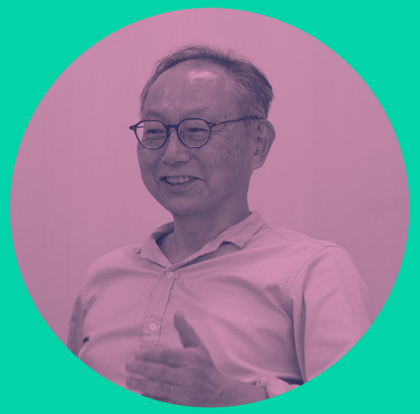

Message to Young Readers

Students at the high school level are often highly enthusiastic and express a strong desire to pursue a particular field. But surprisingly, these are often the same students who end up stagnating. There's no need to rush into deciding on a research focus so soon. Your four years at university should be spent exploring a variety of subjects for a well-rounded education. During that time, you can cultivate interests that develop naturally and try to find a graduate program that aligns with those interests.

Thinking too much about what you want to do too early on can narrow your perspective. Read a wide range of books, watch different kinds of movies, and acquire a broad education. Cherish the process of discovering what genuinely interests you, and then pursue that path.

> I would like you to cherish the process of acquiring broad knowledge and discovering what truly interests you.

What is Bio2Q?

Bio2Q is a world-class research center at Keio University. It aims to use quantum computing and AI to analyze the interaction between Human Biology and Microbiome, revealing uncharted territories of the human body and developing new treatments for intractable diseases.

It is the first private university to be selected for the World Premier International Research Center Initiative (WPI) program promoted by the Ministry of Education, Culture, Sports, Science and Technology (MEXT).

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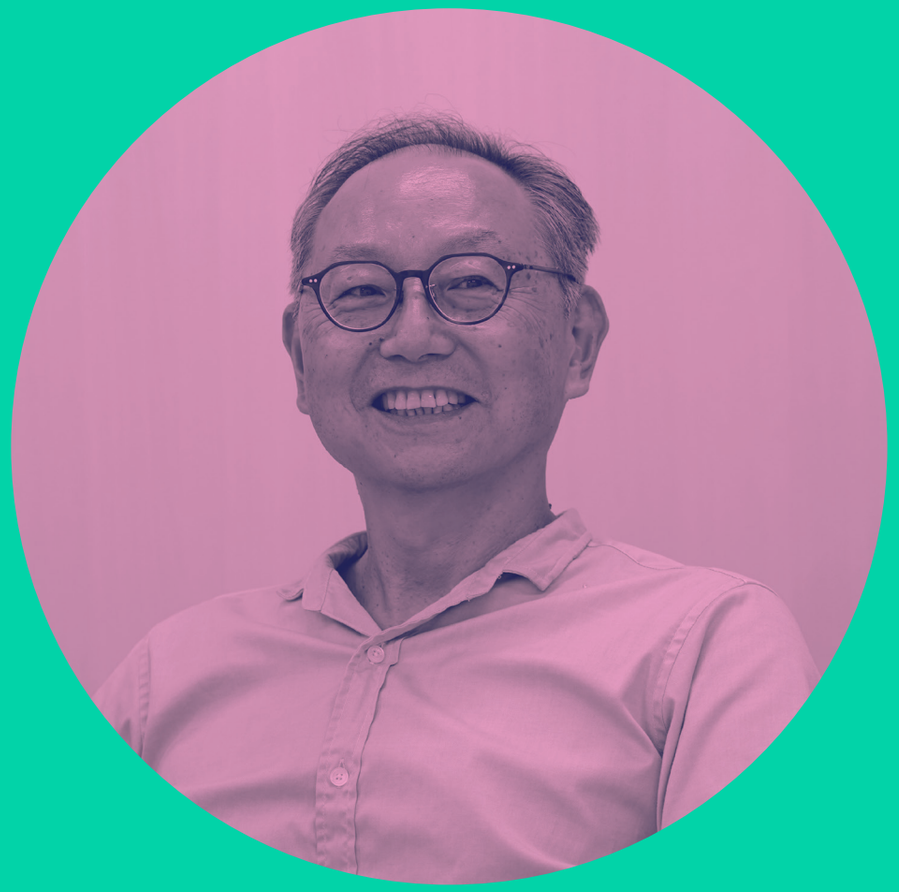
WPI Research Center
Keio University
Bio2Q Human Biology Microbiome Quantum Research Center
wpi



