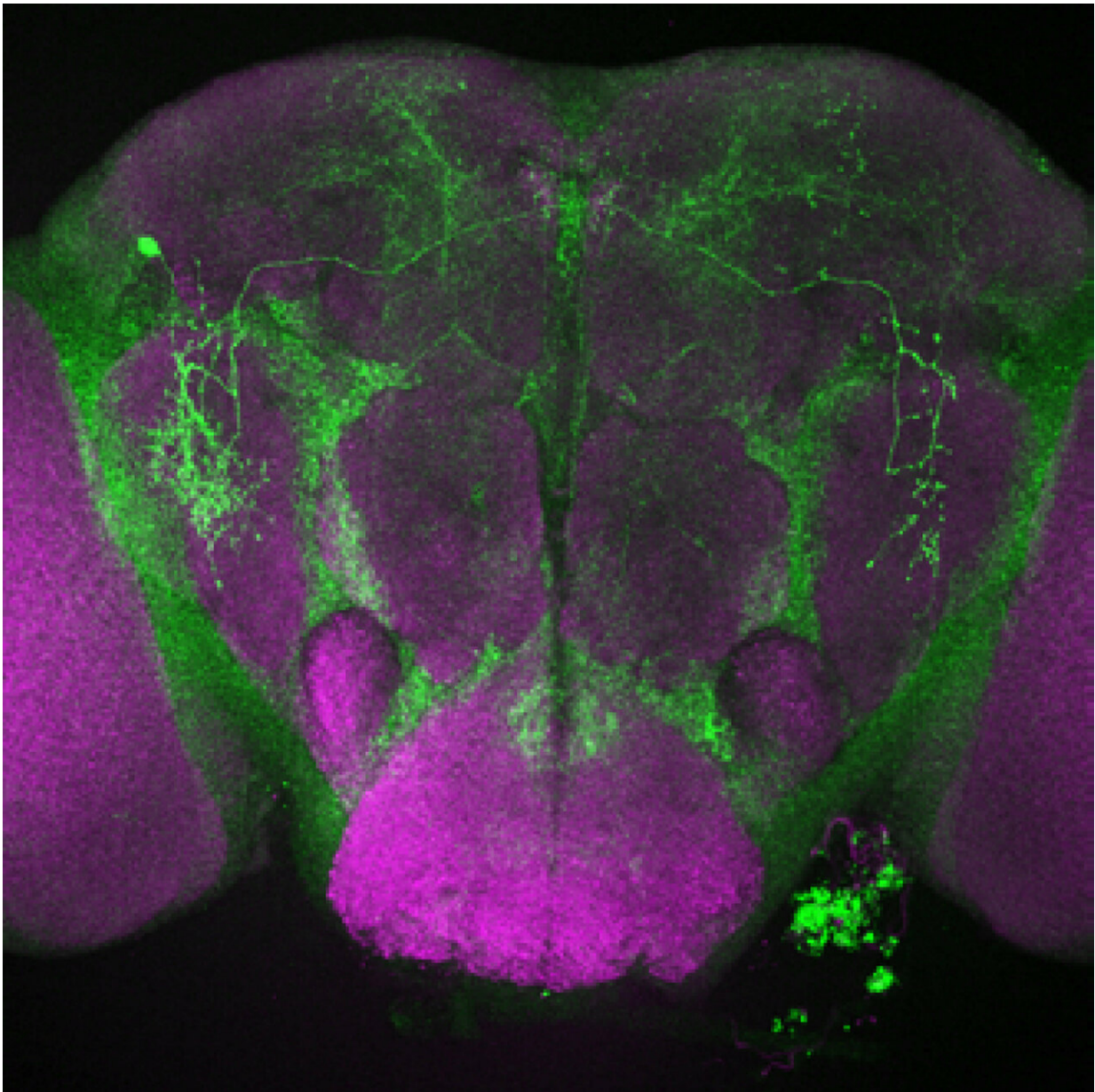


# To sleep, perchance to heal: Newly discovered gene governs need for slumber when sick

January 31 2019

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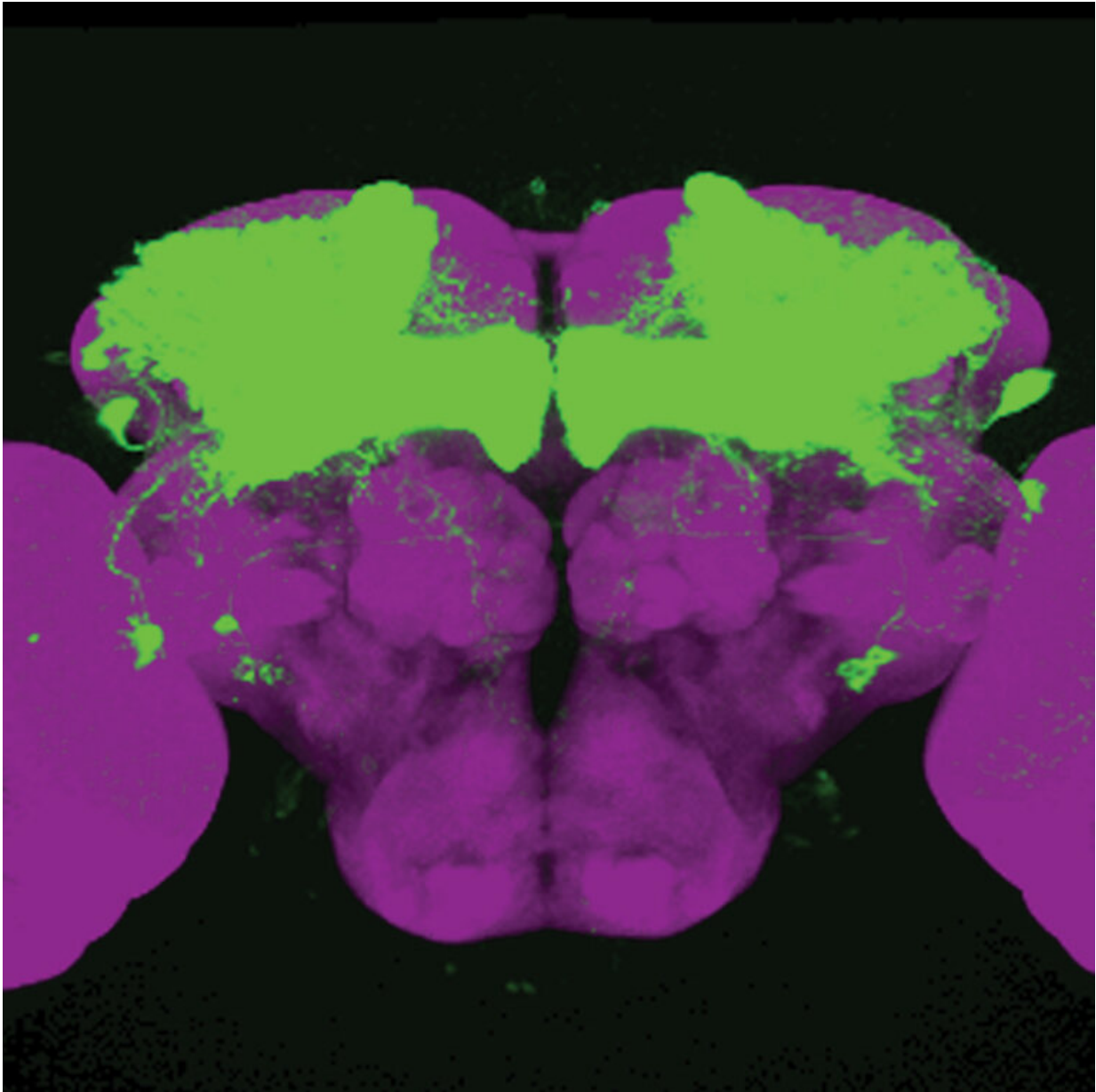
A fruit that fly has been infected with bacteria, showing nemuri expression (green) in the brain -- a single neuron and its projections on either side of the brain. Credit: Amita Sehgal, Perelman School of Medicine, University of Pennsylvania; *Science*

Humans spend nearly one-third of their lives in slumber, yet sleep is still one of biology's most enduring mysteries. Little is known about what genetic or molecular forces drive the need to sleep—until now. In a study of over 12,000 lines of fruit flies, researchers from the Perelman School of Medicine at the University of Pennsylvania have found a single gene, called nemuri, that increases the need for sleep. These findings are published today in *Science*.

The NEMURI protein fights germs with its inherent antimicrobial activity and it is secreted by cells in the brain to drive prolonged, [deep sleep](#) after an [infection](#).

"While it's a common notion that [sleep](#) and healing are tightly related, our study directly links sleep to the [immune system](#) and provides a potential explanation for how sleep increases during sickness," said senior author Amita Sehgal, Ph.D., a professor of Neuroscience and director of Penn's Chronobiology Program.

Without the nemuri gene, flies were more easily aroused during daily sleep, and their acute need for an increase in sleep—induced by [sleep deprivation](#) or infection—was reduced. On the other hand, sleep deprivation, which increases the need for sleep, and to some extent infection, stimulated nemuri to be expressed in a small set of fly neurons nestled close to a known sleep-promoting structure in the brain. Overexpression of nemuri increased sleep in bacteria-infected flies and led to their increased survival compared to non-infected control flies.



