IgA nephropathy: autoimmune nature of the disease

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Studies of molecular and cellular interactions involved in the pathogenesis of the most common glomerulonephritis - IgA nephropathy - revealed the autoimmune nature of this disease. Altered glycan structures of the unique hinge region of the heavy chains in IgA1 molecules in patients with this disease lead to the exposure of antigenic determinants which are recognized by unique anti-glycan antibodies of IgG or IgA1 isotypes resulting in the formation of nephritogenic immune complexes in the circulation and their deposition in the glomerular mesangium. Deposited immune complexes induce proliferation of resident mesangial cells, increased production of extracellular matrix proteins and cytokines, and ultimately the loss of glomerular function. Structural elucidation of the nature and biological activity of immune complexes should provide a rational basis for effective, immunologically-mediated interference with the formation of nephritogenic immune complexes as a disease-specific therapeutic approach.