Bio2Q Researchers

Professor Haruhiko Siomi

Bio2Q Administrative Director/Genome Dynamics Team PI

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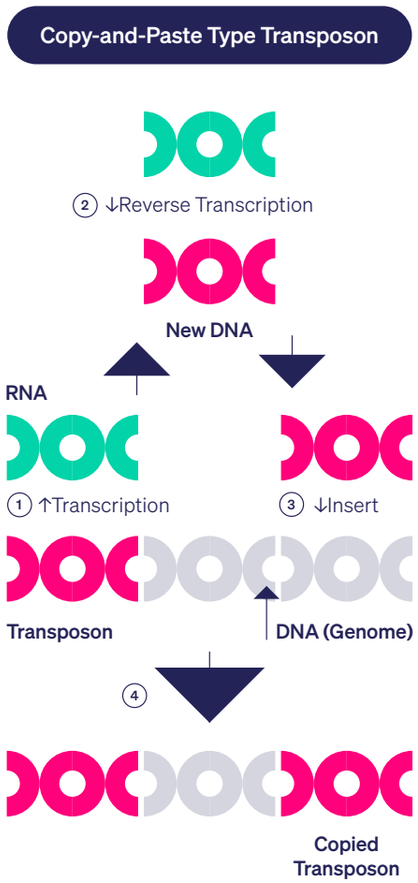
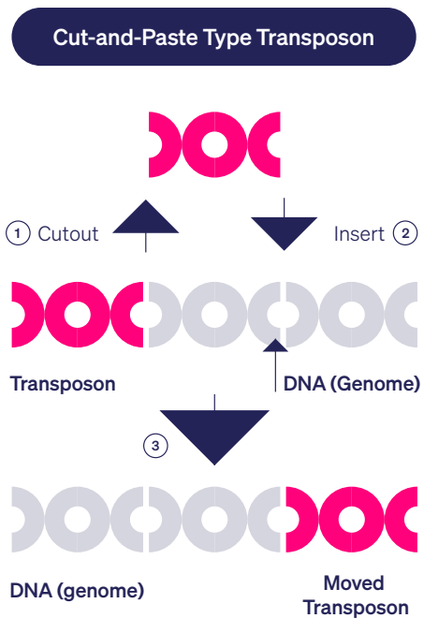




Please tell us about your lab's research.

Our lab's research focuses on the study of early embryos within the field of developmental biology, with a specific emphasis on transposons, also known as transposable elements or "jumping genes," in genomes. Within the genome, which refers to the complete set of chromosomes that we have, these are called transposons.

When transposons insert themselves into essential genes, they can become the cause of diseases. On the other hand, when considering evolution over a long time scale, it is believed that transposons have contributed to changes in genome structure and function by moving around and making many copies of themselves.

For example, humans and chimpanzees are different species. If we trace back the evolutionary path, there was a divergence at some point, leading to species differentiation. Although humans and chimpanzees use almost the same set of genes, they are controlled differently. The variation in gene usage contributes to the differences between species. Transposons are thought to have played a significant role in such species differentiation.

Transposons (mobile genetic elements) are thought to be closely related to evolution.

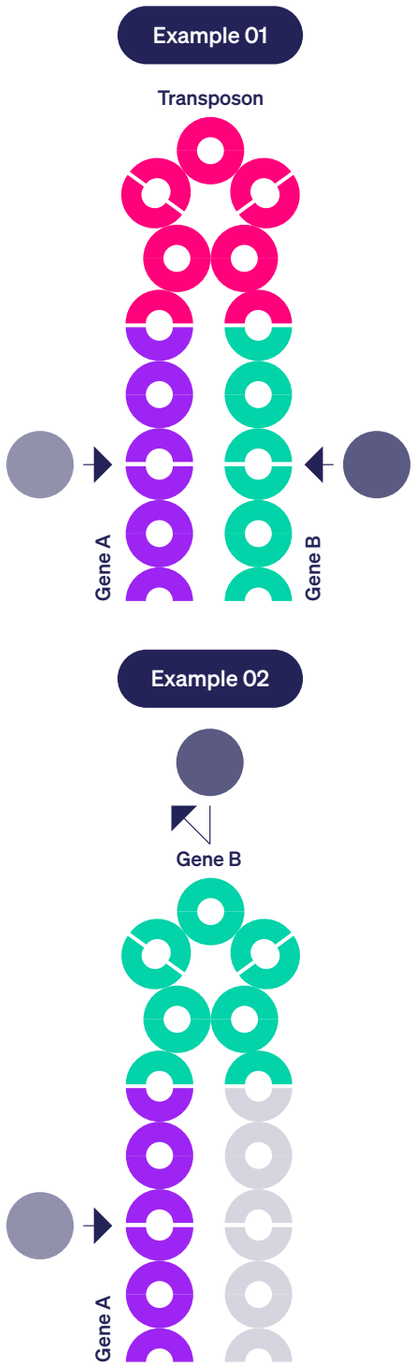
How do transposons move?