Expression of the *nemuri* gene (green) in neurons in the brain of a fruit fly.  
Credit: The University of Pennsylvania

In response to infection, NEMURI appears to kill microbes, most likely in the peripheral parts of the fruit fly body, and increases sleep through

its action in the brain. Several molecules like NEMURI, which is an antimicrobial peptide (AMP), have multiple functions that help combat infection, but its sleep-promoting role may be just as important for host defense, the researchers suggest, given that increased sleep during sickness promotes survival in the flies.

What's more, the authors note that cytokines such as interleukin-1 (IL-1), an immune cell molecule, are implicated in human sleep. IL-1 can function in the same pathway as AMPs, and it accumulates after prolonged wakefulness and appears to promote sleep. In mammals, cytokines can induce production of AMPs, but AMPs may also affect the expression of cytokines. Given this interwoven relationship, the researchers conclude that NEMURI is a working link between immune function and sleep.

"The NEMURI protein is a genuine driver of keeping sleep on track under conditions of high sleep need like when we're sick," said first author Hirofumi Toda, Ph.D., a postdoctoral fellow in Sehgal's lab. "In the next phase of our work, we plan to investigate the mechanism by which NEMURI drives sleep."

**More information:** H. Toda et al., "A sleep-inducing gene, *nemuri*, links sleep and immune function in *Drosophila*," *Science* (2019). [science.sciencemag.org/cgi/doi ... 1126/science.aat1650](https://science.sciencemag.org/cgi/doi/10.1126/science.aat1650)

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Provided by Perelman School of Medicine at the University of Pennsylvania

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