Frontier Biosciences group

Graduate School of Frontier Biosciences

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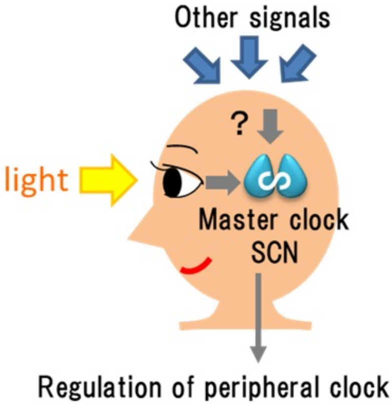
The circadian clock (biological clock) is an important system that living things have acquired to adapt to the daily cycle of environmental changes associated with the Earth's rotation.

In mammals, the circadian clock in the suprachiasmatic nucleus (SCN) of the hypothalamus acts as the central clock that generates autonomous oscillation. In order to synchronize the internal environmental rhythms with the external environmental rhythms, the central clock controls the appropriate phase relationship between its own autonomous oscillation and the periodic changes of the environment, and sends the information to the peripheral clocks throughout the body (see the figure below). As a result, various physiological phenomena such as sleep/wakefulness, body temperature, and hormone secretion show rhythms with peaks at appropriate times. Light is the most powerful environmental factor (zeitgeber) that affects the phase and/or period of circadian rhythms, but it is known that environmental factors other than light, such as meal timing and social interactions, also have effects on circadian rhythms. We aim to clarify at the molecular level how various environmental factors affect the circadian clock. We are also studying the aftereffects of environmental factors on circadian rhythms, that is, the plasticity of the circadian clock.



Mammalian circadian clock

The mammalian circadian clock is located in the suprachiasmatic nucleus (SCN) of the hypothalamus at the bottom of the brain. The SCN is a small nucleus with a diameter of about 300 µm on one side. After the SCN is lesioned, all circadian rhythms of the body disappear. Also, the cultured SCN isolated from the brain continue to oscillate autonomously in a cycle of about 24 hours as long as the cells are alive. Since the discovery of clock genes, the central mechanism of the autonomous oscillation of the circadian clock has been clarified. Clock genes in the SCN are expressed with a clear and significant rhythm. The feedback loop of transcription and translation of these clock genes and their own transcriptional regulation by their proteins is the core mechanism of the circadian clock.

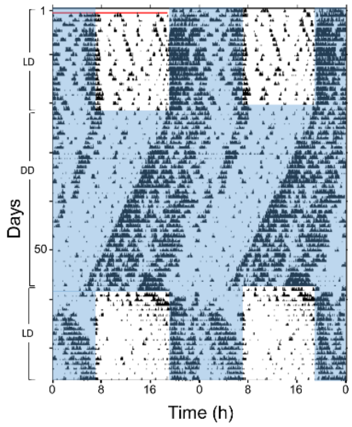


Figure: Mouse behavioral rhythm in 12hr light:12hr dark cycles (LD) and constant dark conditions (DD).
The activity rhythm in DD is free running.

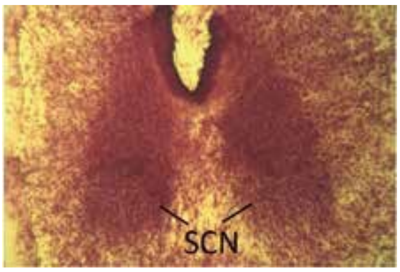


Figure: The SCN in culture, showing circadian rhythm after transfer to culture

Various zeitgebers that affect the circadian clock

Various environmental factors change the phase and free-running period of the circadian clock. Among them, light is the strongest environmental factor that shifts the phase of circadian clock, and its effect depends on the phase (time) of the circadian clock. We are investigating the phase dependency of effects, in which light drives the phase shift of circadian rhythms only at nighttime. Also, when a mouse is placed under exotic lighting conditions, the period of circadian rhythm changes and its effect lasts for a long time as an aftereffect. We are also interested in this kind of plasticity phenomenon of circadian rhythm and are conducting research on the mechanisms of the circadian clock involved in the phenomenon. This research is expected to lead to the elucidation of the close relationship between our physical/mental disorders and the malfunction of our circadian clock. We are also searching for factors other than light that affect the phase and period of the circadian clock.

Circadian clocks of diurnal and nocturnal animals

Nocturnal animals such as experimental mice (C57BL/6, BALB/c, etc.) are active at night. On the other hand, diurnal animals such as humans are awake during the day. Although the activity rhythm of both is in the antiphase relationship, the neural activity of the SCN is high in the daytime and low in the nighttime in both diurnal and nocturnal animals. However, it is not yet clarified whether the properties of the circadian clock in the SCN are the same for diurnal and nocturnal. Therefore, in order to understand the human circadian clock, we are investigating the properties of the circadian clock of diurnal animals using the diurnal primate common marmoset.

Let's unravel the mystery of the mammalian circadian clock.

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