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

See next page for additional authors

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.