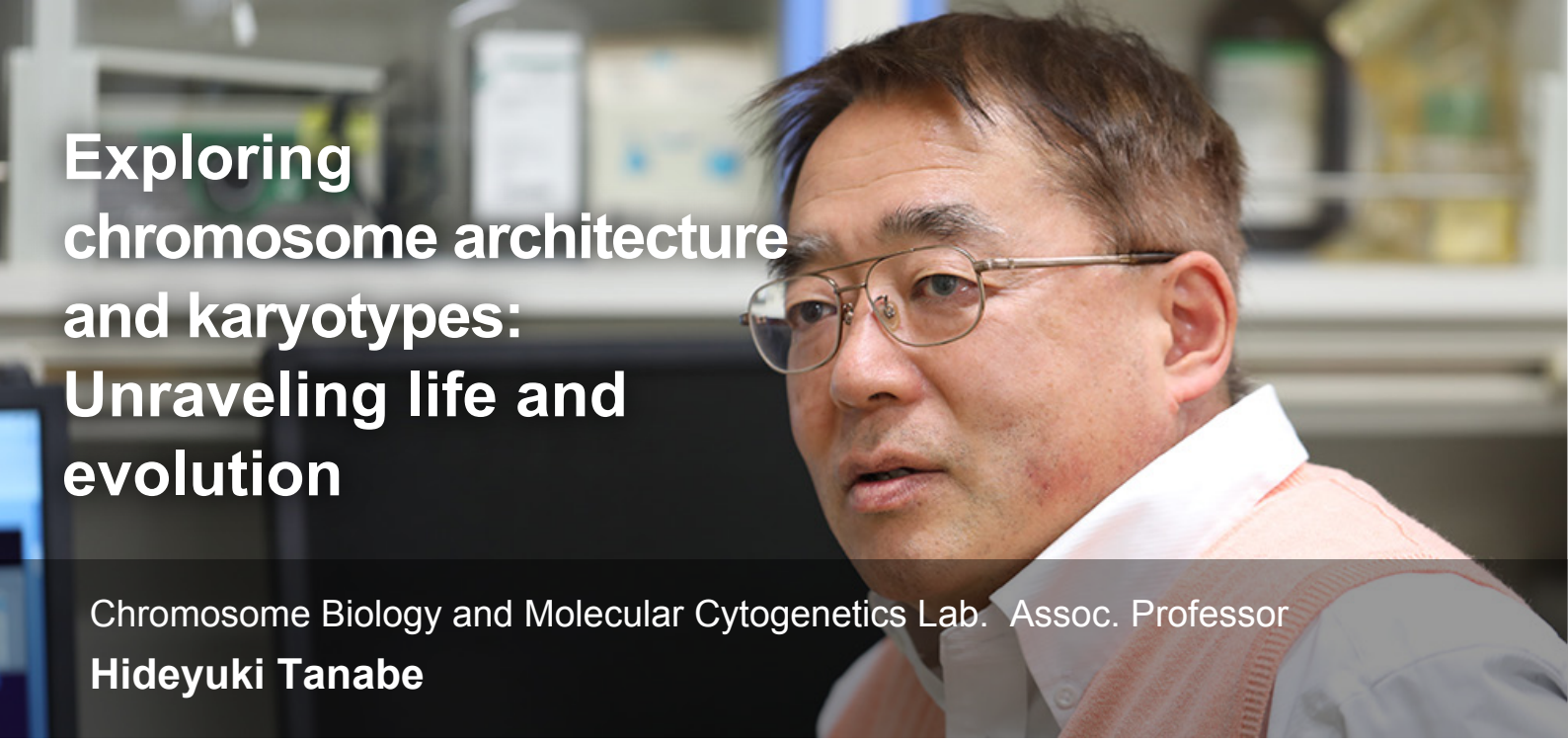

Exploring chromosome architecture and karyotypes: Unraveling life and evolution

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Q. What is the one thing you want to know the most right now?

