

# BioResource Now!

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Shohei Mitani (Tokyo Women's Medical University, School of Medicine)

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Research and Bioresources <NO.20>

## National BioResource Project "C. elegans"

Shohei Mitani, Professor  
(Tokyo Women's Medical University,  
School of Medicine)

### Is a Generational Transition Taking Place in the Community of Nematode Researchers?

The National BioResource Project (NBRP) *C. elegans* has, since its inauguration in 2002, collected and preserved deletion mutants of *Caenorhabditis elegans* by using its genomic information, opened its database to the public, and distributed deletion mutants upon request. It is my pleasure that we have continuously executed these research activities for a very long time and with consistent results.

In June 2015, the International Worm Meeting, convened biennially, was held at the University of California, Los Angeles. In the meeting, the plenary session introduced the history of nematode research, and memorial photographs of the principal laboratory of Dr. Sydney Brenner, who had initiated genetic analysis using nematodes, were exhibited. I was a little surprised to know that some young researchers knew little of the history of nematode research and were seeing these photographs for the first time.

Dr. Brenner  
(from the Cyber Museum of  
Genetics, National Institute  
of Genetics)



There was a proposal that opinions on how to manage the community of nematode researchers should be exchanged after the meeting. The atmosphere within the community has been changing gradually. The reason for this change may be that an influential figure, who began to study nematodes under the guidance of Dr. Brenner, and has been leading the community since then, will retire soon. Such a topic cannot be taken up in the research field, the history of which is longer than that of nematodes. However, at present, only those researchers, who started studying nematodes around the time that Dr. Brenner published his paper in 1974, or afterwards, remain in the community. I think that a generational transition in the community is taking place.

Genetic resources, including mutants of *C. elegans*, have continuously been used for genetic research in the past 40 years. However, new technologies and resources have been introduced one after another since 1998, when whole-genome sequencing was completed for *C. elegans*. Dr. Brenner proposed the idea that a complete picture of genetics could be obtained using nematodes. I feel that Dr. Brenner's idea has gradually been realized.

It is true that we have recently been able to solve problems using advanced technologies, which could not be solved 40 years ago, and we have discovered many new life phenomena, which were not known before. However, it may be only an illusion that Brenner's idea has gradually been realized.

### Reunion with Resources

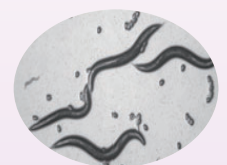
The core facility of NBRP *C. elegans* ships deletion mutants of *C. elegans* to laboratories around the world; each laboratory uses the shipped mutants for its research, and researchers in each laboratory publish their research results in the form of a paper. Consequently, we are "reunited" with our resources through these papers. I often find parts of research results obtained using nematodes in leading scientific magazines, and I am surprised to find the sophisticated use of our resources. Here, I introduce two recent research results below.

**Paper 1** reports the results of research on the lifespan of organisms, which has been a familiar theme for research in nematodes for a long time. Regarding research on the lifespan of organisms using nematodes, a lot of data has already been accumulated. I sometimes wonder whether this indicates a new direction. However, I do believe that new creativity is facilitated with a generational transition.

It is well known that when insulin signaling is impaired, a downstream transcription factor called FOXO (DAF-16 in *C. elegans*) is activated, which prolongs the lifespan of the individual organism. This phenomenon is seen not only in *C. elegans*; a similar phenomenon occurs in other model organisms. Basically, a series of insulin signaling pathways are considered to play an important role in determining lifespan.

The so-called dauer larva formation abnormal (DAF)-16 protein, the output of insulin signaling, has often been analyzed in association with dauer larva formation in *C. elegans*. However, paper 1 proposed a new concept. When the larvae of *C. elegans* are bred under conditions involving insufficient food (causing impaired insulin signaling), the larvae do not always undergo the dauer larval stage (when larvae transition to the adult stage, they do not pass through the dauer larval stage), but their lifespan is greatly prolonged.

This phenomenon is well known, and is thought to occur under the control of the above-mentioned FOXO transcription factor in many cases. Paper 1 revealed that another transcription factor, called SKN-1, was involved in determining lifespan, independent of dauer larva formation. SKN-1 action was directed at the modeling of the extracellular matrix (a mutant called *tm3411* distributed by the core facility was used for these experiments).



*Caenorhabditis elegans*  
(from the Cyber Museum of  
Genetics, National Institute  
of Genetics)

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In nematodes, collagen is the main component of the exoskeleton. It is quite interesting that a structure that protects the internal organs of an individual from external hazards plays an important role in preventing aging, especially since aging has been studied with a focus on glycolipid metabolism. If “healthy skin” is an important factor for anti-aging in nematodes, nematodes may have similar feelings as humans—recently, the color and gloss of my skin have declined....



