

Chrono, the last piece of the circadian clock puzzle?

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All organisms, from mammals to fungi, have daily cycles controlled by a tightly regulated internal clock, called the circadian clock. The whole-body circadian clock, influenced by the exposure to light, dictates the wake-sleep cycle. At the cellular level, the clock is controlled by a complex network of genes and proteins that switch each other on and off based on cues from their environment.

Most genes involved in the regulation of the [circadian clock](#) have been characterized, but Akihiro Goriki, Toru Takumi and their colleagues from RIKEN and Hiroshima University in Japan and University of Michigan in the United States knew that a key component was missing and sought to uncover it in mammals.

In the study, the team performed a genome-wide chromatin immunoprecipitation analysis for genes that were the target of BMAL1, a core clock component that binds to many other [clock genes](#), regulating their transcription.

The authors characterize a new circadian gene that they name Chrono. They show that CHRONO functions as a transcriptional repressor of the negative feedback loop in the mammalian clock: the protein CHRONO binds to the regulatory region of clock genes, with its repressor function oscillating in a circadian manner. The expression of core clock genes is altered in mice lacking the Chrono gene, and the mice have longer circadian cycles.

"These results suggest that Chrono functions as a core clock repressor," conclude the authors.

In addition, they demonstrate that the repression mechanism of Chrono is under epigenetic control and links, via a glucocorticoid receptor, to metabolic pathways triggered by behavioral stress.

These findings are confirmed by another study by the University of Pennsylvania, also published in *PLOS Biology* today. In the study, John Hogenesch and his team prove the existence of Chrono using a computer-based analysis.

Provided by RIKEN

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