Circadian oscillation of a cyanobacterium doesn't need all three Kai proteins to keep going

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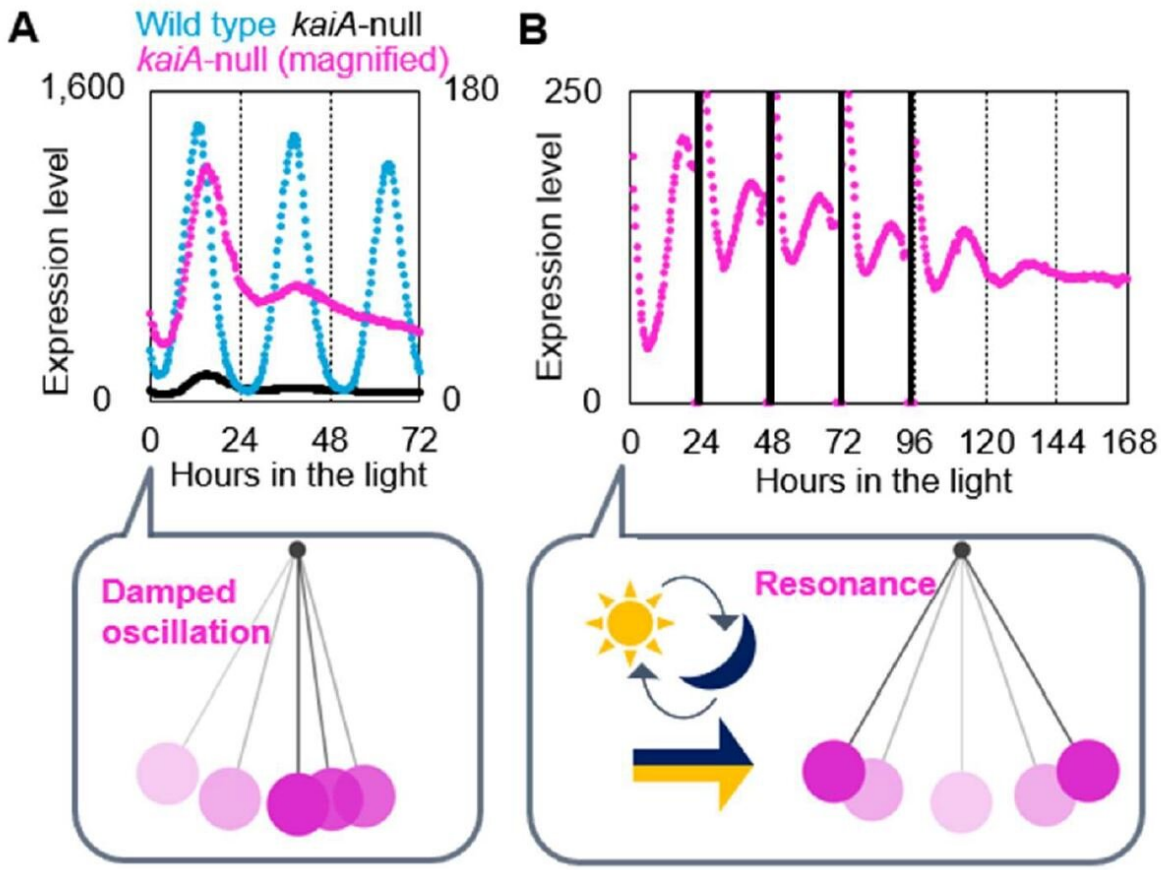

Inactivating KaiA does not stop but damps circadian oscillations of the cyanobacterial' circadian clock (A). The amplitude of the damped oscillation is elevated by resonance with external cycles (B). Credit: Iwasaki Laboratory, Waseda University

Circadian rhythms are driven by a highly autonomous, self-sustaining circadian clock within cells, telling us when to sleep or wake up in a 24-hour cycle.

This mechanism can also be found in other organisms, including in primitive, photosynthetic bacteria known as cyanobacteria. In cyanobacteria, three types of proteins known as KaiA, KaiB, and KaiC work together like gears of a clock to create the rhythms. According to previous studies, all three Kai proteins are required for the circadian clock of cyanobacteria to function, and lacking KaiA could abolish oscillations.

However, in a recent study published in *Nature Communications*, scientists from Waseda University, Kyushu University, and Ritsumeikan University presented an observation of dampened, low-amplitude circadian oscillations in the absence of KaiA in the cyanobacterium Synechococcus elongatus.

Hideo Iwasaki, professor of cell biology at Waseda University and the corresponding author of this study, actually recorded such weak circadian rhythms during an experiment conducted more than 20 years ago, but at the time, it was dismissed as a discrepancy and overlooked. However, when a graduate student from his laboratory pointed out the same subtle oscillations while observing gene expression patterns of a genomic variant of cyanobacteria lacking KaiA, Iwasaki knew something was going on.

"We spent much time and energy in conducting experiments, such as monitoring rhythms with a technique called the bioluminescence reporter, to understand physiological importance and molecular mechanisms of the damp circadian oscillations, as well as to establish

our theoretical perspective because we had a hunch that our findings would overturn conventional knowledge," Iwasaki says. "Our findings are the results of efforts made by the graduate student who noticed the oscillations, who is the first author of this paper, and by the talented researchers we collaborated with. I would like to thank everyone involved for their dedication and hard work."

Iwasaki adds, "We also found that the dampened rhythms resonate with external cycles with a period of 24 to 26 hours, meaning that its natural frequency is similar to that of a circadian clock. So, in a day-night altered environment, low-amplitude oscillations could theoretically act as a circadian clock to regulate various activities within cells and adapt to change in the cyclic environment."

Though much research has been done on the circadian clock, there has been a tendency for researchers to shy away from studying dampened circadian oscillations because of the difficulty in analyzing them and their phenotypes being not particularly intriguing, but Iwasaki believes that there needs to be more focus on the topic.

"Based on our results, we could hypothesize that the circadian clock did not become autonomous and self-sustaining all of a sudden, but instead, gradually evolved from low-amplitude oscillations," says Iwasaki. "From the evidence that some cyanobacteria in the natural environment do not possess KaiA, perhaps obtaining and losing KaiA happened multiple times along its evolution, and it could be that some cyanobacteria do not have KaiA for good reasons. Through further studies on dampened circadian oscillations, we could be unveiling a great mystery with physiological and evolutionary significance."

Iwasaki and his team are interested in further investigating the roles that dampened circadian oscillations play. If similar circadian mechanisms can be observed among higher plants and mammals, it may be able to

manipulate our circadian rhythms more accurately by applying dampened circadian oscillations and resonation.

More information: Naohiro Kawamoto et al, Damped circadian oscillation in the absence of KaiA in Synechococcus, *Nature Communications* (2020). DOI: 10.1038/s41467-020-16087-x

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