

Sorting complement dysregulation in renal disorders (ESPN 2014.5).

Number of rare devastating renal disorders is associated with the dysregulation of complement system, a part of the innate immune system. Important complement-mediated renal disorders include: C3 glomerulopathies (C3G), immune-complex-mediated glomerulonephritis (IgGN) and atypical hemolytic uremic syndrome (aHUS).

In many cases, these disorders have overlapping etiologies. Diagnosis often relies on renal biopsy, which is an invasive procedure for the patient and in case of aHUS should be avoided due to increased chance of bleeding caused by thrombocytopenia. Moreover, current understanding of exact complement pathology in each of these disorders is still limited.

Here we hypothesize that these disorders have different patterns of complement activation biomarkers in fluid phase, which should correspond with biopsy and clinical findings and can be analyzed in serum and/or EDTA plasma samples.

In collaboration with the Department of (Pediatric) Nephrology, University Hospitals Leuven, Belgium (Prof. dr. Kathleen Claes/ Prof. Dr. Ben Sprangers) we aim to study complement activation in these renal diseases. This collaboration will allow us to combine clinical and laboratory expertise of the departments with strong track record in diagnostics and treatment of complement-mediated renal diseases. It will also allow recruiting enough patients for the three patient groups mentioned above.

This is a highly relevant project, which will allow getting more insight into pathology of various complement-mediated glomerular diseases. In the future, it may allow developing diagnostic techniques based on EDTA plasma/serum biomarkers. These tests will distinguish disorders with alternative complement pathway activation in the fluid phase (such as C3G) from disorders caused by complement activation at the cell surface (aHUS) and from disorders that involve activation of the classical pathway (IgGN). Furthermore, it would be possible to monitor patients for early signs of the disease relapse and guide the development of individual treatment schemes for complement inhibition therapy.