Systems Biology of Mammalian Circadian Clocks

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MAMMALIAN circadian clock is a complex and dynamic system consisting of complicatedly integrated regulatory loops and displaying the various dynamic behaviors including i) endogenous oscillation with about 24-hour period, ii) entrainment to the external environmental changes, and iii) temperature compensation over the wide range of temperature.

The logic of circadian clock is difficult to elucidate without 1) comprehensive identification of network structure[1-3], 2) prediction and validation based on measurement and perturbation of its behavior[4], and 3) design and implementation of artificial networks of identified structure and observed dynamics[5].

First, we comprehensively determined the transcriptional circuits composed of 20 transcription factors, and three type of DNA elements[1,2]. The following quantitative measurement, and static and dynamic perturbation of clock circuits revealed a topological and functional vulnerability in mammalian clocks[3,4].

Second, to derive and prove transcriptional logic of mammalian circadian clocks, we develop mammalian cell culture system, where we can design and implement artificial transcriptional circuits to physically simulate natural circadian transcriptional circuits. Using this system, we report transcriptional logic to generate day-time and night-time transcriptional output as well as diverse transcriptional outputs with various timings[5].

Reference

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