EXPERIMENTAL ARTHRITIS

Stability of T_{REG} cells induced *ex vivo* boosts prospects for cellular therapies

“Plasticity associated with so-called ‘natural’ T_{REG} cells may preclude their therapeutic use,” says Song Guo Zheng, explaining that regulatory T (T_{REG}) cells have a tendency to switch to type 17 T helper (T_H17) cell programming in inflammatory milieu. “We were much more successful in suppressing disease when we generated induced T_{REG}s from conventional CD4⁺ T cells,” adds Zheng.

T_{REG} cells, which express the key marker Foxp3, have a role in suppressing inflammation and might form a future cell-based therapy for rheumatic disease. Natural T_{REG} (nT_{REG}) cells can suppress the induction of experimental arthritis, but are not effective in established disease. Another problem is that, *in vitro*, proinflammatory cytokines convert nT_{REG} cells to T_H17 cells, which would potentially exacerbate, rather than attenuate, arthritis.

In a study now published in *Arthritis & Rheumatism*, Zheng and colleagues used the collagen-induced arthritis mouse

model of rheumatoid arthritis to compare antigen-specific thymus-derived nT_{REG} cells with iT_{REG} cells (induced *ex vivo* using TGF-β). In contrast to nT_{REG} cells, iT_{REG} cells resisted conversion to T_H17 cells and remained fully functional after transfer into the mice. iT_{REG} cells were also superior to nT_{REG} cells in ameliorating established arthritis.

Practically, iT_{REG} cells are easier to obtain in sufficient numbers than nT_{REG} cells, but much remains to be done before they could be used clinically. “A complicated problem,” according to Zheng, is how much T_H17 conversion occurs *in vivo*, which, he says, “will require a significant effort to find answers.”

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Original article Kong, N. *et al.* Antigen-specific TGF-β-induced regulatory T cells but not natural T_{REG}s ameliorate autoimmune arthritis by shifting the balance of T_H17 toward T_{REG} cells. *Arthritis Rheum.* doi:10.1002/art.34513