

Press Release

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Worm genetics reveal important pathways for sleep regulation

Using an unbiased genetic approach in worms, researchers from the University of Tsukuba find that tissues in the body regulate sleep via pathways that are important for making and disposing of proteins

Tsukuba, Japan - Although the regulation of sleep—how much, when, and how sleep occurs—is mainly considered to be controlled by the brain, sleep deprivation also affects the body, and signals from the body can affect sleep. However, the ways in which the body regulates sleep are largely unknown. In a recent study published in *Cell Reports*, Japanese researchers have revealed that sleep in worms is regulated by the body via cellular pathways that maintain proper protein function, from synthesis to degradation.

When exploring the body's regulation of sleep, it can be difficult to know where to start. The researchers from the University of Tsukuba chose to use an unbiased investigative technique known as forward genetic screening. To do this, they first applied a chemical to cause random mutations in about 500 worms, and then used a video-based monitoring system to identify the worms that slept much more or less than average. When they identified such worms, they looked at what mutations they had, how the mutations affected the sleep.

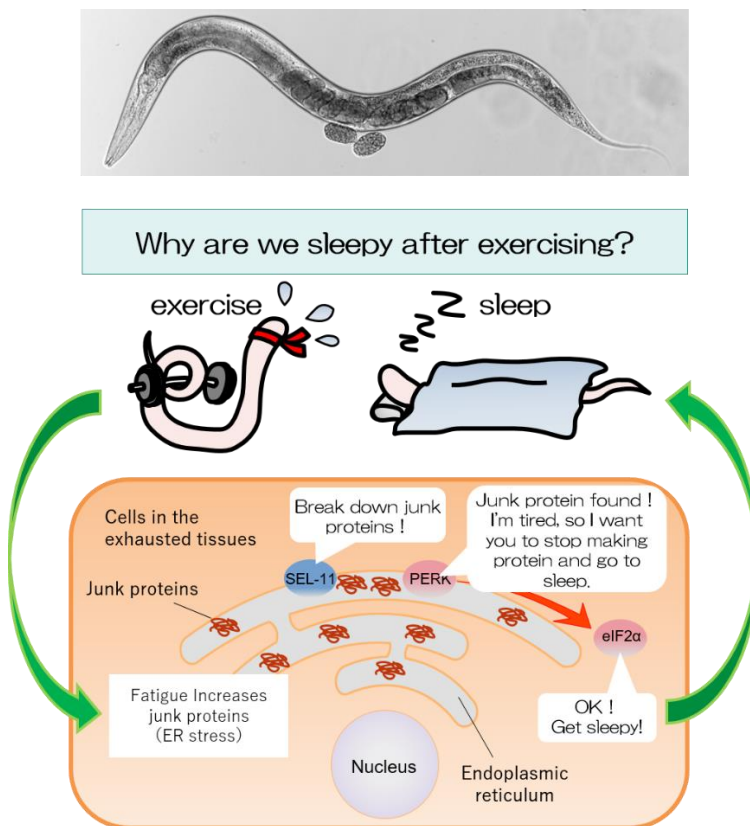
“Using this method, we were able to identify that mutations in the *sel-1* and *sel-11* genes were associated with longer sleep duration,” says senior author of the study Professor Yu Hayashi. “Both genes code for proteins that are part of the endoplasmic-reticulum-associated protein degradation pathway, which helps cells to get rid of proteins that are misfolded.”

The researchers also found that mutations in *mars-1*, which is important for protein synthesis, were associated with prolonged sleep in the worms. Moreover, although *sel-1*, *sel-11*, and *mars-1* were expressed in a wide range

of tissues, when the researchers made the worms express normal versions of some of these genes in skin cells led to normal sleep patterns. These results indicated that protein-regulating pathways in the body are indeed important for controlling sleep.

“We were also able to identify some downstream pathways that are involved in sleep regulation by modifying the expression of proteins in the worms,” says Professor Hayashi. “Furthermore, when we tested our results from worms in mice, we found that these pathways also seem to regulate sleep in mammals.”

Sleep disturbances are widely considered to influence inflammation and immunity, and may contribute to diseases such as inflammatory bowel disease and arthritis. A better understanding of how sleep is regulated is thus key to disease prevention. The results of this study add to a growing body of literature on sleep regulation and are hoped to improve sleep disturbance therapies in the near future that may prevent inflammatory diseases such as arthritis.



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Summary: Researchers from the University of Tsukuba have found that, in worms, protein-regulating pathways in the body help to control sleep. Moreover, some of the worm-related findings were replicated in mice, indicating that these peripheral pathways are also important in mammals. These results add to our growing knowledge around sleep regulation and may inform therapies to reduce human sleep disturbances in the future.

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Bibliographic information

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