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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]

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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

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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 Foxp3\textsuperscript{gfp} “knock-in” mice and myelin oligodendrocyte glycoprotein (MOG)\textsuperscript{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 MOG\textsuperscript{35–55} emulsified in complete Freund’s adjuvant, MOG\textsuperscript{35–55}-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.