Frandsen
P17.03	Peter Agergaard	O04.02	Peter Martin Hjørnet Kamper
P01.05	Philipp Harbig	P34.01	Pia Damgaard Colding
P16.03	Pia Kirkegaard	P05.09	Pia Møller Faaborg
P03.02	Raffaella Mangnoni	P18.05	Rasmus Boye Kjellerup
P12.05	Rasmus Haarup Lie	P10.06	Rasmus Pold
O03.02	Rasmus Sode-Carlsen	P13.08	Rebekka Vibjerg Bækgaard Thomsen
P28.04	René Ernst Nielsen	P05.08	René Frydensbjerg Andersen
P17.02	Rikke Jørgensen	P08.08	Rikke Vestergaard
P07.04	Rita Maria Delgado Silva Marques	P04.06	Rune Dupont Birkler
P26.07	Rune Thomsen	P20.08	Ruta Tuckuviene
P03.06	Sabina Jelen	P29.03	Sabrina Maria Gade Sundbye
P29.01	Sanna Lemming Kjær	P31.01	Sanne Kragh Kjær
P33.04	Sidse Kringelholt	P32.07	Signe Groth Renvillard
P28.10	Simon Hjerrild	P18	Simon Lønbro Jensen
P19.10	Simon Rasmussen	P23.09	Sine Nygaard Langerhuus
P11.06	Sofie Gry Pristed	P09.05	Sophie Constantin Lütken
P22.01	Stefan W. Harders	P01.01	Steffen Møller-Larsen
P27.07	Stephen Austin	P34.08	Stine Maria Lund Andersen
P16.04	Stine Yde Nielsen	P06.08	Stinne Pulkkinen Schmidt
P25.08	Susie Mikkelsen	P24.09	Søren Beck
P25.10	Søren Egedal Degn	P36.02	Søren Schou Olesen

P08.11	Súsanna Við Streym Thomsen	P21.03	Tanja Eiersted Molzen
P11.05	Tanja Tvistholm Sikjær	P12.04	Thais Almeide Lins Pedersen
P03.09	Thaneas Prabakaran	P12.07	Thomas Dalsgaard
P23.05	Thomas Damgaard Sandahl	P22.10	Thomas Greve
P05.05	Thomas Guldager Knudsen	P09.09	Thomas Krusenstjerna-Hafstrøm
P28.02	Thomas Maribo	P22.02	Thomas Reinert
P20.05	Thomas Svava Nielsen	P32.08	Thomas Urban
O02.05	Thomas Wittenborn	O04.06	Tina Rask Emholdt
P03.05	Tina Storm	P19.05	Tine Gregersen
P03.03	Tine Qvistgaard	P04.07	Tine Steen Rubak
P19.02	Tomasz Kazimierz Wojdacz	P28.03	Torben Albert Devantier
P09.07	Torben Harsløf	P21.07	Torben Stamm Mikkelsen
P05.06	Torsten Bloch Rasmussen	P07.08	Trine Borup Andersen
P04.10	Trine Brogaard	P29.09	Trine Christensen
P33.07	Trine Dalsgaard	P15.05	Trine Guldberg
P18.04	Trine Silkjær	P24.05	Trine Tramm
P05.02	Trine Østergaard	P18.10	Troels Schepler
P09.10	Troels Thim	P34.10	Tue Asger Kruse Rasmussen
O01.04	Tue Fryland	P32.01	Tue Hartmann
P13.04	Ulla Kampmann Opstrup	P12.06	Ulla Kristine Møller
P25.09	Ulrik Vindelev Elstrøm	P26.01	Vagn Erik Lisbjerg Johnsen
P21.08	Vanda Turcanova	P14.06	Vibeke Bregnballe
P27.08	Vibeke Fuglsang Bliksted	P02.01	Yonglun Luo
P06.04	Yu Wang	P05.07	Zhenping Liu