Addressing leptin resistance

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LEPTIN WAS CLONED IN 1994 and shown to be secreted from adipocytes (5). This and subsequent studies demonstrated that leptin is made and secreted in proportion to the fat content of individual adipocytes (4). Under normal physiological conditions, the concentration of circulating leptin is inversely related to body fat, or energy, content (2). It is transported past the blood-brain barrier and acts via specific receptors in the arcuate nucleus of the hypothalamus to activate anorexigenic pathways; that is, leptin reduces food (energy) intake. Leptin also increases energy expenditure (2). Thus it is eminently reasonable to hypothesize that leptin is a lipostatic signal.

As might have been expected from such an important control system, the story is turning out to be much more complex. In diet-induced obesity, circulating leptin level is very high and the relationship between the body's content of fat/energy and leptin concentration is lost (2).

These and similar findings have led to the concept of leptin resistance, which is thus defined as a failure of leptin signaling leading to dysregulation of energy balance and body weight.

Analogous events do occur in other endocrine control systems. For instance, high circulating levels of ANG II lead to downregulation at many peripheral sites of the major subtype, AT1, of the angiotensin receptor (3). Nevertheless, the concept of leptin resistance remains poorly understood. The study in this issue by Bowen et al. (1) reports a well conceived, designed, and executed set of experiments that examine leptin resistance. The authors provide evidence that many factors contribute to leptin resistance. Some, such as strain and gender, are intrinsic to the organism, whereas others, such as housing conditions, are clearly environmental. Furthermore, the experiments point to interactions between leptin signaling and both extrinsic and intrinsic modifying factors.

REFERENCES

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