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Clock gene plays role in weight gain, study finds

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Scientists at the University of Virginia and the Medical College of Wisconsin have discovered that a gene that participates in the regulation of the body's biological rhythms may also be a major control in regulating metabolism. Their finding shows that mice lacking the gene Nocturnin, which is regulated by the circadian clock in the organs and tissues of mammals, are resistant to weight gain when put on a high fat diet and also are resistant to the accumulation of fat in the liver. This new understanding of weight gain could potentially lead to therapies for inhibiting obesity and for treating its effects on health.

The study is published this week in the journal *Proceedings of the National Academy of Sciences.*

"It's been known for some time that there are many links between the circadian clock and various aspects of physiology and metabolism," said Carla Green, the study's lead author and an associate professor of biology at the University of Virginia. "This study suggests that Nocturnin is part of the network that the circadian clock uses to control important aspects of metabolism. A better understanding of Nocturnin's function could eventually lead to medical treatments that could counteract the problems of obesity, which has become a major issue in modern society."

Biological clocks are the body's internal timekeepers that regulate organs and activity/rest cycles by controlling energy levels, alertness, growth, moods and the effects of aging. Research in this field has many health

implications for dealing with aging, jet lag, sleep disorders, shift work and dieting.

Green and her colleagues used regular mice and genetically altered mice in which the Nocturnin gene was knocked out. The Nocturnin-deficient mice were divided into two groups; one group fed a normal diet, the other a very high fat diet. A group of normal mice were also fed a high fat diet. The researchers found that both groups of the genetically altered mice maintained normal weight and activity levels, and, of particular interest, the ones fed the high fat diet gained only slight weight even over long periods of time. The normal mice on the high fat diet, however, "ballooned," gaining more than twice the weight of the Nocturnin-deficient mice. And when the mice were dissected, the researchers discovered that the normal mice had, as expected, large concentrations of fat on their livers, whereas the altered mice had normal levels of fat in their livers.

"We were quite amazed at what we found," Green said. "We thought that over time, as we continued to feed the mutant mice the high fat diet, that they would eventually gain weight at some expected rate, but it never happened. These mice continued to stay slim while the normal mice nearly doubled in weight and developed fatty livers."

Green said it is possible that, "after a great deal of further research, a drug possibly could be developed that would inhibit Nocturnin and reduce the risk of developing obesity."

Clock genes in the body's organs operate in conjunction with a central time keeper in the brain, the hypothalamic suprachiasmatic nucleus, but also work somewhat independently, resulting in a complex system of oscillators regulating various functions of the body.

Scientists are working to better understand how the genes and proteins of

the circadian clock in mammals affect not only activity cycles but also metabolism, which are tied to feeding cycles. Circadian rhythms were set in motion early in the history of life on the planet, and tied through evolution to the astronomical cycles that effect Earth's environment, the rise and setting of the sun, and the passing of seasons.

Source: University of Virginia