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LUPUS NEPHRITIS

NGAL: not just an innocent bystander?

Neutrophil gelatinase-associated lipocalin (NGAL) has shown promise as a biomarker for lupus nephritis. "However, whether NGAL is actually involved mechanistically in antibody-mediated nephritis was not known," states Chaim Putterman of the Albert Einstein College of Medicine, New York. Now, new data from Putterman and collaborators suggest that NGAL does, indeed, have a role in lupus nephritis pathogenesis.

Their data demonstrate that kidney, serum and urine NGAL levels were increased in correlation with disease severity in nephrotoxic nephritis—a mouse model of lupus nephritis. By applying this antibody-dependent nephritis model to NGAL knockout mice, the researchers revealed that NGAL deficiency considerably reduced proteinuria and improved renal histopathology compared with wild-type mice. By contrast, recombinant NGAL exacerbated renal disease and accelerated mortality in wild-type mice with nephritis, in comparison with controls. However, NGAL did not affect renal histology in mice without nephritis.

"We discovered several mechanisms by which NGAL may contribute to nephritis, by activating nuclear factor κB signaling, promoting expression of inflammatory mediators including MCP-1, IP-10, and VCAM-1, and inducing apoptosis in renal resident cells," explains Putterman. "Investigating the role of NGAL in mouse strains susceptible to lupus nephritis will be important for understanding its role in spontaneous disease, and might provide evidence for a new therapeutic target in renal disease associated with systemic lupus erythematosus," he concludes.

David Killock

Original article Pawar, R. D. *et al*. Neutrophil gelatinase-associated lipocalin is instrumental in the pathogenesis of antibody-mediated nephritis. *Arthritis Rheum*. doi:10.1002/art.33485