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Serological extracellular matrix fragments may serve as early kidney damage biomarkers in children with defects in Alport genes

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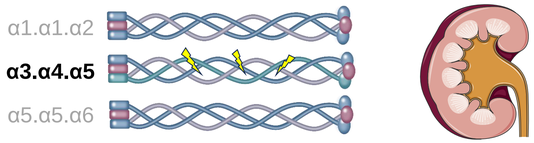
INTRODUCTION & AIM

Alport syndrome is a **genetic disorder** caused by variants in ***COL4A3, COL4A4,*** or ***COL4A5***, which encode **type IV collagen**. The α3.α4.α5(IV) collagen network is a critical structural component of the **glomerular and tubular basement membranes** within the kidney's **extracellular matrix (ECM).**

Type IV collagen triple helices

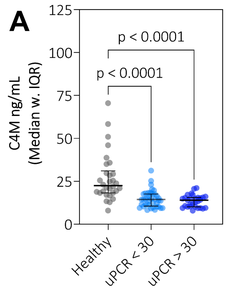


Variants in this network compromise basement membrane integrity, leading to cell injury, inflammation, and **fibrotic remodeling** of the surrounding **interstitial matrix,** which contributes to progressive kidney dysfunction

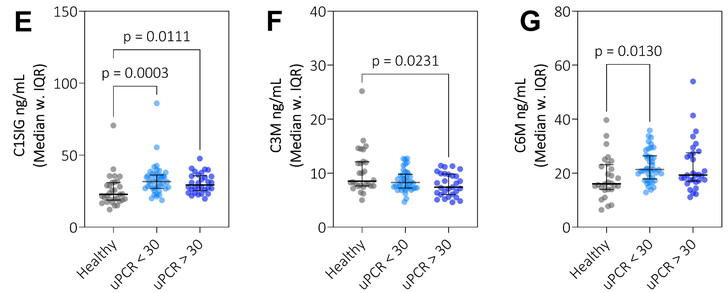
We aim to identify **serological protease-generated fragments** of the **ECM** as potential **early biomarkers** of kidney damage.

RESULTS

Basement membrane biomarkers



Interstitial matrix biomarkers



Differences between groups were assessed using the Kruskal-Wallis non-parametric test. Statistical significance was set at $p < 0.05$.

METHODS

Serological biomarkers quantified using ELISAs*

ECM degradation

C1SIG	Type I collagen
C3M	Type III collagen
C4M	Type IV collagen
C6M	Type VI collagen
NIC	Nidogen
LG1M	Laminin

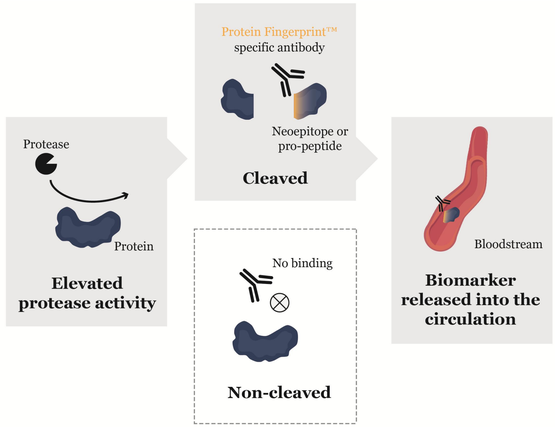
ECM formation

PRO-C3	Type III collagen
PRO-C6	Type VI collagen

ECM turnover

PRO-C4	Type IV collagen

*ELISAs are developed by Nordic Bioscience



Age- and sex-matched healthy children (n =30)

Children with Alport syndrome

uPCR<30 (n =41) — Baseline

uPCR>30 (n =30) — Follow-up

CONCLUSIONS

The following biomarkers were **altered** in children with Alport syndrome, compared to healthy donors, before the onset of detectable proteinuria:

- ↓ **C4M, LG1M, NIC** (basement membrane degradation)
- ↓ **PRO-C3 and PRO-C6** (interstitial matrix formation)
- ↑ **C1SIG and C6M** (interstitial matrix degradation)
- ↑ **PRO-C4** (basement membrane turnover)

These biomarkers could potentially indicate **early kidney damage** and enable earlier initiation of **kidney-protective treatments** in children with Alport syndrome.

HAVE QUESTIONS OR WANT TO CHAT?
PLEASE REACH OUT Solveig Groen, ssg@nordicbio.com