


Study of design principle underlying infradian rhythms and its application

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Project Information	Project Number : 24H00058	Project Period (FY) : 2024-2028	
	Keywords : biological clocks, circannual rhythm, circasemilunar rhythm		

Purpose and Background of the Research

● Outline of the Research

Pufferfish, corals, and sea turtles spawn during the full or new moon. On the other hand, mating, migration, and hibernation of various animals occur during specific seasons. Humankind has been fascinated by this mysterious animal physiology and behaviors, as noted in Aristotle's *Historia Animalium*. These phenomena are controlled by endogenous biological clocks, such as the "circasemilunar clock" and "circannual clock" that tick "infradian rhythms" with cycles longer than 24 hours. However, the mechanisms driving this rhythmicities remain unknown in all organisms. We recently identified circasemilunar and circannual genes in pufferfish, medaka, and rhesus monkeys that show distinct infradian rhythms. The aim of this study is to clarify the underlying mechanisms of infradian rhythms and understand the physiological functions and diseases governed by the moon and seasons.

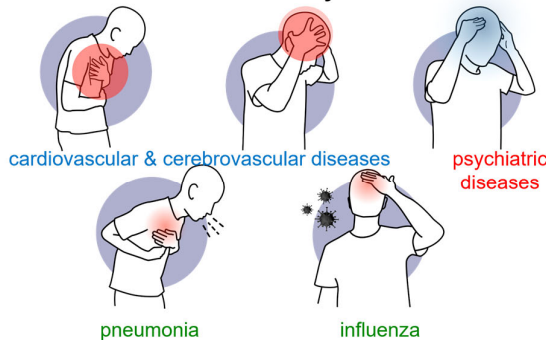
Circasemilunar rhythm



mating
delivery

menstrual cycle
bipolar disorder
sleep

Circannual rhythm



Higher mortality rate in winter

Figure 1. Various aspects of physiology and several diseases are under the control of the infradian clock; however their underlying mechanisms remain unknown

● Background of research

Organisms have evolved biological clocks to better adapt to cyclic environmental changes. The reproduction of gnus, bipolar disorder, menstrual cycle and sleep in humans exhibits lunar rhythms. On the other hand, there are seasonal variations in morbidity owing to cardiovascular and cerebrovascular diseases, influenza, pneumonia, depression, bipolar disorder, and schizophrenia. Most of these conditions become more severe and exhibit higher mortality rates in the winter. Although the mechanism of the circadian clock has been uncovered over the past several decades, the mechanisms of infradian rhythms remain unknown.

● Purpose of this study

We previously identified the signal transduction pathway for seasonal sensing (Fig. 2). The aim of this study is to elucidate the mechanisms of infradian rhythms and understand the physiological functions and diseases governed by infradian rhythms.

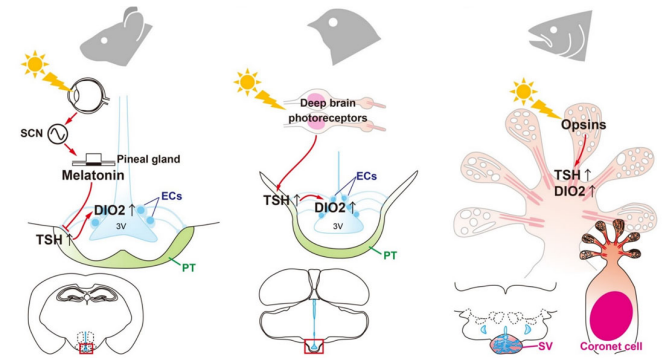


Figure 2. Mechanisms for vertebrate seasonal sensing

Expected Research Achievements

● Elucidation of the mechanism of the circasemilunar rhythms

We have recently identified the 'spring tide gene' and the 'neap tide gene' in pufferfish. We also searched for conserved transcription factor binding motifs in the upstream regions of the spring tide and neap tide genes and discovered a transcription factor binding motif common to the spring tide genes. In this study, we attempt to uncover the gene networks that regulate the circasemilunar rhythm.

● Elucidation of the mechanism of circannual rhythms

The hypothalamus and pituitary glands of medaka kept under natural outdoor conditions were analyzed monthly for two years, and seasonally oscillating genes were identified. Monthly analyses under constant conditions have also identified 'circannual genes' that show a yearly rhythm under both natural and constant conditions (Fig. 3). Furthermore, by analyzing 80 tissues of rhesus monkeys kept outdoors every two months throughout the year, we identified seasonally oscillating genes. Therefore, the aim is to uncover the underlying mechanisms of the circannual rhythms based on these datasets.

● Understanding physiology and diseases regulated by the moon and seasons.

Human bipolar disorder, menstrual cycles, and sleep exhibit lunar rhythms. Cardiovascular and cerebrovascular diseases, pneumonia, influenza, and psychiatric disorders are more severe in winter and mortality rates increase markedly during this period. However, the mechanisms through which these diseases exhibit infradian rhythms are unknown. We aim to uncover the molecular mechanisms underlying these physiological processes and diseases. The results of this study are expected to improve the quality of life and animal production.

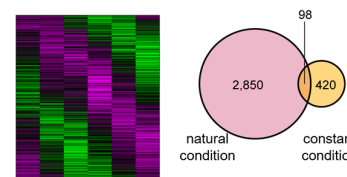


Figure 3. Identification of circannual genes in medaka

