



Shaping Tomorrow's Nephrology: Insight-Driven Kidney Care

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Large-scale OLINK blood proteomic profiling identifies novel prognostic biomarkers for disease progression in IgA nephropathy

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Objectives : Predicting disease progression and adverse kidney outcomes in IgA nephropathy remains a critical clinical challenge. This study aimed to characterize the disease-specific blood proteomic profile and discover novel prognostic biomarkers associated with kidney function decline in IgA nephropathy.

Methods : We conducted a comprehensive plasma proteomic analysis of 319 subjects, comprising 193 patients with biopsy-proven IgA nephropathy and 126 controls, which included 38 healthy individuals, 63 with minimal change disease, and 25 with membranous nephropathy. The Olink Explore HT platform was utilized to robustly quantify 5,401 circulating proteins. The primary outcomes were defined as a composite event of the first occurrence of either estimated glomerular filtration rate (eGFR) <15 ml/min/1.73m², dialysis, transplantation, or $>50\%$ reduction of eGFR. Statistical analyses encompassed principal component analysis, uniform manifold approximation and projection, K-means clustering, pathway enrichment, and multivariate Cox proportional hazards models.

Results : Dimensionality reduction techniques demonstrated distinct clustering patterns separating patients with IgA nephropathy from control groups. Differential expression analysis identified 82 highly specific proteins with consistent estimate directions. Unsupervised K-means clustering revealed distinct patient subgroups that were significantly associated with an eGFR < 60 mL/min/1.73 m² and International IgA nephropathy risk prediction tool scores. After rigorous adjustment for baseline kidney function and the exclusion of non-specific markers, 105 proteins remained significantly associated with adverse kidney events. Gene set enrichment analysis highlighted pathways related to cell adhesion and apoptotic processes. Crucially, multivariate Cox regression, adjusted for age, sex, estimated glomerular filtration rate, and proteinuria, identified six independent prognostic biomarkers: TSNAIP1, DCN, LUZP2, TAFI5, OGN, and UMOD.

Conclusions : Large-scale proteomic profiling successfully elucidated pathophysiological signatures specific to IgA nephropathy. The six newly identified prognostic biomarkers offer a promising non-invasive tool for accurate clinical risk stratification and outcome prediction.

Figure.png



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