New Medical Science Arising from iPS Cells

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It is a great pleasure and honor to receive the 2010 Kyoto Prize for me leading a research team at Kyoto University. I would like to take this opportunity to express my heartfelt appreciation to President Kazuo Inamori and the many others at the Inamori Foundation, as well as the members of the prize selection organization.

Today, I am thrilled to see such a large audience here at these commemorative lectures. To tell you the truth, I have had the opportunity to speak at this venue about five times since the beginning of this year, but I have never seen the hall packed like this before. I understand that there are also a large number of people who are watching a transmission of this lecture from the second venue. I am truly delighted to be given the opportunity to speak to you on this wonderful occasion.

An orthopedic surgeon turning to fundamental research

As a student, I was dedicated to the sports of judo and rugby; however, possibly due to the fact that I was not a born athlete, I often found myself getting injured. Mentioning fractures alone, I must have broken my bones on at least ten different occasions. Out of curiosity, yesterday I tried to count the number of bones I had broken from head to toe, but there were so many that it made me want to give up. It suffices to say that just my nose was broken at least two times. I wanted to be an orthopedic surgeon and entered Kobe University’s School of Medicine. Needless to say, I broke several bones while playing rugby even when I was a medical student, but after completing my course there I became a resident physician at a hospital in Osaka to undergo training in orthopedic surgery. Unfortunately, after undergoing my residency for two years or so, I realized that I had little or no talent as a surgeon.

The first operation that I performed in my life was the surgical removal of an atheroma, which is a small benign tumor, like a lump of fat that forms directly beneath the skin. An ordinary orthopedic surgeon would take only ten minutes to finish, but to the utter amazement of my supervisor and nurses, it took me a total of two hours. I thought that I was useless as a surgeon and began thinking of ways that I could be of some help. And so, I gave up my career as a surgeon and have since dedicated my time to fundamental research.
Two things that I learned in the United States

I learned about fundamental research for four years at Osaka City University’s Graduate School of Medicine, but I still felt the need for further studies to become a more grounded researcher. For some reason, I decided to go to the United States rather than staying in Japan. I’m not sure why, but I didn’t give much thought to studying in Europe at that time, and I was intent on traveling to the States. So, I closely checked classified ads in well-known foreign scientific journals like Nature and Science to send out applications to every research institute in the States offering a researcher position that I might be interested in.

However, to my great regret I was merely a rather incompetent surgeon with only three to four years’ experience as a researcher, and so it was not easy to find an American institute that would agree to put a strange young Japanese man on their payroll. I kept writing letters only to receive no reply. I did receive a response from a researcher in San Francisco, though, and after talking on the phone for about 30 minutes we reached an agreement. This was probably around November (in 1992), and that commendable researcher kindly invited me to come over in the following April upon finishing my graduate school.

The man in question was Dr. Thomas Innerarity of the Gladstone Institute of Cardiovascular Disease. Back then, the Gladstone Institute was housed in a more than 100-year-old brick building, and I spent about three years there from 1993 to 1996 (Fig. 1). After receiving a Ph.D. from the university, one may undergo additional research training as a postdoctoral fellow, and it was at the Gladstone that I was accepted for a postdoctoral position.

This is Dr. Tom Innerarity, the benevolent researcher who had the courage to offer me the position (Fig. 2. left). This picture was taken in 1995. Under his guidance, I was able to enjoy a highly fulfilling life as a researcher in the United States. Of the many things that I learned there, “VW” and “NAT1” serve as the foundation of what I am doing at present (Fig. 3).

Actually, it was not Dr. Innerarity who taught me “VW,” but Dr. Robert Mahley, who was at that time President of the Gladstone Institutes (Fig. 4). Dr. Mahley and his wife have kindly come all the way from San Francisco to Kyoto to congratulate me on receiving the Kyoto Prize. Dr. Mahley has been a long-time driver of Volkswagen vehicles, and so “VW” could obviously stand for Volkswagen, but there is another meaning behind it: “Vision and Hard Work.” About ten and some years ago, he told me
that, as long as I held onto those two ideas, I would surely be successful as a researcher and human being. Ever since then, I have always kept these notions of “V” and “W” in mind.

It is often said that the Japanese are good at working hard, but they may not have visions. I must say that this generalization applies to me. I think that I work very hard, but I often find myself not knowing exactly what I am doing. Dr. Mahley showed me the importance of having a clear vision, and working hard to fulfill that vision.

