Scientists find that our cells' power plants run on timers

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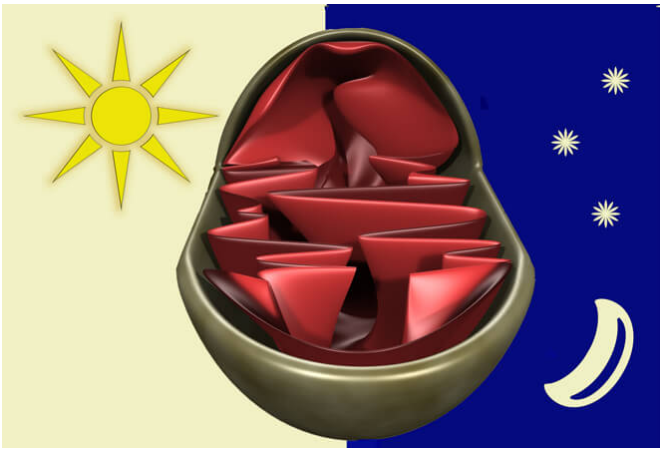

The circadian clock regulates the mitochondria's utilization of nutrients throughout the day

When one eats may be as important as what one eats. New research at the Weizmann Institute of Science and in Germany, which recently appeared in the *Proceedings of the National Academy of Sciences* (*PNAS*), suggests that the cells' power plants - the mitochondria - are highly regulated by the body's biological, or circadian, clocks. This may help explain why people who sleep and eat out of phase with their circadian clocks are at higher risk of developing obesity, diabetes and metabolic syndrome.

Dr. Gad Asher of the Weizmann Institute's Biomolecular Sciences Department, who led the study, explains that circadian clocks, which are found in living things from bacteria to flies and humans, control our rhythms of sleep, activity, eating and metabolism. "In a sense," he says, "it's like a daily calendar, telling the body what to expect, so it can prepare for the future and operate optimally."

Dr. Adi Neufeld-Cohen, of Asher's group, in collaboration with Dr. Maria S. Robles and Prof. Matthias Mann of the Max Planck Institute of Biochemistry in Germany, looked for circadian changes in the mitochondria that, by creating peaks and dips in the cells' energy levels, would also help regulate their day-night cycles. The group identified and quantified hundreds of mitochondrial proteins, finding that the quantities of a whopping 40% peak once a day. Further research identified the proteins making up the mitochondrial circadian clock that regulates these activities. Surprisingly, most of the circadian proteins in the mitochondria peaked four hours into the daylight part of the cycle (in mice, which are active at night).

Among the essential proteins the researchers uncovered was a key enzyme that determines the rate of sugar use for energy production. This protein reaches its maximal amount four hours into daylight, suggesting that the mitochondria's capacity for burning sugar peaks around this time, as well. To check, the researchers provided mitochondria with sugar and found that at around hour four, respiration and glucose utilization were indeed at their highest. They also found that the protein responsible for the entry of fatty acids into the mitochondria only peaks at the eighteenth hour and, again, tests showed fat processing was optimal at the same time.

In mice with a genetic mutation that interferes with their overall biological clocks, the amounts of these proteins did not change over the course of the day, and the decomposition activity of fats and sugars was steady throughout.

"These findings support previous findings in our lab in which we showed that if mice eat only at night, when they are active, rather than throughout the day and night, they will eat the same amount of calories but their liver lipid levels will be 50% lower," says Asher. "In other words, the outcome depends not only on what you eat but also on when you eat it. If we could be more aware of the timing of our cellular activities, we might be able to take

advantage of various nutrients in a healthier way."

More information: Adi Neufeld-Cohen et al. Circadian control of oscillations in mitochondrial rate-limiting enzymes and nutrient utilization by PERIOD proteins, *Proceedings of the National Academy of Sciences* (2016). DOI: 10.1073/pnas.1519650113

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