Type IIFN signaling in T regulatory cells modulates chemokine production and myeloid derived suppressor cells trafficking during EAE

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Abstract

Interferon-β has therapeutic efficacy in Multiple Sclerosis by reducing disease exacerbations and delaying relapses. Previous studies have suggested that the effects of type I IFN in Experimental Autoimmune Encephalomyelitis (EAE) in mice were targeted to myeloid cells. We used mice with a conditional deletion (cKO) of the type I IFN receptor (IFNAR) in T regulatory (Treg) cells to dissect the role of IFN signaling on Tregs. cKO mice developed severe EAE with an earlier onset than control mice. Although Treg cells from cKO mice were more activated, the activation status and effector cytokine production of CD4+Foxp3- T cells in the draining lymph nodes (dLN) was similar in WT and cKO mice during the priming phase. Production of chemokines (CCL8, CCL9, CCL22) by CD4+Foxp3- T cells and LN resident cells from cKO mice was suppressed. Suppression of chemokine production was accompanied by a substantial reduction of myeloid derived suppressor cells (MDSCs) in the dLN of cKO mice, while generation of MDSCs and recruitment to peripheral organs was comparable. This study demonstrates that signaling by type I IFNs in Tregs reduces their capacity to suppress chemokine production, with resultant alteration of the entire microenvironment of draining lymph nodes leading to enhancement of MDSC homing, and beneficial effects on disease outcome.

Biography:

Shalini Tanwar has a strong background in cellular aspects of inflammation, immunology and autoimmunity with specific focus on cellular cross talk between B and T lymphocytes during development and T regulatory cells and myeloid derived suppressor cells (MDSCs) in neurodegenerative model of autoimmunity (EAE).

Speaker Publications:

1. "A role for apoptosis-inducing factor in T cell development"
2. "Role of apoptosis-inducing factor (Aif) in the T cell lineage"
3. "Functionally significant metabolic differences between B and T lymphocyte lineages"
4. "Type1 IFN signaling on Tregs modulates the migration of Myeloid Derived Suppressor Cells"
5. "Regulation of Myeloid Derived Suppressor Cell (MDSC) dynamics by T regulatory cells"

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