Division of Seasonal Biology (Adjunct)

Adjunct Professor
YOSHIMURA, Takashi

Specially Appointed Assistant Professor:	*SHINOMIYA, Ai*
	SHIMMURA, Tsuyoshi
Visiting Graduate Student:	*SENGA, Takumi*
	ADACHI, Daisuke
	SHIMO, Takayuki
Visiting Undergraduate:	*NAKATSUKASA, Mana*
Technical Assistant:	*BABA, Nayumi*
	AKAMA, Akiko
Secretary:	*OKUBO, Masayo*

Animals living outside the tropics adapt various physiology and behavior to seasonal changes in the environment. As animals use changes in day length and temperature as seasonal cues, these phenomena are referred to as photoperiodism and thermoperiodism, respectively. Medaka provides an excellent model to study these mechanisms because of their rapid and robust seasonal responses. In addition, genomic sequences and transgenic approaches are available in this species. In this division, we are trying to uncover the underlying mechanisms of seasonal adaptation.

I. Identification of deep brain photoreceptor

It has been known for more than a century that non-mammalian vertebrates receive light information directly within the deep brain to adapt to seasonal changes in day length. However, the identity of the deep brain photoreceptor remained unclear.

Cerebrospinal fluid (CSF)-contacting neurons extend knob-like dendrites into the ventricular cavity (Figure 1). This dendritic structure resembles those of photoreceptor cells in the developing retina and the pineal organ. Thus, the CSF-contacting neurons have been suggested to function as a deep brain photoreceptor.

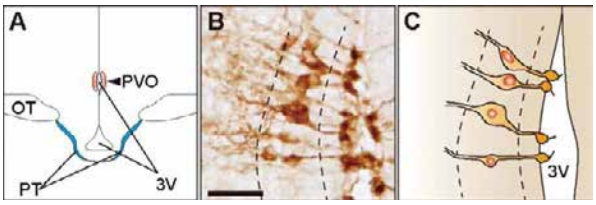

Figure 1. (A) Schematic drawing of the quail mediobasal hypothalamus. PVO: paraventricular organ; PT: pars tuberalis of the pituitary gland; 3V: third ventricle; OT: optic tract. (B) OPN5-positive CSF-contacting neurons in the PVO. (C) Schematic drawing of representative OPN5-positive CSF-contacting neurons in the panel (B).

1-1 Intrinsic photosensitivity of OPN5-positive CSF-contacting neuron

In a previous study, we demonstrated localization of a novel photopigment, OPN5 in the CSF-contacting neurons of quail. We used whole-cell patch-clamp analysis to demonstrate that OPN5-positive CSF-contacting neurons in the PVO are intrinsically photosensitive.

1-2 Involvement of OPN5-positive CSF-contacting neuron in the seasonal reproduction

We examined the effect of siRNA-mediated OPN5 knockdown on long day induction of springtime hormone, thyrotropin (thyroid stimulating hormone: TSH). Long day-induction of TSH was suppressed by the OPN5 knockdown, suggesting that OPN5 is involved in the seasonal regulation of reproduction. To our knowledge, this is the first demonstration of the intrinsic photosensitivity of deep brain CSF-contacting neurons.

II. Involvement of tissue-specific post-translational modification in seasonal time measurement

TSH is a glycoprotein secreted from the pituitary gland. Pars distalis-derived TSH stimulates the thyroid gland to produce thyroid hormones, whereas pars tuberalis-derived TSH acts on the hypothalamus to regulate seasonal physiology and behavior as a springtime hormone. However, it had not been clear how these two TSHs avoid functional crosstalk. We found that this regulation is mediated by tissue-specific glycosylation. Although pars tuberalis-derived TSH was released into circulation, it did not stimulate the thyroid gland. The pars distalis-derived TSH is known to have sulfated bi-antennary *N*-glycans, and sulfated TSH is rapidly metabolized in the liver. By contrast, pars tuberalis-derived TSH had sialylated multi-branched *N*-glycans; in circulation, it formed the macro-TSH complex with immunoglobulin or albumin, resulting in the loss of its bioactivity. Glycosylation is fundamental to a wide range of biological processes. However, this is the first demonstration of its involvement in preventing functional crosstalk of signaling molecules in the body.

