Scientists discover how gene mutation reduces the need for sleep

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A mutation in the gene DEC2 allows for some people to be natural short sleepers. Credit: University of California, San Francisco

It's every over-achiever's dream: a gene mutation that allows them to function normally with just four to six hours of sleep a night instead of the normal eight.

In 2009, UC San Francisco neurology professor Ying-Hui Fu, Ph.D., discovered a mutation in the gene DEC2 in a family of natural short

sleepers – people who go to bed at a normal time (11 p.m. to midnight) but wake up naturally at 5 in the morning. "These are not people who've trained themselves to wake up early. They're born this way," says Fu.

A new study in mice by Fu's lab – published in *PNAS* on March 12, 2018 – reveals how the DEC2 mutation seen in human short-sleepers may allow them to survive and thrive on just a few hours of sleep.

The researchers engineered mice to have the same mutation in the DEC2 gene seen in human short sleepers. They discovered that DEC2 helps control levels of orexin, a hormone involved in maintaining wakefulness. (The sleep disorder narcolepsy is caused by too little of this hormone.) The mutation in DEC2 seems to work by partially releasing the brakes on orexin production.

DEC2 helps regulate circadian rhythms, the natural biological clock that dictates when hormones are released and influences behaviors such as eating and sleeping. DEC2 oscillates on a circadian schedule: rising during the day, but falling at night.

The new study suggests that DEC2 may lower your level of alertness in the evening by binding to and inhibiting MyoD1, a gene that turns on orexin production. Before dawn, DEC2 fades away, allowing MyoD1 to stimulate orexin production to wake you up and keep you alert throughout the day.

Fu says the mutation seen in human short sleepers weakens DEC2's ability to put the breaks on MyoD1, leading to more orexin production and causing the short sleepers to stay awake longer. "The role of DEC2 is likely to make sure orexin is expressed in the right amount at the right time of day. It's the time-keeper to make sure orexin levels match the circadian rhythm," she explains.

The DEC2 mutation is very rare, but there are other gene mutations that act on different pathways to cause natural short sleep. Fu is studying these genes with the goal of better understanding sleep and its impact on our health.

More information: Arisa Hirano et al. DEC2 modulates orexin expression and regulates sleep, *Proceedings of the National Academy of Sciences* (2018). DOI: 10.1073/pnas.1801693115

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