CHAPTER 16
Food Intake, Circuitry, and Energy Metabolism

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References


Ahima, R.S., Prabakaran, D., Mantzoros, C., et al. (1996) Role of leptin in the neuroendocrine response to fasting. *Nature*, 382, 250–252. [A seminal piece of work which establishes leptin NOT as a hormone to make you stop eating, but a hormone that functions to let your brain know that you have no fat, and to turn on the starvation response.]


Farooqi, I.S., Bullmore, E., Keogh, J., Gillard, J., O’Rahilly, S. and Fletcher, P.C. (2007a) Leptin regulates striatal regions and human eating behavior. *Science*, **317**, 1355. [The first evidence of leptin playing a role in the ‘hedonic’ aspects of eating behavior. Leptin-deficient humans are unable to discriminate foods of different nutritional and reward value. However, upon leptin replacement, these patients are then able to make a ‘value judgment’ on food.]


Huszar, D., Lynch, C.A., Fairchild-Huntress, V., et al. (1997) Targeted disruption of the melanocortin-4 receptor results in obesity in mice. *Cell*, 88, 131–141. [Report of Mc4r deficiency in mice and the fact that it results in a dominantly inherited obesity. All the other previous models have been recessive disorders. Heterozygous mutant mice display an intermediate phenotype compared to homozygous mice.]


Kruide, H., Bieberrmann, H., Luck, W., Horn, R., Brabant, G. and Gruters, A. (1998) Severe early-onset obesity, adrenal insufficiency and red hair pigmentation caused by POMC mutations in humans. *Nature Genetics*, 19, 155–157. [The direct evidence for pro-opiomelanocortin, the precursor for the melanocortin peptides including α- and β-MSH, having a critical role to play in the control of food intake and body weight, with mutations causing severe obesity, red hair, and isolated ACTH deficiency in humans.]


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Montague, C.T., Farooqi, I.S., Whitehead, J.P., et al. (1997) Congenital leptin deficiency is associated with severe early-onset obesity in humans. *Nature*, 387, 903–908. [The first report of a human monogenic obesity syndrome, when two cousins were found to have homozygous loss-of-function mutations in their leptin gene, and showing the relevance of leptin signaling in the control of human food intake and body weight.]


Ollmann, M.M., Wilson, B.D., Yang, Y.K., et al. (1997) Antagonism of central melanocortin receptors in vitro and in vivo by agouti-related protein. *Science*, 278, 135–138. [Report of the cloning of AgRP and a description of how it plays an important role in the control of food intake by competing with α-MSH to bind to the MC4R, where it acts as an antagonist, resulting in an increase in food intake.]


Stunkard, A.J., Harris, J.R., Pedersen, N.L. and McClean, G.E. (1990) The body-mass index of twins who have been reared apart. *New England Journal of Medicine*, **322**, 1483–1487. *These two papers by Stunkard et al. are seminal publications, setting up the now widely accepted notion that genetics plays a critical role in the determination of body shape and size. Stunkard first studied fraternal versus identical twins, then followed this up with a study on twins raised apart, thereby showing that your genes play a larger role in determining your body weight than the environment you are raised in.*


the neurotropin receptor TrkB in the control of human food intake and body weight, with mutations in the gene leading to dominantly inherited obesity and developmental delay.]


