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Research and Bioresources〈NO.13〉

New Transcriptional Regulatory Mechanism in the Development of the Dorsal and Ventral Regions in Animals

Kaoru S. Imai[1] and Yutaka Satou[2]

1: Former Specially Appointed Assistant Professor, Graduate School of Science, Kyoto University, and Restart Postdoctoral Fellowship, the Japan Society for the Promotion of Science

2: Associate Professor, Graduate School of Science, Kyoto University

Ascidians

Ascidians are chordates, and the Urochordata (Tunicata), including ascidians, is a group of animals that are the closest relatives to Vertebrata. In fact, the shape of an ascidian larva is similar to that of a tadpole. When you look at the tadpole-type larva, you can understand that ascidians are closely related to us. Since the genome of ascidians (genome size is 160 Mb and the number of genes is approximately 16,000) is much simpler than that of Vertebrata, this simple genome provides a great advantage in genome-level studies [1] (Fig. 1) .

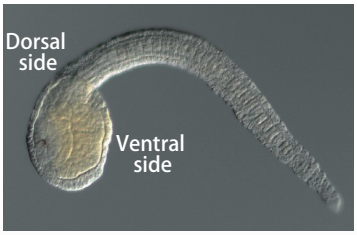

Fig.1: Ascidian tailbud embryo just before hatching Tadpole-type tailbud embryo

Dorsal and Ventral Differentiation in Animals

The dorsal and ventral regions are differentiated in animal bodies with few exceptions, and this differentiation occurs at the initial stage of development. For the dorsal and ventral differentiation, a secretory protein called BMP*1 is involved in most cases. In vertebrate animals (e.g., frogs), BMP is expressed in the ventral region and multiple molecules that inhibit the action of BMP (called antagonists) are expressed in the dorsal region [2]. Previously, we revealed the outline of a gene regulatory network that controls ascidian embryogenesis [3]. However, we could not find the evidence that played a decisive role in the regulation of BMP in the dorsal and ventral differentiation in ascidians.

Dorsal and Ventral Regions in Ascidian Tailbud Embryos

Is it true that, unlike in other animals, the BMP molecule is not involved in the dorsal and ventral differentiation of ascidians? (Are ascidians such special animals?) In order to answer this question, we analyzed the differentiation mechanism during the developmental period between neurula and tailbud embryos, because epidermal cells differentiate in several regions along the dorsal-ventral axis in ascidians. We found that when the dorsal and ventral regions developed, the secretory molecule BMP was expressed in the ventral region to form this region, similar to other animals. Unlike the BMP molecule, a secretory protein called Admp*2, which is similar to BMP, was expressed in the dorsal region. However, Admp was necessary to form the ventral region, similar to the BMP molecule.

In the process of analyzing the differentiation mechanism in detail, we detected a new protein (antagonist) that was specifically bound to Admp to inhibit the action of Admp (this protein is called Pinhead) [4]. In fact, Pinhead was expressed after receiving Admp signals; thus, a negative feedback exists between Admp and Pinhead (indicating that BMP and Admp are proteins required to form the ventral region and Pinhead is a protein required to inhibit the formation) (Fig. 2) .

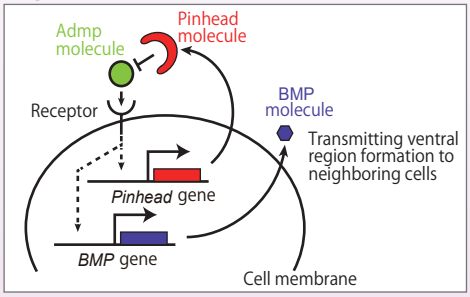

Fig. 2: Feedback between Admp and Pinhead

New Transcriptional Regulatory Mechanism

It was interesting that the *Pinhead* gene inhibited the *Admp* gene not only at the protein level but also at the transcription level; i.e., expression of the *Admp* gene was inhibited. This is due to the gene arrangement in the genome, i.e., *Pinhead* and *Admp* are coded by adjacent genes. In other words, when the *Pinhead* gene is transcribed, an interaction occurs between the enhancer and the promoter*3 resulting in DNA loop formation. In the loop, there is an enhancer of the *Admp* gene. Consequently, the enhancer is physically isolated. By inhibiting the *Admp* gene at both the protein and transcription levels, the development of the ventral region is appropriately controlled (Fig. 3).

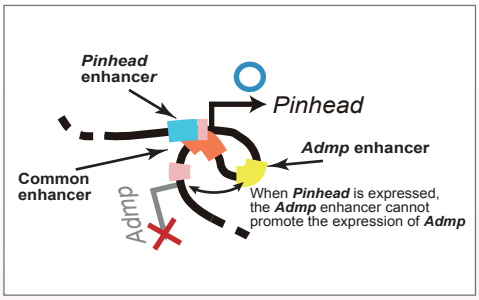

Fig. 3: Reason why the *Admp* gene cannot be expressed when the *Pinhead* gene is expressed. The region in pink indicates the promoter.

