Press release

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Basic information

Name: Lu Wen Email: luwen@clin.au.dk Phone: +45 50657642

Department of: Clinical Medicine

Main supervisor: Professor Henrik Birn, Department of Biomedicine, Aarhus University

Title of dissertation: Interaction between megalin, microRNA-148b, and complement proteins in IgA nephropathy and other kidney diseases

Date for defence: 26-01-2018 at (time of day): 14:30 Place: Lille Anatomisk Auditorium, Aarhus University, Building 1231, room 424, Wilhelm Meyers Alle' 3, Aarhus C

Press release (Danish)

Sammenspillet mellem megalin, microRNA-148b og komplementproteiner i IgA-nefritis og andre nyresygsdomme.

Et nyt PhD-studie udgående fra Klinisk Institut ved Aarhus Universitet kaster lys over samspillet mellem megalin, microRNA og komplementproteiner i forbindelse med IgA-nefritis og obstruktiv nyresygdom. Fundene har betydning for vores forståelse af sygdomsudviklingen ved disse tilstandes såvel som andre nyresygdomme. Projektet er gennemført af Dr. Lu Wen, som forsvarer sin PhD-afhandling den 26. januar, 2018.
Allerede i dag tyder en række observationer på, at den tubulære proteinoptagelse er abnorm ved visse nyresygdomme betinget af en ændret funktion af receptorproteiner megalin. Da megalin spiler en vigtig rolle for optagelsen af filtrerede proteiner, vil kan dette have betydning for sygdomsudviklingen og for udskillesen af sygdomsmarkører i urinen. De mekanismer, der regulerer syntesen af megalin i nyren er imidlertid ikke faslagte. Formålet med dette projekt har været at undersøge, om microRNA kan regulere udtrykket af megalin i forbindelse med ensidig, obstruktiv nefropati (UUO) i mus og ved IgA-nefritis hos mennesker, samt hvorvidt ændringer i udtrykket af megalin hænger sammen med ændringer i udskillesen af markører for nyreskade i urinen. På baggrund af transfektionsstudier, undersøgelser i mus udsat for UUO og gennem analyser af miR-148b og megalin i nyrebiopsimateriale både fra patienter med IgA-nefritis og patienter med ikke-prolifirative nyresygdomme, har vi vist, at miR-148b hæmmer syntesen af megalin ved UUO og IgA-nefritis. Målinger af koncentrationerne af komplementproteiner i serum og urin både hos patienter med IgA-nefritis og patienter med ikke-proliferative nyresygdomme har vist, at høje koncentrationer af komplementproteiner i urinen ser ud til at afspejle skade på nyretubuli og nedsat megalinfunktion. Megalin synes således at kunne spille en rolle for udviklingen af proteinuri og for udskillesen af sygdomsmarkører ved IgA-nefritis og muligvis også ved andre nyresygdomme.

Forsvaret af ph.d.-projektet er offentligt og finder sted den 26/01/2018 kl. 14:30 i Lille Anatomisk auditorium,Bygning 1231, Aarhus Universitet, Wilhelm Meyers Alle' 3, 8000 Aarhus C. Titlen på projektet er "Interaction between megalin, microRNA-148b, and complement proteins in IgA nephropathy and other kidney diseases". Yderligere oplysninger: Dr. Lu Wen, e-mail: luwen@clin.au.dk, tlf. +45 50657642.

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Press release (English)

Interaction between megalin, microRNA-148b, and complement proteins in IgA nephropathy and other kidney diseases

A new PhD study from the Department of Clinical Medicine, Aarhus University, provides new knowledge about the interaction between megalin, microRNAs, and complement proteins in IgA nephropathy and obstructive kidney disease, which may have implications for understanding disease progression in these and possibly other renal conditons. The project was carried out by Dr. Lu Wen, who is defending her dissertation on 26/01/2018.

Current evidence indicates that some kidney diseases may be associated with abnormal renal tubular protein reabsorption caused by dysfucntion of the megalin receptor. Considering the important role of megalin for the tubular uptake of filtered proteins, this may have implications for disease progression and for the urinary excretion of disease markers. So far the pathophysiological mechanism regulating megalin expression in kidney has been unclear. The aim of the project was to examine if microRNAs are involved in the regulation of megalin expression in unilateral ureteral obstruction (UUO) in mice and IgA nephropathy in humans, and whether alterations of megalin expression may be associated with changes in the urinary excretion of established markers of kidney injury. By performing cell transfection, examining the mice model of UUO, and analysing miR-148b and megalin expression in kidney biopsy tissue from patients with IgA nephropathy, we found that miR-148b can negatively regulate megalin expression in UUO and IgA nephropathy. By analysing the serum and urinary complement protein levels in IgA nephropathy patients and non-proliferative chronic kidney disease patients, we found that higher levels of urinary complement proteins in IgA nephropathy may reflect tubular damage with impaired megalin function. Thus, megalin could play an important role for the progression of proteinuria and urinary excretion of disease markers in IgA nephropathy and possibly other kidney diseases.

The defence is public and takes place on 26/01/2018 at 14:30 in Lille Anatomisk Auditorium , Aarhus University, Building 1231, room 424, Wilhelm Meyers Alle' 3, 8000 Aarhus C. The title of the project is "Interaction between megalin, microRNA-148b, and complement proteins in IgA nephropathy and other kidney diseases". For more information, please contact Dr. Lu Wen, email: luwen@clin.au.dk, Phone +45 50657642.

Assessment committee:

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