TH1 AND TH17 PATHWAYS DETERMINE OPPOSITE RESULTS OF INTERFERON BETA TREATMENT OF EXPERIMENTAL AUTOIMMUNE ENCEPHALOMYELITIS AND RELAPSING-REMITTING MULTIPLE SCLEROSIS


Interferon beta (IFNβ) is the main treatment for multiple sclerosis (MS). However, this treatment is not always effective. Here we see a striking congruence in outcome between responses to IFNβ in experimental autoimmune encephalomyelitis (EAE) and relapsing-remitting MS (RRMS). IFNβ is effective in reducing EAE induced by Th1 cells, but exacerbated disease induced by Th17. Effective treatment in Th1 EAE correlated with increased IL-10 in spleens. In Th17 disease, IL-10 was unchanged by treatment, although unexpectedly IFNβ still reduced IL-17 without benefit. Both inhibition of IL-17 and induction of IL-10 depended on interferon gamma (IFNγ). The absence of IFNγ signaling resulted in ineffective IFNβ therapy in EAE. In RRMS, IFNβ nonresponders had higher IL-17F in serum compared with responders. Nonresponders had worse disease with more steroid usage and more relapses than responders. Hence, IFNβ is proinflammatory in Th17-induced EAE. Moreover, high IL-17F in serum predicts nonresponsiveness to therapy with IFNβ in RRMS.