Another important thing that I learned about in the States is “NAT1,” which is the name of a new gene that I discovered in a project Tom and I were involved in. To be precise, we were engaged in cancer research at the time that we first discovered this gene, but it was not until I returned to Japan and continued my research that I realized that the NAT1 gene plays an essential role in embryonic stem cells, or ES cells for short.

**What are ES cells?**

Let me explain what ES cells are. Human life—just like that of mice and frogs—begins when one egg cell and one sperm cell join together to become a fertilized egg. A single fertilized egg then divides repeatedly over several days until it becomes an embryo, or a mass of ten or so cells, and nidates in the mother’s uterus. In other words, pregnancy begins when an embryo attaches into the uterine wall, after which it develops one organ after another to eventually become a baby. It may sound a little sad for the embryo, but immediately before it makes it to the uterine wall, that is, before pregnancy occurs, the embryo can be removed from the uterus, taken apart, and cultivated in a laboratory for a few weeks. This is how an ES cell can be created (Fig. 5). Because it is a stem cell made from an embryo, it is called an “embryonic stem cell.” In 1981, more than 20 years ago, British scientists successfully derived the world’s first ES cells from mouse embryos.

ES cells have two distinctive properties of immense potential that no other cells possess (Fig. 6). First, their proliferation potency is extremely high. It is quite simple to multiply one ES cell into one hundred million. If you have the facilities and finances, you can even increase that number to one trillion. The proliferation occurs at a surprising rate. The other property of ES cells is that they are capable of developing into any kind of cell in a body, including a nerve cell and a muscle cell. It is said that there are more than 200 different kinds of cells that make up the adult body. This property is referred to as “pluripotency.”

As I used mice to study the NAT1 gene that I discovered in the United States, I realized that this gene plays an extremely crucial role in pluripotency, the second
significant property of ES cells. I never suspected this at all when I first discovered
NAT1, but from that time on I began to have a strong interest in finding out why ES
cells have abilities that cannot be found in other cells, and I have continued my research
on ES cells for more than ten years ever since then.

As such, it is safe to say that “VW” and “NAT1,” which I acquired at the
Gladstone Institute, provide the foundation of my research.

**Overcoming “Post America Depression”**

Having led a fulfilling research life in the United States, I came home highly motivated
to pursue my research interests in Japan, but became ill in less than a year. I had an
illness called PAD (Fig. 7). I believe that there are many medical professionals in the
audience, but I doubt that any of you have heard about this disease named PAD. That is
because it is a name that some people and I jokingly came up with. PAD stands for
“Post America Depression.”

In the United States, all I had to do was become absorbed in my favorite
thing—doing research—day in and day out at the wonderful institute established by Dr.
Mahley. I was fortunate enough to be blessed with wonderful staff members, and did not
have to worry about where my research funds were coming from. I also had many
persons nearby with whom I was able to discuss my research findings. It was simply an
ideal environment for a researcher. However, things were completely different in Japan.
First of all, research funds did not come easily. I brought three mice for research with
me from the States and named one of them Tom and treated him like a pet. We have a
phrase in Japan, “multiply like mice,” referring to the way that they increase so rapidly:
the first three became twenty in one month, and two hundred in six months. In the States,
too, they breed exponentially, but there is always someone who takes care of the mice,
and researchers only need to worry about the experiments, whereas in Japan, the
researchers have to take care of their own mice. I ended up spending days not knowing
if I were doing research or simply taking care of the mice.

What was even more trying was that there were few people around me who
understood what I was doing. I was working hard on the research of mouse ES cells at a
university medical department, when my senior researchers suggested that I should try
something different that would be of some value to medical science, even though they
too found my research interesting. Then I began to feel down, eventually reaching the
point where I began to think that I should give up my career as a researcher and return
to a job as a surgeon where, even if I were clumsy, I could still be of some help. At that
time, I really was on the verge of discontinuing my research.

Fortunately, two events occurred then that helped me to recover from PAD. First, human ES cells were generated in the United States in 1998. A professor at the University of Wisconsin-Madison, Dr. James Thomson, took a human embryo immediately before it became implanted in order to derive human ES cells with properties of rapid proliferation and pluripotency to differentiate into a wide range of cell types like mouse ES cells. Before that, there had only been mouse ES cells, and I too was studying mice, but now we were finally able to obtain human ES cells.

