COMMENTARY ON: **COEXPRESSION OF LEPTIN RECEPTOR AND PREPRONEUROPEPTIDE Y MRNA IN ARCUATE NUCLEUS OF MOUSE HYPOTHALAMUS. MERCER JG, HOGGARD N, WILLIAMS LM, LAWRENCE CB, HANNAH LT, MORGAN PJ, TRAYHURN P. *J NEUROENDOCRINOL*. 1996; 8: 733-5.**

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Leptin, a circulating hormone secreted by the adipocytes of mammalian white fat, exerts anorectic effects in part by inhibiting the release of Neuropeptide Y (NPY) from the arcuate nucleus of the hypothalamus (1). NPY neurons are well-documented to have primary orexigenic effects on food intake and energy balance (2, 3). This Rapid Communication by Mercer et al (4) is the most cited article published in the Journal of Neuroendocrinology and provides histological evidence that NPY neurons in the arcuate express leptin receptors. Double *in situ* hybridization against preproNPY mRNA and a sequence common to all splice variants of the leptin receptor showed that leptin receptors co-localize at some but not all NPY neurons in the arcuate nucleus. Over the next 20 years, these results contributed to the seminal findings that leptin can directly inhibit these neurons (5-7) and over time, can help rewire the structure of synaptic inputs to NPY neurons (8). Fasting increases the expression of NPY mRNA (9) and stimulates the spike firing of NPY neurons (7). If unopposed, this influence of NPY neurons can be interpreted as a frank starvation response, by coordinating the suppression of energy expenditure and stimulating voracious feeding (10). Leptin inhibits NPY gene expression (11) and reverses fasting-activated neural changes at NPY neurons (7). This effect of leptin on NPY neurons represents a negative feedback that reassures the brain that NPY-driven feeding has refilled energy stores in the body. This article by Mercer et al (4) provides the first clue that leptin may directly regulate NPY neurons to mediate central energy balance.

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