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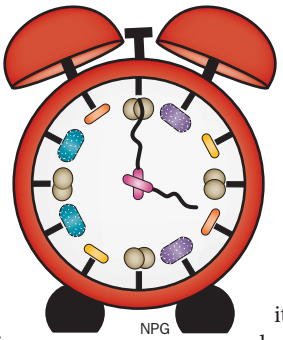
METABOLISM

Bacterial–host interplay in circadian regulation of metabolism

Disrupted circadian rhythms in mice and humans lead to changes in the composition and function of the microbiota that in turn affect the host metabolism, reveal Eran Elinav and colleagues in *Cell*.

The increased prevalence of metabolic diseases in Western countries is associated with lifestyle changes, such as "the tendency to disrupt normal circadian sleep–wake patterns, for instance by frequent flying to different time zones or performing shift work," comments Elinav.

The researchers saw that the abundance of different taxonomic groups of bacteria in the microbiota of mice changes in a circadian pattern, and metagenomic sequencing also revealed circadian fluctuations in bacterial functional activity. Analysis of *Per1/2*$^{-/-}$ mice, whose circadian clock is impaired, showed that a functional host clock is required for these normal circadian changes of the microbiota. Elinav and colleagues also observed that these oscillations depend on the rhythmic consumption of food by the host mice. Analysis of faecal samples from two humans also showed a circadian rhythmicity in the composition and function of the microbiota. "These findings establish a principle by which a symbiotic community of host and microorganisms can coordinate their activity to the day–night variations in the environment," says Elinav.



To mimic the human conditions of jet lag and shift work, the researchers designed an experiment in which the exposure of mice to light was advanced by 8 h on the first day, an advance that was maintained for 3 days, after which the mice were shifted to the initial day–night pattern; this procedure was then repeated several times. This regimen was associated with loss of rhythmic physical activity, irregular rhythm of food intake and reduced oscillations in the composition of the microbiota. Importantly, mice that experienced the procedure had greater weight gain and more glucose intolerance than control mice when both groups consumed a high-fat diet, and antibiotic treatment attenuated these differences.

"Large cohort studies are warranted to examine the effect of circadian disruption on the intestinal microbial community and its consequences for metabolic dysregulation," comments Elinav. "Our inner microbial rhythm represents a new therapeutic target that may be exploited in future studies to normalize the microbiota in people whose lifestyle involves frequent alterations in sleep patterns, hopefully to reduce or even prevent their risk of developing obesity and its complications."

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Original article Thaiss, C. A. *et al.* Transkingdom control of microbiota diurnal oscillations promotes metabolic homeostasis. *Cell* doi:10.1016/j.cell.2014.09.048