Top Interview

photo：Ryuichi Yagi

Director of Center for iPS Cell Research and Application, Kyoto University

Dr. Shinya Yamanaka

Life possesses unknown, hidden potential. I wish to release it.

Dr. Shinya Yamanaka, the director of the Center for iPS Cell Research and Application, Kyoto University was awarded the Nobel Prize in Physiology or Medicine with Dr. John Gurdon, a professor at Cambridge University. The prize recognizes them for being the first in the world to successfully develop induced pluripotent stem cells (iPS cells) which are generated from somatic cells such as skin cells and are capable of differentiating into the cells of any tissues or organs. The generation of iPS cells is anticipated to bring about a revolution in the medical and biological world. We had the privilege of interviewing Dr. Shinya Yamanaka who led the successful research.

The key to success is VW (Vision and Work Hard)

It is generally said that fundamental research such as that on iPS cells takes time until you achieve results. What has motivated you to advance your research whose results would not appear immediately, Dr. Yamanaka?

I used to work as a clinician and felt a sense of fulfilment in contributing to each patient's treatment. But on the other hand, I met many patients who were suffering from diseases that were incurable by contemporary medicine, and in each case, I was chagrined. Afterwards, although I decided to transfer from clinical medicine to fundamental medicine, I am still determined to contribute to medical treatment for patients as a physician. Regarding clinicians, they give one-to-one treatment to each patient and the results of their treatment become apparent in a short, critical term such as a few days, a week or a month. As for fundamental research, however, it takes much longer period until results are produced, say, a year, 10 years or even 50 years. Although it takes time, once a piece of fundamental research achieves a good result, there is a possibility that the result will be able to contribute to the treatment of hundreds of thousands of patients.
Fundamental research cannot be carried out by just one researcher alone, and sometimes the baton is passed on to the next generation. That is, we can say that clinicians are 'sprinters' who run at a full tilt, while fundamental researchers are 'relay road race runners' who hand over the baton.

In moving into fundamental research, was it easy for you to switch your mode from 'a sprinter' to 'a relay road race runner'?

Fundamental research is much more likely to end up in failure than meet with success. When I faced difficulty, a word from a hospital manager whom I respected picked me up a lot. He used to be a surgeon, but ended up hanging up his scalpel and changing careers to become a hospital manager. His words encouraged me greatly. He said 'I was working hard as a surgeon and did a lot of surgery, and therefore I felt really sad when I gave it up. But now I have a clear vision to establish a substantial hospital in order to provide better medical services to hundreds and thousands of patients. Isn't your vision the same as mine?'

You described the importance of VW (Vision and Work Hard) in your book. When did your vision catch you?

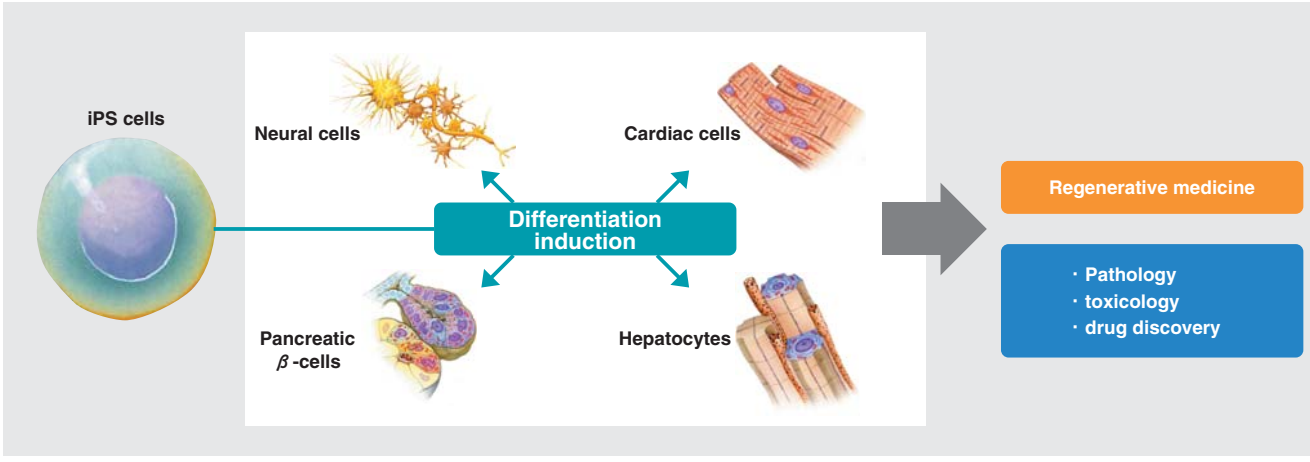
When the hospital manager gave me his words, I was 31 years old and it was before I left for the US for study. That was when I started to have a vision. To me, going to the US for study meant giving up my career as a clinician, so I was very unsure whether I should leave or not. Then, he said what he said to me and I started thinking that my vision is 'curing as many patients as possible at once rather than being involved in one-to-one treatment.'

Has your vision changed after having developed iPS cells? What is your current vision for the future?

