Single dose of antigen-specific regulatory Tr1 lymphocytes can prevent acute and chronic arthritis

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Introduction:
Tr1 cells have been characterized as induced T regulatory lymphocytes inhibiting inflammation in various chronic inflammatory models. Based on these data, a clinical trial is ongoing in inflammatory bowel disease. However, the therapeutic potential of these cells has not been yet evaluated in rheumatoid arthritis.

Methods:
Collagen type II specific Tr1 clones were obtained from TCR transgenic mice and expanded in vitro. Clones were screened based on cytokines profile and in vitro immuno-suppressive activity. DBA-1 mice were used for both acute and chronic arthritis models.
Acute arthritis model used anti-collagen antibodies. For chronic arthritis, mice were immunized at day 0 and 21 with bovine collagen.
Hind paw swelling and clinical signs of arthritis were evaluated for acute and chronic arthritis as described in the literature.

Results:
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.
In both acute and chronic arthritis, Tr1 clones administered once, as semi-preventive treatment, significantly inhibit the development of arthritic disease, shown by reduction of disease severity and incidence. We also observed a dose-dependent efficacy of this Tr1 cell therapy. More importantly, preliminary data indicate that administration of Tr1 clones after the disease onset could also reduce disease severity and incidence in chronic arthritis.

Conclusions:
Single dose of Tr1 cell administration showed a reduction of disease incidence and severity in both acute and chronic arthritis confirming the clinical potential of these induced T regulatory lymphocytes.

Keywords:
Regulatory T cells / Arthritis / Cell therapy