

Protein-Protein Interactions in the Cyanobacterial KaiABC Circadian Clock

Martin Egli, *Department of Biochemistry, Vanderbilt University, School of Medicine, Nashville, Tennessee 37232, USA.* E-mail: martin.egli@vanderbilt.edu

Circadian clocks are self-sustained biochemical oscillators. Their properties include temperature compensation, a time constant of approximately 24 h, and high precision. These properties are difficult to explain by known biochemical reactions. The ultimate explanation for the mechanism of these unusual oscillators will require characterizing the structures, functions, and interactions of their molecular components. We are analyzing the biological clock in the simplest cells that are known to exhibit circadian phenomena, the prokaryotic cyanobacteria, whose basic clock is composed of three essential genes, *kaiA*, *kaiB* and *kaiC* [1]. The structures of all three Kai proteins have recently been reported ([2], reviewed in 3]), along with phosphorylation sites in KaiC that are crucial for sustaining the oscillation [4]. Very recent research has demonstrated that the KaiABC clock keeps time in the absence of a transcriptional-translational oscillatory feedback loop [5] and that the circadian oscillation of KaiC phosphorylation can be reconstituted *in vitro* [6]. This means that the clock made up of recombinant KaiC, KaiA and KaiB proteins in the presence of ATP and Mg²⁺ ticks in an Eppendorf tube! The presentation will summarize the status of structural work on Kai proteins and efforts to begin to understand their complexes.

[1] Ishiura M., et al., *Science*, 1998, **281**, 1519. [2] Pattanayek R., et al., *Molec. Cell*, 2004, **15**, 375. [3] Johnson C.H., Egli M., *Nature Struct. Mol. Biol.*, 2004, **11**, 584. [4] Xu Y., et al., *Proc. Natl. Acad. Sci. U.S.A.*, 2004, **101**, 13933. [5] Tomita J., et al., *Science*, 2005, **307**, 251. [6] Nakajima M., et al., *Science*, 2005, *in press*.

Keywords: protein-complexes, protein-crystallography, protein-phosphorylation