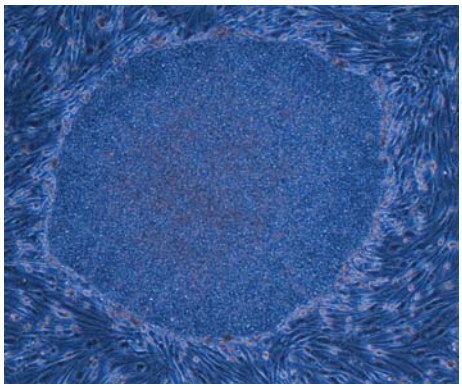
When I first developed iPS cells, I was thinking that they would be able to contribute mainly to regenerative medicine. However, now, I think that making a contribution to developing new drugs is more significant. The process of creating new drugs utilizing iPS cells is as follows: First, we create iPS cells from cells of patients who are suffering from intractable diseases and make those iPS cells differentiate into the cells of the affected part in order to recreate the disease outside the body. Then, we develop new drugs that can alleviate the condition. Of course, regenerative medicine is important, but now, I think that the development of new drugs is the field where iPS stem cells can really contribute. As for my current vision for the future, I would like it if many researchers and companies used iPS cells in order to develop new drugs all over the world. Particularly, I hope that new drugs will be developed in Japan.

Has iPS cells already been used in the development of new drugs?

In early June 2013, the International Society for Stem Cell Research met in the US and there were a lot of presentations on developing new drugs using iPS cells. Since the number of presentations has increased a lot, I had an impression that new drug development was improving. However, it takes about 10 years to develop a drug because once a candidate for a new drug is found, the safety and the efficacy need to be determined, then,

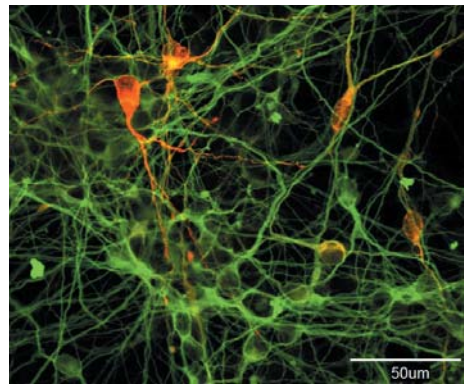


Induced pluripotent stem (iPS) cells are highly anticipated to be utilized for determining the causes of diseases, developing new drugs and regeneration medicine such as cell transplant treatment.



iPS cells derived from adult human dermal fibroblasts

©Shinya Yamanaka, Center for iPS Cell Research and Application, Kyoto University



Dopaminergic neurons derived from human iPS cell

©Asuka Morizane, Center for iPS Cell Research and Application, Kyoto University

the clinical testing also needs to be done, and finally, it can come onto the market as a new drug. Unfortunately, iPS cells can't magically shorten 10 years to three days. But by utilizing iPS cells, they can make various contributions such as finding candidates for new drugs and conducting tests with iPS cells for toxicity studies which could only be done artificially before the discovery of the cells. What's more, I really anticipate that iPS cells might be able to shorten 10 years to five years or multiply the probability of the candidates being made into final products as new drugs.

You need someone who complete this jigsaw puzzle

Did you notice anything different after you started research in the US?

The biggest thing I noticed was the difference in human resources. In the US, a venture capital sets as large a budget as a national project in Japan and launches a company where a team of experts – experts of developing drugs, regulations and intellectual property specialists – is organized in order to work on commercial production all at once. I particularly feel a difference between Japan and the US in the way they do things. There are many excellent human resources in Japanese private companies. However, there is no way to invite them to universities to conduct research together. Universities in Japan do not have positions for patent experts or for people from drug companies. In universities, a project is usually set up in five-year units; therefore, the period of employment needs to be within those units. Furthermore, salaries are lower than those of private companies. Under such circumstances, it is impossible to organize a team in the way venture capitals in the US do.
I like to think of a team project as a jigsaw puzzle. Researchers are important pieces, but the puzzle cannot be completed with only those pieces. A project needs a lot of pieces such as intellectual property specialists, public relations experts, fund raising experts, specialists to advance cooperation with authorities such as the Ministry of Health, Labour and Welfare, experts on bioethics, and people who have experience developing drugs in a drug company. The person who plays the most important role here is the person who completes the jigsaw puzzle with these pieces. Someone like a manager or the CEO of the project, who has the ability to form a clear view of the pieces and to put them in the most suitable places plays the most important role here, I think.

Are researchers suitable for the role of CEO?

No, researchers cannot play the role of the CEO. Currently, I am carrying out a role similar to that of a CEO, but this is a problem. I have trained to be a researcher and I am confident about it, however, I have not trained to be a CEO. My father was the owner of a small company and he told me, his only son, 'you are definitely not cut out to be a CEO, so become a doctor or a researcher.' which shows how much I am not suited to being a CEO. Regarding the example of the US, the CEO decides the direction of the project – whether it is a jigsaw puzzle about regenerative medicine, about new drug development or about something we have never thought about. And we must pay the CEO a large salary. This is the biggest difference between Japan and the US.

