

It's all connected: Daily changes in mouse gut bacteria moves with internal clock, gender

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By now, the old saw, "You are what you eat," has been well-used in describing the microbiome. However axiomatic that phrase may be, a new study has also found that who and when that consumption is done can affect microbiome make-up. Changes in the abundance of mouse gut bacteria, over a 24-hour cycle, particularly in females, is tied to rhythms in the internal clock, according to work published online this week in the Early Edition of the *Proceedings of the National Academy of Science*, by researchers from the Perelman School of Medicine at the University of Pennsylvania.

In mammals, most physiological, metabolic, and behavioral processes follow a daily, or circadian, rhythm, adapting to changing light in the environment. Recent studies of the mouse [microbiome](#) have found that the microbes that live in mammals have their own circadian behavior, which has been shown to be linked to host feeding time. However, how this all ties together has not been fully clarified.

Doctoral student Xue Liang, working with the labs of authors Garret A. FitzGerald, MD, FRS, chair of the department of Systems Pharmacology and Translational Therapeutics, and Frederic Bushman, PhD, chair of the department of Microbiology, analyzed [circadian rhythms](#) in abundance and type of microbiota in the gut and feces of mice using genetic sequencing. They found that the absolute abundance of Bacteroidetes, a large group of rod-shaped bacteria common in the gut and skin of animals, and relative species make-up of the microbiome, changed over a 24-hour cycle. What's more, this rhythmicity was more

pronounced in female mice.

Normally, during the daytime, when the mice are resting and consuming less food, Bacteroidetes are predominant, reaching the highest abundance toward the end of the light phase. The influence of food may reflect the varying nutrient availability to bacteria. Components in host diet and mucus in the intestines provide carbon sources to the bacteria. Several strains of Bacteroidetes have evolved to use host mucous carbon when dietary carbon is in short supply, which may partially explain the blooming of Bacteroidetes in the resting phase.

But how are [internal clock](#) and sex involved in setting up these patterns? When the Penn team disrupted the clock gene *Bmal1*, any trace of a 24-hour cycle in the composition of fecal microbiota in both male and [female mice](#) was eliminated. *Bmal1* deletion also induced changes in bacterial abundances in feces, with differential effects based on sex. Although microbiota in both males and females exhibited circadian rhythmicity, females showed more significant oscillation than males. However, the effect of host sex is secondary to the host circadian clock in shaping the rhythmicity, because *Bmal1* deletion abolished the rhythmicity irrespective of sex.

"Although host behavior, such as time of feeding, is recognized to play a large role in explaining these intertwined cycles, we show that sex interacts with the [circadian clock](#), and these factors collectively shape the circadian rhythmicity and composition of the fecal microbes in mice," says first author Liang. "Our findings suggest the need to consider circadian factors and host gender in the design of microbiome studies and highlight the importance of analyzing absolute abundance in understanding the microbiome and its influence on physiology, and possibly inflammatory bowel disease."

More information: *PNAS*

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