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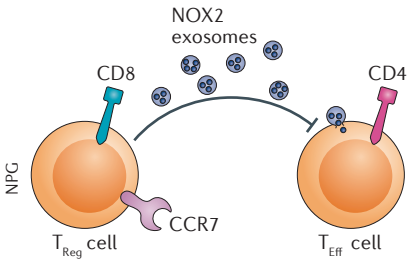
VASCULITIS SYNDROMES

Dysfunctional CD8 T_{REG} cells implicated in GCA

> the manipulation of NOX2 and CD8 T_{REG} cells [could be] an attractive future therapeutic target

A new study proposes a role for CD8 T_{REG} cells in the pathogenesis of giant cell arteritis (GCA). A team of researchers led by Cornelia Weyand at Stanford University have discovered a novel mechanism by which CD8 T_{REG} cells are able to suppress the proliferation of CD4 T cells. By releasing exosomes containing NADPH oxidase 2 (NOX2), CD8 T_{REG} cells dampen and halt the immune processes involved in chronic inflammation and autoimmune diseases. "The effect begins after minutes of cell–cell contact, but has long-lasting impact and suppresses the expansion of CD4 T cells," says Weyand.



Vital immune functions associated with T_{REG} cells are progressively lost with age, leading Weyand and colleagues to hypothesize that the increased risk of infection and bias towards inflammation that occurs in the immune system of older people is associated with a loss of T_{REG} cells. In the study, Weyand explains, "We first defined ageing-related changes in healthy individuals and found that the frequency of CD8 T_{REG} cells declines progressively with age." The team also discovered that CD8 T_{REG} cells from older individuals are deficient in NOX2, which impairs their suppressive capacity.

In order to assess the relevance of CD8 T_{REG} cell-mediated suppression in autoimmunity, the researchers investigated the frequency of CD8 T_{REG} cells in patients with psoriatic arthritis (PsA), small-vessel vasculitis (SVV) or GCA. They found that numbers of CD8 T_{REG} cells were age-appropriate in patients with PsA and SVV. However, this was not the case for patients with GCA, regardless of whether or not they were undergoing therapy with steroids. "Patients with GCA lack CD8 T_{REG} cells", says Weyand, "depriving them of the protective anti-inflammatory action of such cells."

Induced overexpression of NOX2 in CD8 T_{REG} cells from older individuals was able to rescue the suppressor function of these cells both *in vitro* and *in vivo*, making the manipulation of NOX2 and CD8 T_{REG} cells an attractive future therapeutic target, something that Weyand and colleagues are looking to investigate further. "Our ongoing work is focussed on rebuilding these CD8 T_{REG} cells in patients with GCA as well as in older healthy individuals," she concludes.

Joanna Collison

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