【Grant-in-Aid for Specially Promoted Research】

Biological Sciences

Title of Project : Circadian pacemaker of cyanobacteria by clock protein KaiC

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Research Area : Biology
Keyword : Circadian clock, clock protein, KaiC, ATPase

【Purpose and Background of the Research】

From bacteria and fungi to plants and animals, circadian clocks are ubiquitous endogenous biological timing mechanisms that adapt to daily alterations in environmental conditions.

We reconstituted the self-sustained circadian oscillation in phosphorylation state of the cyanobacterial clock protein KaiC by incubating it with KaiA protein, KaiB protein, and ATP. KaiC also has novel mechanisms for synchronization. Thus, the Kai protein clock is inheritantly designed as the master pacemaker of cyanobacterial circadian clock.

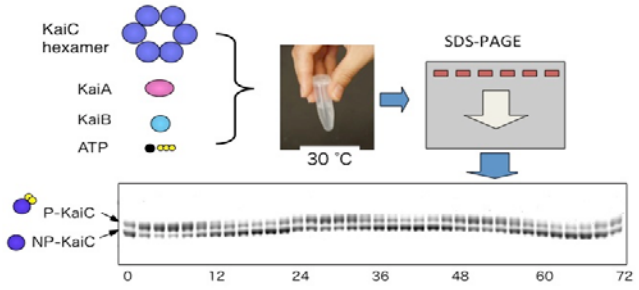

Fig. 1 In vitro reconstitution of circadian clock-2005

Moreover, we showed that KaiC possesses extremely weak but temperature-compensated ATPase activity (10-15 ATPs/day/KaiC) and that activities of wild-type KaiC and five period-mutant proteins are directly proportional to their *in vivo* circadian frequencies, indicating that the ATPase activity defines the circadian period. Based on these observations, we propose the KaiC ATPase activity as the most fundamental pacemaking reaction underlying circadian periodicity of cyanobacteria.

【Research Methods】

How KaiC protein that forms hexamer attains such extraordinary characteristics that apparently contradict with the normal chemical reaction? We proposed the intramolecular negative-feedback regulation of ATPase activity could generate tension inside the KaiC hexamer to suppress the activity and to gain circadian period determination. In this study, we will analyze the biochemical and genetical approaches to the ATPase activity of KaiC to explain a time-keeping function of KaiC. We also try to understand function of KaiC at atomic level by introducing dynamic structural biology.

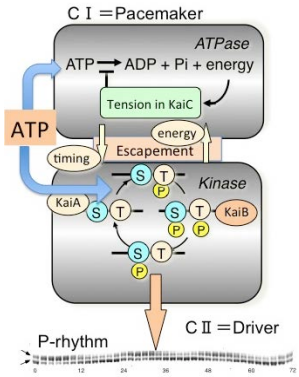

Fig. 2 KaiC clock model

【Expected Research Achievements and Scientific Significance】

1) This project could explain one of the final questions of circadian biology, that is, to explain how living organisms remember 24 h period and how it was stablilized against temperature. 2) This study could reveal the circadian clock of many eukaryote, because biochemical process by protein activity are recently reported to affect circadian period.
3) This study might find novel function of proteins that is not included current list of protein function, such as enzyme, motion, chemical reactor, etc.

【Publications Relevant to the Project】

・*Nakajima M, et al. Science 308, 414-5 (2005)*
・*Terauchi K, et al. Proc. Natl Acad. Sci. USA. 104, 16377-81 (2007)*

【Term of Project】 FY2012-2016

【Budget Allocation】 315, 500 Thousand Yen

【Homepage Address and Other Contact Information】

http://clock.bio.nagoya-u.ac.jp/web/index.htm