In the genomes of other animals, from insecta to amphibia, the *Pinhead* gene is coded in a locus adjacent to that of the *Admp* gene (unfortunately, both the *Pinhead* and *Admp* genes seem not to exist in Homo sapiens). This high level of conservation indicates that the origin of the regulatory mechanism can ascend to the origin of bilateria (Fig. 4).

↳To the next page

*1 BMP is the abbreviation for bone morphogenetic protein. BMP is secreted into the extracellular environment and is used for transmitting signals to neighboring cells. Approximately 10 types of BMPs exist in Homo sapiens and at least 2 types exist in ascidians. In fact, BMP of ascidians described in this newsletter is called BMP 2/4.

*2 Admp is the abbreviation for anti-dorsalizing morphogenetic protein. The Admp molecule is similar to the BMP molecule. Similar to BMP, Admp is involved in the transmission of signals to neighboring cells.

*3 The enhancer and promoter: Both are regions in the DNA required for gene expression to produce RNA (transcription). A protein common to all genes and required for transcription is bound to the promoter. To the enhancer, a protein called a transcriptional regulatory element, which differs according to the sequence of the enhancer, is bound to enhance binding of the common protein to the promoter.

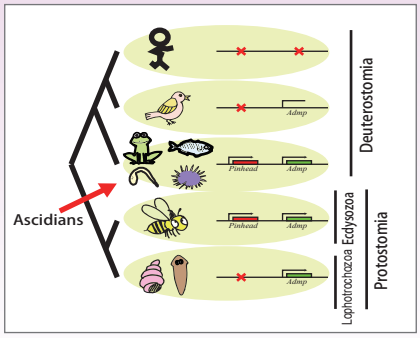

Fig. 4: The arrangement of the *Pinhead* and *Admp* genes in the genome has been widely conserved throughout animal evolution

Conclusion

The ascidian used in our experiment was *Ciona intestinalis*. This ascidian is distributed in almost all the seas around the world, and foreign researchers collect this ascidian as experimental material even now. In Japan, wild-type species of ascidians are abundantly and continuously available via the National BioResource Project. The present study was mainly possible because of this well-established material provision system.

References

1. Dehal P, Satou Y, Campbell RK *et al*: **The draft genome of Ciona intestinalis: insights into chordate and vertebrate origins**. *Science* 2002, **298**(5601):2157-2167.
2. De Robertis EM: **Spemann's organizer and the self-regulation of embryonic fields**. *Mech Dev* 2009, **126**(11-12):925-941.
3. Imai KS, Levine M, Satoh N *et al*: **Regulatory blueprint for a chordate embryo**. *Science* 2006, **312**(5777):1183-1187.
4. Imai KS, Daido Y, Kusakabe TG *et al*: **Cis-acting transcriptional repression establishes a sharp boundary in chordate embryos**. *Science* 2012, **337**(6097):964-967.

Finding Vulnerabilities in Software

Ongoing Column [No. 76] 10min.

We use various kinds of software on our PCs, but software can often be vulnerable to security problems (hereafter "vulnerabilities"). Software makers and distributors (hereafter "vendors") release software updates when vulnerabilities are discovered, but it is important that users check the available information about vulnerabilities, as it may take some time before software updates are issued, and there are cases where an automated update notification is not sent out.
Using JVN, the Japan Vulnerability Notes tool (an information portal site for software vulnerabilities) at http://jvndb.jvn.jp/en/apis/myjvn/mjcheck.html, you can obtain information about software vulnerabilities, including their impact and countermeasures, by filtering using various criteria, such as the software name, the severity of the vulnerability, and the date on which the vulnerability was discovered.

First, access the MyJVN website link above using a web browser. When you access the website for the first time, click on the [Default] button (Fig. 1). A default list of software products will be displayed. Click on [Finish] to view a list of the vulnerabilities associated with these products.

Since only the vulnerabilities found in the default list of software are displayed, you should register other software that is installed on your PC.

Click on the [Setup] button on the vulnerabilities listing screen (Fig. 2) in order to add or remove software for which you would like vulnerability information to be displayed.

To change the display filter, such as vendor, software, severity and updated date, click on the [Edit] button (Fig. 3).

