Leptin increase in multiple sclerosis associates with reduced number of CD4+CD25+ regulatory T cells

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We analyzed the serum and cerebrospinal fluid (CSF) leptin secretion and the interaction between serum leptin and CD4+CD25+ regulatory T cells (TRegs) in naïve-to-therapy relapsing-remitting multiple sclerosis (RRMS) patients. Leptin production was significantly increased in both serum and CSF of RRMS patients and correlated with IFN-γ secretion in the CSF. T cell lines against human myelin basic protein (hMBP) produced immunoreactive leptin and up-regulated the expression of the leptin receptor (ObR) after activation with hMBP. Treatment with either anti-leptin or anti-leptin-receptor neutralizing antibodies inhibited in vitro proliferation in response to hMBP. Interestingly, in the RRMS patients, an inverse correlation between serum leptin and percentage of circulating TRegs was also observed. To better analyze the finding, we enumerated TRegs in leptin-deficient (ob/ob) and leptin-receptor-deficient (db/db) mice and observed the significant increase in TRegs. Moreover, treatment of WT mice with soluble ObR fusion protein (ObR:Fc) increased the percentage of TRegs and ameliorated the clinical course and progression of disease in proteolipid protein peptide (PLP139-151)-induced relapsing-experimental autoimmune encephalomyelitis (R-EAE), an animal model of RRMS. These findings show an inverse relationship between leptin secretion and the frequency of TRegs in RRMS and may have implications for the pathogenesis of and therapy for multiple sclerosis.