Behind the scenes of cutting-edge research

Today’s guest is Dr. Mika Yoshimura. She’s an expert on bioinformatics who analyzes a huge amount of data from a NGS (Next Generation Sequencing). Her role does not usually get a lot of attention but as a woman who works in the male-dominated field of information systems, she sparkles my curiosity more than usual.

Dive into BDR’s intriguing research

Single cell analysis

Yakushiijii (MY): So jumping right in, based on the fact that you belong to the Laboratory for Bioinformatics Research, would you prefer to work in a “dry” lab environment doing bioinformatics, such as data analysis, rather than in a “wet” lab doing experiments?

Yoshimura (MY): Yeah, that’s true! I don’t do any “wet” lab experiments at all. My team mainly works on developing the technology for high-throughput single cell RNA sequencing single cell RNA-seq). This is the technology that analyses RNA transcribed from DNA in each single cell to determine the characteristics of individual cells in a cell population can be analyzed. For instance, we can even observe the difference between the state of each cell during the process in which IRS cells become another type of cell.

In addition to that, in my opinion, by expressing the data in a matrix format, mathematical formulae can be used to analyse them which, in turn, allows us to examine them from various angles.

I didn’t think research was for me

MY: Have you always done this kind of work before you came to RIKEN?

MY: In both undergraduate and graduate school, I didn’t think I was a research student. At my first job, I got a job at an IT company after graduate school.

MY: There were various reasons, but one of the main reasons is that I didn’t think research was for me.

MY: That’s a great career. What made you decide to return to academia?

Mika Yoshimura

Expert Technician, Laboratory for Bioinformatics Research

After earning a Ph.D. from Tokyo Medical and Dental University, she worked at an IT company several years until an internship opportunity called her back to academic research. Currently, she is working on constructing a workstation for single cell RNA analysis as well as analyzing data from point research. Her hobby is apparently gaming.

Various types of infrastructure

HY: How would you describe the infrastructure?

MY: My lab does not use a “wet” lab. Even the analysis was based on the data I collected from the experiments that I conducted myself, so I wasn’t familiar with computers at all. But for some reason, I got a job at an IT company after graduate school.

HY: Why? (laughing)

MY: There were various reasons, but one of the main reasons is that I didn’t think research was for me. First of all, I got a job as a fresh graduate at a system integrator company and then I moved to a software package development company and eventually accepted a part-time job in data analysis as well as analyzing data from point research. Her hobby is apparently gaming.

HY: That’s a great career. What made you decide to return to academia?

I think it’s because it makes it easier to understand the infrastructure when each of them is already analyzed individually.

In the past, the bulk RNA-seq was the mainstream method in which all cells were processed together for expression analysis by using single cell RNA-seq, the characteristics of individual cells in a cell population can be analyzed. For instance, we can even observe the difference between the state of each cell during the process where IRS cells become another type of cell.

In addition to that, in my opinion, by expressing the data in a matrix format, mathematical formulae can be used to analyse them which, in turn, allows us to examine them from various angles.

Bulk analysis

Since cells are processed together in one tube, the data obtained is just an average of those cells.

Single cell analysis

Data for individual cells can be obtained since cells are processed respectively.

Single cell analysis will reveal a lot of things that we didn’t know before.

The platform that supports the analysis is also evolving fast.

We need to keep updating…

HY: Well, technology is advancing rapidly. “Wet” lab researchers are quite smart as they are capable of learning some level of coding skills. Some of them can write codes that can analyze the data to a certain degree. However, we also have a package that is close to becoming the global standard for single cell RNA-seq analysis, which is written in R that is often used in the field of statistical processing. While R is useful, for economics, it draws us to create various charts that are useful for our research.

MY: R is more flexible.

MY: It makes it easier to draw graphs and diagrams.

HY: I’m not sure I need as much as single cell RNA-seq does, but this is the work I do.

MY: Hey! I’m looking forward to it!

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POSTSCRIPT

This interview felt to me as if I was getting a look behind the scenes of the existing world of single cell analysis. I’m sure there are many things I didn’t quite understand but I feel a renewed appreciation for the people who support such cutting-edge research even though they are not in the spotlight.