Then, ES cells suddenly came under the spotlight due to their potential benefits to medical science. If human ES cells could be multiplied in large quantities to generate various cell types, such as nerve cells, cardiac cells, or pancreatic cells, there would be a possibility of curing patients with spinal cord injuries, cardiac failures, and diabetes by transplanting cells that could generate healthy nerve cells, cardiac cells, and insulin. Expectations were suddenly high that ES cells might be used for regenerative medicine (Fig. 8). I had long been advised to do research that would contribute to medicine, but the tide had changed overnight. At that time I happily recovered my spirits, knowing that ES cell research could be beneficial to medical science.

However, there is a positive and negative side to everything. Human ES cells have truly wonderful potential, but they can only be derived from fertilized eggs and embryos. Because of this, transplanting cardiac cells differentiated from ES cells into a patient with a heart disease can result in immune rejection because, after all, they are someone else’s cells. Furthermore, we are presented with an ethical issue: Should we allow the destruction of human embryos—the very germination of a human life—even if it is for the sake of developing medical science or helping patients (Fig. 9)? Naturally, there are still many people around the world who oppose the research of human ES cells. In spite of all this controversy, for me the birth of human ES cells significantly helped to ease my Post America Depression.

Another major event occurred to me in the following year. In 1999, I moved from the Osaka City University to the Nara Institute of Science and Technology, or NAIST, where I was given my own laboratory for the first time (Fig. 10). This national institute offers a splendid research environment, which is on par with that of its counterparts in the United States. With an abundance of research funds, NAIST draws many talented researchers and graduate students from around the country. Now that I had my own laboratory there and human ES cells had become a reality, my PAD began to disappear, allowing me to continue with my work without having to revert to a career as an inept orthopedic surgeon.
Establishing a new vision that overcomes issues with ES cells

So, I took up my new position at NAIST on December 1, 1999, and the first thing I did there was to prepare for the Year 2000 computer software problem. I still remember going there at midnight on New Year’s Eve of 1999 to check if the electric power had failed.

With the Year 2000 problem ending without a hitch, I was ready to resume my research, and I thought that I should have an appealing vision. Otherwise, I was afraid that graduate students entering NAIST in April would not choose my laboratory. The NAIST Graduate School of Biological Sciences had more than 20 research laboratories for biology alone, which scrambled for some 120 new students from around the country every spring when the school year begins. The choice was up to the students. Mine was a small fledgling laboratory and, while laboratories are usually supervised by professors, I was still an associate professor and had no professor above me. Although the laboratory bore my name, its space and number of staff were half the size of other laboratories because of my position as an associate professor. I was still in my thirties then, and completely unknown with little research funds. And so, I was really concerned about whether any students would choose to conduct research in my laboratory. Because NAIST is composed solely of graduate schools, it would be extremely awkward if I did not gain even a single student. After much deliberation about how I could convince students, I remembered the words of Dr. Mahley, and decided that I should set forth an appealing vision. You cannot increase funds in a short amount of time, but you can create a vision. I thought really hard and finally came up with the long-term goal of my laboratory, which was “the generation of ES-like pluripotent stem cells.”

I began studying ES cells because a gene that I discovered in the United States happened to be one that plays a key role in ES cells. When human ES cells were generated, the possibility arose that my research would be of great use to medical science. However, human ES cells needed to be derived from human embryos, which is a highly controversial subject. I thought that such issues with ES cells might be resolved if I could induce cells that function like ES cells from the patients’ own somatic cells, such as those taken from the skin, rather than from someone else’s fertilized eggs. A process of reverting differentiated cells to a state similar to that of fertilized eggs is known as “reprogramming” by scientists. My vision was to “reprogram” skin cells into ES-like cells (Fig. 11).

