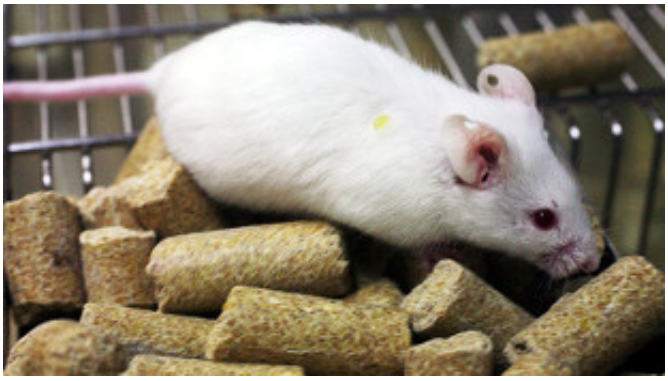
Gut Microbes Influence Circadian Clock

Metabolites produced by gut microbes in mice can affect the animals' circadian rhythm and metabolism.

By Anna Azvolinsky | April 16, 2015



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The mammalian gut microbiome is involved in controlling the circadian rhythm of its host, according to a mouse study published today (April 16) in *Cell Host & Microbe*. In both mice and humans, timing of feeding and diet type can impact the bacterial populations of the gut. Now, Eugene Chang of the University of Chicago Medical Center and his colleagues have found that mouse gut microbiota produce metabolites in diurnal patterns, and these can influence the expression of circadian clock genes in the liver.

The results provide additional support for the idea that the gut microbiome is dynamic, said Satchidananda Panda of the Salk Institute for Biological Studies who was not involved in the work. "At night, we go to bed with a bunch of bugs in our stomachs and wake up in the morning with a different set of bugs," said Panda. "The implications are pretty big because there are more bacterial cells in our guts than the number of cells in our body and these species produce different enzymes and factors that have a big impact on our overall metabolism."

Joseph Takahashi, who studies mammalian circadian rhythm at the University of Texas Southwestern Medical Center but was not involved in the current work, noted in an e-mail that this study is the latest in a string of experiments linking circadian rhythm to the gut microbiome.

The mammalian sleep-wake cycle is known to play a role in metabolism. Rodent studies have shown that such circadian rhythm can be altered by high-fat diets. In humans, perturbed sleep patterns can lead to increased appetite and an increased risk of obesity and diabetes.

Panda and his colleagues recently showed that the gut microbes of mice fed a high-fat diet did not fluctuate diurnally as they did in mice fed control food. Another recent study, led by Weizmann Institute of Science's Eran Elinav, pointed to similar oscillation of gut bacteria in humans.

"The finding that our microbiome also exhibits diurnal rhythms is interesting since virtually every cell in

the body has a circadian clock, and it is therefore likely that a coordinated diurnal change in the microbiome could be complementary to the circadian rhythms in metabolism in peripheral tissues," Takahashi told *The Scientist*.

For the present study, Vanessa Leone—a postdoctoral fellow in the Chang lab—and her colleagues first observed that, compared with control animals, germ-free mice did not gain as much weight when fed a high-fat diet. Compared with control animals, the germ-free mice also showed different circadian clock gene-expression patterns in their livers.

"In the face of high-fat feeding . . . we see a dysbiosis in community structure and function . . . which shifts host metabolism in a negative direction leading to diet-induced obesity," Leone explained in an e-mail to *The Scientist.*

"The circadian rhythm of these mice is disrupted at the molecular level, which is very surprising and says that the gut microbiome plays a role in circadian rhythm not only in the peripheral organ, but also in the central nervous system," said Panda.

Analyzing gut microbe-produced metabolites in the animals' guts, Leone, Chang, and their colleagues found that beneficial bacteria produced the short-chain fatty acid butyrate at levels that varied diurnally in mice fed a control diet, but not those fed a high-fat diet. Hydrogen sulfide, in contrast, was produced a diurnal pattern in the guts of mice on a high-fat diet, but not in mice fed regular food.

"Our working hypothesis is that gut microbes sense what, when, and how much is eaten, producing metabolic signals that feed into the regulation of circadian networks which control our metabolism," said Chang. "High-fat, western-type diets alter these microbial signals in a way that disturbs circadian functions to promote obesity."

"The nice thing here is that the authors show that removal of the [gut] microbiome has an effect on circadian rhythm," said Panda. "Figuring out why this happens is the next big question."

V. Leone et al., "Effects of diurnal variation of gut microbes and high-fat feeding on host circadian clock function and metabolism," *Cell Host & Microbe,* doi:10.1016/j.chom.2015.03.006, 2015.

Tags

physiology, mouse study, Molecular clock, metabolism, gut microbiota and circadian clocks

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fits with other timings in nature and acient texts. thanks

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I wonder how this applies to people who work overnight for 7 days straight then are off for 7 days? Perhaps if they maintained a low (bad fat) fat diet they wouldn't be at risk for obesity?

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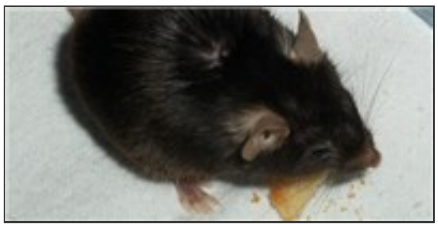

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