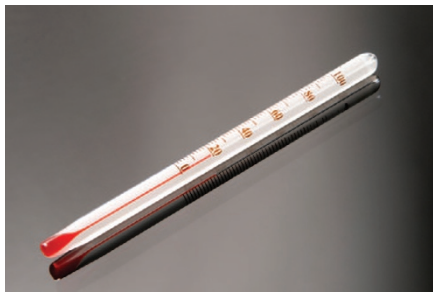
Mice heat up to burn more fat

Recent genetic studies have demonstrated a key role of the brain's endogenous opioid system in energy homeostasis. Administration of general opioid receptor antagonists reduces food intake and body weight in rodent models of obesity, while agonists of these receptors increase food intake. Though this system presents an attractive target of drug-based treatments for obesity, general modifications to the opioid system can have multiple effects on analgesia, addiction, depression and anxiety, prompting researchers to look for a more specific target for preventing obesity. Now researchers have found that blocking the delta opioid receptor (DOR) alone creates resistance to weight gain by stimulating gene expression promoting thermogenesis in mice (*FASEB J.* **26**, 3483–3492; 2012).

Ruben Nogueiras (University of Santiago de Compostela-Instituto de Investigación Sanitaria, Santiago de Compostela, Spain) and Michael A. Statnick (Lilly Research Laboratories, Indianapolis, IN) analyzed mice that were genetically modified to lack



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DOR. These mice were fed either a regular diet or a high energy diet (HED) containing greater amounts of fat and sugar. They found that, in comparison with regular mice fed the HED, the genetically modified HED-fed mice gained less weight and had lower fat mass. The mice lacking DOR also had lower plasma lipid levels as well as less storage of fat in the liver.

The DOR-deficient mice also showed higher energy expenditure than regular mice. Since the mice showed no increase in locomotor activity, this increased energy expenditure had to be the result of some other mechanism. The body surface temperature of the DOR-deficient mice was higher near major sources of brown adipose tissue, leading the scientists to believe that deleting DOR in the mice stimulated the expression of other genes in brown fat tissue that promoted thermogenesis. The mice were also better able to maintain a higher core body temperature in response to being in a cold environment. In other words, the mice lacking DOR seemed to resist becoming obese by burning the excess fat in their diets to produce body heat.

These findings support the hypothesis that overactivation of opioid receptors may contribute to the development of obesity when there is prolonged consumption of high-fat, caloric diets. Gerald Weissmann, Editor-in-Chief of the *FASEB Journal*, said in a press release, "This exciting research identifies genes that activate brown adipose tissue to increase our burning of calories from any source. It may lead to a safe diet pill in the future."

Kara Rosania

OF MICE AND MICROGRAVITY

In the longest animal space journey yet undertaken, three male C57BL/J10 mice flew aboard the Space Shuttle Discovery to the International Space Station and lived there for 91 days in a specially designed housing unit before returning to Earth on the Space Shuttle Atlantis. The Italian Space Agency funded and organized the project to gather information that could be used to reduce the health risks to humans during prolonged space missions.

Like other living organisms on Earth, humans are adapted structurally and functionally to the planet's gravitational field. Exposure to reduced gravity (or microgravity) in space thus affects almost all physiological systems, sometimes causing serious health problems that persist even after a return to normal gravity. These problems may become more pronounced during prolonged exposure to microgravity, as in interplanetary travel.

The systems most affected by microgravity include blood circulation, bone tissue and skeletal muscle and reproduction. Gene and protein expression are also thought to be altered. Data on these systems were collected from the astronaut mice and from control mice and then analyzed by 20 research groups from 6 countries.

Researchers headed by Angela Maria Rizzo (Università degli Studi di Milano, Italy) identified that damage to cells due to oxidative stress may be related to the reduction in red blood cell number and blood plasma volume known as 'space anemia' (*PLoS One* **7**, e32361; 2012). Sara Tavella (Università degli Studi di Genova, Italy) and her team reported tissue loss in weight-bearing bones, owing to both increased resorption and decreased deposition, that was partially prevented by overexpression of pleiotrophin (*PLoS One* **7**, e33179; 2012). A collaborative effort headed by Romeo Betto (Institute of Neuroscience, Padova, Italy), Diana Conte (University of Bari, Italy) and Stefano Schiaffino (Venetian Institute of Molecular Medicine, Padova, Italy) found that slow-twitch muscle underwent microgravity-induced atrophy, whereas fast-twitch muscle seemed to resist atrophy (*PLoS One* **7**, e33232; 2012). Francesco Saverio Ambesi-Impiombato (Istituto Nazionale di Ricovero e Cura per Anziani, Rome, Italy) and colleagues noted structural and functional changes to the thyroid and dysfunctional spermatogenesis in the astronaut mice, suggesting that long-term exposure to microgravity could lead to reproductive dysfunction in male mammals (*PLoS One* **7**, e35418; 2012). And a group led by Yoshinobu Ohira (Osaka University, Japan) found that brain expression of many genes and proteins involved in a wide range of biological functions was influenced by exposure to microgravity (*PLoS One* **7**, e40112; 2012).

Monica Harrington