Read other Interviews
**BDR Research Highlights**

**01** Stem cells exert tight control over the timing of brain development

Brain stem cells, or radial glia, give rise to all the neurons in the cerebral cortex, and are stretched between the apical and basal membrane surfaces. The transition of some radial glia from symmetrical to asymmetrical division that later leads to brain expansion has been thought to be governed by changes in the mitotic spindle orientation in radial glia relative to the apical surface. But a new study by Fumio Matsuzaki and Bruce Fujita in the Lab for Cell Asymmetry showed that while manipulating spindle orientation of early-stage radial glia did cause the radial glia to detach from the apical surface, it did not necessarily lead to their migration. Instead, early-stage radial glia can extend "implants" that reattach to the apical surface allowing symmetric division to proceed. This discovery could also shed new insights into our understanding of mammalian brain evolution.


**02** Mechanical forces shape animal "origami" precisely despite "noise"

The reproducibility of form, shape, and characteristic appearance is a key feature of our development that is made possible because their instructions are coded in our DNA. What is puzzling, however, is how this reproducibility is achieved despite genetic variation and developmental "noise" resulting from environmental, physical and chemical fluctuations. An international team led by Yu-Chan Wang (Lab for Epithelial Morphogenesis) discovered that a genetic "blueprint" for tissue bending, despite specific instructions down to the single-cell level, is insufficient to explain developmental consistency. The mechanical forces that sculpt the embryo turn out to be the noise-producing culprit, and unexpectedly, play a previously overlooked role that ensures the precision in tissue bending— a true double-edged sword.


**03** Exploring the molecular dynamics of the new coronavirus

Makoto Taji and his colleagues in the Lab for Computational Molecular Design used the KDDI supercomputer to analyze the structural dynamics of the main protease of SARS-CoV-2, the virus that causes the new coronavirus disease, COVID-19. The raw data of the ten microsecond-long simulation has been published on Mendeley Data (doi 10.17632/2vpdhekylzy.2) for use by researchers around the world.

**04** RIKEN group leads world in single-cell transcriptome profiling

Single-cell RNA-seq (scRNA-seq), a technique used to characterize the transcriptomes of individual cells in a sample, is currently a focus of intense research. Many scRNA-seq protocols are now available, but as they all have marked differences in standards, an international group has benchmarked 13 different methods using a unified reference sample resource. The group, led by Holger Heyn of the Centro Nacional de Análisis Genómico in Spain, found that the Quarta-seq2 method, developed by Joshniko’s lab for Bioinformatics Research, was covered the best method developed to sequence single-cell RNA.


**05** New staining technique visualizes whole organs and bodies

Hiroki Ueda, Etoue Suzuki and colleagues from the Lab for Synthetic Biology have established an optimized three-dimensional (3D) tissue-staining and observation technique, named CUBI- histophotons, based on existing tissue clearing technology the lab previously developed. Their recent study details how the new technique can be used to stain tissue and label cells in mouse brains, human brains, and whole mammalian bodies. This technique will allow detailed anatomic morphology and whole-organ comparisons between species at the cellular level.


**06** Finding more chromosome structures by assuming less

Some talk to people in their neighborhood, while others talk to people outside their communities but still in the same city. Likewise, chromosomes possess different types of structural features closely interacting structures on a small scale are called TADs and longer range interacting structures on a larger scale are called compartments. Now, Yuichi Tanaguchi, Yosimuro Kunito and Simon Lacroute in the Lab for Cell Systems Control have developed a new clustering technique for analyzing data derived from HiC experiments that allow them to identify multiple structural features at different scales at once and to associate them with a characteristic tree.


**07** A new biomarker for the aging brain

Toshikazu Aoi, deputy team leader of Lab for Brain Connectomics Imaging and his collaborators have identified changes in the aging brain related to blood circulation. In their study, they found that natural age-related enlargement of the ventricles, a condition called ventriculomegaly, was associated with a lag in blood drainage from a specific deep region of the brain. The lag can be detected early with magnetic resonance imaging (MRI), making it a potential biomarker for predicting ventriculomegaly and the aging brain, which can then be treated quickly.


