

NBRP Zebrafish

News Letter March 2023



Thank you for your continued support of the National BioResource Project (NBRP)-Zebrafish. The first year of the fifth phase of the NBRP Zebrafish Research Project is almost over. We are especially pleased to receive many requests for resource deposition.

We look forward to your cooperation in the coming fiscal year.

Users' Voices

Dr. Kazu Kikuchi of the National Cerebral and Cardiovascular Center Research Institute gave us an article on small fish research and his comments on the NBRP Zebrafish.

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I arrived at the National Cerebral and Cardiovascular Center Research Institute (NCVC) in 2019 as Director of Department of Cardiac Regeneration Biology (formerly Department of Regenerative Medicine and Tissue Engineering). Together with a gradually increasing number of lab members (**Fig. 1**), I am currently working on regeneration research using zebrafish and the establishment of Danionella, a novel small fish model that is transparent throughout its body. The opportunity to write this article has given me a chance to reflect on my involvement in small fish research.

My first encounter with small fish models dates back to 2005. I had completed graduate school in 2003 and had been working as a postdoctoral fellow in the Department of Immunology at Duke University for about two years. I was interested in the regulation of cell differentiation and was working on blood cell differentiation in mice at the time. I had published several papers and things were going well, but as I looked at the FACS dots every day, I began to think that I would like to do research which brings out more visually appealing results. Then one day, I happened to attend a seminar where a PI I didn't know was giving a presentation on cardiac regeneration. As I listened, I realized that it was a study using adult zebrafish. Although his research was still in its early stages due to the lack of precedent, I was impressed by his presentation in which he attempted to construct a hypothesis from limited data and to get closer to the mechanism. When I asked the student who he was, he said the speaker was Ken Poss, a young PI who had just started his own research in the Department of Cell Biology. I emailed him and he immediately responded that I should come to his office.

I was nervous because some students talked about him as a demanding PI, but Ken was a very calm person when we met face to face. He was very humble and even slightly self-deprecating, but I was very impressed by his quiet confidence in his own research, and I was very interested in working with him. Ken's presentation had been well-received around me, and I had assumed that there were no open positions, so I was surprised to hear that there was a shortage, but at the same time I saw it as an opportunity. I was surprised to hear that there was a shortage of staff, but at the same time I thought it was an opportunity. Ken was surprised but appeared very happy to hear of my decision, but I was a bit confused by his reply, "I would hire you if you were not a mass murderer."

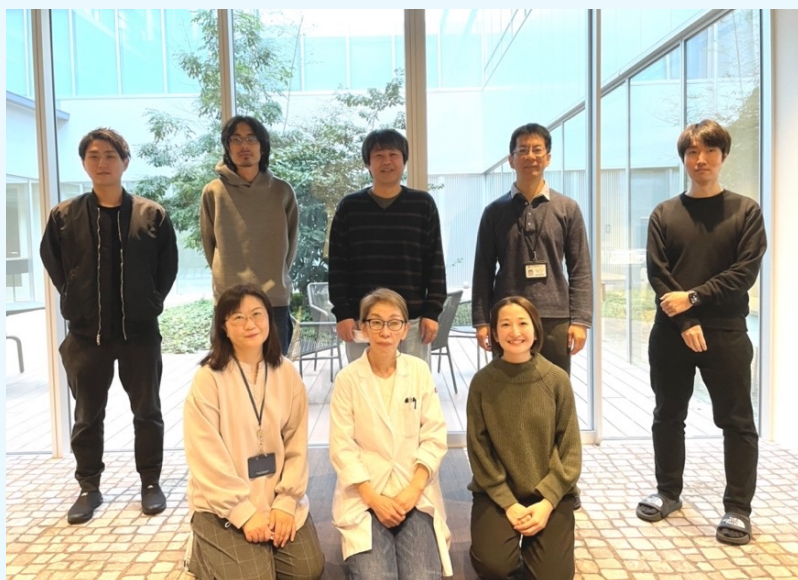


Fig.1 Members of Department of Cardiac Regeneration Biology. The author is in the center of the back row.

At the Poss Lab, we first discussed the general theme and direction of the project, and then each member was free to pursue his or her own research. Progress and prospects were presented at the lab meetings, which rotated every three months or so. Everything was new to me, having changed fields, and I experimented until late at night every day, staying up all night preparing for every lab meeting I was in charge of. Most projects in the Poss Lab were generally vague, and we could not envision the final form of the paper from the beginning, but rather, through trial and error, gradually began to see the form. After presenting the core data at the lab meeting, we discussed the direction of the paper in Ken's office. With our notebooks in front of us, we think about various interesting scientific developments and ways to combine the data, and the experiments that will be needed in the future become clear. We often rediscovered new significance in dead data or useless transgenics. These meetings were my favorite time, and I believe that what I learned during these meetings supports my current research.

After several papers were published, I was recommended to apply for a PI position. Since I had little intention of going back to Japan, I accepted several interviews as I was approached. As a result, I decided to go to the Victor Chang Cardiac Research Institute in Sydney, Australia, a small, homey institute. One of the reasons I did not stay in the U.S. was that Ken was working at a furious pace at the time and I felt it would be easier to establish my independence if I changed countries. Another important reason was that Sydney, which I visited for an interview, was a very beautiful city and I liked it very much.

