Distinct and nonredundant in vivo functions of IFNAR on myeloid cells limit autoimmunity in the central nervous system.

The action of type I interferons in the central nervous system (CNS) during autoimmunity is largely unknown. Here, we demonstrate elevated interferon beta concentrations in the CNS, but not blood, of mice with experimental autoimmune encephalomyelitis (EAE), a model for CNS autoimmunity. Furthermore, mice devoid of the broadly expressed type I IFN receptor (IFNAR) developed exacerbated clinical disease accompanied by a markedly higher inflammation, demyelination, and lethality without shifting the T helper 17 (Th17) or Th1 cell immune response. Whereas adoptive transfer of encephalitogenic T cells led to enhanced disease in Ifnar1(-/-) mice, newly created conditional mice with B or T lymphocyte-specific IFNAR ablation showed normal EAE. The engagement of IFNAR on neuroectodermal CNS cells had no protective effect. In contrast, absence of IFNAR on myeloid cells led to severe disease with an enhanced effector phase and increased lethality, indicating a distinct protective function of type I IFNs during autoimmune inflammation of the CNS.