

Gwangju Institute of Science and Technology

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Professor Young-Joon Kim's research team investigates the circadian rhythm mechanism of egg formation

- Professor Young-Joon Kim's team from the School of Life Sciences at GIST (Gwangju Institute of Science and Technology, President Kiseon Kim) revealed the mechanism by which the somatostatin neuropeptide* released by the brain's biological clock generates oogenesis** circadian rhythm.
 - * Neuropeptide: Neuroproteins are relatively small-sized proteins that neurons use to communicate with each other. Neuroproteins are known to be involved in a wide range of brain functions, including food intake, metabolism, reproduction, social behavior, learning, and memory, and sleep.
 - ** oogenesis: It is the process of generating mature eggs from the female ovary's reproductive stem cells. The generation of the eggs of the fruit fly, Drosophila melanogaster, is divided into 14 steps. The juvenile hormone, the main reproductive hormone of the fruit flies, allows the egg in stage 7 to mature into the egg in stage 8, which starts to accumulate egg yolk, inducing oogenesis.
 - The research team applied neuronal activity regulation technology and gene expression manipulation technology to grow insulin located in the brainstem region of 6 pairs of DN1p(posterior dorsal neurons)* out of about a hundred thousand neurons in the Drosophila brain. It was discovered that the circadian rhythm of oogenesis was created by periodically suppressing the



activity of hormone-secreting cells, and through this, the secretion rhythm of JH(juvenile hormone), a reproductive hormone that promotes oogenesis, is generated.

- * Posterior dorsal neuron 1, DN1p: A part of 150 biological clock neural networks reported in the Drosophila brain. It has high morning activity due to the influence of the M-nerve, which increases in the morning. In previous studies, it was reported that this nerve induces circadian behavioral rhythm changes under the influence of temperature and light. In this study, it was found that the nerve is an essential biological clock in determining the rhythm of oogenesis.
- Animals have evolved to optimize the reproductive period for successful reproduction. Large mammals have a gestation period of at least 6 months, breed in the fall to give birth in spring. Small mammals and birds with a short gestation period mainly breed in spring and give birth in summer. The biological clock of animals is estimated to play an important role in determining the breeding period by detecting changes in the length of day and night according to the season, but the mechanism for determining the breeding period of females is unknown.
 - The fruit fly Drosophila melanogaster is an important model animal for circadian clock research. The researchers who isolated the circadian clock gene PERIOD from the fruit fly won the 2017 Nobel Prize in Physiology or Medicine. The fruit fly's brain has about 150 nerves that perform the circadian clock function, creating a circadian rhythm of various physiological processes such as the hormone secretion rhythm along with the behavioral cycle of the fruit fly. However, how the brain circadian clock generates the oogenesis cycle, which is important for the formation of the reproductive period, remains unknown.
- The research team was the first to discover that allatostatin-C*, a somatostatin-based neuropeptide periodically released by DN1p biological clock nerves, inhibits the secretion activity of insulin growth hormone cells.
 - * Somatostatin/ Allatostatin-C: As a kind of neuroprotein, it has high evolutionary conservation, such as found in not only invertebrates but also vertebrates. It was first reported as a role in inhibiting the production and secretion of growth



hormone invertebrates and is known to inhibit the secretion of the gonadotropinreleasing hormone that regulates the secretion of reproductive hormones.

- Allatostatin-C is a homolog to somatostatin, which is known to inhibit the secretion of gonadotropin-releasing hormone, which regulates the secretion of reproductive hormones in vertebrates, including mammals. The hypothesis is that it will generate a cycle of hormone secretion activity.
- Professor Young-Joon Kim said, "The causal relationship between the allatostatin-C release biotic clock nerve, secretion of the reproductive hormone, and the rhythm of oogenesis, which was first discovered in this study, is to reveal the neurological and molecular mechanisms that determine the reproductive period of vertebrates, which is still unknown. We look forward to providing important insights."
- This research was conducted with the support of the integrated Institute of Biomedical Research supported by GIST, the senior researcher support project supported by the National Research Foundation of Korea, and the Korea Drosophila Resource Center. The research results were published online on January 26, 2021, in the *Proceedings of the National Academy of Sciences*, a worldrenowned journal in the field of natural sciences.

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