**08** Mice need kinetochores rich in a microtubule crosslinker to achieve error-free oocyte division

Animal oocytes are susceptible to errors during the segregation of genetic material. These errors can result in miscompanies and congenital disorders such as Down syndrome. Tomoya Kikuma and Shuhei Yoshida from the Lab for Chromosome Segregation and collaborators have found that mice need kinetochores (the main point of attachment for spindle microtubules) rich in the microtubule crosslinker Prcl to achieve error-free formation of spindles during oocyte cell division. Significantly, the team found that kinetochores in humans are not rich in Prcl. This difference between mouse and human oocytes could go a long way to explaining why oocyte division in humans is more error prone than that in mice.


**BDR Research Tour**

**Molecular Imaging Facility (MI R&D Center Building, Kobe Campus)**

*Introduction*

We can observe what is going on inside the body without causing damage or harm, and visualize tissue organization, cell function, and molecular dynamics.

*View of the MI R&D Center Building from the Port-liner’s Inyo Center Station. “MI” is short for molecular imaging. To the right of the building is the RIKEN Integrated Innovation Building (IB).*

*PET/CT scanner for animals. We are carrying out basic research on the role of positron emission tomography (PET) not only for diagnosing cancers—already commonly used in hospitals—but also for diagnosing various other diseases and for drug discovery.*
The BDR’s Clinical Translational Research Program aims to merge demands of clinical settings with cutting-edge basic research. Two researchers with clinical knowledge and experience are leading respective teams under this program with the goal of advancing our understanding of diseases as well as developing applications for regenerative medicine. We will introduce these two labs here.

**Hematopoietic Stem Cell Research**  
**Miyanishi Lab**

- **Senior scientist** Masanori Miyanishi, who is the research leader, two graduate students, two technical staff and two visiting scientists.
- We are involved in a wide range of research from basic to applied research to understand the biological characteristics of hematopoietic stem cells (HSCs), which produce all blood cell types in the body, and maximize their potential for uses in clinical settings.
- We have established the world’s best method for identifying, purifying and analyzing HSCs, which are surprisingly scarce with only one found among 100,000 blood cells, with high reproducibility. We also have expertise in functional screening to identify genes involved in homeostasis of the hematopoietic system.
- It is important to determine the best direction for research and development by accurately understanding the needs of the clinical field and the patients. We are working in collaboration with many different researchers with the desire to deliver new technology to the clinical field as quickly as possible.

**iPSC-based Cardiovascular Medical Research**  
**Masumoto Lab**

- **Senior scientist** Hidetoshi Masumoto, who is the research leader, one visiting scientist, one technical staff and one student trainee.
- We are striving to generate heart tissue from induced pluripotent stem cells (iPSCs) and replicate the function of the heart in a culture system for use in regenerative medicine and drug discovery research with the goal to create new medical treatments.
- We have established techniques for generating the different types of cells that comprise the heart from human iPSCs, and have also integrated these techniques with cell engineering technology to generate 3D artificial tissues.
- For example, being able to transplant a heart generated by iPSCs would be the ultimate goal of basic research, but this is still expected to take a long time to achieve. Besides pursuing basic research, it is therefore necessary to determine which research and developments made so far can be used clinically, and to make an effort to bring these benefits to the clinic.

**What are the advantages of doing clinical translational research at BDR?**

- There are researchers working in various research fields at BDR, and it is easy to engage with them in collaborative research.

**What is remarkably unique about the laboratory?**

- For example, being able to transplant a heart generated by iPSCs would be the ultimate goal of basic research, but this is still expected to take a long time to achieve. Besides pursuing basic research, it is therefore necessary to determine which research and developments made so far can be used clinically, and to make an effort to bring these benefits to the clinic.

**What is the laboratory conducting?**

- We are striving to generate heart tissue from induced pluripotent stem cells (iPSCs) and replicate the function of the heart in a culture system for use in regenerative medicine and drug discovery research with the goal to create new medical treatments.

**How many members are in the laboratory?**

- Senior scientist Hidetoshi Masumoto, who is the research leader, one visiting scientist, one technical staff and one student trainee.