You mean the CEO who comes up with a vision is significant for a project. It is said that Japanese people are good at 'W' (Work hard) but not good at 'V' (Vision). What do we need to have a vision?

I don't think that all the pieces of the jigsaw need to have a vision. If each piece starts developing its own vision and starts moving off on its own, the jigsaw puzzle would just break apart. When each piece has a role to fulfil, that's a vision. The role to indicate the vision is for the CEO, not for the pieces. A uniform system of role-share has been established in the US. Venture capital brings someone with an excellent vision to a project as the CEO. If they do not like the vision of the CEO, they replace the CEO with somebody else no matter how brilliant the CEO is. As a result, sometimes the direction of the company changes completely with the replacement of the CEO. As this process goes on, the pieces start falling into place.

The connection between the life sciences and the social sciences is important

iPS cells proved that animal cells possess the ability of pluripotent differentiation as vegetable cells do. Do you think the flexibility to develop into anything is the nature of life?

We still do not know what the nature of life is. In order to come close to the answer, we, researchers and doctors in the life sciences, need to be modest. As medical science develops, a lot of diseases have become curable. But what we can see now is

just the tip of the iceberg appearing above the water. iPS cells allow us to see a part of what's below the surface of the sea which we had not been able to see before. Life possesses a lot of hidden potential. We tend to pay attention to the parts we can see, but I think giving more support for research that tries to see invisible part is very important. Let's take a simple example here. Limbs of newts regenerate even after they are cut off. Even if we cut a planarian into 16 parts, they have an ability to become 16 living bodies. Some researchers very seriously study the reason why limbs of newts are regenerative but those of human beings are not. If they could make limbs of human beings regenerate, this is exactly what we would call a dream treatment. But I actually realised that, through the research on the iPS cells technology. Something that is thought to be a dream now will not necessarily be a dream after 100 years. Life possesses unknown, hidden potential. I wish to release it.

It would be great if society possessed the ability to regenerate as well.

Yes, I wish it would. Human beings have been repeating foolish actions like war. I want to believe that human beings are wise; however, as far as I look back in their history, I have to say that they are not. From the perspective of the social sciences, I cannot be positive about the question as to whether human beings have been improving or not. On the other hand, can the life sciences contribute to a step in the progress of human beings? My answer for this question is not completely positive when I think about the fact that the development of nuclear technology was utilized to create atomic bombs. There is also a possibility that life sciences could lead to stupid consequences. Therefore, we cannot deny the possibility that iPS cells could be used in the wrong way.
I think scientists should not confine themselves in their laboratories as they used to in the past. Researchers should open up to the world. The rapid-paced progress of science and technology today allows us to do things very quickly which we were not able to do in the past. It would be good if the influence of science and technology is exercised on the cure of diseases; however, there is a possibility that social systems might collapse if science and technology were used to extend our life-span to 120 or 150 years. We need to get ready for and consider this kind of situation. I think, now, we are in the situation where the life sciences and the social sciences cannot exist apart from each other.

It might be important to put jigsaw puzzles together not only by researchers but also with people who think about society.

We, researchers tend to think that what we do is entirely right and that we conduct our research for society. However, if we view ourselves objectively, it turns out that we are not always right. We cannot easily say what is right or not. Therefore, it is very important for researchers to think about their relation to society in order to avoid thinking about things just from their own points of view.

Interviewers:
Masaki Tachibana, Director and Senior Corporate Executive Officer, Sumitomo Mitsui Banking Corporation
Kenichi Nakamura, General Manager CSR Department, Sumitomo Mitsui Banking Corporation
Takekazu Inoue, Manager, the Japan Research Institute, Limited.

PROFILE

Shinya Yamanaka
Born in Osaka city in 1962. After graduating from Kobe University Graduate School of Medicine, he received his PhD from Osaka City University Graduate School of Medicine and Faculty of Medicine. After completing a postdoctoral fellowship at Gladstone Institute in the US, he was assigned as an assistant professor at School of Medicine, Osaka City University in 1996. And then in 1999, he became an associate professor at Research Education Center for Genetic Information, Nara Institute of Science and Technology and was assigned a professorship in 2003. In 2004, he arrived at his post as a professor at the Institute for Frontier Medical Sciences, Kyoto University and became the Director of Center for iPS Cell Research and Application at the Institute for Integrated Cell-Material Sciences, Kyoto University. From April in 2010, he has held a position as the Director of the Center for iPS Cell Research and Application, Kyoto University.

Overview of the institute

iPS Cell Research and Application, Kyoto University (CiRA)
Founded: The 1st of April, 2010
Address: 53 Kawahara-chō, Shōgoin, Sakyō-ku, Kyōto 606-8507, Japan
Director: Dr. Shinya Yamanaka
Mission: As the world's first core institute dedicated to leading iPS research, the pursuit of the possibilities of iPS cells, the promotion of research collaboration, and the cultivation of and exchange between young scientists.
Website URL: http://www.cira.kyoto-u.ac.jp/j/