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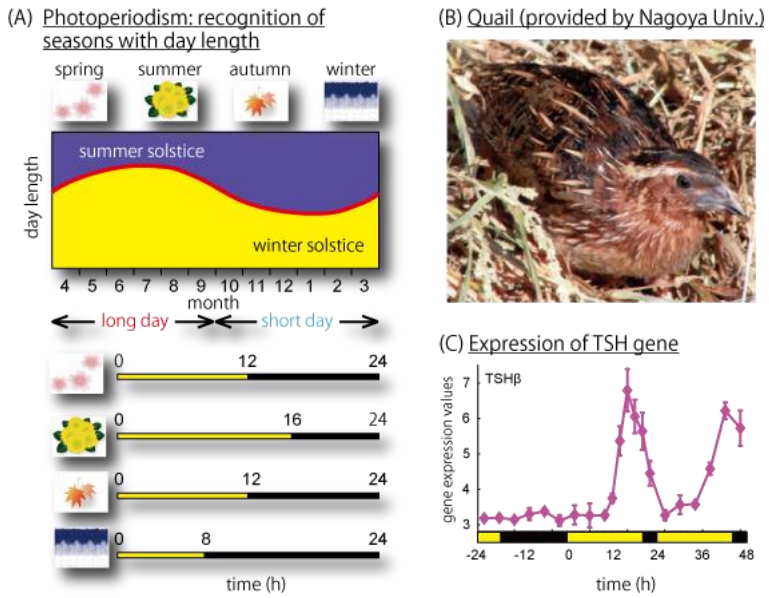
**Spring comes to the field**

*March 26, 2008* – The circadian rhythm that runs on an approximately 24-hour cycle is perhaps the best-known biological clocks, but many animals such as hibernating bears and migratory birds also follow a longer-term rhythm that regulates seasonal behaviors from feeding to reproduction. The molecular underpinnings of this "biological calendar," however, have largely remained a mystery.

A new collaborative study between Takeya Kasukawa of the CDB Functional Genomics Unit (Hiroki R. Ueda, Unit Leader) and Takashi Yoshimura's group at Nagoya University and others now reveals a "spring hormone" that works to trigger seasonal breeding in the Japanese quail, *Coturnix japonica*. In work published in *Nature*, the group found that the hormone thyrotrophin (TSH), which is secreted from the anterior lobe of the pituitary gland in response to light exposure mimicking that of a long day in spring, triggers seasonal breeding in this domestic fowl.




A) Many animals adjust their daily rhythms to the length of day in a given season. B) The quail used in this research is a common domestic fowl in Japan, and exhibits highly sensitive responses to seasonal change. C) On being shifted into a long-day light exposure regime, TSH levels are elevated by 14 H after midnight of the first day of exposure.

The work was enabled by the application of DNA microarray technology to the quail, which serves as a useful model for the study of seasonal breeding due to its rapid and dramatic responsiveness to changes in day length. As with many birds, the Japanese quail maintains gonads of small size in non-breeding periods, reducing its load, developing them to functional size only at the start of mating season. Yoshimura's group had previously shown that thyrotrophin secretion was one of the earliest events in the long day-induced pathway.

The joint project began with a comprehensive analysis by DNA microarray of changes in gene expression when birds raised in short day length conditions were shifted to a longer light exposure environment, similar to the change in day length from winter to spring. Of the nearly 30,000 genes analyzed, roughly 300 showed changes in expression level associated with the day length shift, with TSH being the earliest responder. Further study revealed that this hormone is triggered in the pars tuberalis, a section of the anterior pituitary lobe, and binds to its receptor, TSHR, in the overlying hypothalamus, enabling it to bypass the blood-brain barrier and enter the brain.

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The group next looked for a possible interaction between thyrotrophin and a second factor known as type-2 deiodinase, or DIO2, which Yoshimura's lab had previously shown to be important in gonad activation, and found that TSH indeed upregulates DIO2. They confirmed this in vivo by injecting TSH into cerebral ventricles, which stimulated both DIO2 expression and gonadal growth.

In addition to the identification of this molecular pathway involved in seasonal breeding, the discovery of the role of the pars tuberalis put paid to a longstanding question of the function of this hitherto mysterious structure. The new link between TSH, which is known for its roles in thermoregulation and metabolism, and reproduction also represents an important discovery, that may lead to new insights into seasonal biological cycles with implications in fields ranging from animal husbandry to seasonal affective disorders.

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