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Evaluation of KCa3.1 as a Urinary Biomarker for the Monitoring of Disease Activity in IgA Nephropathy

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Background: IgA Nephropathy (IgAN) is the most common primary glomerulonephritis in the world. After diabetes, it is rapidly becoming a leading global cause of renal morbidity. 20-50% will develop ESRF within 10 years and at present, determining the likely course at diagnosis is difficult. Biopsy is the only definitive method to monitor progression. There is a clinical need for the identification of less-invasive methods.

KCa3.1 is a calcium activated potassium channel shown to be involved in fibrosis. Work in our lab has shown synthesis of KCa3.1 varies in vitro in mesangial cells and proximal tubule epithelial cells (when stimulated by pathogenic IgA1) in a dose dependent manner.

We hypothesise that KCa3.1 can be a useful marker, specific for IgAN disease activity in vivo.

Methods: The primary outcome was the presence or absence of KCa3.1 in urine samples. IgAN (n=50), disease (n=46) and healthy (n=28) samples were corrected for creatinine. Western blotting and densitometry were used to quantitate KCa3.1 profiles. Immunohistochemistry was used to identify renal origin of KCa3.1.

Results: KCa3.1 was found in all patients with IgAN (n=50), some disease controls (n=16) but no healthy controls. Presence was different in IgAN v DC ($p<0.0001$) and IgAN v HC ($p<0.0001$). The densitometry values also showed a difference between IgAN v DC ($p<0.00001$) and IgAN v HC ($p<0.00001$). Immunohistochemistry showed predominant staining within the proximal tubules. Densitometry values were not associated with proteinuria, haematuria or GFR. Performance measures found KCa3.1 was 100% sensitive and 65% specific.

Conclusion:KCa3.1 is not specific to IgAN thus limiting it's usefulness as a biomarker for disease. However, given existing evidence to suggest it's involvement in fibrogenesis with the consistent identification of KCa3.1 in all IgAN samples, KCa3.1 may be involved in IgAN fibrogenesis which may be a potential therapeutic target.

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