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Our monthly newsletter features a variety of information, highlighting current domestic and international issues concerning bioresources.

## Research and Bioresources No.1

### Mechanisms used by vertebrates to perceive the onset of spring, as clarified by quail models

Takashi Yoshimura, Graduate School of Bioagricultural Sciences, Nagoya University

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The next month's issue will be "Human-derived bioresources."



## Research and Bioresources No.1

### Mechanisms used by vertebrates to perceive the onset of spring, as clarified by quail models

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In regions at altitudes beyond the temperate zone, the environment changes dramatically depending on the season. In order to adapt to this yearly cycle of seasonal transformation, animals chirp, migrate, breed, and hibernate during specific seasons. Seasonal changes in animal behavior are thoroughly described in texts as early as *Historia Animalium*, written by Aristotle; this apparently miraculous ability of animals has fascinated us for more than 2,300 years.



Temperature and precipitation are important environmental factors that change with the seasons; however, most organisms rely not on these signs, but on the length of the day, or photoperiod, to perceive the progression of the calendar. Temperature and precipitation vary from year to year, as seen in the occasional mild winter, cold summer, and unusually dry rainy season, and thus do not provide reliable information. By contrast, solstice and equinox days arrive regularly every year; therefore, day length represents extremely accurate seasonal information and it makes sense that most organisms rely on day length to serve as their calendars. The behavior of animals that change their physiological functions according to day length is called photoperiodism.

*Drosophila* and mice hardly react to seasonal changes and thus have been considered inappropriate as model animals for elucidating the control mechanisms behind photoperiodism in animals. On the other hand, birds show some significant seasonal changes. Because birds must maintain as light a bodyweight as possible in order to fly, their reproductive organs develop only in the mating season. The weight of a male bird's testis, for example, increases more than 100-fold in a two-week period in response to changes in day length. No other animals react to the change in day length so rapidly and dramatically as birds do. Therefore, birds, and especially quail, are considered the best model organisms to study photoperiodism. Aichi prefecture is famous not only for Nagoya cochins, but also as Japan's largest quail-producing area; therefore, research on fowl, such as quail and chickens, is traditionally active in our Graduate School of Bioagricultural Sciences at Nagoya University.



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## Announcements (Details are available at <http://www.nbrp.jp/>)

- **Human induced pluripotent stem (iPS) cell and embryonic stem (ES) cell bank project was initiated.**
  - Technical training on simple vitrification methods is organized.
    - Dates: April 10, 24(Fri.), May 8, 15, 22, 29(Fri.), June 5, 19 (Fri.)
    - Time: 13:00-16:00
    - Place: Cell Engineering Division, RIKEN BioResource Center
- **Lecture Series for the Standardization of Culturing and Analyzing Human Pluripotent Stem Cells: No. 1 "Xeno-free Culturing"—Possibilities, Issues, and Validations for the Applications of Pluripotent Stem Cells**
  - Date and Time: 11:00-17:30 on Thursday, June 25, 2009.
  - Place: Auditorium on the first floor of Building C, Center for Developmental Biology, RIKEN

The Japanese Association for Laboratory Animal Science launched a serial article on NBRP animal resources in "Experimental Animals"—the in-house journal—beginning from the second issue of Vol. 58.



Domestic quail have been kept by warriors and called "Naki-uzura" since the Muromachi era and are known as the only animal species to have been domesticated in Japan, as the name Japanese quail (*Coturnix japonica*) implies. For these reasons, we attempted to elucidate photoperiodism control mechanisms by using quail as model animals.



Physiological studies conducted between the late 1960s and the 1990s identified the control center of photoperiodism in the medial basal hypothalamus (MBH) in the brain. Accordingly, we then used differential analysis to examine the genes whose expression is induced by long-day treatment. We identified *DIO2*, which encodes a type 2 deiodinase that activates thyroid hormones, as a key gene in the control of photoperiodism. Specifically, the expression of *DIO2* in the MBH as a result of long-day treatment typically converts T4 (thyroxine; a low-active thyroid hormone) to T3 (triiodothyronine; an active thyroid hormone). This induces a morphological change in the brain that causes it to secrete gonadotropin-releasing hormone (GnRH), which initiates reproductive activities\*1).



