Göteborg, 2021

The role of glycoproteins in glomerular pathophysiology

Akademisk avhandling

Som för avläggande av medicine doktorsexamen vid Sahlgrenska akademin,
Göteborgs universitet kommer att offentligen försvaras
i hörsal Arvid Carlsson, Medicinaregatan 3, Göteborg
Torsdagen den 23 september 2021, klockan 13.00

av Alina Khramova

Fakultetsopponent:

Rikke Nørregaard, PhD, Dr.Med., Associate Professor, Aarhus University

Department of Clinical Medicine, Aarhus University Hospital, Aarhus, Denmark

Avhandlingen baseras på följande delarbeten:

I. Proteoglycans contribute to the functional integrity of the glomerular endothelial cell surface layer and are regulated in diabetic kidney disease

Khramova A, Boi R, Friden V, Björnson Granqvist A, Nilsson U, Tenstad O, Oveland E, Haraldsson B, Ebefors K and Nyström J.
Scientific Reports (2021) 11:8487

II. Adaptive remodeling of mesangial extracellular matrix proteoglycan composition during IgA nephropathy

Khramova A, Noborn F, Buvall L, Larson G, Ebefors K and Nyström J.
Manuscript

III. Galactose-deficient IgA levels in blood and urine in patients with IgA nephropathy

Khramova A, Eliasdottir S, Saeed A, Guron G, Ebefors K and Nyström J.
Manuscript

SAHLGRENSKA AKADEMIN
INSTITUTIONEN FÖR NEUROVETENSKAP OCH FYSIOLOGI

GÖTEBORGS UNIVERSITET

Göteborg, 2021

The role of glycoproteins in glomerular pathophysiology

Alina Khramova

Department of Physiology, Institute of Neuroscience and Physiology,
Sahlgrenska Academy at University of Gothenburg, Sweden, 2021

Abstract

Chronic kidney disease (CKD) is increasing worldwide and has a prevalence of around 10%. With time patients are at risk of losing their renal function and will need dialysis or transplantation for survival. There are no specific treatments available and mechanisms behind the onset and progression of CKD are still not fully investigated. Two of the most common examples of CKD are diabetic kidney disease (DKD) and IgA nephropathy (IgAN). This thesis is focusing on the role of specific glycoproteins in these diseases and possible biomarkers for diagnostic purposes. The first paper demonstrates the importance of proteoglycans (PGs) in the endothelial cell surface layer for an intact glomerular filtration barrier. Loss of PGs from this layer led to increased proteinuria in rats, and analysis of human glomerular tissue and cells cultured in diabetic-like conditions revealed an altered PGs expression. Paper II focused on the role of PGs in the mesangial matrix in IgAN. One of the main reasons for onset of IgAN is considered to be galactose deficient IgA (gd-IgA) containing immune complexes deposited in the mesangium of the kidney. Analysis of human glomerular tissue in combination with mesangial cells treated with gd-IgA revealed increase in PG expression and an altered glycosylation profile of the PGs in IgAN. The last paper concerns the possibility of using gd-IgA as a biomarker for IgAN for early detection and follow up of the disease. Patient urine and serum from the time of the diagnostic biopsy as well as follow up samples were analyzed. Patients with IgAN had higher levels of gd-IgA compared to heathy individuals and patients with other renal diseases. gd-IgA levels in urine did reflect severity of disease but had no prognostic value and at this stage we cannot conclude that gd-IgA is a valuable biomarker for IgAN.

In conclusion, PGs are important for a normal function of the glomerular filtration barrier and loss of PGs leads to proteinuria. On the contrary increased levels of PGs in the mesangial matrix is part of the progression of IgAN. These findings highlight the importance of PGs in glomerular function and disease. In addition, we investigated the possibility of using gd-IgA as a biomarker for IgAN, but with inconclusive results calling for further investigation.

Keywords: Proteoglycans, extracellular matrix, IgA nephropathy, diabetic kidney disease

ISBN: 978-91-8009-448-1 (TRYCK)
ISBN: 978-91-8009-449-8 (PDF)