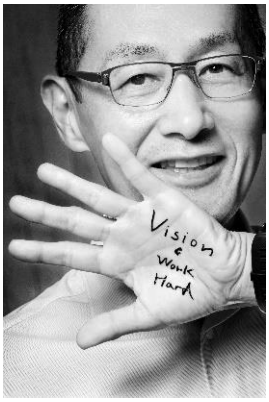
Yamanaka Shinya | Medicine

Discovered that mature body cells such as skin cells can be reprogrammed to stem cells (iPS cells). He received the Nobel Prize in Physiology or Medicine together with John Gurdon in 2012 for his groundbreaking research.



Why should young people study sciences? What advice would you give them?

Studying sciences is one way to understand nature including human beings and make the unknown known, which will contribute to building a better world and improving the well-being of people. I hope many young people with a flexible mindset would be interested in science and explore nature with new ideas. Science is full of surprises.

What role models did you have and why were they role models?

Some senior researchers I worked with are role models for me. For example, I respect Dr. Robert Mahley, the founding president of the Gladstone Institutes, where I worked for three years as a postdoctoral fellow in my 30s. He had strong leadership skills and nurtured a lot of young researchers to become outstanding scientists. I strive to be a leader like him.

Tell me about your formative years? What did your father teach you?

My father was running a small factory manufacturing parts for sewing machines, and I grew up watching him designing and making the parts. When I was a junior high school student, he got injured at work. He had to have a blood transfusion, which resulted in him getting infected with viral hepatitis. In those days, the virus responsible for his hepatitis had not been identified, thus there was no cure. By watching him become weaker and weaker, I became interested in medicine and decided to become a doctor. When I graduated from a medical school, he was very sick and must have been in pain. However, whenever I gave him

treatment such as infusion, he seemed like he was smiling. There was still no cure and he passed away soon after. It was very shocking to me. I could not help my own father, together with other patients suffering from intractable diseases. This experience prompted me to become a scientist since it is medical research that changes intractable to tractable.

When did you first realize that a mistake is not a mistake, but a clue to a new way?

When I was a graduate student at Osaka City University Graduate School of Medicine, I performed my first experiment regarding blood pressure to prove a hypothesis set by my supervisor, Dr. Katsuyuki Miura. The results of the experiment showed his hypothesis was wrong, but Dr. Miura and I were so excited about the unexpected results. I investigated how that happened and wrote my doctoral dissertation on the analysis. This experience made me realize that unexpected results are the best chances to make new discoveries.

In 1993, you wrote 30 letters to universities in the United States to get a job and do research there. How did you know that America was so important for your life as a researcher?

I wanted to learn methods to create genetically modified mice, which is an essential technique to study how a specific gene works. In Japan, few pharmacology laboratories used transgenic mice at the time, so I decided to go to the US to learn the advanced technique. I used to learn English through radio programs, in which lives in the US were vividly described. This was another reason why I wanted to live in the US.

You lived in the U.S. for several years and in 1996, you returned to Japan. The lifestyle is completely different and also as a scientist it was a shock. Your standards were high, but the environment for researchers was very different. You became depressed. What helped you to get out of that situation?

I suffered from post America depression (PAD). However, in 1999, I was hired as an associate professor at Nara Institute of Science and Technology (NAIST) and had my own laboratory for the first time in my life. By having this great opportunity, I was able to overcome PAD and continue my career as a scientist.

Sometimes you were desperate and thought about giving up. What made you get up again and again?

Advice from books and the people I admire have helped me a lot when going through difficult times. When I felt desperate because my work was not going well, I used to read self-help books. One of the impressive lessons I learned from them was that you need to crouch down to fly higher. I was also encouraged by Dr. Susumu Tonegawa, the 1987 Nobel Prize in Physiology or Medicine laureate. When I attended his lecture, I asked a question: ``In Japan, many scientists think that research continuity is important. What do you think about this?" I often changed research themes because I encountered unexpected results in my experiments, and I was wondering if this approach to research was okay. His answer was something like, "If you find an interesting theme, you should do it." I was delighted to hear that.

In the USA you learned presentation skills. A key idea for success as a scientist. Why is this so important?

It is very important for researchers to talk about research findings in a way that is accurate and easy to understand for not only other researchers but also the public. The presentation skills I acquired in the US became a powerful tool for me to get a faculty post and research grants. Also, scientists are responsible for explaining their sciences and technologies so that the public can understand how they affect their everyday lives and have their opinions on issues arising from them. It is important for researchers to communicate their research clearly.

How did you feel at the moment of your discovery?