There are two main mechanisms of movement: copy-and-paste and cut-and-paste. In the copy-and-paste mechanism, the transposon's DNA is transcribed into RNA, and this RNA is then reverse-transcribed to create a new DNA copy. This new DNA copy is then inserted into another part of the genome through the action of specific proteins, effectively increasing the number of copies in the genome. This mechanism is common in mammals, where each transposition event increases the number of copies by one, leading to genome enlargement.

The cut-and-paste mechanism involves the transposon cutting itself out and then re-inserting itself into a different part of the genome. Since it cuts itself out, the number of copies generally does not increase. This mechanism is more common in plants.

Do transposons have a specific role?

As mentioned earlier, transposons are involved in genome enlargement and are believed to create new mechanisms for controlling gene expression. In other words, they are a source of genetic innovation. In a sense, the differences between humans and chimpanzees can be attributed to where transposons are inserted. For instance, if there is a transposon insertion between genes A and B in humans but not in chimpanzees, it may cause genes A and B to be expressed differently in humans and chimpanzees. About half of the human genome consists of transposons and their remnants. Until recently, transposon research focused exclusively on diseases caused by transposition. However, if they were entirely harmful, there should have been mechanisms to eliminate them. The fact that they have not been eliminated suggests that transposons may play some important role. In our lab, we are exploring the positive aspects of transposons and studying what happens when transposons are inactive.



In Example 01, genes A and B are untangled (open), allowing gene expression control factors (transcription factors or chromatin modification factors) to access the DNA and enable expression.

In Example 02, the structure of gene B changes due to a transposon insertion, preventing gene expression control factors from accessing the DNA, resulting in an inability to express the gene.

With the mouse as a model animal, we have found that suppressing the expression of transposons, specifically those expressed around the 2-cell stage of early embryos, leads to developmental abnormalities. This research provides evidence that the expression of transposons is essential for normal development, which is a groundbreaking discovery.

So, transposons are helpful in the process of a fertilized egg developing into an embryo?

Yes, in terms of of their positive aspects, transposons are essential for embryonic development and are believed to be closely related to evolution. Transposons can be expressed in response to stress. For example, transposons can be activated when cells experience stress, such as a sudden increase in external temperature, exposure to UV radiation, or infection by bacteria or viruses. From an evolutionary perspective, stress represents a change in the environment. To adapt to a new environment and leave behind individuals better suited for survival, different genome sequences need to be created. If transposons are expressed and transposed in germ cells in response to stress, when the fertilized egg develops into an individual, with a new transposon insertion(s), which may be better adapted to the new environment.

Humans have experienced major pandemics on the order of centuries, such as the Spanish flu in the early 1900s, which resulted in millions of deaths worldwide. However, individuals have diverse genome sequences, so even when exposed to the same virus, some may succumb quickly, while others may recover despite experiencing high fever. The diversity in our genome sequences ensures that some individuals will survive. One of the mechanisms that is thought to contribute to this diversity from an evolutionary standpoint is the transposition of transposons in response to stress.

What would you say is one of the more interesting experiences you've had during your time in research?

A significant moment was when we realized that transposons, which until then had been mainly considered as causes of diseases, were actually indispensable for normal development. For researchers, there's no equivalent of hitting a home run in front of tens of thousands of cheering fans. Even with the most groundbreaking discoveries, there are typically no more than a few people present, who may remark how incredible it is. Major discoveries tend to be quiet affairs.

* 2-cell stage embryo: The stage at which the fertilized egg undergoes division, resulting in two cells.