Blocking of p38 and transforming growth factor ? receptor pathways impairs the ability of tolerogenic dendritic cells to suppress murine arthritis

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Objective Dendritic cells (DCs) modulated with lipopolysaccharide (LPS) are able to reduce inflammation when therapeutically administered into mice with collagen-induced arthritis (CIA). The aim of this study was to uncover the mechanisms that define the tolerogenic effect of short-term LPS-modulated DCs on CIA. Methods Bone marrow-derived DCs were stimulated for 4 hours with LPS and characterized for their expression of maturation markers and their cytokine secretion profiles. Stimulated cells were treated with SB203580 or SB431542 to inhibit the p38 or transforming growth factor ? (TGF?) receptor pathway, respectively, or were left unmodified and, on day 35 after CIA induction, were used to inoculate mice. Disease severity was evaluated clinically. CD4+ T cell populations were counted in the spleen and lymph nodes from inoculated or untreated mice with CIA. CD4+ splenic T cells were transferred from mice with CIA treated with LPS-stimulated DCs or from untreated mice with CIA into ot