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Mice serve as research models to study mechanisms of obesity

Thomas W. Gettys, Louisiana State University

If current estimates prove accurate, half of the American population will be clinically obese by the year 2030—up from about 30% today. Being obese predisposes one to a number of additional health problems, including hypertension, heart disease, and diabetes.

The direct costs of treating complications of obesity, plus the indirect costs from lost productivity, represent a $100 billion annual burden on the U.S. economy. Given that these costs are expected to double in the next 30 years, an effective treatment for obesity is the subject of intense study.

Fat accumulates in the body in adipose tissue. The historic view has been that this tissue is a passive participant in the process, merely acting as a repository for excess consumed calories.

That perception changed with the discovery of leptin by Jeffrey M. Friedman at Rockefeller University in late 1994. Researchers now recognize that this peptide is a satiety hormone produced by adipose tissue that communicates the status of energy stores to the brain.

The discovery of leptin energized the study of obesity. It revealed adipose tissue as a complex endocrine organ. Research has shown that it serves not only as the source of leptin but also as an important target for brain-mediated effects on how energy is utilized in the body.

ANIMAL MODELS OF OBESITY HAVE ACCELERATED THE PACE OF DISCOVERY IN OBESITY RESEARCH. PICTURED ARE OBESITY-PRONE AND OBESITY-RESISTANT MICE.

Models of Obesity

The epidemic of obesity in Westernized societies is strongly linked to consumption of high-fat diets. Some people appear to be particularly sensitive to high-fat diets and have a significantly higher tendency to deposit body fat, even when consuming similar amounts of food.

A similar variation in sensitivity to dietary fat has been documented in mice – particular strains readily become obese

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after consuming high-fat diets over time. These susceptible mouse strains provide excellent models to study the developmental stages of a syndrome that is highly analogous to human obesity.

How Leptin Works

After being released from adipose tissue, leptin travels via the bloodstream to the brain, where it crosses the blood-brain barrier and binds to specific receptors in the hypothalamus. These receptors produce a coordinated series of responses to match rates of energy utilization with rates of food intake.

These responses include specific effects on gene expression in adipose tissue, which increase rates of energy utilization. When this system is functioning properly, the amount of energy burned always matches the amount of energy consumed so that there are no excess calories to deposit as fat in adipose tissue. Body weight remains stable and obesity is avoided.

With support from USDA's National Research Initiative (NRI) Competitive Grants Program, researchers at Louisiana State University's Pennington Biomedical Research Center are studying fat-resistant and fat-sensitive mouse strains.

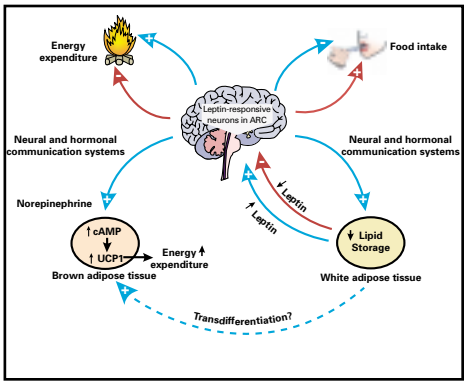
They have found substantial evidence that obesity-resistant mice maintain their ability to respond to leptin, while obesity-prone mice become progressively less responsive.

The latter state is called leptin resistance. The researchers are seeking to dissect the mechanisms responsible for compromising the central recognition of—and peripheral responses to—leptin in diet-induced obesity.

Impact

Leptin resistance is a cardinal feature of human obesity. It represents a breakdown in the communication system between adipose tissue and the brain, which regulates stabilization of body weight.

The researchers expect that fundamental new insights into the causes of leptin resistance will serve as the basis for developing effective new strategies for treating this most prevalent and debilitating condition.



COMMUNICATION NETWORKS BETWEEN ADIPOSE TISSUE AND THE BRAIN PREVENT EXCESS BODY FAT DEPOSITION. COMPROMISED FUNCTION OF THESE SYSTEMS ALLOWS OBESITY TO DEVELOP.

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