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Complement and the kidney landscape

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ection that is common to all children in all age groups, including the new born period. The diagnosis of urinary tract infection is established with certainty by urine culture. Additional investigations can be done to help confirm the diagnosis, such as Interleukin-6 urine (IL-6). Increased number of IL-6 urine is useful to help quickly checks the occurrence of pyelonephritis. Complement activation has emerged as a critical pathogenic contributor in a number of kidney diseases. Complement activation, which occurs normally is aggravated in kidney disease and ultimately contribute to glomerulosclerosis and tubulo-interstitial fibrosis, leading to loss of renal function. Administration of eculizumab, a complement inhibitor, ameliorates kidney pathology in diseases such as IgA nephropathy and aHUS. With a number of complement inhibitors, antagonists and antibodies in the pipeline, this is an exciting time in identifying the settings where complement therapeutics can help alleviate symptoms and pathology. Our lab studies the role of different complement proteins in immune complex mediated diseases such as lupus and dense deposit disease (DDD). Complement factor H is a critical regulator of the complement pathway. Inherited mutations in CFH can account for DDD, atypical hemolytic uremic syndrome, and age-related macular degeneration. The former can be associated with excessive systemic complement activation from dysfunctional CFH, while the latter two are associated with mutations affecting the ability of CFH to bind to anionic surfaces such as on endothelial cells in the glomerular and retinal capillary walls. Using the serum sickness model in which mice were injected daily with horse spleen apoferritin for 4 weeks, our results revealed that mice with factor H deficiency (CFH−/− mice) displayed greater accumulation of immune complexes within the glomeruli than wild-type mice. In addition, there was reduced glomerular injury in CFH−/−C5aR−/− mice, indicating that signaling by C5a is an important cause of injury. Microarray analysis and exosome analysis revealed increase in macrophages in CFH−/− mice. Interestingly, increased M2 (anti-inflammatory) macrophages in the kidneys of the CFH−/−C5aR−/− mice was observed compared to the kidneys of the CFH−/− mice. Further, for the first time, using a 2D glomerular filtration barrier model, our studies reveal a new role for FH in kidney architecture and function. What these results tell us about human disease will be discussed.

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