1-1-2007

Su.32. Myelin-specific Regulatory T Cells Accumulate in the Central Nervous System, but Fail to Suppress Pathogenic Effector T Cells at the Peak of Autoimmune Inflammation [abstract only]

Thomas Korn
Harvard Medical School

Mohamed Oukka
Harvard Medical School

Jay Reddy
University of Nebraska - Lincoln, jayreddy@unl.edu

Estelle Betelli
Harvard Medical School

Amit Awasthi
Harvard Medical School

next page for additional authors

Authors
Thomas Korn, Mohamed Oukka, Jay Reddy, Estelle Betelli, Amit Awasthi, Raymond Sobel, Kai Wucherpfennig, and Vijay K. Kuchroo

Published in *Clinical Immunology* (2007) Supplement, 123: S152-S153. DOI: 10.1016/j.clim.2007.03.073.

FOCIS 2007 – 7th Annual Meeting, San Diego, California, June 7-11, 2007
Federation of Clinical Immunology Societies

Poster Session Abstracts
Sunday, June 10
Autoimmune Neurologic Diseases

Su.32. Myelin-specific Regulatory T Cells Accumulate in the Central Nervous System, but Fail to Suppress Pathogenic Effector T Cells at the Peak of Autoimmune Inflammation

Thomas Korn, Mohamed Oukka, Jay Reddy[a], Estelle Bettelli, Amit Awasthi, Raymond Sobel[b], Kai Wucherpfennig[c], Vijay Kuchroo

Center for Neurologic Diseases, Harvard Medical School, Boston, Massachusetts, USA
[a]Affiliation 2012: University of Nebraska-Lincoln, Lincoln, Nebraska, USA
[b]Department of Pathology, Stanford University, Stanford, California, USA
[c]Department of Cancer Immunology and AIDS, Dana Farber Cancer Institute, Harvard Medical School, Boston, Massachusetts, USA

Treatment with ex vivo generated regulatory T cells (Treg) has been regarded as highly attractive therapeutic approach for autoimmune diseases. However, the dynamics and function of T-reg in autoimmunity are not well understood. Thus, we developed Foxp3gfp "knock-in" mice and myelin oligodendrocyte glycoprotein (MOG)35–55/IAb tetramers to track autoantigen-specific effector T cells (T-eff) and T-reg in vivo during experimental autoimmune encephalomyelitis, an animal model for multiple sclerosis. Following immunization with the encephalitogenic peptide MOG35–55 emulsified in complete Freund's adjuvant, MOG35–55-tetramer-reactive, Foxp3+ T-reg expanded in the peripheral lymphoid compartment and readily accumulated in the central nervous system (CNS), but did not prevent the onset of disease. During disease onset, the MOG-tetramer+ T-eff population in the CNS increased faster than the population of antigen-specific T-reg. At the peak of disease, the ratio of T-reg vs. T-eff was 1:17 which dramatically changed into 1:2 at the beginning of recovery. Foxp3+ T-reg isolated from the CNS were fully competent in suppressing naive MOG-specific T cells. However, Foxp3+ T-reg failed to control encephalitogenic T-eff which in contrast to T-eff from the peripheral immune compartment, secreted

IL-6 and TNF when they were isolated from the CNS at the peak of disease. Our data suggest that in the face of inflammation, the regulation of autoimmunity by CD4+Foxp3+ T-reg in situ may not be accomplished simply by changing the numerical balance of antigen-specific pathogenic vs. regulatory T cells, but may require the control of tissue inflammation as well.