

Press release

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Basic information

Name: Angela Pärn Email: angela.parn@biomed.au.dk Phone: +37256251645

Department of: Biomedicine

Main supervisor: Simon Glerup

Title of dissertation: The Role of PCSK9 in the Brain

Date for defence: 26. February 2021 at (time of day): 15.00 Place: Online via Zoom (link available by contact with Angela Pärn)

Press release (Danish)

PCSK9s rolle i hjernen - Virtuelt P.hd. forsvar - Angela Pärn

Et nyt ph.d. projekt fra Aarhus Universitet, viser at hæmning af PCSK9 i mus, både under udvikling og i voksenliv ikke har nogle uønskede neurologiske konsekvenser. Dette er vigtige resultater da de supplerer troen på at PCSK9 hæmmer er en sikker behandling for patienter der lider af forhøjet kolesterol.

Protein convertase subtilisin/kexin type 9 (PCSK9) er et protein der er involveret i regulering af lavdensitetslipoprotein (LDL) metabolisme samt plasma kolesterol niveauer. Hæmning af PCSK9 sænker plasma kolesterol effektivt, og antistoffer rettet mod PCSK9 er i klinisk brug. Derudover er et medikament, der fuldstændigt blokerer PCSK9 syntesen for nyligt blevet godkendt.

Mens PCSK9 hovedsagelig er udtrykt i den udviklende samt voksne lever, findes det også i andre væv, inklusive i hjernen. Bemærkelsesværdigt er PCSK9 ekspressionen i hjernen højst i løbet af den kortikale og cerebellære udvikling. Derfor er det blevet foreslået, at PCSK9 har en vigtig rolle i udviklingen af hjernen samt dens homeostasis. I den forbindelse er det vigtigt at sikre at hæmning af PCSK9 ikke har nogle neurologiske bivirkninger.

Fokus i denne tese var at undersøge konsekvensen af ændret PCSK9 aktivitet under udviklingen og i den voksne hjerne i mus. Resultaterne viser, at selvom vi finder nogle ændringer i hjernens lipidsammensætning hos mus der ikke har PCSK9, så giver hverken overekspression af PCSK9 eller mangel på PCSK9 under hjernens udvikling nogle større konsekvenser for hjernens funktion i mus. Det samme gør sig gældende for lav plasma kolesterol årsaget af PCSK9 mangel i voksenlivet. Derfor supplerer vores resultater troen på, at nuværende og fremtidige medikamenter der hæmmer PCSK9 er sikre for patienterne.

Dette er et nyt ph.d.-projekt fra Aarhus Universitet, Health. Projektet er gennemført af Angela Pärn, der forsvare det d. 26/2

Forsvaret af ph.d.-projektet er offentligt og finder sted den 26/2 kl. 15.00 virtuelt via Zoom. Titlen på projektet er "The Role of PCSK9 in the Brain". Yderligere oplysninger: Ph.d.-studerende Angela Pärn, e-mail: angela.parn@biomed.au.dk, tlf. +37256251645.

Bedømmelsesudvalg:

Olav M Andersen, PhD, Institut for Biomedicin, Sundhedsvidenskabelige Fakultet, Aarhus Universitet, Danmark - Formand for udvalget

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Press release (English)

The Role of PCSK9 in the Brain - Online PhD defense - Angela Pärn

Proprotein convertase subtilisin/kexin type 9 (PCSK9) is a protein that is involved in the regulation of low-density lipoprotein (LDL) metabolism and plasma cholesterol levels. Its therapeutic inhibition efficiently lowers plasma cholesterol, and antibodies directed against PCSK9 are in clinical use.

Furthermore, novel drugs that completely block PCSK9 synthesis have been recently approved. While PCSK9 is mostly expressed in the developing and adult liver, it is also present in several other tissues, including the brain. Intriguingly, PCSK9 expression in the brain peaks during cortical and cerebellar development and decreases markedly thereafter. Accordingly, PCSK9 has been proposed to have an important role in brain development and homeostasis. Thus, it is important to assure that the long-term inhibition of PCSK9 has no potential adverse neurological effects. The focus of this thesis was to study the consequences of altered PCSK9 activity in developing and adult mouse brain. The results demonstrate that although we find moderate changes in the brain lipids of PCSK9 KO mice, neither overexpression nor deficiency of PCSK9 during brain development nor low plasma cholesterol resulting from PCSK9 deficiency in adulthood has major consequences for brain functioning. Accordingly, our results complement the belief that the current and future PCSK9-inhibiting therapies are safe to use on patients.

The project was carried out by Angela Pärn, who is defending her dissertation on the 26th of February.

The defence is public and takes place at 26. February 2021 at 15.00 online via Zoom. The title of the project is "The Role of PCSK9 in the Brain". For more information, please contact PhD student Angela Pärn, email: angela.parn@biomed.au.dk, Phone +37256251645.

Assessment committee:

Olav M Andersen, Associate Professor, PhD, Department of Biomedicine, Faculty of Health, Aarhus University, Denmark - Chairman of the committee

Annik Prat, PhD, Researcher at Clinical Research Institute of Montreal (IRCM), Canada

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