【Grant-in-Aid for Scientific Research (S)】

Broad Section G

Title of Project： Understanding the seasonal adaptation mechanism and its application

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Research Project Number：19H05643　Researcher Number：40291413
Keyword：photoperiodism, seasonal adaptation, medaka, chemical genomics

【Purpose and Background of the Research】

Organisms exposed to seasonal changes in the environment, such as daylength, temperature, and precipitation, are known to adapt their physiology and behavior, including reproduction, hibernation, migration and molting accordingly. How these organisms sense these seasonal changes, remains unknown. In addition, the mechanistic nature that drives the seasonally regulated physiology remains unclear. Furthermore, morbidity in humans, owing to cardiac, cerebrovascular, infectious, and psychiatric diseases, is seasonal, and peaks in winter. At high latitudes, about 10% of population suffer from winter depression, and high suicide rates are a serious social issue. However, the underlying mechanism is yet to be determined.

Medaka is an excellent model because of its robust responses to seasonal changes in daylength and temperature, as well as the availability of genome-editing techniques. The difficulties in manipulating genes in some species (e.g., quail and sheep) and the unclear seasonal responses in other species (e.g., zebrafish and mouse), presents medaka as an ideal system for these studies (Fig. 1). Furthermore, small teleosts, such as zebrafish and medaka, are emerging models for the study of complex disorders and are becoming powerful models in pharmacogenetic studies.

In this study, we aim to investigate the genetic basis of the seasonal sensing mechanism by using the medaka fish. We will also investigate the molecular basis of seasonally regulated physiology by assessing gene expression on a genome-wide scale in tissue samples collected every month over a period of two years. Furthermore, compounds that rescue the winter phenotype will be developed using a chemical genomics approach.

【Research Methods】

Medaka populations captured at higher latitudes show more robust responses to daylength and temperature alterations than do the populations found at lower latitudes. Our genetic analysis of this fish has already detected significant quantitative trait loci. The candidate genes will be evaluated to understand the genetic basis of the seasonal sensing mechanism.

The RNA-seq analysis of the two-year time-series samples identified seasonally oscillating genes in the medaka fish. We plan to elucidate the molecular basis of the seasonally regulated physiology and behavior.

A multi-omics analyses, together with a chemical screening of the winter medaka to understand and rescue the winter phenotype, will also be performed.

【Expected Research Achievements and Scientific Significance】

Living organisms adapt to seasonal alterations on earth. Although this phenomenon has attracted great interest, the underlying mechanism remains unknown and this is a fundamental question in biology. This study is expected to uncover the genetic and molecular bases of these mechanisms in vertebrates and develop compounds that could regulate the seasonal adaptation mechanisms in animals.

【Publications Relevant to the Project】

- Shimmura T, et al., Dynamic plasticity in phototransduction regulates seasonal changes in color perception. *Nature Communications* 8, 412 (2017)
- Tamai TK, et al., Identification of circadian clock modulators from existing drugs. *EMBO Molecular Medicine* 10, e8724 (2018)
- Nakayama T et al., Seasonal regulation of the lncRNA *LDAIR* modulates self-protective behaviors during the breeding season. *Nature Ecology & Evolution* 3, 845-852 (2019)

【Term of Project】

FY2019-2023

【Budget Allocation】

153,500 Thousand Yen

【Homepage Address and Other Contact Information】

https://www.agr.nagoya-u.ac.jp/~aphysiol/

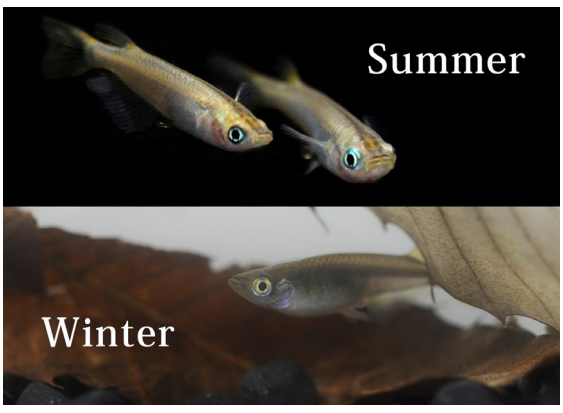

Figure 1 Medaka shows clear seasonality.