



A novel biomarker of laminin turnover is associated with mortality and disease progression in chronic kidney disease

Nielsen, Signe Holm; Guldager Kring Rasmussen, Daniel; Fenton, Anthony; Jesky, Mark; Ferro, Charles; Karsdal, Morten; Genovese, Federica; Cockwell, Paul

Published in:
Nephrology, Dialysis, Transplantation

Link to article, DOI:
[10.1093/ndt/gfx102.S0015](https://doi.org/10.1093/ndt/gfx102.S0015)

Publication date:
2017

Document Version
Publisher's PDF, also known as Version of record

[Link back to DTU Orbit](#)

Citation (APA):
Nielsen, S. H., Guldager Kring Rasmussen, D., Fenton, A., Jesky, M., Ferro, C., Karsdal, M., Genovese, F., & Cockwell, P. (2017). A novel biomarker of laminin turnover is associated with mortality and disease progression in chronic kidney disease. *Nephrology, Dialysis, Transplantation*, 32(Suppl. 3).
<https://doi.org/10.1093/ndt/gfx102.S0015>

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

LG1M levels in serum and urine from a large prospective cohort of patients with high-risk CKD.

METHODS: A novel immunoassay targeting a specific MMP-9-generated neo-epitope fragment of LAMC1 (LG1M) was used to measure the fragment levels in urine and serum from 492 patients from the Renal Impairment in Secondary Care (RIISC) study, a prospective cohort of patients with high-risk CKD. Patients were monitored for a median follow-up time of 2.5 years. Progression of CKD was defined as a decline in eGFR of more than 30%, or starting renal replacement therapy as a definition of end-stage-renal disease (ESRD) within 12 months. Associations between LG1M levels in both serum and urine for progression of CKD were assessed by a multivariable logistic regression model with forward selection, while adverse outcomes were assessed by Kaplan-Meier and Cox regression analysis.

RESULTS: Forty-six patients (11%) of 411 patients who were alive and under follow-up at 12 months had progressed. During the study 102 patients developed ESRD and 65 patients died. Both urinary and serum levels of LG1M showed an inverse linear correlation with baseline eGFR (Spearman's correlation coefficient $r=-0.43$, $p<0.0001$ and $r=-0.17$, $p=0.0002$, respectively). Serum but not urinary LG1M levels were significantly associated with progression of CKD within 12 months ($p<0.01$), but were not included in the final model for prediction of whether the patients developed ESRD. Urinary LG1M levels were significantly associated with death; patients in the highest LG1M tertile were 4.5 ($p<0.0001$) times more likely to die than patients in the first tertile. Urinary LG1M levels were included in the final model for prediction of mortality (HR 1.25, 95% CI 1.04-1.51, $p=0.02$).

CONCLUSIONS: The novel biomarker LG1M reflecting glomerular basement membrane remodeling is associated with disease progression, development of ESRD, and mortality in high-risk CKD patients.

SO015

A NOVEL BIOMARKER OF LAMININ TURNOVER IS ASSOCIATED WITH MORTALITY AND DISEASE PROGRESSION IN CHRONIC KIDNEY DISEASE

Signe Holm Nielsen^{3,1}, Daniel Guldager Kring Rasmussen¹, Anthony Fenton², Mark Jesky², Charles Ferro², Morten Karsdal¹, Federica Genovese¹, Paul Cockwell²

¹Biomarkers and Research Nordic Bioscience Herlev Denmark, ²Department of Renal Medicine Queen Elizabeth Hospital Birmingham United Kingdom and ³Department of Biotechnology and Biomedicine Technical University of Denmark Lyngby Denmark

INTRODUCTION AND AIMS: Patients with chronic kidney disease (CKD) have increased risk of progressing to end-stage renal disease (ESRD) and a high mortality rate. One of the major underlying causes of progression of renal failure is renal fibrosis, which is caused by dysregulated extracellular matrix (ECM) remodeling. The laminin $\gamma 1$ (LAMC1) chain is a constituent of the laminin types present in the glomerular basement membrane (GBM), and its turnover may be altered in CKD. Fragments of LAMC1 could quantify GBM turnover in human CKD and reflect pathological tissue changes. We developed an immunoassay targeting LG1M, a neo-epitope of LAMC1 generated by matrix metalloproteinases (MMPs). We then measured