Adoptive transfer of IL-10 producing regulatory Tr1 lymphocytes inhibits chronic arthritis

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IL-10 producing regulatory Tr1 cells has been characterized as induced T regulatory lymphocytes inhibiting inflammation in various chronic inflammatory models. Based on these data, a clinical trial is ongoing in Crohn's Disease. However, the therapeutic potential of these cells has not been evaluated in Rheumatoid Arthritis.
Tr1 clones specific for Collagen II were obtained from TCR transgenic mice and expanded in vitro. Clones were screened based on Tr1 like cytokines secretion profile and in vitro suppressive activity on bystander T-cell proliferation. Tr1 clones were administrated to DBA-1 mice immunized twice with collagen II and developing a chronic arthritis.
Selected clones showed in vitro antigen specificity, Tr1 cytokine profile ($IL10^{high}/IL4^{neg}$) and IL10- and TGFβ-dependent suppressive activity. In contrast to nTreg, Tr1 cells expressed regulatory markers (CD25, Foxp3) only after activation. Collagen-specific Tr1 cell transfer prevents arthritis development by inhibiting both collagen-specific IgG2a production and Th17 cell expansion in vivo. Importantly, adoptive transfer of collagen II specific Tr1 cells after the onset of the disease also inhibits incidence and severity. Based on these results, a production process of human collagen II-specific Tr1 cells was set-up from the blood of Rheumatoid Arthritis patients giving rise to potent suppressive IL-10 producing Tr1 cells.
Tr1 cell adoptive transfer showed a reduction of disease incidence and severity in chronic arthritis in mice. These data and the feasibility of arthritic patient's derived Tr1 cell production set the stage for further clinical development of collagen II specific Tr1 cells in joint diseases.

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