Subsequently, the chicken genome was sequenced in December 2004, and genome-wide genetic analysis of birds became possible. Using a genome-wide time-course analysis, we searched gene groups whose expression levels changed when the quail's growing environment was switched from short-day to long-day conditions. In response to the long-day treatment, thyroid-stimulating hormone (TSH) was induced in a region called the pars tuberalis, which had been functionally unknown and had received little attention. Further functional analysis determined that the TSH induced in the pars tuberalis binds to TSH receptors in the MBH and thereby functions as a master controlling factor that regulates reproductive activities via the expression of *DIO2*, a key gene regulating photoperiodism\*2). In conventional endocrinology and physiology, TSH, as the name implies, is secreted from the anterior pituitary into the bloodstream and stimulates the thyroid gland. However, a series of our studies elucidated a novel function of TSH as a "spring hormone"; that is, when it acts in the brain, TSH transfers information about the onset of spring to the brain in order to initiate reproductive activities.



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Meanwhile, we questioned whether TSH also functions as a spring hormone in mammals. In order to examine this hypothesis, we used mice as research models. It is conventional thought that mice are incapable of reacting to seasonal change, since they are reproductively active throughout the year, as humans are. However, based on my experience in raising mice for more than 10 years, I was personally assured that mice are also capable of responding to the seasons; for example, they tend not to give birth in winter, even under conditions of constant room temperature and light. Through our investigations of the mouse brain, we found that TSH and *DIO2* levels respond to changes in day length in mice, just as we observed in quail. Moreover, we showed that the day length information was not transferred in TSH-receptor knockout mice. These results confirmed that TSH is also a master controlling factor in the regulation of photoperiodism in mammals. ※3

Utilization of the unique properties of a wide variety of organisms is the path that will allow us to comprehend the ingenuity of various biological activities. A further enrichment of bioresources is awaited. ■



#### <References>

- ※1: Yoshimura *et al.*, *Nature* 426, 178-181 (2003)
- ※2: Nakao *et al.*, *Nature* 452, 317-322 (2008)
- ※3: Ono *et al.*, *PNAS* 105, 18238-18242 (2008)



### Erudite Lecture Series by Dr. Benno: No. 5

#### Why are we constipated?

According to research, nearly one out of every two women (48%) suffers from constipation. It is not widely known, however, that there are several types of constipation. Some people are late risers and do not have time to wash in the morning; thus, they skip bowel movements on weekdays and only defecate on the weekend with the aid of laxatives; these people suffer from so-called weekend defecation syndrome. Others are constipated because of stress and need several administrations of enemas per day to defecate; this is stress-related constipation. These days, people also suffer from frequent constipation caused by excessive dieting, deviant food habits that involve eating primarily low-fiber breads and sweets, and encopresis, a condition in which patients involuntarily vacate feces little by little every four to five days; this is seen even among children. These types of constipation plainly reflect the aging of the bowels.



Constipated patients tend to have pimples and poor, sallow complexions. Constipation induces harmful bacteria in the colon to produce toxins, which are then absorbed through the wall of the large intestine into the blood and circulated throughout the whole body. Consequently, the activity of bacteria indigenous to the skin is enhanced. In addition, the accumulation of gases and toxins in the colon causes detrimental effects to the body and further accelerates constipation.

In particular, women who skip breakfast or chill their bodies by wearing miniskirts in the cold since junior high or high school repress the urge to defecate. Feelings of social impropriety, such as embarrassment or being teased about going to the restroom, are also causes of fecal continence. Furthermore, constipation may result from insufficient exercise. These days, many young people lack exercise and are weak in their abdominal and back muscles—and thus, too powerless to empty their bowels. Eating food does not guarantee the evacuation of the bowels without the aid of sufficient muscular force. ☹️

Now, let us consider laxatives. Some laxatives inhibit the absorption of water in the colon, thereby maintaining sufficient water content in the feces for smooth defecation. In other words, bowel movement is activated by creating a diarrhea-like condition. Other laxatives stimulate the muscles of the bowels, targeting people whose peristaltic motions are too weak, due to lack of exercise or aging. This type of laxative also acts on the nervous system and thus will become ineffective upon continuous administration. This leads people to administer increasingly stronger doses of laxatives and further depresses natural bowel movements.

