INJECTION OF ANTIGEN-SPECIFIC REGULATORY TR1 LYMPHOCYTES PROTECTS MICE FROM SEVERE COLLAGEN-INDUCED ARTHRITIS

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Introduction Tr1 cells have been characterised as induced T regulatory lymphocytes (Treg) inhibiting inflammation in various chronic inflammatory models. Based on these data, a phase I/II clinical trial is currently under investigation in Crohn’s disease (TxCell). However, the therapeutic potential of these cells has not yet been evaluated in rheumatoid arthritis. In this study, the authors investigated the therapeutic potential of bovine type II collagen (bCII) specific Tr1 cells, isolated from TBC mice, in the experimental model of collagen-induced arthritis (CIA).

Methods Collagen type II specific Tr1 clones were obtained from T cell receptor transgenic mice and expanded in vitro. Selected clones showed in vitro antigen specificity, Tr1 cytokine profile (IL-10 high/IL-4 neg) and IL-10- and transforming growth factor β-dependent suppressive activity. Male DBA/one mice were immunised with bCII and 10×10⁶, 3×10⁶, 1×10⁶, 0.3×10⁶ of Tr1 cells were injected (intravenously) 28 days postimmunisation. Hind paws swelling and clinical signs of arthritis were scored, as well as biological parameters such as the level of anti-bCII antibodies in the sera of treated mice and the cytokine profile of bCII specific T cells.

Results One single injection of 3×10⁶ or 1×10⁶ of Tr1 cells at day 28, in ongoing arthritis, significantly inhibits the development of arthritic disease, shown by reduction of disease severity and incidence. In contrast the injection of 0.3×10⁶ and 10 M of Tr1 cells did not improve the clinical signs of arthritis. The analysis of the bCII specific T cell responses following euthanasia of the mice injected with 3×10⁶ and 1×10⁶ of Tr1 cells revealed a decrease of anti-bCII specific antibodies in the sera, a decrease of proliferation of bCII specific T cells and a slight increase of IL-10 secreted by activated splenocytes. Importantly, these preliminary data indicate that a single injection of Tr1 cells at disease onset could reduce disease severity and incidence in experimental arthritis.

Conclusions Single dose 3×10⁶, 1×10⁶ of Tr1 cell administration showed a reduction of disease incidence and severity in CIA demonstrating the therapeutic potential of Tr1 cells in arthritis and confirming the clinical potential of these induced Treg.