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An interview with Shin-Ichi Nishikawa

Shin-Ichi Nishikawa is Group Director of the RIKEN Center for Developmental Biology in Kobe, Japan, where his stem cell research focuses on understanding the mechanisms involved in cell differentiation. He joined *Development* as an editor in 2009. We interviewed Shin-Ichi to find out about his interest in developmental biology, about the event that made him change career from being a practicing physician to a researcher, and his current research interests.

Looking back, when do you first remember being interested in science?
This was quite early in my life, when I was still a pupil at elementary school. I remember very clearly the day that the Sputnik satellite was launched by the Soviet Union – on October 4, 1957. I heard the news and was amazed that something the size of a beach ball had been sent into orbit around the Earth. We didn't know it then, but this was the dawn of the space age, the beginning of the space race and the start of my life-long passion for science.

What path did you follow in your early career?
I was desperate to work in a scientific field but I was not good at maths or physics, so becoming a researcher in physics or space technology wasn't really an option. I decided to study medicine and got my MD at the Kyoto University School of Medicine in 1973. I then worked as a chest physician for about 7 years, completing an internship and residency at the Kyoto University Chest Research Institute. My plans at that stage were to carry on in medicine, and I would very likely have stayed on track if I had not caught hepatitis when treating one of my patients.

What prompted the change to scientific research and the move to Germany?
Getting ill with hepatitis was a life-changing experience for me. It made me recognise the risks involved in practising medicine and it also prompted me to think about what I wanted out of my life. I was also able to view my own illness from the point of view of an interested scientist and I became very interested in the process by which a simple inflammation irreversibly develops to a chronic inflammation. I had observed this from taking care of patients with diseases such as tuberculosis, sarcoidosis and chronic berylliosis, and I was able to feel it at first hand. I went to the Institute for Genetics at the University of Cologne for two years and then came back to Kyoto, to the Chest Disease Research Institute as associate professor in the Department of Microbiology in 1983. My main focus of research at that stage was the immune reaction.

How did you first realise that you had a passion for stem cell research?
In the late 1980s, I came across a paper by Mike Dexter on the long-term culture of haematopoietic cells. At that time, I had been searching for a method to generate B lymphocytes from bone marrow progenitors, but didn't yet have any specific interest in stem cells. By learning the process involved in Dexter's long-term bone marrow culture, I became fascinated by the fact that stem cell systems include self-renewing immature stem cells, differentiating cells and stromal cells. These three cell types work together to form the microenvironment that allows stem cell differentiation to be recapitulated in culture. When I got the opportunity to investigate my own project in Japan, I decided that my first major research target should be the molecular mechanisms that underlie the interaction between this microenvironment and stem cells.

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What has been your most successful scientific collaboration?
Without doubt, it was our work in association with Leonard Schultz of the Jackson Laboratory (Bar Harbor, ME, USA), when we discovered that the recessive osteopetrosis (*op*) mutation on

chromosome 3 is within the coding region for macrophage colony-stimulating factor (M-CSF; now known as Csf1). This protein was initially thought to be required to produce macrophage progenitor cells. With the help of Len, we were able to show for the first time that there is a single base pair insertion in the coding region of the M-CSF gene that generates a stop codon. Len is a genuine mouse geneticist and maintained a large colony of the *op/op* strain; he not only sent us this genetically clean *op/op* strain, but also taught us all the requirements for maintaining it. I have also heard that as we came close to completing the sequencing, he even stopped sending the *op/op* strain to other laboratories.

What is your main research focus at the moment?
Currently, our major focus is on how the haematopoietic stem cells (HSCs) that generate blood cells throughout life are generated in embryos. It is somewhat puzzling to me that a detailed description of this process has remained obscure despite the long history of developmental haematology. We have been investigating this for the last decade, and I believe that we have now defined this process in detail, which is a great achievement.

Our work has specified four distinct intermediate stages between primitive mesoderm cells and HSCs. Several lines of evidence, including our own experiments, have now shown that endothelial cells are the direct precursors of the definitive HSC. Currently, my team has four senior post-

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docs, three junior post-docs and five technicians. One-third of our resources is spent working on this, concentrating particularly on the role of Etv2 in specifying the lateral mesoderm that gives rise to endothelial cells and HSCs.

What is your main interest outside science and do you get enough time to pursue it?

I have always been interested in all kinds of human cultural activities, including music (mainly classical), paintings and philosophy. I am always trying hard to find time. In recent years I have increased the amount of international travel that I do, and I have found that this provides an unexpected opportunity to read more books.

I am also working on a book. It is about science but not about my work – an analysis of the process of science and how it has diverged from philosophy with a particular focus on the history of philosophy and the work of Descartes, Hume and Kant.

Why did you become an editor at *Development*?

As I will be leaving active scientific research for the world of retirement in several years, I felt that this would be the right time for me to make some contribution to society and to the world of science publishing. Thus, I said yes without hesitation when I got the invitation from Olivier. I find that *Development* is excellent for stimulating a good and lively dialogue among authors, reviewers and editors.

I see my role as expanding the journal to publish more cell-oriented, rather than organism-oriented, developmental biology. The latter has been the traditional, more orthodox approach, but stem cell research has really opened up the cellular focus in development. If I am able to contribute by collecting some good stem cell biology papers during my time as an editor, I will be very happy.

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