Although laxatives exhibit immediate effects, it is a great mistake to choose laxatives as a treatment for constipation. Their use will deteriorate the condition of constipation unless the person also makes an effort to resolve or at least alleviate it by changing his or her dietary habits. Please be aware that the frequent use of laxatives or anticonstipation agents will worsen constipation and ultimately become ineffective.



10 minutes

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### Developer tools in Internet Explorer 8

Microsoft released Internet Explorer (IE) 8 on March 19, 2009. According to Net Applications\*1, the market share of major browsers as of March 2009 was as follows: IE7, 46.54%; Firefox 3.0, 19.66%; IE6, 18.36%; and IE8, 1.83%. Developers and designers of web applications are required to make them compatible not only with IE6 and IE7, but also with IE8. Microsoft has provided the long-standing IE Developer Toolbar, an IE developer tool that should be installed separately from the browsers. In IE8, however, IE8 Developer Tools\*2 are provided together with the browser, and some functions have been enriched in comparison with the earlier IE Developer Toolbar.

To initiate IE8 Developer Tools, run IE8 and then choose "Developer Tools" from "Tools" in the menu bar, or press F12 on the keyboard. The analysis result of the website being browsed in IE8 will be displayed on the screen of the IE8 Developer Tools (Fig. 1). Some of the enhanced functions of the new tool set are introduced below.

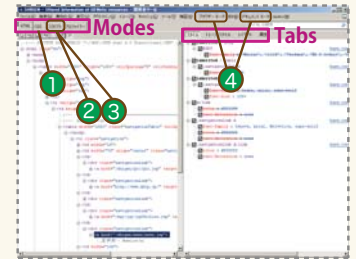



Fig. 1: IE8 Developer Tools

#### Reference Websites

- \*1: Browser Version Market Share  
<http://marketshare.hitslink.com/browser-market-share.aspx?qprid=2>
- \*2: Information Technology No. 31 in BioResource Newsletter Vol.4 No.4  
[http://www.shigen.nig.ac.jp/shigen/news/n\\_letter/2008/newsletter\\_v4\\_n4.html#column](http://www.shigen.nig.ac.jp/shigen/news/n_letter/2008/newsletter_v4_n4.html#column)

#### Enhanced Functions

- 1 Extended display, editing, and analysis of cascading style sheets (CSS) and elements  
The new toolbar adds functions such as displaying CSS properties inherited from a parent element and visualizing CSS layouts in selected components.
- 2 Debugging JavaScript (JScript)  
This function can be activated by selecting the "Script" tab and clicking on the "Start Debugging" button. Breakpoints can be set and local and custom variables can be viewed and edited under the "Locals" or "Watch" tabs when the debugger pauses.
- 3 Profiling JavaScript (JScript) performances  
This function can be activated by selecting the "Profiler" tab and clicking on the "Start Profiling" button. Go to the website that you wish to profile and after it is displayed, click on the "Stop Profiling" button to display the profile report. This function is useful to identify time-consuming processes in the script.
- 4 Switching browser modes  
Without installing both IE7 and IE8, you can simply switch between 3 browser modes, "IE7," "IE8," and "IE8 Compatibility View" to test how websites will be rendered on IE7 and IE8. In addition, there are 3 options for document modes, "Quirks Mode," "IE7 Standards Mode," and "IE8 Standards Mode." 

I would like to recommend to developers who use IE7 to upgrade to IE8 and try the Developer Tools.

(Gaku KIMURA)

**Editor's Note** Dr. Takashi Yoshimura received the Japan Society for the Promotion of Science Prize in fiscal year 2008 for his research introduced in this issue, "Seasonal Clock Percepts Coming of Spring in Vertebrate – Quail as a Model Animal." His unique and pioneering research made maximal use of bioresources and received great recognition. This news is extremely delightful and encouraging for people engaged in bioresource projects. I would like to offer Dr. Yoshimura my most sincere congratulations for his achievements. (Y.Y.)

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