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Research finds circadian rhythms dominate all life functions, plays significant role in metabolism

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Colorado State University researcher Andrey Ptitsyn.

New research from Colorado State University shows that the function of all genes in mammals is based on circadian - or daily - rhythms. The study refutes the current theory that only 10 percent to 15 percent of all genes were affected by nature's clock.

While scientists have long known that circadian rhythms regulate the behavior of the living, the study shows that daily rhythm dominates all life functions and particularly metabolism. The new study presents oscillation as a basic property of all genes in the organism as opposed to special function of some genes as previously believed.

Understanding how genes interact with and regulate health and disease

Knowing about oscillation properties of genes involved in metabolism is essential for understanding how genes interact with and regulate health and disease. Colorado State University researcher Andrey Ptitsyn's new analysis of data collected through several studies establishes a baseline oscillation in 98 to 99 percent of all genes through advanced computer algorithms. Most of these genes have never been previously reported as changing their expression level in a daily cycle. Some of these genes, considered "housekeeping," have been used as a stable reference platform in gene expression studies.

"Anyone who diets, for example, knows you shouldn't eat late, and now we are getting closer to understanding why exactly," said Ptitsyn, a researcher in the Bioinformatics Center at the College of Veterinary Medicine and Biomedical Sciences. The center is located in the Department of Microbiology, Immunology and Pathology. "We discovered that all genes have a significant change in pattern of activity - or expression - throughout the day. Every pathway of gene expression is affected by circadian rhythms, and the timing of the rhythms from each group of genes that are synchronized is important."

Clues for developing ways to treat people who overeat

Ptitsyn also discovered alternative short and long copies of some genes oscillating in the opposite phase. These genes are essential components of leptin signaling system, responsible for the sensation of satiety after eating. The oscillating pattern varies in different organs and determines the effect of leptin on regulation of the energy balance. Better understanding gene oscillation may provide researchers with clues for developing ways to treat people who overeat because of impaired leptin signaling.

Circadian rhythms are biological rhythms that cycle over a period of about 24 hours and regulate timing for most physiological functions and behaviors such as sleeping, eating and activity.

As a checks-and-balances procedure, Ptitsyn analyzed the sets of data with several mathematical approaches to achieve the same results. The research also shows that gene oscillation is significantly more organized when mammals are exposed to regular periods of day and night. Oscillation can become chaotic in states of consistent lighting or lack of lighting, but it never stops.

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Comparing the complex system in which the genes function to an AC power grid, Ptitsyn made the discovery by plotting the expression of 20,000 genes on a scale of frequency, or intensity, over a two day period and sorting them by phase or timing of oscillation. Where previous studies have failed, the Colorado State study uses advanced algorithms that have the capacity to identify patterns in such a large number of genes.

Impact of daylight and darkness

Ptitsyn discovered that gene activity oscillates in a "finely orchestrated" system and gene expression can be impacted by daylight and darkness - or a lack of both. For example, while gene expression oscillates in mice exposed to a constant state of dim light or darkness, the groups of genes that typically oscillate together - such as genes responsible for the function of an organ or a specific tissue - are chaotic under this state and don't function as a group. Lack of orchestration can be easily confused with the lack of oscillation. This makes the rhythm much harder to detect.

"It's like a conductor walking away from an orchestra during a performance; each musician continues to play, gradually going out of key with the others," said Ptitsyn. That is one likely reason why researchers previously missed the impact of circadian rhythm on all genes.

Synchronization with other genes

Depending upon environmental factors, groups of genes can function in a synchronized manner, shifting in time against each other and working in what resembles a domino effect.

However, very few genes are found to be oscillating in the same phases in different tissues or organs. In fact, only about 5 percent of all genes fall into the same phase or timing of peaks and valleys. Synchronization with the activity of the other genes and genes in different organs is a very important and highly specific part of gene function.

In addition, genes can oscillate with different amplitude - the swing between the highest and the lowest point. Genes are expressed at very different levels, but most of them have the same relative change throughout the day. However, some genes show significant change in the amplitude in different organs or in response to a changing environment.

"When we standardize genes onto a common scale that measures levels of expression, we could not find a single gene that did not oscillate," Ptitsyn said.

Visit the Colorado State University Bioinformatics Center online at:
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