Fig. 1: Configuration screen during initial access

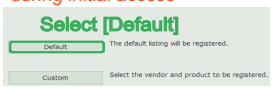

Fig. 2. List of vulnerabilities

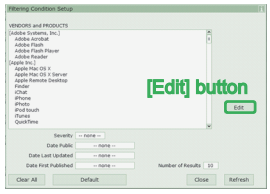

Fig. 3. Check configurations

Fig. 4. Filtering condition setup screen

1 Select software vendors

From the list of vendors on the left hand side, select the vendor whose vulnerabilities you wish to view, and then click on the [>>] button in the middle of the screen to move it to the list on the right hand side. Click on [Next] to continue to the next step (Fig. 4).

2 Select software

Click on a vendor in the list on the left hand side of the screen to view a list of software products that the vendor supplies. Select the software you wish to add to the filter and click on the [>>] button in the middle of the screen to move the software to the list on the right. Software listed on the right hand side will be used as the filter for displaying vulnerabilities. Next, click on [Next] to set up filtering conditions.

3 Set up filtering condition

Specify the filtering criteria by selecting severity, discovery date, or update date, and click on the [Finish] button to view vulnerabilities filtered according to the criteria that you have selected.

To view detailed vulnerability information for each software item, click on the [VEND] button at the upper left of the screen (Fig. 5-①) to switch the view, and click on a vulnerability heading for that software (Fig. 6).

Fig. 5.
List of vulnerabilities (switch display order)

Displayed detailed vulnerability information

①	Overview	Overview of the vulnerability
②	Affected systems	Software versions affected by the vulnerability
③	Impact	Possible attacks that can exploit the vulnerability, and the severity of the vulnerability
④	Solution	Countermeasures and workarounds
⑤	Advisory, reference information	Link to the website that publishes information on this vulnerability
⑥	Revision history	Discovery date, update date, and release date

Fig. 6. Detailed vulnerability information

Note: Filter settings for the Vulnerability Countermeasure Information Tool are saved in the browser' s cookie. Deleting the cookie will erase the filter settings.

As shown above, you can reduce the risk of a computer virus infection and decrease exposure to the attacks of malicious third parties by understanding software vulnerabilities and taking countermeasures using the information and advice provided with this tool.

In addition to the tool described above, the IPA (Information Technology Promotion Agency, Japan) website at http://www.ipa.go.jp/index-e.html also has details on information security and common vulnerabilities. Why not take a look?

(Hiroki Watanabe)

Recommended Book ! 〈NO.12〉

"A Baroque Thinker in the Forest"

Written by Shinichi Nakazawa (Kodansha Gakujutsu Bunko, 2006)

Shinichi Nakazawa, the author of this book, is a philosopher, a thinker, and a religious scholar. This book vividly describes the overview of Minakata Kumagusu, who was a genius with extensive knowledge, a remarkable memory, and who flourished about 100 years ago (the original book was published in 1992). I, the critic of this book, came to this book in relation to "Minakata Kumagusu as a researcher of myxomycetes." This book freely describes not only "myxomycetes and autopoiesis" (Chapter 5) but also Minakata Folklore (Chapter 4), ecology (Chapter 6), and a unique world view called Minakata Mandala (Chapter 7). My capacity is insufficient to understand the whole picture of this book. Therefore, I introduce this book by quoting a part of it.
"The universe has been formed as a huge mystery. … .the mysterious universe has been enfolding an indefinite number of pleats in its inside. The universe is inexhaustible and limitless. The entire universe has been enveloped in the holomovement of mandala, i.e., Mahavairocana, and its new figures have appeared one after another in human intellectuality while changing and moving. This phenomenon can only be observed by using a microscope. What a mysterious place the universe is where humans live! Science can exist to observe and enjoy the mysterious universe. Only science studied by those who sufficiently know the enjoyment can really enrich humans. Minakata had pursued only this type of science throughout his life. He was not interested in anything other than this type of science at all…" excerpted from Chapter 2 (K. N.).

Contact Address

Genetic Resource Center, National Institute of Genetics
1111Yata, Mishima-shi, Shizuoka 411-8540, Japan
Tel.: 055-981-6885 (Yamazaki)
E-mail： brnews@shigen.info

Editor's Note

The last issue of the newsletter in 2012 involved "a switch that differentiates the dorsal and ventral regions in ascidians" published in Science, and the authors of this article explained the scientific content to outsiders for easier understanding. It is interesting that although the dorsal and ventral regions in ascidian larvae are differentiable, these regions are considered difficult to differentiate in adult ascidians. Those who have not seen *Ciona intestinalis* should access the website of the National BioResource Project at http://marinebio.nbrp.jp/.
The Recommended Book! section will not be continued after this issue. Mr. K. N., the critic of this book, is an avid reader regardless of the category, and has selected a book every month with great efforts. Mr. K. N. wrote the final book review to excite the readers' curiosity.
BioResource now! successfully completed its 8th year. We are deeply grateful to the authors and readers of this newsletter. Have a good New Year (Y. Y.).

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