At the Victor Chang, we were desperate to get grants anyway in order to retain our labor costs and zebrafish breeding expenses. At the time, the grant success rate in Australia was at an all-time low, and I had several PI friends who closed their labs and quit. It must be a global trend, but even in Australia, people wanted more clinical research, and it was very difficult to get a zebrafish research project through. Dr. Richard Harvey, a world-renowned cardiac embryologist, had an office next door to mine, and he was as hungry as a shark to get grants and keep his research going with 10 or more postdocs at any time. I had three postdocs at the best of times, and usually one at the low end. I learned how hard it is to keep up with research when I saw Richard working alone in his office on an empty weekend, paying close attention to every word of the grant application, and working tirelessly on his revision.

Perhaps because of Australia's isolation from the rest of the world, research groups are actively organized within the country. At that time, the name of Dr. Naoki Mochizuki, Director General of the NCVI, came up frequently in conversations with several zebrafish researchers. This connection developed and I unexpectedly decided to move to the NCVI in 2019. I thought that a new theme was appropriate for a new start, and decided to start two research projects: one is cardiac regeneration research using mice, and the other is imaging research using *Danionella*, pursuing my yearning for visual research. *Danionella* is a related species of zebrafish, but it is a small fish that is transparent throughout its body, not only as a juvenile but even as an adult (Fig. 2). It has the potential to analyze systemic responses during tissue injury, organ connections, pathogenesis and progression, and stem cell functions involved in the maintenance of adult tissues while still alive. The possibility of genetically analyzing the mechanism of maintenance of tissue transparency is also very interesting.



Fig.2 Wild-type (top) and pigment-deficient (bottom) *Danionella* adults. *Danionella* strains were kindly provided by Dr. Benjamine Judkewitz (Humboldt University).

After arriving at the NCVI, I had been collecting funds to expand the zebrafish breeding racks, and it was during this time that Dr. Mochizuki asked me if I was interested in “transparent Medaka fish” which is how I came to know about *Danionella*. I was looking into the housing and husbandry recommendations for Medaka fish, but when I opened the package sent by Dr. Judkewitz of Humboldt University, I found that it was not Medaka fish at all. A transparent, very beautiful small fish came out, and the members of the lab became motivated at once. It has now been about a year since we started large-scale breeding, and we are beginning to see transgenics, and I am very much looking forward to future developments.

After arriving at the NCVI, I joined the Japanese Medaka and Zebrafish Research Group and was honored to organize the 28th Japanese Medaka and Zebrafish Meeting in 2022. I would like to take this opportunity to thank once again everyone who participated in the meeting. I was also honored to participate in the steering committee of the NBRP Zebrafish, where I learned for the first time about the high level of contribution of this project. I believe that this is a world-class project that combines the quality of the provided resources with a high level of public spirit. I would like to provide my continuous effort to ensure that this project is properly maintained and developed in the future.

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I entered the field of small fish research by chance, but fortunately, I have been able to continue my zebrafish research up to now, which enables me to grow through encounters with a variety of researchers. I also feel very fortunate to have quickly become a member of the wonderful small fish research community after moving to Japan. I look forward to continuing to work with you in the future.

Call for Deposit

- Would you like to be a depositor? -

RIKEN Center for Brain Science (RIKEN CBS) is Core center for zebrafish strain conservation and has a facility that can accommodate 200,000 fish. We are willing to accept deposits of strains from external research institutions, so please do not hesitate to deposit your strains with us. When depositing, the intellectual property rights of the depositor are protected.

- Sperm cryopreservation is available -

Sperm cryopreservation is the best way to back up your strain. Send us your fish and we will process and preserve a sample as soon as possible. We recommend 3-5 healthy male fish for processing, which will provide enough sperm for 45 IVFs.

Frozen sperm samples are backed up and stored at RIKEN CBS and National Institute for Basic Biology to prevent loss in disasters. We will be able to respond to your needs as much as possible.

Please feel free to contact us for more information. We look forward to working with you.

Notice

-Revision of price list-

Effective April 1, 2023, price list of the RIKEN CBS will be revised. Due to changes in the salary system for fixed-term employees at RIKEN, there will be changes in the unit price of personnel expenses and the unit price of supplies, which will necessitate a revision to the actual fees. Thank you for your understanding.

New price list

	Unit	Fee (JPY)	
		non-profit institution	profit institution
Adults	strain	7,400	14,800
Eggs	strain	7,330	14,660
In vitro fertilized-egg	strain	15,480	30,960
Box	shipment	510	1,020
Heat pack	shipment	540	1,080
Bleeding	strain	31,770	63,540

Organizations

NBRP Zebrafish is conducted by the following three institutes.

- Core center -

RIKEN Center for Brain Science
Principal Investigator Hitoshi Okamoto

-Sub-Core center-

National Institute of Genetics
Principal Investigator Koichi Kawakami

-Sub-Core center-

National Institute for Basic Biology
Principal Investigator Shin-ichi Higashijima

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