

Press release

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Basic information

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Department of: Biomedicine

Main supervisor: Prof Poul Henning Jensen

Title of dissertation: Investigating markers of inclusion and non-inclusion α -synuclein aggregate pathology in

Parkinson's disease and related disorders

Date for defence: 16/5-2024 at (time of day): 13.00 Place: AIAS auditorium (building 1632)

Press release (Danish)

Nye markører for nervecelle-sygdom ved Parkinsons syge

Parkinsons sygdom er en neurodegenerativ sygdom karakteriseret af bevægelsesforstyrrelse og en række forstyrrelser af anden art. Neuropatologisk forefindes prominent tab af nerveceller i specifikke hjerneområder samt karakteristiske ophobninger af proteinet alfa-synuclein, såkaldte Lewy-legemer. I de seneste år har der været spekuleret i, at mindre former for alfa-synuclein aggregater, som ikke er organiseret i Lewy-legemer, spiller en vigtig rolle i sygdommen. Dog har kun få studier påvist sådanne små aggregater i vævsprøver, primært pga. tekniske begrænsninger.

I dette ph.d.-projekt, udført på Aarhus Universitet, udviklede vi et nyt alfa-synuclein proximity ligation assay til at påvise små aggregater i cellemodeller og hjernevæv fra afdøde patienter. Vi sammenlignede resultaterne fra vores metode med traditionel immunhistokemi til at påvise Lewylegemer og kan demonstrere, at vores metode påviser flere syge nerveceller langt tidligere i sygdommen. Vi viser desuden, at patienter med en genetisk form for Parkinsons uden Lewy-legemer - en kuriositet, vi pt. ikke kan forklare - har små alfa-synuclein aggregater i hjernen, hvilket indikerer en fælles sygdomsmekanisme. Slutteligt undersøgte vi udviklingen af fosforylering på serin-129 i alfa-synuclein, en typisk markør for sygdom, og evaluerede potentialet i at hæmme denne fosforylering som behandling af Parkinsons sygdom.

Projektet er gennemført af Nanna Møller Jensen, der forsvarer det d. 16/5.

Forsvaret af ph.d.-projektet er offentligt og finder sted den 16/5 kl. 13.00 i AIAS auditorium, Aarhus Universitet, Høegh-Guldbergs Gade 6B, 8000 Aarhus C. Titlen på projektet er "Investigating markers of inclusion and non-inclusion α -synuclein aggregate pathology in Parkinson's disease and related disorders".

Yderligere oplysninger: Ph.d.-studerende Nanna Møller Jensen, e-mail: nanna.mj@biomed.au.dk, tlf. 6022 6553.

Bedømmelsesudvalg:

Associate Professor Peter Bross (chairman of the committee and moderator of the defence) Research Unit for Molecular Medicine, Aarhus University and Aarhus University Hospital, Aarhus, Denmark

Associate professor and Chief consultant Liisa Myllykangas University of Helsinki and Helsinki University Hospital, Finland

Professor George Tofaris, Professor of Neurology & Translational Neuroscience and Consultant Neurologist

Nuffield Department of Clinical Neurosciences and Kavli Institute for Nanoscience Discovery, University of Oxford, United Kingdom



Press release (English) New markers for neuropathology in Parkinson's disease

Parkinson's disease is a neurodegenerative disorder characterized by motoric dysfunction and a range of non-motoric disturbances. Neuropathologically, it features prominent neuronal loss in specific areas of the brain as well as characteristic alpha-synuclein protein inclusions called Lewy bodies. In recent years, smaller types of alpha-synuclein aggregates not organized into Lewy bodies have been hypothesized to be highly involved in disease pathogenesis, though few studies have shown these aggregates in tissue samples, mainly due to technical limitations.

In this PhD project, carried out at Aarhus University, we developed a novel alpha-synuclein proximity ligation assay to detect such small aggregates in cell models and post-mortem human tissue sections. We compared the results from our new assay with traditional immunohistochemistry to detect Lewy bodies and show that our assay detects more pathology at much earlier timepoints in disease. We also demonstrate that a genetic variant of Parkinson's disease without Lewy bodies - a curiosity currently left unexplained - does contain the smaller types of aggregates, pointing to a common disease mechanism. Lastly, we investigated the temporal development of phosphorylation at serine-129 of alpha-synuclein, a common disease marker, and examined the potential of its inhibition as a treatment target.

The project was carried out by Nanna Møller Jensen who is defending her dissertation on 16/5.

The defence is public and takes place on 16/5 at 13.00 in AIAS auditorium, Aarhus University, Høegh-Guldbergs Gade 6B, 8000 Aarhus C. The title of the project is "Investigating markers of inclusion and non-inclusion α -synuclein aggregate pathology in Parkinson's disease and related disorders". For more information, please contact PhD student Nanna Møller Jensen, email: nanna.mj@biomed.au.dk, Phone +45 6022 6553.

Assessment committee:

Associate Professor Peter Bross (chairman of the committee and moderator of the defence) Research Unit for Molecular Medicine, Aarhus University and Aarhus University Hospital, Aarhus, Denmark

Associate professor and Chief consultant Liisa Myllykangas University of Helsinki and Helsinki University Hospital, Finland

Professor George Tofaris, Professor of Neurology & Translational Neuroscience and Consultant Neurologist

Nuffield Department of Clinical Neurosciences and Kavli Institute for Nanoscience Discovery, University of Oxford, United Kingdom

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