CD200 Regulation can Promote Recovery from Autoimmunity in Experimental Autoimmune Encephalomyelitis

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Abstract

Experimental Autoimmune Encephalomyelitis (EAE) is a prototype disease used for the study of multiple sclerosis (MS) in humans. Recent evidence suggests a role for CD200 in regulating T cell priming outside the central nervous system (CNS) [1]. However, the cell-level effects of CD200 down-regulation on dendritic cells' phenotypes remain unknown.

We have developed ARTIMMUS [2], an agent-based simulation of murine EAE. Using ARTIMMUS, we have explored the potential cell-level consequences of CD200 regulation of dendritic cells (DC). Two mechanisms were explored: 1) A reduction in DC priming capacity of T cells and 2) A promotion of DC type II cytokine secretion.

We have found that CD200 down-regulation of DC priming capacity promotes autoimmunity. At the population, T_{REG}-priming DCs are subjected to more CD200 down-regulation than their T_H1-priming counterparts. On its own, this potential mechanistic consequence of CD200 down-regulation does not support recovery from autoimmunity. We also found that DC cytokine profile switching substantially promotes type II deviation of the autoimmune response, even in the presence of perforin knockout simulations, where CD8 T_{REG} are unable to directly apoptose autoimmune T_H1 cells. Hence, CD200-supported type II deviation strongly supports recovery from EAE.

These two potential mechanisms, which individually have opposing effects regarding recovery from EAE, when combined in simulation appear to support the view that CD200 regulation can promote recovery from autoimmunity.

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References

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