Jeffrey Friedman - Abstract

Leptin is an adipose tissue hormone that maintains homeostatic control of adipose tissue mass. This endocrine system thus serves a critical evolutionary function by protecting individuals from the risks associated with being too thin (starvation) or too obese (predation). Mutations in leptin or its receptor cause massive obesity in mice and humans, and leptin can effectively treat obesity in leptin deficient patients. Most obese patients have high endogenous levels of leptin indicating that they are leptin resistant with a variable response to exogenous leptin. The identification of leptin has thus provided a framework for studying the pathogenesis of obesity in the general population. Leptin also links changes in nutrition to adaptive responses in other physiologic systems with effects on insulin sensitivity, fertility, immune function and neuroendocrine function (among others). Leptin is an approved treatment for generalized lipodystrophy, a condition associated with severe diabetes, and has also shown promise for the treatment of other types of diabetes and for hypothalamic amenorrhea an infertility syndrome in females.

The identification of leptin has also advanced our understanding of the neural mechanisms that control feeding. Current research focuses on specific neural populations in the hypothalamus and other brain regions. The function of these neural subtypes is being evaluated by modulating their activity using optogenetics as well as by using a method that enables the non-invasive control of neural activity by a magnetic field.