38 IMMUNOSUPPRESSIVE DX5+ T CELLS ARE POTENT INHIBITORS OF TH-1 RESPONSES VIA MODULATION OF DCS

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Background and objectives DX5+CD4+ T cells have been shown to have both a protective- and therapeutic effect on collagen-induced arthritis. This protective effect was associated with an increase in IL-10 production. To understand the mechanisms used by DX5+ T cells to dampen Th1-associated inflammation in CIA, the authors recently studied their immunomodulatory action on CD4+ T cells. These studies revealed that these cells are very effective in modulating Th1-cell responses through direct effects on CD4+ T cells by

production of IL-4. In the presence of DX5+ T cells, IFNγ production was inhibited whereas IL-10 secretion was induced in responding CD4+ T cells. To further define additional mechanisms applied by DX5+ T cells to inhibit Th1-immunity, the authors studied the effects of DX5+ T cells on DC function.

Materials and methods D011.10 (OVA specific TCR Tg) mice were used for the generation of bone marrow DCs (BMDCs) and for the isolation of CD4+ T cells.

BMDCs were cultured with DX5+ or DX5- supernatants for 3 days. LPS was added after 1 day of incubation. The DCs obtained were cultured at 0.4×10^6/ml with OVA323–339 peptide and OVA specific CD4+ T at 1×10^6/ml in total volume of 150 µl for 3 days. At day 3, the secretion of cytokines was determined by flow cytometry.

12p70 levels in BMDCs cell culture supernatants were measured by ELISA.

Results The authors demonstrate that DX5+ T cells can also indirectly inhibit Th1 responses through modulation of DC. DX5+ T cells robustly inhibit IL-12-production by DC. This effect was dependent on IL-10 produced by DX5+ T cells and does not require cell-cell contact. In addition, DX5+ T cells modulate the surface phenotype of LPS-matured DC as high levels of the "co-inhibitory" molecules PD-L1 and PD-L2 were induced. Importantly, OVA-specific CD4+ T cells primed by DC exposed to DX5+ T cell supernatant produced less IFNγ as compared to their counterparts primed by conventional DC. Addition of IL-12 restored IFNγ production. When IL-10 derived form DX5+ T cells was neutralised, DC re-established their ability to produce IL12 and to efficiently prime Th1 responses.

Conclusion These data show that DX5+ T cells cannot only directly inhibit Th1-cell immunity, but also indirectly through the modulation of DC.