Nature Reviews Rheumatology | Published online 24 Mar 2016; doi:10.1038/nrrheum.2016.43

SYSTEMIC LUPUS ERYTHEMATOSUS

Compromised pDC–B_{REG} cell crosstalk

A new study published in *Immunity* implicates aberrant crosstalk between plasmacytoid dendritic cells (pDCs) and $CD24^{+}CD38^{hi}$ regulatory B (B_{REG}) cells in the pathogenesis of systemic lupus erythematosus (SLE).

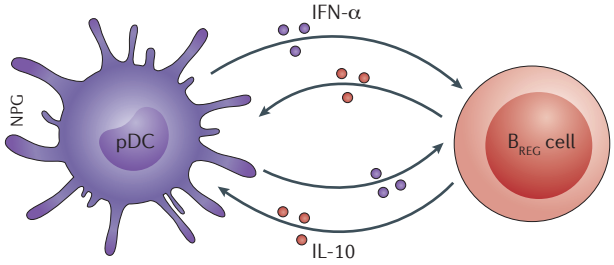
Previous work had shown a reduced frequency and function of immunosuppressive IL-10-producing B_{REG} cells in patients with SLE, but the signals required for the differentiation of B_{REG} cells were unknown. Claudia Mauri and colleagues have shown for the first time in healthy human cells that IFN-α produced by pDCs induces the *in vitro* differentiation of B_{REG} cells, which in turn negatively regulate pDC activity through IL-10.

The authors sought to determine whether this bidirectional crosstalk is aberrant in SLE. Co-culture experiments showed that pDCs from patients with SLE were significantly inferior to those from healthy individuals in inducing the expansion of healthy IL-10^{+} B_{REG} cells. On the basis of their experiments implicating IFN-α in pDC–B_{REG} cell crosstalk and the established association between elevated type I IFN signalling and SLE, Mauri and colleagues proposed that excessively high levels of IFN-α production by dysregulated pDCs could underlie the reduced induction of IL-10^{+} B_{REG} cells in SLE. Indeed, exposing healthy B cells to high concentrations of IFN-α reduced IL-10 production to levels similar to those produced by B cells from patients with SLE.

The authors showed that in addition to defective communication from pDCs to B_{REG} cells, reciprocal communication was impaired in SLE: healthy B_{REG} cells, but not those from patients with SLE, were able to suppress IFN-α production by healthy pDCs. The authors hypothesize that aberrant pDC–B_{REG} cell crosstalk creates a "vicious cycle that contributes to the pathogenesis of disease".

Notably, the function of pDCs and B_{REG} cells from patients with SLE who had a clinical response to rituximab — but not cells from non-responders — was comparable to that of healthy cells, which further implicates pDC–B_{REG} cell crosstalk in the pathogenesis of SLE and suggests that normalization of this crosstalk could be part of the therapeutic mechanism of rituximab. The authors suggest targeting pDC–B_{REG} cell crosstalk as a potential therapeutic approach. "Our future work will focus on harnessing the suppressive capacity of B_{REG} cells to treat autoimmune diseases," explained Madhvi Menon, the first author of the paper.

Lydia Shipman



ORIGINAL ARTICLE Menon, M. *et al.* A regulatory feedback between plasmacytoid dendritic cells and regulatory B cells is aberrant in systemic lupus erythematosus. *Immunity* 44, 683–697 (2016)