Press release

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Basic information

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Department of: Biomedicine

Main supervisor: Marina Romero-Ramos

Title of dissertation: "Neuroprotective role for the CD163 receptor in the alpha-synuclein induced Neurodegeneration in Parkinson's disease"

Date for defence: Thursday 24 February 2022 at (time of day): 09:00-12:00 Place: Eduard Biermann Auditorium 1252-204, Aarhus University, Bartholins Allé 3, 8000 Aarhus C.

Press release (Danish)
Involveringen af den monocytiske CD163 receptor i alpha-synuclein-induceret neurodegenering i Parkinsons sygdom.

Parkinsons sygdom er en af de hurtigst voksende neurologiske sygdomme, og det anslås, at omkring 12 millioner mennesker vil være påvirket af sygdommen i 2024. Der findes ingen kur mod Parkinson, og meget forskning er stadigvæk nødvendigt for at finde potentielle terapeutiske mål. Et af de centrale neuropatologiske træk ved Parkinson er tilstedeværelsen og ophobningen af intra-neuralt misfoldede aggregater af alpha-synuclein (α-syn) protein. Derudover spiller immunforsvaret en vigtig rolle i sygdommen, hvilket er hoved-fokus i denne afhandling. Dette projekt er udført af Sara Raquel Almeida Ferreira, som vil forsvare sin afhandling den 24/02-2022.
Traditionelt bliver Parkinson klassificeret som en "hjerne"-sygdom, men i dag er det accepteret at sygdommen er styret af mange faktorer, hvor både nerve- og immune systemet er påvirket, og begge bidrage til den symptomatiske præsentation af sygdommen. Derudover foreslås det, at ikke kun hjernens, men også de perifere immunceller er involveret i den inflammatoriske proces, som er associeret med neurodegeneringen i Parkinson. Det er vigtigt at forstå, at misfoldet α-syn ikke kun er associeret til det neuronale komponent af sygdommen, men også til immunresponsen. Dette skyldes at α-syn kan fungere som et pro-inflammagen, både for mikroglia-celler i hjernen og for monocytter i det perifere system, fx de monocytter som udtrykker CD163 cellereceptoren.
Det primære fokus i denne afhandling var at undersøge involveringen af den monocyt-specifikke CD163 receptor i α-syn-induceret neurodegenering i Parkinson. Dette ph.d.-projekt er baseret på tre studier, der er præsentereret som to udgivet artikler og et manusskift. Den første publikation er en gennemgang og opsummering af allerede eksisterende litterærtur omhandlende α-syn pro-inflammatoriske effekt på immunceller. Det andet studie havde til formål at undersøge involveringen af CD163 monocytter i Parkinson. I dette studie bruges opløselig CD163 (sCD163), den kløvede form af proteinet, som en markør for monocyt aktivering, og som en potentiel biomarkør i Parkinson. Derudover karakteriseres CD163's rolle i det α-syn-associeret immunresponse. I det tredje studie modelleres Parkinson i en CD163-knockout mus, hvorved CD163's rolle i de α-syn-inducerede immun- og patologiske processer kunne evalueres.
Data indsamlet under denne ph.d. giver en vigtig indsigt i en ny rolle for CD163 receptoren i Parkinsons sygdom og bidrager dermed til et nyt sygdoms-modificerings mål til fremtidig forskning.

Forsvaret af ph.d.-projektet er offentligt og finder sted den 24/02-2022 kl. 09.00 i Eduard Biermann Auditorium 1252-204, Aarhus Universitet, Bartholins Allé 3, 8000 Aarhus C. Titlen på projektet er "Neuroprotective role for the CD163 receptor in the alpha-synuclein induced neurodegeneration in Parkinson's disease". Såfremt COVID-19 situationen ikke tillader et fysisk forsvar, vil forsvaret foregå online. I givet fald kan man anmode om deltagelse via Zoom ved at kontakte ph.d.-studerende Sara Raquel Almeida Ferreira via e-mail på sara.ferreira@biomed.au.dk.

Bedømmelsesudvalg:

Professor Gregers Wegener, MD, Ph.D., Translationel Neuropsykiatrisk Afdeling, Institut for Klinisk Medicin, Aarhus Universitet, Danmark

Professor Veerle Baekelandt, Ph.D. Laboratorium for Neurobiologi og Genterapi, Institut for Neurovidenskab, Leuven Universitet, Belgien

Professor Nadia Stefanova, MD, Ph.D. Sektion for Klinisk Neurobiologi, Neurologisk Afdeling, Innsbruck Medical Universitet, Østrig

Press release (English)

Involvement of the monocytic CD163 receptor in the alpha-synuclein-induced neurodegeneration in Parkinson's disease

Parkinson's disease (PD) is the fastest growing neurodegenerative disease with an anticipated prevalence of 12 million persons affected by 2040. No cure has been yet found for PD, and much research is needed to define novel therapeutic targets. In PD, the intraneuronal aggregation of alpha-synuclein (α-syn) constitute the pathological neuronal hallmark of the disease. Besides this, PD also includes a significant immune component, which constitutes the main focus of the thesis presented. The project was carried out by Sara Raquel Almeida Ferreira, who is defending her dissertation on 24/02-2022.

Classically approached as a brain disease, it is now accepted that PD has a multifactorial nature, with both nervous and immune systems affected and associated to its symptomatic presentation. It is suggested that not only brain, but also peripheral immune cells are involved in the inflammation associated to the PD neurodegenerative process. Importantly, misfolded α-syn is central to not only the neuronal event, but also to the immune response. This is so, because α-syn can act as a pro-inflammagen on microglia in the brain and also monocytes in the periphery, such those expressing the CD163 receptor.The main focus of this doctoral dissertation was to investigate the involvement of the monocytic CD163 receptor in the α-syn induced neurodegeneration in PD.

The PhD project was based on three studies presented as 2 published articles and one manuscript. In the first study, the existing literature addressing α-syn pro-inflammatory effects on immune cells was reviewed. The second study aimed to investigate the involvement of CD163 monocytes in PD. It defines soluble CD163 (sCD163), the cleaved form of the protein, as a marker of monocytic activation and potential biomarker in PD; and characterizes its role in the immune response associated to α-syn. The third study aimed to evaluate the CD163 role in the α-syn-induced immune and pathological events by modelling the disease in a CD163 knock out mouse line.

The data generated during the PhD provides valuable insights into the novel role for the CD163 receptor in PD, providing the scientific field with a new target for disease modification.

The defence is public and takes place on 24/02 at 9.00 AM in Eduard Biermann Auditorium 1252-204, Aarhus University, Bartholins Allé 3, 8000 Aarhus C. The title of the project is "Neuroprotective role for the CD163 receptor in the alpha-synuclein induced Neurodegeneration in Parkinson's disease". The defense may be converted to an online event due to COVID-19. In this case, a Zoom-link will be provided by contacting PhD Student Sara Raquel Almeida Ferreira via e-mail: sara.ferreira@biomed.au.dk.

Assessment Committee

Professor Gregers Wegener, MD, Ph.D., Translational Neuropsychiatry Unit, Department of Clinical Medicine, Aarhus University, Denmark

Professor Veerle Baekelandt, Ph.D. Laboratory for Neurobiology and Gene Therapy, Department of Neurosciences, Leuven University, Belgium

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