Circadian rhythm-metabolism link discovered

July 24 2008

Paolo Sassone Corsi 1.

UC Irvine researchers have found a molecular link between circadian rhythms – our own body clock – and metabolism. The discovery reveals new possibilities for the treatment of diabetes, obesity and other related diseases.

Paolo Sassone-Corsi, Distinguished Professor and Chair of Pharmacology, and his colleagues have identified that an essential protein called CLOCK that regulates the body's circadian rhythms, works in balance with another protein called SIRT1 that modulates how much energy a cell uses.

"This interplay has far-reaching implications for human illness and aging, and it is likely vital for proper metabolism," said Sassone-Corsi, one of the world's leading researchers on circadian rhythms. The study appears in the July 25 issue of *Cell*.

Circadian rhythms of 24 hours govern fundamental physiological functions in almost all organisms. The circadian clocks are intrinsic time-tracking systems in our bodies that anticipate environmental changes and adapt themselves to the appropriate time of day.

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

It is estimated that up to 15 percent of our genes are regulated by these circadian clocks. Sassone-Corsi identified in 2006 that the protein CLOCK is an essential molecular gear of the circadian machinery.

Now, he and his colleagues have shown that the protein SIRT1 counterbalances the function of CLOCK. Even though SIRT1's function differs from CLOCK's, the two proteins interact, creating a bond that is finely regulated in the cell.

SIRT1 senses energy levels in the cell; its activity is modulated by how many nutrients a cell is consuming. It also helps cells resist oxidative and radiation-induced stress, and for this reason SIRT1 is known to help control the process of aging.

CLOCK and SIRT1 are both part of the epigenome, which consists of proteins existing in connection with a cell's DNA that take external environmental factors and make the cell's genes behave differently, even though those genes do not structurally change.

"When this balance between these two vital proteins is upset, normal cellular function can be disrupted," Sassone-Corsi said. "Because of the role these two enzymes play, changes in our sleep patterns or our diets can directly be translated into how our cells act."

The findings also suggest that proper sleep and diet could help maintain or rebuild the CLOCK-SIRT1 equilibrium and may help explain why lack of proper rest or disruption in our normal sleep patterns is known to increase hunger, which can lead to obesity and related illnesses and can accelerate the aging process.

The specific interaction between CLOCK and SIRT1 also could lead to the development of drugs aimed at facilitating healthy metabolism, thereby helping to solve major social and medical problems such as diabetes and obesity.

Source: University of California - Irvine