



POSTER PRESENTATION

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# Interaction with activated monocytes enhances cytokine expression and suppressive activity of human CD4<sup>+</sup>CD45RO<sup>+</sup>CD25<sup>+</sup>CD127<sup>low</sup> regulatory T cells

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## Introduction

Despite the high frequency of CD4<sup>+</sup> T cells with a regulatory phenotype (CD25<sup>+</sup>CD127<sup>low</sup>FoxP3<sup>+</sup>) in the joints of patients with rheumatoid arthritis (RA), inflammation persists. Regulatory T cells (Tregs) can be converted into pro-inflammatory IL-17-producing cells by inflammatory mediators, particularly IL-1 $\beta$ .

## Aim

To investigate whether activated monocytes, which are abundantly present in the rheumatic joint and potent producers of IL-1 $\beta$ , induce pro-inflammatory cytokine expression in Tregs and whether this impairs Treg function.

## Materials and methods

The presence and phenotype of CD4<sup>+</sup>CD45RO<sup>+</sup>CD25<sup>+</sup>CD127<sup>low</sup> T cells (memory Tregs) and CD14<sup>+</sup> monocytes in the peripheral blood (PB) and synovial fluid (SF) from patients with RA was investigated by flow cytometry. FACS-sorted memory Tregs from healthy controls were co-cultured with autologous *in vitro*-activated monocytes and anti-CD3 monoclonal antibody. Intracellular cytokine expression, phenotype and function were determined by flow cytometry, ELISA and proliferation assays.

## Results

Patients with RA showed higher frequencies of CD4<sup>+</sup>CD45RO<sup>+</sup>CD25<sup>+</sup>CD127<sup>low</sup> Tregs and activated CD14<sup>+</sup> monocytes in SF relative to PB. We demonstrate that activated monocytes induced an increase in the percentage of IL-17<sup>+</sup>, IFN $\gamma$ <sup>+</sup> and TNF- $\alpha$ <sup>+</sup>, but also IL-10<sup>+</sup> Tregs. Blocking and reconstitution experiments revealed that the observed increase in IL-17<sup>+</sup> and IFN $\gamma$ <sup>+</sup> Tregs was driven by monocyte-derived IL-1 $\beta$ , IL-6 and TNF- $\alpha$  and was mediated by both CD14<sup>+</sup>CD16<sup>-</sup> and CD14<sup>+</sup>CD16<sup>+</sup> monocyte subsets. Despite enhanced cytokine expression, cells maintained their CD25<sup>+</sup>FoxP3<sup>+</sup>CD39<sup>+</sup> Treg phenotype and showed enhanced capacity to suppress proliferation and IL-17 production by effector T cells.

## Conclusion

Tregs exposed to a pro-inflammatory environment show increased suppressive activity.

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