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Genetic switch for circadian rhythms discovered

December 12 2007

University of California, Irvine researchers have identified the chemical switch that triggers the genetic mechanism regulating our internal body clock.

The finding, which uncovers the most specific information about the body's circadian rhythms to date, identifies a precise target for new pharmaceuticals that can treat sleep disorders and a host of related ailments. The study appears in the Dec. 13 issue of *Nature*.

Paolo Sassone-Corsi, Distinguished Professor and Chair of Pharmacology, found that a single amino acid activates the genes that regulate circadian rhythms. Amino acids are the building blocks of proteins, and Sassone-Corsi was surprised to find that only a single amino acid activates the body-clock mechanism because of the complex genes involved.

"Because the triggering action is so specific, it appears to be a perfect target for compounds that could regulate this activity," Sassone-Corsi said. "It is always amazing to see how molecular control is so precise in biology."

Circadian rhythms are the body's intrinsic time-tracking system, which anticipates environmental changes and adapts to the appropriate time of day. They regulate a host of body functions, from sleep patterns and hormonal control to metabolism and behavior. About 10 percent to 15 percent of all human genes are regulated by circadian rhythms.

Disruption of these rhythms can profoundly influence human health and has been linked to insomnia, depression, heart disease, cancer and neurodegenerative disorders.

The gene CLOCK and its partner BMAL1 trigger circadian rhythms. Sassone-Corsi and his research team discovered last year that CLOCK functions as an enzyme that modifies chromatin, the protein architecture of a cell's DNA.

In this current study, the Sassone-Corsi team learned that a single amino acid in the BMAL1 protein undergoes a modification that triggers the genetic chain of events involved with circadian rhythms.

Sassone-Corsi notes that if this amino-acid modification is impaired in any way, the switching mechanism can be thrown off, which can be the genetic underpinning of circadian-rhythm-related ailments. Currently, Sassone-Corsi is testing antibodies that can target this BMAL1 amino-acid activity.

Source: University of California - Irvine