Role of leptin in autoimmune system

Health & Medicine

Leptin is one of the most important hormones secreted by adipose tissue and its implication in energetic homeostasis at central level has been largely described. Leptin is exerted at the development, proliferation, anti-apoptotic, maturation, and activation levels. Indeed, LepRs have been found in neutrophils, monocytes, and lymphocytes, and they belong to the family of class I cytokine receptors. The overall leptin action in the immune system is a pro-inflammatory effect, activating pro-inflammatory cells, promoting Th1 responses, and mediating the production of the other pro-inflammatory cytokines, such as TNF-α, IL-2, or IL-6. Leptin is therefore able to modulate both innate and adaptive immune response. Moreover, several studies in human revealed that leptin levels associated with autoimmune disorders, infections and endocrine/metabolic diseases, thus suggesting a central role of leptin in immune homeostasis and in the pathogenesis of several inflammatory disorders.

Multiple sclerosis (MS) is a chronic, immune-mediated, inflammatory disorder of the central nervous system (CNS) myelin. The disease is characterized by autoreactive T-cells that traffic to the brain and the spinal cord and injury myelin, with the result of chronic or relapsing-remitting paralysis. 13Analysis of the disease susceptibility in naturally leptin-deficient ob/ob mice before leptin replacement revealed resistance to both active and adoptive experimental autoimmune encephalomyelitis (EAE) that was reversed by leptin administration. Leptin replacement converted Th2- to Th1-type response and shifted IgG antibodies from IgG1 to IgG2a. In addition, it has also been recently observed that a serum leptin surge precedes the onset of EAE in susceptible strains of mice. This peak in serum leptin is correlated

with inflammatory anorexia, weight loss, and development of a pathogenic T-cell response against myelin.

In human MS, it has been reported that secretion of leptin is increased in serum and cerebrospinal fluid (CSF) of naïve-to-treatment MS patients and positively correlated with the secretion of interferon (IFN) in CSF and inversely with the percentage of circulating regulatory T-cells (TRegs), a key cellular subset in the suppression of immune and autoimmune responses, involved in the maintenance of T-cell tolerance. In addition, TRegs in patients with MS were not only inversely related to the leptin levels but also were reduced in percentage and absolute numbers when compared with healthy controls. This suggests that the number of TRegs can be affected by leptin secretion13. The evidence that a significant increase of leptin secretion occurs in the acute phase of MS and that this event positively correlates with CSF production of IFN is of particular interest for the pathogenesis and clinical follow-up of patients with MS. Increased secretion was present in both the serum and CSF of MS patients and determined loss of correlation between leptin and body mass index (BMI).