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OR.76. Myelin Specific Regulatory T-Cells Expand from Naturally Occurring Regulatory T-Cells and Accumulate in the CNS during EAE [abstract only]

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Oral presentations

#3202-Controlling Inflammatory Reactions
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10:30 a.m.-12:30 p.m.

OR.76. Myelin Specific Regulatory T-Cells Expand from Naturally Occurring Regulatory T-Cells and Accumulate in the CNS during EAE

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FoxP3 is a lineage specific marker for regulatory T-cells (Treg). We have generated FoxP3 knock-in (KI) mice by introducing a bicistronic GFP reporter into the endogenous FoxP3 locus, allowing us to faithfully track T-reg in vivo. Recently, we have also generated a MOG 35-55/IAb-tetramer. The combination of these two technologies enables us to study the in vivo behavior of myelin specific T-reg and effector T-cells (T-eff) during EAE. Upon immunization with MOG 35-55, we identified a population of MOG-tetramer-reactive T-reg in the peripheral lymphoid compartment. T-reg trafficked to the CNS where they were readily detected as early as day 10 following immunization. At this stage and till the peak of the disease, an overwhelming number of T-eff also targeted the CNS. Thus, the ratio of T-reg and T-eff at the initiation of disease was 1:15. However at the onset of recovery, this ratio changed in favor of T-reg (T-reg/T-eff close to 1:1). As shown by MOG-tetramer staining, myelin specific T-cells accumulated in significant numbers only in the CNS, but

not in the spleen. At the peak of disease, about 9% of the CNS-derived CD4+ T-cells were MOG-specific T-eff and 0.5% were MOG-specific T-reg. At that time, about 30% of all T-reg in the CNS produced IL-10. During recovery, even 50% of the CNS-derived T-reg were IL-10 producers compared to only 10% in the peripheral immune compartment. Finally, we found that MOG-specific T-reg were not recently converted, but derived from the pool of naturally occurring T-reg since the transfer of GFP-(FoxP3 KI) T-cells into congenic recipients followed by immunization with MOG 35-55 did not result in the appearance of GFP+ T-cells. We conclude that MOG-specific T-reg are expanded from naturally occurring T-reg and migrate to the CNS during EAE where they constitute a pool of long-lived regulatory T-cells.