Nature Reviews Nephrology | Published online 13 Mar 2017; doi:10.1038/nrneph.2017.38

LUPUS NEPHRITIS

T-bet$^+$ B cells mediate renal injury in lupus

> T-bet$^+$ B cells represent the pathogenic subset

B cells have an important role in autoimmune diseases, including systemic lupus erythematosus (SLE). Thus, targeting pathogenic autoreactive subsets of B cells is a promising therapeutic strategy. New research by Kira Rubtsova and colleagues shows that T-bet$^+$ B cells promote rapid autoantibody secretion, have a critical role in the development of renal damage, and accelerate mortality in mouse models of SLE and lupus nephritis. "These data suggest that T-bet$^+$ B cells represent the pathogenic subset, which indicates that they can serve as a novel therapeutic target for patients with SLE," explains Rubtsova.

The researchers previously identified accumulations of CD11c$^+$T-bet$^+$ B cells in aged female mice, and in mice and patients with autoimmune diseases. To explore the contribution of this subset of B cells to SLE and lupus nephritis, they specifically deleted T-bet in B cells in three mouse models of SLE, including the SLE1,2,3 model, which develops renal damage. In these mice, T-bet ablation prevented the formation of spontaneous germinal centres, mitigated renal damage (as evidenced by an absence of proteinuria and reductions in glomerular damage and IgG–C3 complex deposition), reduced total autoantibody titres in the long-term (~1 year) and improved survival. B-cell specific deletion of T-bet also decreased B-cell and T-cell activation in the SLE mice.

Rubtsova and co-workers now plan to develop a depleting drug to specifically target T-bet$^+$ B cells. "Such a drug will have a tremendous advantage for patients with autoimmune diseases, as it will not lead to global immune suppression, as current therapies often do, but will specifically target the pathogenic cells," says Rubtsova.

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ORIGINAL ARTICLE Rubtsova, K. *et al.* B cells expressing the transcription factor T-bet drive lupus-like autoimmunity. *J. Clin. Invest.* http://dx.doi.org/10.1172/JCI91250 (2017)

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