Press release

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Basic information

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Department of: Biomedicine

Main supervisor: Olav M. Andersen

Title of dissertation: Novel insights into SORL1: unraveling the role of the fourth autosomal-dominant Alzheimer's disease gene

Date for defence: 16/09/2021 at (time of day): 15.00 Place: Online via Zoom

Press release (Danish)
Nye indsigter i SORL1: opklaring af rollen for det fjerde autosomal dominante Alzheimer's sygdomsgen

Alzheimer's demens (AD) er en neurodegenerativ sygdom, som er den mest hyppige form for demens. AD ætiologien er forbundet med mange forskellige faktorer og genetiske studier har påvist varianter i adskillige gener som er associeret med sygdom. Iblandt disse findes SORL1 genet, kodende for sortilin-related receptor SORLA, som nu anses for en af de centrale genetiske determinanter for AD. Det er dog stadig uklart hvordan specifikke SORL1 varianter er patologisk forbundet med AD. Derfor er en dybere forståelse for dette gen og dets translationelle produkt vigtigt for fuldstændig at forstå hvis og hvordan SORL1 mutationer er kausale for AD.
Formålet med dette PhD forløb/studie var at karakterisere SORL1/SORLA yderligere for at finde nye funktionelle aspekter forbundet med AD. Dette var udført/gennemført ved brug af tre forskellige fremgangsmåder. Til at starte med blev en ny missense SORL1 variant i en islandsk familie, som er associeret med AD, karakteriseret med fokus på dens rolle i APP processering og SORLA shedding ved at etablere et in vitro assay. Endvidere var hensigten med formål to at beskirve et nyt human- specifikt transkript, som dannes ved alternativ splicing, i både den raske og syge AD hjerne. Til sidst blev den spatio-temporale karakterisering af SORL1/SORLA undersøgt i nethinden fra en postnatal mus ved at udnytte en musemodel der mangler SORLA samt forskellige molekylærbiologiske teknikker.

Resultaterne er sammenfattet i et nyt ph.d.-projekt fra Aarhus Universitet, Health. Projektet er gennemført af Giulia Monti, der forsvarer det d. 16/09/2021

Forsvaret af ph.d.-projektet er offentligt og finder sted den 16/09/2021 kl. 15.00 online via Zoom. Titlen på projektet er "Novel insights into SORL1: unraveling the role of the fourth autosomal-dominant Alzheimer's disease gene". Yderligere oplysninger: Ph.d.-studerende Giulia Monti, e-mail: gm@biomed.au.dk, tlf. +45 50 21 87 16

Bedømmelsesudvalg:

Thomas Willnow, Professor, PhD (Formand for bedømmelsesudvalget og moderator ved forsvaret) Institut for Biomedicine, Aarhus Universitet

Enrico Tongiorgi, Professor, PhD

Department of Life Sciences, University of Trieste, Italy

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Department of Neurobiology Research, University of Southern Denmark, Denmark

Press release (English)
Novel insights into SORL1: unraveling the role of the fourth autosomal-dominant Alzheimer's disease gene

Alzheimer's disease (AD) is a neurodegenerative disorder representing the most common form of dementia. Aetiology of AD is linked to multiple factors, and genetic studies uncovered several genes associated to disease. Among these, SORL1 encoding the sortilin-related receptor SORLA is now considered one of the main genetic determinants of AD. However, it is still unclear how specific SORL1 variants are pathologically linked to AD. A deeper comprehension of this gene and its translational product is thus key to fully understand if and how SORL1 mutations are causative of AD. The general aim of this PhD study was to further characterize SORL1/SORLA to reveal new functional aspects that could help advancing our knowledge about its role in the pathology. This was carried out following three different approaches. First, a novel missense SORL1 variant associated with AD in an Icelandic family was characterized, focusing on its role in APP processing and SORLA shedding through the establishment of an in vitro assay. Moreover, the second aim was to describe a novel human specific SORL1 transcript produced by alternative splicing in both healthy and AD brain. Finally, the spatio-temporal characterization of SORL1/SORLA was examined in the postnatal mouse retina taking advantage of a SORLA-deficient mouse model and a variety of molecular biology techniques.

The results of the project will be presented and discussed at the defence. The project was carried out by Giulia Monti, who is defending her dissertation on 16/09/2021.

The defence is public and takes place on 16/09/2021 at 15.00 online via Zoom. The title of the project is "Novel insights into SORL1: unraveling the role of the fourth autosomal-dominant Alzheimer's disease gene". For more information, please contact PhD student Giulia Monti, email: gm@biomed.au.dk, Phone +45 50 21 87 16

Assessment committee:

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