expansion of induced Treg cells defined by the CD4+ CD25+ FoxP3+ CD62L− phenotype.

Conclusion In this study, in a strictly hTNF dependent inflammation model, the authors show for the first time that TNF can have different effects on Treg, depending on the duration of exposure and on disease phase. The work also shows that TNF blockade either by TNF-K or infliximab could depend not only on TNF neutralisation but also on Treg upregulation.

A99 DIFFERENTIATION AND ACTIVATION OF REGULATORY T LYMPHOCYTES IN A TNF TRANSGENIC MODEL OF ARTHRITIS, AND THE IMPACT OF PASSIVE OR ACTIVE ANTI-TNF THERAPIES

J Biton,[1] L Semerano,[1,2] L Delavallee,[1] D Lemeiter,[1] M Laborie,[3] G Grouard-Vogel,[3] M-C Boissier,[1,2] N Bessis[1] *[1]EA4222, Li2P, Paris 13 University, Bobigny, France; [2]Rheumatology Department, Hôpital Avicenne, Assistance Publique-Hôpitaux de Paris (AP-HP), Bobigny, France; [3]Neovacs SA, Paris, France*

10.1136/ard.2010.148981.2

Background and objectives Tumour necrosis factor **(**TNF) is a critical cytokine in rheumatoid arthritis. The authors recently demonstrated the efficacy of active immunotherapy against TNF (TNF-K) in a human TNF transgenic (TTg) mouse model of arthritis. Studies with anti-TNF treatments in autoimmune diseases suggest that TNF and TNF antagonists might act through the involvement of a T cells subset, namely CD4+ CD25+ FoxP3+ regulatory T cells (Treg). In the present study, the authors aimed to better characterise the impact on the Treg population of (1) a TNF driven disease, specifically arthritis in TTg mice and (2) active or passive anti-TNF immunotherapy in this same model.

Methods First, untreated TTg mice were euthanised sequentially at the age of 7 weeks, 12 weeks, 17 weeks and 24 weeks. Subsequently, three groups of mice were used: TTg mice given three doses of TNF-K at 15, 16 and 19 weeks of age, TTg mice treated with infliximab and untreated TTg mice. Then in each group, mice were euthanised at 31 weeks. After each euthanasia, the frequency of Treg and the percentage of Treg cells expressing CTLA-4, TNFR2 and CD62L from the spleen and lymph nodes (LN) were determined. Finally, the immunosuppressive activity of the Treg cells was studied.

Results hTNF overexpression induced an initial decline in Treg. Then, once chronic inflammation was established, the frequency of Treg cells increased with time. The authors also observed a progressive and dramatic increase in TNFR2 expression (65.8–88.6% at weeks 7 and 24, respectively, p<0,0001) and MFI on Treg from LN during the course of arthritis. Compared to untreated mice, hTNF blockade with either infliximab or TNF-K resulted in an increased Treg frequency. The study also showed that hTNF blockade induces an upregulation of CTLA-4 expression by Treg cells in LN, accompanied by an increased Treg suppressive activity on CD4+ CD25− effector T cell proliferation. Finally, in LN of infliximab and TNF-K treated TTg mice, the authors observed an