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Understanding T regulatory cell development in the thymus using both in vivo and in vitro models

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Multiple sclerosis (MS) is an autoimmune disease caused by autoreactive T cells attacking myelin sheath proteins in nerve fibers of the central nervous system resulting in paralysis and death. Conventional T cells (cytolytic and helper) initiate disease in MS, and T regulatory cells (Tregs) are conventional T cell suppressors. By studying the development of Tregs, a T cell suppressor, we can stop T cells from attacking myelin sheath proteins and prevent disease progression. All T cells develop in the thymus in three stages: double negative, double positive, and single positive. In the stage of my research's interest, the double positive stage, the T cell undergoes two educational phases, positive and negative selection. In positive selection, an antigen presenting cell (APC) presents a peptide to the T cell's T cell receptor (TCR). If the interaction between the peptide on the APC and TCR has a low affinity, then the T cell survives. However, if the affinity between the peptide and the TCR is high, the T cell dies via apoptosis. We hypothesize that Tregs require a strong affinity between the peptide and TCR to continue to the next educational phase. Interestingly, exposure high affinity peptides resulted in a decrease in Treg apoptosis both in vitro and in vivo. This observation is opposite to conventional T cell selection. We want to determine the ability of medium affinity peptide, PLP-Y, to prevent Treg apoptosis in vitro because ex vivo analysis shows PLP-Y does prevent Treg apoptosis in the thymus. Our results from in vitro experiments, however, did not show prevention of Treg death. Thus, it is likely more peptide is needed to provide the signal strength necessary for prevention of Treg death. Since many autoimmune diseases arise from poor Treg development, a better knowledge of the selection process may lead to potential therapies.