Epstein-Barr virus infection promotes Th1-mediated disease in a humanized immune mouse model of multiple sclerosis

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Infection with the human-tropic Epstein-Barr virus (EBV) is a strong risk factor for multiple sclerosis (MS), though the underlying mechanisms remain unclear. To investigate EBV infection directly, we induced experimental autoimmune encephalomyelitis (EAE) in immunocompromised mice humanized with peripheral blood mononuclear cells (PBMCs) from individuals with or without a history of EBV infection and/or diagnosis of relapsing MS. HuPBMC EAE mice generated from EBV seronegative healthy donors (HD) were less susceptible to developing severe clinical symptoms than EBV seropositive cohorts. Donor EBV seropositivity and RRMS diagnosis led to a significant incremental increase in the human Th1:Treg $CD4^+$ T cell ratio in the brain and spinal cord, as well as increased human cytotoxic $CD8^+$ T cell and murine macrophage infiltration and demyelination. The data indicate that a history of EBV infection, further compounded by a diagnosis of RRMS, promotes Th1-mediated disease in a novel humanized mouse model of MS.