April then arrived, and the heads of each laboratory were given the opportunity
to publicize their laboratories before 120 new students. I of course spoke for my laboratory and eloquently explained my vision. Having spent by that time more than a decade doing fundamental research, I knew that mine would be truly wonderful if it were to bear fruit, but it was such a difficult line of research, which could take twenty or thirty years, maybe longer. However, when I spoke to the 120 students, I deliberately chose not to talk about the difficulties and focused only on how wonderful it would be if it were to become a reality. My trick seemed to work, and three students joined my laboratory. One of them took a job after the master’s course, and the other two—Yoshimi Tokuzawa and Kazutoshi Takahashi—went on to the doctoral course. We also had Tomoko Ichisaka join our laboratory as a technitian. Before it was only me doing the hard work, but now that we were a group of four, we were able to work with not just four times, but sixteen times the energy—no, even more than that.

**How is the body’s blueprint transmitted to each cell?**

It is always a challenge to explain to non-researchers how to realize such a dream as transforming skin cells into ES cells (Fig. 11). Of course, I always do my best to explain, and I hope that I have made myself clear, when someone from the audience tells me, “Dr. Yamanaka, your explanation was all Greek to me, but I certainly realized that you are very enthusiastic about what you do.” It seems that I have yet to properly convey my message, and so I think that I may try a different tactic today. The day before yesterday, Kyoto Mayor Daisaku Kadokawa, Kyoto Governor Keiji Yamada, and President Kazuo Inamori kindly held a reception for the laureates of the Kyoto Prize. On that occasion, Mayor Kadokawa gave me a picture book of Kyoto, which features photos of traditional temples and shrines, geisha in Gion, the Kyoto International Conference Center and other modern buildings, and my favorite Ekiden long-distance relay race. You could say that everything about Kyoto is crammed into this book.

For example, if Mayor Kadokawa were to ask me to reproduce Kyoto in the United States, I would certainly use this picture book as a blueprint. This book tells you everything that you need to know to create another Kyoto, such as how to construct temples and shrines, create a Gion district, and build this wonderful conference hall or a sports arena.

But of course, I could not make everything just by myself. I would need to hire many people and allocate work to them based on the blueprint, saying, “Now, you build temples,” “You make this modern conference center,” “You create Gion,” and “You build a sports arena.” Now, there are two ways to set about doing this.
One strategy is to hand out pages showing temples only to the person who builds temples. This requires that an original book containing all of the pages be kept, because if the pages were all apart, you will not have a complete set of blueprints when you wish to make a third Kyoto. As such, at least one person needs to have a complete set of master blueprints. This is the first strategy.

The other strategy is to purchase a number of these books and hand them to each worker. For the person building temples, you might put bookmarks on the pages of temples and say, “Just check the pages about temples where a bookmark is placed, and make the temples exactly like that.”

Which strategy do you think is better? Each one has its own advantages and disadvantages.

In fact, the same thing happens in our bodies. It is estimated that our body has about 60 trillion cells, which can be classified into over 200 types. However, they all have their origins in a single fertilized egg, which means that the fertilized egg has the complete set of blueprints. We all know that genes are blueprints of cells. There are about 30,000 different genes, and so a fertilized egg essentially contains a huge, 30,000-page-long blueprint collection.

One fertilized egg divides repeatedly, with the result that some cells will develop into intestinal cells, others into skin cells, and still others into stem cells like ES cells. There are two possible ways that this blueprint is communicated: one possibility is that intestinal cells receive pages of intestines only and lose all of the other pages; and the other possibility is that the entire 30,000-page blueprint is communicated to every single cell. The question of which hypothesis is true had been the topic of controversy in biology that had lasted for more than a century.

All cells contain the blueprint for the whole body

This is a book published more than a century ago in 1893 by Dr. August Weismann, which is titled “The Germ-Plasm—A Theory of Heredity (Fig. 12).” In this book, Dr. Weismann supported the first possibility, namely, that only the necessary pages from the blueprint are communicated to each cell. Only germ cells—sperm for men and oocytes for women—have a complete copy, and a new life begins when they become fertilized; however, to a large majority of the other cells, only the pages that they need are transmitted while all others are lost.

Theoretically speaking, this may seem to be the most efficient method. It could be highly wasteful to copy the entire 30,000-page blueprint onto some 60 trillion cells,
and it would be far more efficient to copy only the necessary pages for each cell. Therefore, researchers around the world believed that each differentiated cell had only the blueprint pages that they needed.

However, it gradually became known that such was not the case. In 1962, 70 years after Dr. Weismann published his theory, Dr. Sir John Gurdon of the United Kingdom finally proved it wrong.

