

 AUTOIMMUNITY

## IL-17C promotes immune-mediated glomerular disease

The IL-17 family of cytokines are produced by T helper 17 (T<sub>H</sub>17) cells and have an important role in organ-specific autoimmunity. As most of the studies of this role to date have focused on IL-17A, the specific functions of the other IL-17 cytokines are less well understood. Now, Ulf Panzer and colleagues report a pathogenic role of IL-17C–IL-17 receptor E (IL-17RE) signalling in immune-mediated glomerular disease.

The researchers found that serum levels of IL-17C, but not of IL-17A, IL-17E or IL-17F, were significantly increased in patients with acute anti-neutrophil cytoplasmic antibody-associated crescentic glomerulonephritis compared with healthy individuals. Expression of IL-17C and its specific receptor IL-17RE were also upregulated in a mouse model of crescentic glomerulonephritis. In this model, deficiency of IL-17C or IL-17RE had a protective effect, resulting in a reduction in glomerular crescent formation and tubulointerstitial injury as well as less severe kidney dysfunction compared with wild-type mice. Similarly, IL-17C deficiency

reduced disease severity in a mouse model of lupus nephritis.

“Mechanistically, we provide evidence that the IL-17C–IL-17RE axis directly stimulates the nephritogenic T<sub>H</sub>17 cell response and thereby promotes renal tissue injury in crescentic glomerulonephritis,” says Panzer. “Based on our finding that IL-17C stimulates the T<sub>H</sub>17 cell response upstream of IL-17A, targeting of the IL-17C–IL-17RE pathway may present an intriguing therapeutic strategy for T<sub>H</sub>17-driven autoimmune and inflammatory diseases.”

The researchers are now investigating the therapeutic potential of a neutralizing IL-17C antibody in crescentic glomerulonephritis.

*Ellen F. Carney*

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**ORIGINAL ARTICLE** Krohn, S. et al. IL-17C/IL-17 receptor E signaling in CD4<sup>+</sup> T cells promotes T<sub>H</sub>17 cell-driven glomerular inflammation. *J. Am. Soc. Nephrol.* <https://doi.org/10.1681/ASN.2017090949> (2018)

**FURTHER READING** Krebs, C. F. et al. T helper type 17 cells in immune-mediated glomerular disease. *Nat. Rev. Nephrol.* **13**, 647–659 (2017)