MedicalXpress

Circadian rhythms have profound influence on metabolic output, study reveals

March 19 2012

By analyzing the hundreds of metabolic products present in the liver, researchers with the UC Irvine Center for Epigenetics & Metabolism have discovered that circadian rhythms – our own body clock – greatly control the production of such key building blocks as amino acids, carbohydrates and lipids.

They identified more than 600 liver-originated metabolites, which are the chemical substances created by metabolism that sustain and promote cell health and growth. Approximately 60 percent of these metabolites were found to be dependent on the endogenous circadian clock – many more than expected, as only about 15 percent of the body's genes are regulated by it.

Circadian rhythms over 24 hours govern fundamental biological and physiological processes in almost all organisms. They anticipate environmental changes and adapt certain bodily functions to the appropriate time of day. Disruption of these cycles can seriously affect human health.

Center for Epigenetics & Metabolism director Paolo Sassone-Corsi, lead author on the study and one of the world's preeminent researchers on circadian rhythms, said the liver metabolites reveal how the body clock – through the main circadian gene, CLOCK – orchestrates the interplay between metabolites and signaling proteins in much the same way a conductor leads a symphony.

"Metabolites and signaling proteins – like the horns and strings in an orchestra – need to be perfectly coordinated, and we've found that CLOCK provides that direction," he said.

Since external cues such as day-night lighting patterns and nutrition influence the circadian machinery, metabolites and their relationship to signaling proteins in cells seem to be acutely tied to circadian disruptions. This may help explain, Sassone-Corsi added, some of the primary physiological factors underlying obesity, high cholesterol and metabolic-based diseases like diabetes.

"This interplay has far-reaching implications for human illness and aging, and it is likely vital for proper metabolism," he said. Study results appear this week in the early online edition of the Proceedings of the National Academy of Sciences.

"By identifying the relationship between metabolites and the body clock, we have taken a first step toward a better understanding of how nutrients interact with our metabolism, giving researchers a new opportunity to spot the optimal times for us to get the fullest benefits from the foods we eat and the medications we take," added Kristin Eckel-Mahan, a UCI postdoctoral researcher in biological chemistry and study co-author.

Working with Metabolon Inc., Sassone-Corsi and Eckel-Mahan created the first liver metabolome – the full set of metabolites. With this information, they partnered with Pierre Baldi, director of UCI's Institute for Genomics & Bioinformatics, and his graduate student Vishal Patel to analyze the data and build CircadiOmics, a Web-based data system that provides detailed profiles of the metabolites and related genes in the liver and the underlying networks through which they interact. The CircadiOmics address is http://circadiomics.igb.uci.edu.

"Within CircadiOmics, we were able to integrate this circadian

metabolite data with multiple other data sources to generate the first comprehensive map of the liver metabolome and its circadian oscillations and develop regulatory hypotheses that have been confirmed in the laboratory," said Baldi, Chancellor's Professor of computer science. "CircadiOmics is being expanded with metabolic data about other tissues and conditions and will be invaluable to further our understanding of the interplay between metabolism and circadian rhythms in healthy and diseased states."

Provided by University of California - Irvine