**Paper 2** discusses a study performed within the core facility. Although three human *BCL7* genes (*A*, *B*, and *C*) exist on different chromosomes, only one *C. elegans* homolog (*bcl-7*) exists. Paper 2 discusses experiments involving functional analysis using the above-mentioned differences. A previous paper reported that deletion of *BCL7B*, which occurs in Williams syndrome, might cause tumors in humans. However, detailed mechanisms are unknown. In a *bcl-7* deletion mutant (*tm5268*) of *C. elegans*, a phenomenon is observed wherein stem cell differentiation ceases at an early stage and their nuclei remain juvenilized.

In human tumor cell lines, when *BCL7* is knocked down, a similar phenomenon is observed, and the expression levels of a stem cell marker increase. Therefore, *BCL7* may be an important factor in determining the malignancy of a tumor.

**Paper 1**

Ewald et al. Dauer-independent insulin/IGF-1-signaling implicates collagen remodelling in longevity. *Nature* 519, 97 (2015, March)

**Paper 2**

Uehra et al. The Tumor Suppressor *BCL7B* Functions in the Wnt Signaling Pathway. *PLoS Genet.* 2015;11(1):e1004921.

## Characteristics of Spear Phishing and Countermeasures

## Ongoing Column [No. 97]



In June 2015, Japan Pension Services made a public announcement that they had fallen victim to a spear phishing attack. Owing to the critical nature of the incident, which amounted to a breach of 1.25 million personal records, this issue was reported extensively by various media outlets. The trend of damages being caused by spear phishing is said to be rising yearly, with the targets of these attacks ranging from companies, to government agencies, to individuals. In this article, I would like to outline the characteristics of spear phishing and present countermeasures that can be used to defend against them.

### Characteristics of Spear Phishing

- **Email with content that has been customized for a specific target**  
Spear phishing emails feign the body of the message to make it appear as if it is a real business communication.
- **User's computer becomes infected with malware when an attachment is opened**  
There are known attacks that implant malware onto a target's computer via attachments. Successful attacks are possible not only with executable files such as .exe and .bin, but also with other file types such as Word, Excel, and PDF files.
- **Attacks can be delivered via malicious code embedded in HTML mail**  
Emails can be in plain text or HTML format. HTML emails can have embedded images or scripts, making a variety of attacks possible. Extra caution must therefore be taken with HTML emails, as the simple act of opening such an email can trigger the launch of an attack.

### Countermeasures

- **Do not open suspicious emails**  
Check the sender email address and subject. If you notice anything odd about an email, such as a hitherto unknown domain in the sender email address, or if the subject contains non-Japanese kanji characters, the best strategy is to not open the email, and report it to your organization's IT administrator. You should also be aware that sender email addresses can be easily forged, and so this on its own cannot be used as the basis to determine whether an email is legitimate.
- **Configure your email client to not automatically execute HTML mails**  
This is a required countermeasure to protect yourself if you happen to open a suspicious email that is in HTML format.
- **Never open file attachments unless you can trust the email**  
File extensions can be forged. The rule of thumb is to never open file attachments, regardless of the file format, unless you are absolutely certain that the email can be trusted.
- **Avoid clicking on shortened URLs**  
It is difficult to ascertain the website to which a shortened URL (Fig. 1) is linked. Consequently, shortened URLs are often used for attacks in which a link redirects to a malicious website. Unless the email can be trusted unconditionally, avoid clicking on links that use shortened URLs. Of course, if a linked website is not known to you, then you should avoid clicking on its link even if the URL is not shortened.

Because targeted phishing attacks are carefully forged manually, the reality is that threats from such attacks cannot be thwarted completely. However, by paying attention to a number of key points, individuals can reduce their risk of exposure. Caution exercised by individual users on top of organizational-level countermeasures is essential in order to avoid falling victim to spear phishing attacks.

(Kyoei Matsuno)



Fig. 1. Example of a shortened URL. Here, Google's URL shortening service is used to shorten SHIGEN's website address. It is difficult to deduce the original URL of a shortened URL, and phishing emails take advantage of this characteristic.

Answers to the problems in using the codon table in the previous month's issue  
Problem 1: MADRID Problem 2: MANILA

### Contact Address

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

### BioResource Information

(NBRP) www.nbrp.jp/  
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(JGR) www.shigen.nig.ac.jp/wgr/jgr/jgrUrList.jsp

### Editor's Note

I think the community of nematode researchers is well integrated; the community has a culture of generously sharing research resources, which includes both materials and information. With the passing of one generation of researchers, next generation researchers, who have taken over, will introduce new technologies and concepts, and provide elegant leadership. The number of researchers using nematodes in various fields, including basic research and the medical sciences, has seemed to increase in recent years. It is the privilege of resource providers to be “reunited” with the resources they provided via these publications, and to be stimulated and impressed at times by new knowledge (Y. Y.).

