sorting. Supernatants from cultures of these cells were then tested for their capacity to suppress proliferation of freshly purified T cells. Approval for this study was obtained from the Local Ethics Review Committee.

Results IL-10-secreting T cells are derived from populations of differentiating Th1 effector T cells as they also secrete IFN γ . The authors observed that the cytokine expression profile of CD3/CD46-activated T cells is heavily influenced by the amount of IL-2 present during activation. Thus, in the presence of low IL-2, CD3/CD46-activation induces strong IFN γ -secretion and a proinflammatory effector phenotype. High IL-2 induces a 'switch' from IFN γ^+ T cells, via an IFN γ^+ /IL-10 $^+$ state, to an IL-10 $^+$ phenotype. CD46-induced IFN γ^+ /IL-10 $^+$ and IL-10 $^+$ cells are suppressive. By contrast, analysis of T cell populations from patients with inflammatory arthritis such as RA and JIA reveals that progression to the IL-10 $^+$ state is blocked even in the presence of high exogenous IL-2. In addition, CD3/CD46-activated T cells produce 20–30 times more IFN- γ than IL-10.

Conclusions CD46 activation during T cell response initiation supports IFN γ secretion to combat infection while expansion of the effector response provides high IL-2 and the signal to switch to IL-10 production and resolution of the immune response. This regulatory switch appears to be defective in chronic inflammatory disease.

A112 CD3/CD46-MEDIATED GENERATION OF IL-10-SECRETING T CELLS IS DEFECTIVE IN RHEUMATOID ARTHRITIS

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Background and objectives Control of effector T cell responses to foreign and self-antigens through interleukin (IL)-10-producing Th1 cells and adaptive IL-10 $^+$ Tregs is vital for limiting immune pathology during infection and for preventing autoimmunity. However, the mechanisms that regulate their production remain incompletely understood. CD46 is the receptor for the C3b/C4b components of complement. The authors have previously demonstrated that activation of human CD4 T cells through the T-cell receptor and the complement regulator CD46 induces Tr1 like IL-10-producing Tregs. The authors set out to study factors that regulate the generation of IL-10 producing Tregs during normal immune homeostasis and to determine whether this pathway is defective in chronic inflammatory disease, such as rheumatoid arthritis.

Materials and methods CD4 T lymphocytes were purified from PBMC of normal donors or PBMC and synovial fluid of rheumatoid arthritis (RA) and JIA patients using CD4 MicroBeads prior to activation with anti-CD3 and anti-CD46 mAb in the presence or absence of increasing concentrations of IL-2. After 36 h cytokine production was determined using the Th1/Th2 cytokine bead array. Cells were stained using the IFN γ and IL-10 cytokine secretion assay kits in combination and IFN γ^+ , IFN γ^+ /IL-10 $^+$ and IL-10 $^+$ cells isolated via cell