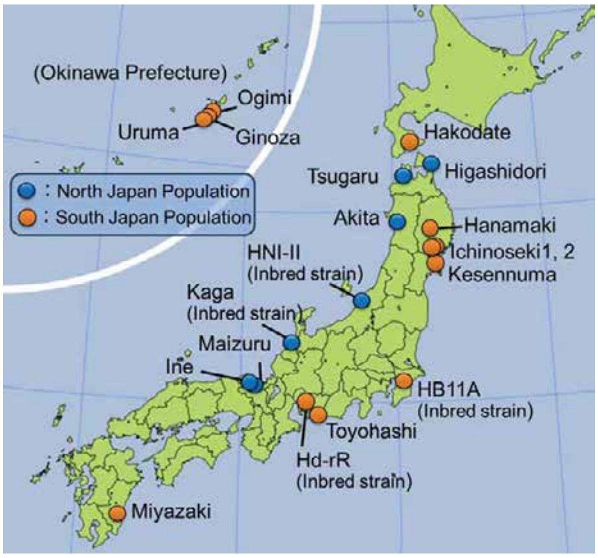

Figure 2. Medaka populations collected and used in our study.

III. Genome-wide association study of seasonal time measurement

It is well established that the circadian clock is somehow involved in seasonal time measurement. However, it remains unknown how the circadian clock measures day length. Additionally, it is not known how animals adapt to seasonal changes in temperature. It has been reported that medaka populations that were caught at higher latitudes have more sophisticated responses to day length and temperature. For example, medaka fish caught in Hokkaido have a critical day length (i.e., duration of light period required to cause a response) of 13 h, while those caught in Okinawa have an 11.5 h critical day length. To uncover the underlying mechanism of seasonal time measurement, we are planning to perform a genome-wide association study in medaka populations collected from various latitudes all over Japan.

3-1 Variation in seasonal responses with latitude in medaka fish

To perform a genome-wide association study, we have collected thousands of medaka fish from all over Japan (Figure 2). We have examined the effects of changing day length and temperature to determine the critical day lengths and critical temperatures that will cause seasonal responses in the gonad and we found differences in critical day length between medaka from higher latitudes and lower latitudes (Figure 3).

IV. Transcriptome analysis of seasonality in medaka fish

Homeotherms such as birds and mammals do not show clear seasonal responses to changing temperature. In contrast, poikilothermal animals also use changing temperature as a calendar. Medaka provides an excellent model to uncover this mechanism. To elucidate the signal transduction pathway regulating seasonal reproduction in medaka fish, we have examined transcriptome analysis. We identified hundreds of genes that respond to day length and temperature changes.

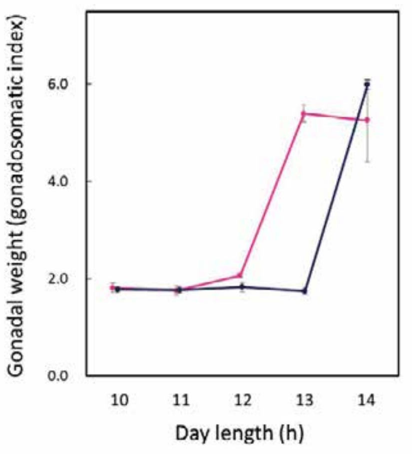

Figure 3. Different critical day length between medaka from higher latitudes and lower latitudes.

Publication List

〔Original papers〕

- Ikegami, K., Liao, X.H., Hoshino, Y., Ono, H., Ota, W., Ito, Y., Nishiwaki-Ohkawa, T., Sato, C., Kitajima, K., Iigo, M., Shigeyoshi, Y., Yamada, M., Murata, Y., Refetoff, S., and Yoshimura, T. (2014). Tissue-specific post-translational modification allows functional targeting of thyrotropin. Cell Reports 9, 801-809.
- Nakane, Y., Shimmura, T., Abe, H., and Yoshimura, T. (2014). Intrinsic photosensitivity of deep brain photoreceptor. Curr. Biol. 24, R596-R597.

〔Original paper (E-publication ahead of print)〕

- Ikegami, K., Atsumi, Y., Yorinaga, E., Ono, H., Murayama, I., Nakane, Y., Ota, W., Arai, N., Tega, A., Iigo, M., Darras, V.M., Tsutsui, K., Hayashi, Y., Yoshida, S., and Yoshimura, T. Low temperature-induced circulating triiodothyronine accelerates seasonal testicular regression. Endocrinology 2014 Nov 18.

〔Review articles〕

- Nakane, Y., and Yoshimura, T. (2014). Universality and diversity in the signal transduction pathway that regulates seasonal reproduction in vertebrates. Front. Neurosc. 8, 115.
- Shinomiya, A., Shimmura, T., Nishiwaki-Ohkawa, T., and Yoshimura, T. (2014). Regulation of seasonal reproduction by hypothalamic activation of thyroid hormone. Front. Endocrinol. 5, 12.