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 (T_{Regs}) 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 T_{Regs} was also observed. To better analyze the finding, we enumerated T_{Regs} in leptin-deficient (*ob/ob*) and leptin-receptor-deficient (*db/db*) mice and observed the significant increase in T_{Regs}. Moreover, treatment of WT mice with soluble ObR fusion protein (ObR:Fc) increased the percentage of T_{Regs} and ameliorated the clinical course and progression of disease in proteolipid protein peptide ($PLP_{139-151}$)-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 T_{Regs} in RRMS and may have implications for the pathogenesis of and therapy for multiple sclerosis.