

Synthesizing Artificial Wet Cell?!

Current State & Social/Cultural Implications

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Circadian rhythms are endogenous oscillations with a period of ~24 h that is temperature-compensated and synchronized to environmental cues such as light and temperature. Recently we have broken a dogmatic hypothesis for generating circadian rhythms based on ‘transcription-translation feedback’ process in cyanobacteria. Circadian rhythm in phosphorylation state of a master clock protein KaiC continued even after elimination of transcription and translation processes. This finding led us to reconstitute posttranslational cycling *in vitro* by incubating three clock proteins and ATP. Although this was the first *in vitro* reconstitution of circadian rhythms, we still do not know the chemical dynamics to generate such oscillations. This is an example that reconstitution or ‘synthesis’ *per se* is not always accomplished based on logical design of cell functions, but provides spectacular biochemical tool for further analysis. Interestingly, in cyanobacteria almost all gene promoters, including clock gene promoters, are driven in a circadian fashion, meaning genome-wide transcriptional control by protein-based chemical oscillator. To address how transcriptional rhythm functions in the circadian system, we are trying transplantation of the Kai-based clock to *E. coli*, and designing artificial inputs and outputs to it. This is so called ‘semi-synthetic’ approach to analyze as-yet-unknown property of a certain gene/protein of interest network (e.g. Kai-based clock). I also report synthetic gene network studies in insect cells in collaboration with Dr. Akira Matsumoto (Kyushu Univ.).

Recent movements in ‘synthetic biology’ has led to an attempt to reconstitute various cellular functions, including circadian rhythms as mentioned above, in model bacterial cells and in a test tube. Future target of such approaches may be synthesizing or reconstituting an artificial wet cell. Recently, some young scientists in Japan, including some of participants in this meeting, have formed a consortium to discuss its aims, possibility and technical problems as well as its social and ethical concerns. Summary of various opinions from the consortium will be presented.