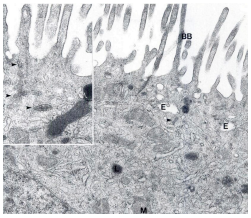
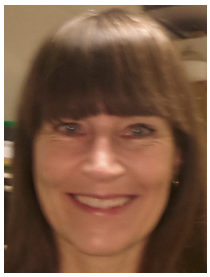
AARHUS UNIVERSITY
DEPARTMENT OF BIOMEDICINE



Cell Biology & Physiology

Rikke Nielsen (will not be present the 31st)
rn@biomed.au.dk

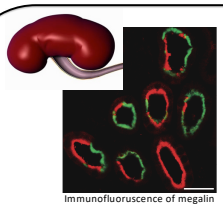


Background

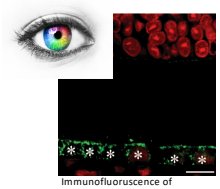
The low-density lipoprotein receptor (LDLR) family are vital endocytic receptors involved in the pathogenesis of severe diseases including cardiovascular disease, dementia and kidney disease. The receptors play diverse roles in many biological processes such as lipoprotein metabolism, protease degradation, clearance of proteins and protein signaling and are therefore prime candidates for exploring molecular roles in diseases and ultimately development of novel treatments.

Megalin (LRP2) is a member of the LDLR family, which is positioned at the surface of epithelia throughout the body also lining important barrier epithelia, such as e.g. in the brain, the retina and the kidney. The function of megalin has mostly been studied in the kidney, where it is known to rescue filtered proteins, vitamins and lipoproteins from urinary loss. However, it is evident from the phenotype of patients lacking the receptor that diseases develops when it is absent.

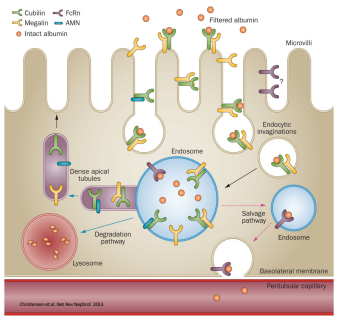
Our overall aim is to understand the role of megalin in the kidney and in the retina of the eye with the perspective to understand diseases in these organs and find new therapeutic entry points.



Immunofluorescence of megalin (red) and CA4 (green) in the kidney.



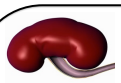
Immunofluorescence of megalin (green) in the retina.



Receptor mediated endocytosis of filtered proteins in the kidney. In this tissue megalin co-operates with the receptor complex Cubam (cubilin and amnionless).

Megalin

Projects and techniques

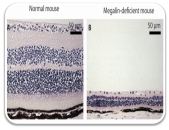


PROJECTS

- Does megalin play a role in progression of kidney disease?
- What is the role of megalin in maintaining homeostasis of e.g. lipids during chronic kidney disease?
- Is megalin downregulating hormone responses in the kidney?
- Can we inhibit megalin by controlling glycosylation?

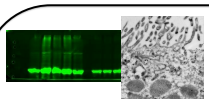
PROJECTS

- Why does megalin dysfunction induce retina degeneration?



Retina degeneration in a megalin knockout mouse.

- Does megalin expression decrease with age and does this play a role in age related eye changes?



METHODS

- Gene modified mice, human material, cell culture.
- Animal work including e.g. urine collection and injections of tracers.
- Western blotting.
- Confocal – and electron microscopy.
- RT-q-PCR.
- Isolation of cells and proteins.

If you are interested in kidney or eye physiology and would like to participate in a research project bridging basic science and clinical problems you are welcome to contact us. This can be either Bsc -, Msc -, Phd – or Research year projects.

We are a dynamic group, at the moment consisting of: 3 permanent staff members, 4 technicians, 2 postdocs, 1 Phd student, 1 Research year student, 1 Msc students and 1 Bsc student. And we are hoping to include you ☺ You will be trained in the required methods by experienced technicians and supervised on a daily basis to ensure progress and problem solving, which is supported by our informal group meetings every second Monday, where we discuss the projects running.

- Nielsen R, Christensen EI, and Birn H. Proximal tubular protein reabsorption – from experimental models to human disease. 2016. *Kidney International.* 89:58-67
- Storm T, Heegaard S, Christensen EI and Nielsen R. Megalin-deficiency causes high myopia, retinal pigment epithelium-macromelanosomes and abnormal development of the ciliary body in mice. 2014. Cell Tissue Res. 358: 99-107