【Grant-in-Aid for Scientific Research (S)】

Biological Sciences (Biology)

Title of Project : An Integrated Multi-scale Approach for Studying Cyanobacterial Circadian Clock System

Shuji Akiyama
(Institute for Molecular Science, Research Center of Integrative Molecular Systems, Professor)

Research Project Number : 17H06165 Researcher Number : 50391842
Research Area : Biophysics
Keyword : Biological Clock, Clock Protein, Cyanobacteria, KaiC

【Purpose and Background of the Research】

Circadian rhythms are self-sustained oscillations with a period of approximately 24 h, enabling organisms to adapt to daily alterations in the environment. So far, many studies have investigated the time-measuring mechanism in the circadian clocks from bacteria to mammals. However, it remains unknown how the period is implemented in clock oscillators and kept unaffected against temperature changes (temperature compensation). In this research project, we will study cyanobacterial circadian clock as a model system and address these questions using a multidisciplinary approach including, biophysics, structural biology, chronobiology, molecular biology, and control engineering.

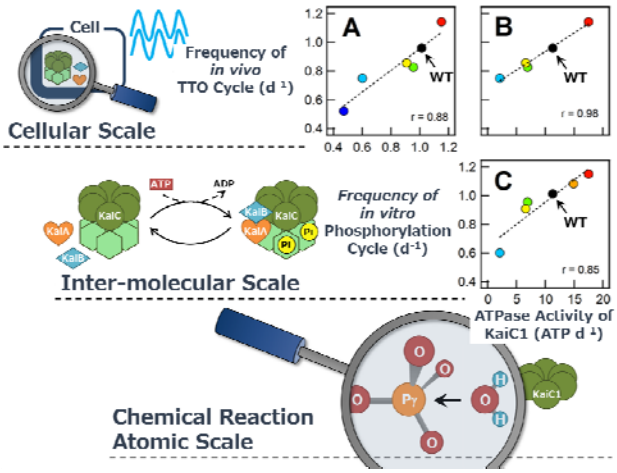

Figure 1 Cyanobacterial Circadian Clock System

【Research Methods】

Both the frequency (reciprocal of the period) and the temperature compensation of cellular rhythms are under strong influences of KaiC, a core clock protein in cyanobacteria. For example, the more *in vitro* ATPace activity of KaiC increases, the higher the frequency of the cellular rhythm becomes (Figure 1, panel B). Taking advantage of this trans-hierarchical correspondence, we will study the mechanisms of the circadian periodicity and temperature compensation both encoded in KaiC in accordance with the following 5 points.

<1> Large-scale screening of KaiC mutants.
<2> Mapping a frequency-to-structure correspondence in KaiC.
<3> Neutron crystallographic study on the active site of KaiC ATPase.
<4> X-ray crystallographic study on KaiC.
<5> Imaging and spectroscopic characterizations of the solution structure and dynamics of KaiC.

【Expected Research Achievements and Scientific Significance】

Results from our research project would provide an answer to the fundamental yet long-standing question in chronobiology: what determines the temperature-compensated 24 h period?

【Publications Relevant to the Project】

・Abe, J., Hiyama, T. B., Mukaiyama, A., Son, S., Mori, T., Saito, S., Osako, M., Wolanin, J., Yamashita, E., Kondo, T., and Akiyama, S. Atomic-scale Origins of Slowness in the Cyanobacterial Circadian Clock. *Science* 349, 312-316 (2015).
・Akiyama, S. Structural and dynamic aspects of protein clocks: How can they be so slow and stable? *Cellular and Molecular Life Sciences* 69, 2147-2160 (2012).
・Murayama, Y., Mukaiyama, A., Imai, K., Onoue, Y., Tsunoda, A., Nohara, A., Ishida, T., Maéda, Y., Terauchi, K., Kondo, T., and Akiyama, S. Tracking and visualizing the circadian ticking of the cyanobacterial clock protein KaiC in solution. *The EMBO Journal* 30, 68-78 (2011).

【Term of Project】 FY2017-2021

【Budget Allocation】 157,400 Thousand Yen

【Homepage Address and Other Contact Information】

http://bms.ims.ac.jp/AkiyamaG/index.html