

## New fruitfly sleep gene promotes the need to sleep

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This is an alpha subunit of the nicotinic acetylcholine receptor accounts for the rye mutant phenotype. Expression pattern of redeye (green). Credit: Amita Sehgal and Mi Shi, PhD, Perelman School of Medicine, University of Pennsylvania; *eLife* 

All creatures great and small, including fruitflies, need sleep. Researchers have surmised that sleep – in any species—is necessary for repairing proteins, consolidating memories, and removing wastes from cells. But, really, sleep is still a great mystery.

The timing of when we sleep versus are awake is controlled by cells in tune with circadian rhythms of light and dark. Most of the molecular components of that internal clock have been worked out. On the other



hand, how much we sleep is regulated by another process called sleep homeostasis, however little is known about its molecular basis.

In a study published in *eLIFE*, Amita Sehgal, PhD, professor of Neuroscience at the Perelman School of Medicine, University of Pennsylvania, and colleagues, report a new protein involved in the homeostatic regulation of sleep in the fruitfly, *Drosophila*. Sehgal is also an investigator with the Howard Hughes Medical Institute (HHMI).

The researchers conducted a screen of mutant flies to identify shortsleeping individuals and found one, which they dubbed redeye. These mutants show a severe reduction in the amount of time they slumber, sleeping only half as long as normal flies. While the redeye mutants were able to fall asleep, they would wake again in only a few minutes.

The team found that the redeye gene encodes a subunit of the nicotinic acetylcholine receptor. This type of acetylcholine receptor consists of multiple protein subunits, which form an ion channel in the cell membrane, and, as the name implies, also binds to nicotine. Although acetylcholine signaling—and cigarette smoking—typically promote wakefulness, the particular subunit studied in the *eLIFE* paper is required for sleep in *Drosophila*.

Levels of the redeye protein in the fly oscillate with the cycles of light and dark and peak at times of daily sleep. Normally, the redeye protein is expressed at times of increasing sleep need in the fly, right around the afternoon siesta and at the time of night-time sleep. From this, the team concluded that the redeye protein promotes sleep and is a marker for sleepiness – suggesting that redeye signals an acute need for sleep, and then helps to maintain sleep once it is underway.

In addition, cycling of the redeye protein is independent of the circadian clock in normal day:night cycles, but depends on the sleep homeostat.



The team concluded this because redeye protein levels are upregulated in short-sleeping mutants as well as in wild-type animals following <u>sleep</u> <u>deprivation</u>. And, mutant flies had normal circadian rhythms, suggesting that their <u>sleep problems</u> were the result of disrupted sleep/wake homeostasis.

Ultimately the team wants to use the redeye gene to locate sleep homeostat neurons in the brain. "We propose that the homeostatic drive to sleep increases levels of the redeye <u>protein</u>, which responds to this drive by promoting sleep," says Sehgal. Identification of molecules that reflect sleep drive could lead to the development of biomarkers for sleep, and may get us closer to revealing the mystery of the <u>sleep</u> homeostat.

Provided by University of Pennsylvania School of Medicine

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