Modeling dynamical T-cell cross-regulation in a mouse model of multiple sclerosis

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The autoimmune disease known as Multiple Sclerosis (MS) is characterized by a degeneration of the myelin sheath of neurons in the central nervous system. The basis of autoimmunity in MS is still unclear, but different possible mechanisms for this pathology have been proposed, including the existence of an imbalance of effector (T_{eff}) and regulatory (T_{reg}) CD4 T cells. Naive T cells are in a quiescent state and become activated by antigens, and subsequently migrate to the infection site. At same time this activity is downregulated by T_{reg} cells. The main goal of this work was to test experimentally a recent theoretical model of T_{eff} ant T_{reg} cell population dynamics proposed for humans[1] to experimental data in an animal model of MS in mice (induced experimental autoimmune encephalomyelitis, EAE). T cells were extracted from spleen tissue (blood filter) and specific T cells for EAE (MOG-specific T cells) were counted by flow cytometry, measuring cell size populations for several days, which allowed us to obtain activation kinetics. We use a predator-prey-like model to describe the interactions between four cell populations (active and resting effector and regulatory cells), supplied by stochastic pulsed inputs representing naïve T cells. Results show that the experimentally monitored active T_{eff} and T_{reg} cell populations qualitatively agree with the model, showing irregular and coordinated spikes in the form of a remitting-relapsing dynamics typical of autoimmune diseases. This model should help us improve our understanding of cell population dynamics in the immune system.

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[1] N. de Mendizábal et al., 'Modeling the effector-regulatory T cell cross-regulation reveals the intrinsic character of relapses in Multiple Sclerosis', BMC Systems Biology **5**, 114 (2011).