IMMUNOLOGY

Tying up the link between TNF and regulatory T cells

In vitro studies of the relationship between tumor necrosis factor (TNF) and regulatory T (T_{REG}) cells have produced contrasting results to date. Now, an *in vivo* mouse study published in *The Journal of Immunology* provides further insight into the potential link between these two key elements of the inflammatory response.

Biton *et al.* chose TNF-transgenic (hTNF-αTg) mice as a TNF-driven model of arthritis in which to study the development of T_{REG} cells and also the effects of TNF blockade on these cells. First, they confirmed that hTNF-αTg mice develop arthritis from 8 weeks of age, and that this disease worsens as the mice age. Analysis of the number of T_{REG} cells in these mice showed that after an initial reduction in comparison to wild-type mice at 7 weeks, the frequency of T_{REG} cells increased to higher levels than seen in the wild-type mice at 24 weeks. The authors conclude that although numbers of T_{REG} cells do recover in hTNF-αTg mice, once arthritis is established these cells are unable to control the inflammation.

Next, the authors used two approaches to block TNF: the anti-TNF antibody infliximab and also a TNF-kinoid, which actively induces expression of anti-TNF antibodies. Either treatment resulted in reduced severity of arthritis and also in increased numbers of T_{REG} cells in comparison to no treatment. In addition, the T_{REG} cells in the treated mice expressed higher levels of CTLA-4 than these cells in untreated mice, and a higher proportion of them was negative for CD62L, findings which suggest that TNF blockade has enhanced the suppressive capacity of the T_{REG} cells in this mouse model.

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Original article Biton, J. *et al.* Interplay between TNF and regulatory T cells in a TNF-driven murine model of arthritis. *J. Immunol.* doi:10.4049/jimmunol.1003372