The blueprint for living organisms is encoded in DNA, and each species has an unique DNA sequence that has been formed during evolution. DNA is bound to histones to form chromatin, and highly bound chromatin build up a structure called as “chromosome.” Within an individual cell nucleus, there is an entire set of multiple chromosomes that is called as the genome. I am interested in why chromosomes have unique structures such as X-shaped ones, why the number and shape of chromosomes (called as a karyotype) differ among species, and how karyotype evolution has occurred during speciation. Namely, what I am most interested in is the structure, function, and evolution of chromosomes. Human genome is composed of 46 chromosomes (Fig. 1), but their structures can be observed only when cells are dividing during mitosis or meiosis.

It is called as “interphase” showing the state of the cell nucleus that is the phase of the cell cycle except mitosis or meiosis. Chromosomes in the interphase nucleus become loose and invisible, but actually each chromosome occupies a specific spatial region as a “chromosome territory” within the nucleus. I am interested in how chromosome territories are arranged in the nuclear space and how cells are functionally regulated, so I am trying to perform not only two dimensional analysis by

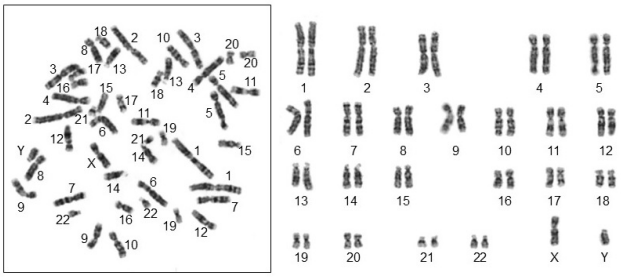


Fig. 1: G-banded human metaphase (left) and its karyotyped panel (right)

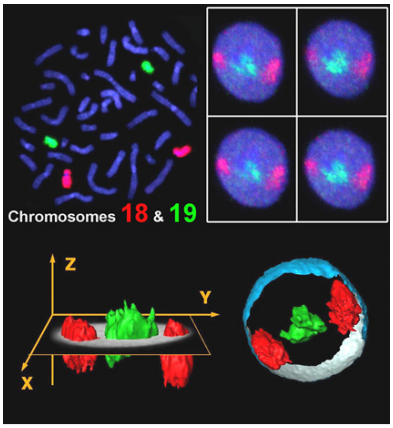


Fig. 2: Procedures for 2D-/3D-FISH analyses

observing metaphases (multicolor-FISH, 2D-FISH techniques) but also three dimensional analysis by investigating nuclear architecture (3D-FISH technique)(Fig. 2).

Q. What do you consider to be a challenge at the moment?

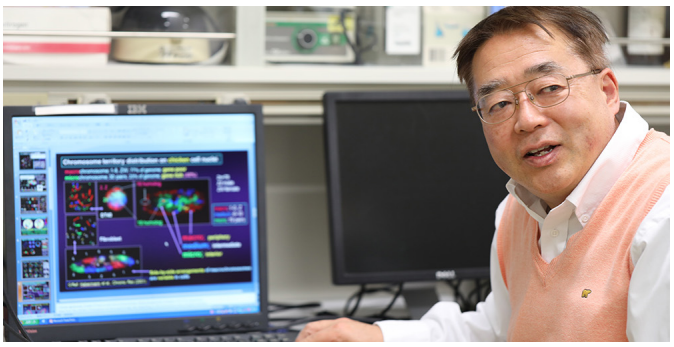
I graduated from the department of anthropology, one day I learned the interesting evidence in a lecture on the evolution of humans and primates, that