When one of my lab members, Dr. Kazu Takahashi, reported to me that he seemed to succeed in converting fibroblasts to cells that looked like embryonic stem cells, I was nearly certain that it must be a contamination or some other mistake. So I told Kazu not to get excited, but instead just repeat the same experiments multiple times. Every time he tried it worked, so we gradually became confident it was not a mistake. Because of this, there was no such a moment like, "Wow, let's have a party!"

You are ambitious. What did you suffer through or do to reach your goal?

In a sense, I died once as a scientist due to PAD. Luckily, I was resuscitated by the great opportunity at NAIST. So I was not afraid of dying again as a scientist and wanted to try something very risky.

Being the first to publish findings is extremely important in science. Only that counts and is the currency. Around 2007 you worked day and night to achieve this goal. How did your environment react, was there much rivalry?

When we discovered a method to make mouse iPS cells in 2005, we did not want to publish it because I knew once we published, many other groups would jump into a race to generate human iPS cells. If we were in industry, we would have never published the mouse iPS cell paper without human data. Since we were in academia, we needed to publish the mouse data alone in order to secure research funding from the government. As I predicted, as soon as we reported the generation of mouse iPS cells, a fierce competition took place. The following year was the busiest and most stressful period of my life.

6 years have already passed since the first announcement that you received the Nobel Prize in 2012 for the discovery that mature cells can be reprogrammed to become pluripotent. That's very unusual. Were you surprised?

Yes, it was very short for me, but at the same time, very long for my fellow recipient, Sir John Gurdon. He showed for the first time that differentiated cells can be reverted back to the embryonic state by means of nuclear cloning in 1962, the year I was born. I really feel the prize was awarded for his seminal discovery. I was extremely lucky to receive it together with him and felt very responsible for bringing iPS cell-based therapies to patients.

You have discovered that mature cells can be reprogrammed to become pluripotent. What applications or possibilities does this have for humans?

iPS cells can be used for regenerative medicine and drug discovery. iPS cells have the ability to proliferate indefinitely and differentiate into any type of cell in the body. Taking advantage of these abilities, we can create large numbers of cells such as neurons, blood cells and heart muscle cells from iPS cells. The iPS cell-derived cells can be used for cell transplantation to

cure diseases and injuries. Clinical trials involving transplantation of iPS cell-derived cells have been conducted for diseases including age-related macular disease, Parkinson's disease, severe heart diseases, subacute spinal cord injury, blood diseases and ovarian cancer.

Another medical application is to explore drug compounds. iPS cells can be generated from patients' somatic cells like blood cells and skin cells, and patient-specific iPS cells can be differentiated into target cells. Researchers use the patient specific iPS cell-derived cells to understand disease mechanisms and discover drug compounds by testing large numbers of chemicals on the target cells. Some research groups started clinical trials for the drugs they found with the iPS cell technology to treat intractable diseases including amyotrophic lateral sclerosis (ALS) and Alzheimer's disease.

Is it already possible to create replacement tissue or organs from iPS cells or will it only be possible in the future?

Some research teams have succeeded in making cell sheets from iPS cell-derived retinal pigment epithelial cells and heart muscle cells, or mini livers and mini brains from iPS cells. Creating more complex tissues and organs from iPS cells is still technologically difficult.

Could your research results not only cure diseases but also stop aging in the future?

iPS cell technology can be used to understand mechanisms of aging and may delay the aging process. However, the purpose of our research is not to stop aging but to develop new cures for intractable diseases to extend healthy life expectancy.

What are the most important qualities that you have developed?

The most important quality for researchers is curiosity. When unexpected results in your research happen, it is important to be interested in why the results were different, rather than thinking it was a failure. When I get an unexpected result, I feel excited and want to know more about it. Curiosity has motivated me to continue my research.

In your youth you did a lot of sports and in 2012 you ran the full Kyoto Marathon to raise 10 million yen. You are very fit. Is physical fitness very important for your thinking?

I run 10 km almost every day and participate in a few marathons a year. Running makes me refreshed and keeps me fit. Physical and mental health is very important for me to think clearly.

How would you describe your personality?

I would describe my personality as hard-working and I am not afraid of taking on new challenges.

Any words of wisdom you would like to pass on?

I would like to pass on the phrase I learned as a postdoctoral fellow at Gladstone: Vision and work hard.

What is your message to the world?

Science and technology have rapidly developed over the past century and greatly contributed to the improvement of people's lives, but we should remember science and technology are double-edged swords. Humans need to make progress to use science and technology wisely for the benefit of the people of the world.