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Friedman studies the molecular and neural mechanisms that regulate food intake and body weight. Genetic studies in mice led to the identification of leptin, a hormone made by fat tissue that plays a key role in controlling appetite and weight. His current work explores the mechanisms by which leptin regulates energy balance and seeks to identify other key regulators of body weight.

Leptin maintains body weight within a relatively narrow range. Increased fat mass increases leptin levels, which in turn reduces body weight; decreased fat mass decreases leptin levels and increases body weight. Defects in the leptin gene are associated with severe obesity, and leptin treatment normalizes weight in these patients. Leptin also improves the severe diabetes and abnormal lipids in patients with lipodystrophy, and is now an FDA-approved treatment for this condition.

Neural Circuits Regulating Food Intake

Leptin acts directly on multiple CNS sites to reduce food intake and body weight in animals and humans, providing an entry point to study the control of feeding. Feeding is a complex motivational behavior controlled by many inputs, including not just leptin but smell, taste, and other hormones. It is not known how or where these multiple inputs are processed to generate a “binary” decision: eat or don’t eat. To begin to address the question of how this complex behavior is switched on (and off), the Friedman lab is using existing and newly developed methods for both identifying novel populations of nerve cells that are linked to feeding and testing their function. Recent studies have identified a key neural population of neurons in the arcuate nucleus that mediates leptin’s effects to reduce food intake in multiple brain regions, including the brain stem, amygdala, and the insular cortex. The next challenge is to establish a hierarchy among these control nodes in order to identify the key node that activates this behavior to the exclusion of other complex behaviors, such as fight, flight, copulation, and grooming. Toward that end, the Friedman lab recently mapped a simple circuit by which leptin controls feeding behavior—a circuit that potentially acts as the target for top down signals that regulate food consumption. In addition, obesity is associated with leptin resistance, which Friedman’s group recently linked to increased activity of the mTor kinase in POMC neurons, a key leptin target neuron.

Regulation of Leptin Gene Expression

The Friedman lab has identified DNA regulatory sequences and a fat-specific long non-coding RNA that control leptin gene expression. They found that mice with a mutation in this RNA, called LncOb, show increased fat mass with reduced leptin levels. Mice that lack LncOb have lower leptin levels than controls and become more obese on a high fat diet, but show significant weight loss after leptin treatment. These studies suggest that obesity with low leptin levels might respond similarly.

Regulation of Fat Innervation

Leptin activates the sympathetic nervous system, which plays an important role in regulating how much energy fat cells store or burn. Recent studies have shown that fat in leptin-deficient animals almost completely lacks sympathetic nerves, and that leptin treatment restores these nerves within 7 to 10 days. Friedman’s lab has established a role for neurons in the hypothalamus that express a protein called BDNF. Blocking BDNF signaling from the hypothalamus to the spinal cord blunts leptin’s ability to induce nerve growth in fat. Current studies seek to understand how BDNF induces adipose tissue nerve growth.

EDUCATION

B.S., 1973
Rensselaer Polytechnic Institute
M.D., 1977
Albany Medical College, Union University
Ph.D., 1986
The Rockefeller University

MEDICAL TRAINING

Internship in medicine, 1977–1978
Residency in medicine, 1978–1980
Albany Medical Center Hospital

POSITIONS

Assistant Professor, 1986–1991
Associate Professor, 1991–1995
Professor, 1995–
Co-director, Kavli Neural Systems Institute, 2015–2016
The Rockefeller University
Associate Physician, 1980–1983
The Rockefeller University Hospital
Assistant Investigator, 1986–1992
Associate Investigator, 1992–1996
Investigator, 1996–
Howard Hughes Medical Institute

AWARDS

Canada Gairdner International Award, 2005
Passano Award, 2005
Jessie Stevenson Kovalenko Medal, 2007
Danone International Prize, 2007
Shaw Prize, 2009
Keio Medical Science Prize, 2009
Albert Lasker Basic Medical Research Award, 2010
Pasarow Award, 2011
BBVA Frontiers of Knowledge Award, 2012
Fondation IPSEN Endocrine Regulation Prize, 2012
King Faisal International Prize, 2013
Harrington Prize for Innovation in Medicine, 2016
Wolf Prize in Medicine, 2019
Breakthrough Prize in Life Sciences, 2020
Princess of Asturias Award for Technical & Scientific Research, 2024
Albany Medical Center Prize in Medicine and Biomedical Research, 2025

HONORARY SOCIETIES

National Academy of Sciences
National Academy of Medicine
Fellow, American Association for the Advancement of Science
Foreign Member, The Royal Society
Associate Member, European Molecular Biology Organization

SELECTED PUBLICATIONS

Tan, B. et al. A cellular and molecular basis of leptin resistance. *Cell Metab.* 37, 723–741 (2025).
Kosse, C. et al. A subcortical feeding circuit linking an interoceptive node to jaw movement. *Nature* 636, 151–161 (2024).
Tan, H.L. et al. Leptin-activated hypothalamic BNC2 neurons acutely suppress food intake. *Nature* 636, 198–205 (2024).
Ilanges, A. et al. Brainstem ADCYAP1+ neurons control multiple aspects of sickness behaviour. *Nature* 609, 761–771 (2022).
Zhang, Y. et al. Positional cloning of the mouse obese gene and its human homologue. *Nature* 372, 425–432 (1994).