is comparison of the chromosomes. I was curious about the differences the number of chromosomes between humans and the great apes, namely, all the great apes (bonobos, chimpanzees, gorillas, and orangutans) have 48 chromosomes, whereas only humans have 46 chromosomes. In other words, it is thought that a pair of chromosome fusions specifically occurred during the evolution in the human lineage (human chromosome 2 = corresponds to the two acrocentric chromosomes of the great apes). This chromosome fusion occurred within the common ancestors of humans, chimpanzees, and bonobos, and then speciation occurred after reproductive isolation, giving rise to the current human species. This means that karyotypic evolution, the formation of human chromosome 2, is thought to have occurred during the process of speciation into the human lineage. The traces of chromosome fusion have been found in the genomes of Neanderthals and Denisovans, suggesting that human chromosome 2 was formed in earlier fossil human populations, but at what stage remains a mystery (the missing link). On July in 2024 a very interesting report was published in Cell issue (https://-doi.org/10.1016/j.cell.2024.06.002) that the mammoth cells have revealed the chromosome structure (number of chromosomes and 3D nuclear structure) due to those were found as kept in freeze-dried condition. It is encouraging that technological advances may allow us to clarify what has been thought to be impossible until now. The divergence date of humans and chimpanzees is considered about 5 million years ago, and if the fossil humans with the well-conditioned are found in the future, the structure within the cell nucleus may reveal the mystery of speciation into humans. In recent years the whole genome analysis of various species has been revealed one after another, however, the chromosome composition in the genome is still unclear in some cases, even if the genome can be decoded. Thus it is important procedures to investigate the karyotype analysis and cytogenetics that are the basis of genome analysis. There are many classical methods of cytogenetics that were developed in the 1970s, it has been entering into the whole genome analysis era so I think it will become more and more important to perform genome analysis in the light of “chromosome” by combining classical cytogenetic methods with FISH and Hi-C techniques.

Q. Could you share your thoughts on the future prospects of this field?

Chromosome composition is an overall picture of the genome as well as the bird’s-eye view of the genome. “The history of the earth is recorded in the layers of its crust; the history of all organisms is inscribed in the chromosomes” (Hitoshi Kihara, 1946) is still frequently quoted in the introductions on the topics of evolutionary biology. By the way, do you think how many species are karyotyped or have examined chromosome compositions? According to the World Conservation Monitoring Center of the United Nations Environment Programme and other organizations, the number of existing species worldwide is estimated to be about 8.7 million (8.7 million ± 1.3 million). However, since this number includes undiscovered and undescribed organisms, the actual number of confirmed species is lower than this, approximately 1.75 million species. Of these, only about 20,000 species, or less than 1% of all species, have known their chromosome compositions and karyotypes. The Society of Chromosome Research, a leading domestic academic organization focusing on animal and plant chromosome research, publishes a “Chromosome Calendar” every year, which includes photographs of 13 animal and plant species (including the cover) and the chromosomes of those species. So far, only about 200 species have been accumulated to date, we expect that this calendar will be published as a book in near future. I personally hope that this effort will be promoted on a large scale, and that in the future (hundreds of

years after many generations have passed), we will aim to create a chromosome composition and karyotype inventory of all species as a human legacy of science.



Q. What was the most enjoyable moment and the most challenging moment during your research?

I felt one of the most enjoyable or fulfilling moments, that was when I was able to prepare a beautiful chromosome spread (preparate). I prepare chromosome preparations by dropping cell suspension onto a glass slide and letting the metaphase spreads develop like a firework. When beautiful metaphase spreads can be finally created and found under the microscope (Figure 1 left is an example), it is impressive and gives me a sense of accomplishment. If the chromosome spreads cannot be prepared accordingly, various subsequent analyses such as chromosome banding analysis, chromosome aberration test, FISH technique etc. will be affected in their accuracy. It may require the feeling of craftsmanship and is close to perform an art within science. On the other hand, the most difficult moment is when I am unable to produce beautiful chromosome spreads. Some species are extremely difficult, depending on the cell types and the animal species. For example, coral larvae must be used at 10 hours after development from fertilized eggs, and the only chance is once a year during the spawning season. Some conditions are difficult to determine, such as sharks that live at low temperatures, which require special culture media containing urea to be adjusted, or long colchicine treatment because their cells divide very slowly. When I could achieve this goal to prepare beautiful chromosome spreads, it is a special feeling.

Q. Do you have a message for undergraduate and graduate students who are interested in joining your lab, and what are your interests outside of research?

To those who are interested in the genomes of organisms, I would like to invite you to take a “chromosome” perspective! If you are interested in trying to observe the chromosomes of your favorite organisms, please contact me. My hobbies include photography in general (nature, landscapes, people, plants and animals), collecting and breeding insects, fish, and amphibians, snorkeling and diving in the ocean, underwater photography, and recently, taking a sauna in the bath, visiting hot springs, etc.