**An analysis of serum biomarkers in IgA nephropathy**

David Wimbury

**INTRODUCTION:** IgA nephropathy (IgAN) is a glomerulonephritis characterised by the mesangial deposition of IgA1-containing immune complexes (IgA-IC). In susceptible individuals this leads to relentless glomerular injury, tubulointerstitial scarring and progressive renal impairment, with 30-40% of patients developing end stage renal disease (ESRD) within 20 years of diagnosis. Two of the key events in the pathogenesis of IgAN are the appearance in the serum of poorly galactosylated IgA1 molecules and the subsequent development of IgA and IgG anti-IgA1 autoantibodies directed against the IgA1 hinge region *O*-linked glycans. The aim of this study was to determine whether the levels of serum biomarkers, with particular focus on factors known to be important in B and T cell activation, are associated with the development of IgAN.

**METHODS:** Serum samples were selected from the UK Glomerulonephritis DNA Bank and the concentrations of 32 candidate biomarkers were measured using Luminex bead-based multiplexing immunoassay (R&D Systems). Comparisons were made based on renal function.

Experiment 1: normal renal function, all serum creatinine (Cr) <110 µmol/l

* 89 IgAN patients
* 89 Membranous Nephropathy (MN) patients, matched for serum Cr with IgAN patients.
* 89 Healthy Subjects (HS), age matched to IgAN patients.

Experiment 2: impaired renal function, all serum Cr >110 µmol/l

* 20 IgAN patients
* 20 MN patients, matched for serum Cr with IgAN patients
* 20 HS, age matched to IgAN patients.

**RESULTS:** Seven of the analysed cytokines (GM-CSF, IFN-gamma, IL-7, IL-12 p70, IL-15, IL-17A and IL-22) were at levels too low to be detected by this assay. Thirteen showed correlation with serum creatinine, seven of which were specific to IgAN (APRIL, BCMA, CD27, CTACK, IGFBP-1 and TACI) and two specific to MN (CD163 and IL-1 RI).

Experiment 1:

Three of the candidate biomarkers were elevated in patients with IgAN and normal renal function when compared to HS (BCMA, MMP-2 and TNF RI). These three and a further 16 were at elevated levels in MN.

Experiment 2:

Eleven candidate biomarkers were increased in patients with IgAN and impaired renal function (APRIL, BCMA, CD27, CD30, CTACK, IGFBP-1, IL-18 BPa, TNF RI, TNF RII, TRAIL and Uteroglobin). Of these, only CTACK was specific to IgAN as the serum levels of the others were also elevated in MN. A further eight were also elevated in MN.

**DISCUSSION:** Previously reported biomarker studies have described associations between a number of biomarkers in this study and the development of IgAN, but have failed to correct for renal function in their study populations. Our data highlight the importance of controlling for renal function when evaluating the importance of serum biomarkers in kidney disease. We have identified a panel of biomarkers elevated in IgAN, of these only CTACK was specific to IgAN. Future work will involve longitudinal studies to examine the impact of this biomarker on disease phenotype and response to therapy.