Dr. Gurdon is still going strong, and is due to visit Kyoto University in two weeks’ time. The year 1962 is the year that I was born, and in that year Dr. Gurdon succeeded in creating a tadpole from the intestinal cell of an adult frog. From a cell that, according to Dr. Weismann’s hypothesis, was supposed only to contain the blueprint pages necessary for intestines, a living, breathing tadpole with a mouth and tail was created.

Dr. Gurdon accomplished it by cloning technology, or nuclear transfer. He caught a frog from somewhere and removed the nucleus from one of its intestinal cells. Now, the nucleus is an important place where the genetic information or the blueprint is stored in a cell. The conventional theory stated that a nucleus taken from an intestinal cell would only contain information on intestines. He then took an unfertilized egg from another frog. An egg is a germ cell, and thus is supposed to have a complete set of blueprints according to the previously held theory. However, he took the nucleus out of an egg and threw it away, inserting into it the blueprint pages taken from the intestinal cell. Nuclear transfer is a very difficult technique, but Dr. Gurdon succeeded and announced the results of his experiment, which stated that, when stimulated, the egg began to differentiate and became a tadpole (Fig. 13). What he proved was that the blueprint in a frog’s intestinal cell at least contains all of the pages necessary for a tadpole.

Then, in 1997, a successful case of nuclear transfer in a mammal was reported with the birth of a sheep named Dolly in the United Kingdom. Her creator was Dr. Sir Ian Wilmut. Dolly was cloned by transferring the nucleus of a milk-producing mammary gland. If you take a cell from a mammary gland and simply cultivate it, you will gain white fluid. Following the conventional theory, a cell from a mammary gland should have only the pages necessary to produce milk, but the nuclear transfer resulted in a complete sheep. In other words, this proved that mammary gland cell contained the complete set of information required to create the individual sheep named Dolly.

**Searching for the “bookmark” in the blueprint**
Thanks to the research work on Dr. Sir. Ian Wilmut’s sheep Dolly and Dr. Sir. John Gurdon’s tadpole, it was proven that every cell holds a complete blueprint. In other words, skin cells and ES cells all share the same blueprint. The difference, however, lies in the “bookmarks,” that indicate which pages are to be read among different types of cells. And it is the transcription factor that serves as a bookmark in a cell.

It has been proven that, if a bookmark, or transcription factor, of a certain cell is inserted into another cell, the characteristics of the cell will change. Dr. Walter Jakob Gehring, who received the Kyoto Prize a decade ago, is among those who proved this.

Some of you might find this to be a little disgusting, but this is a close-up profile of a fruit fly (drosophila) using an electron microscope (Fig. 14). What looks like an eye of the superhero Kamen Rider or Masked Rider here is the right eye of the fruit fly. Because theirs is a compound eye, you can see many small “eyes” within it. The left antenna is normal, with small hairs growing thickly on it. If you look at the right antenna, however, you will find what looks like a cluster of grapes at the tip, even though the eye is the same as that on the left. This in fact is a miniaturized version of the fly’s eye hanging at the tip of the antenna. This occurred because the bookmark necessary to develop eyes had been inserted into the antenna. Inserting only a single bookmark caused an eye to develop where there should have been an antenna. What this proves is that, by simply replacing a bookmark in the common blueprint, the characteristics of cells can be changed.

Based on these research findings, I made my own hypothesis: both skin cells and ES cells share the same blueprint, and they simply use different “bookmarks.” If this is the case, and if we can find the “bookmark” of ES cells and insert it into skin cells, we might be able to create ES-like cells from those cells, just like the eye that developed from the antenna (Fig. 15). Together with other members of my laboratory, we worked hard to discover the “bookmark” of ES cells.

It was just around that time in 2004 that I received a research grant from the Inamori Foundation. Providing research grants is one of the many activities that the Inamori Foundation is involved in other than the Kyoto Prize. I can remember it like it happened yesterday. At the research grant presentation ceremony, President Inamori shook hands with every single recipient and offered words of encouragement. Taking heart after hearing his words that day, I have dedicated myself to the research and discovered many ES cell “bookmarks (Fig. 16).”

**Deriving ES-like cells from skin cells**
By the time I moved to the Institute for Frontier Medical Sciences at Kyoto University in 2004, we had discovered a total of 24 “bookmarks” of ES cells. When we tried to generate ES-like cells by inserting these bookmarks into skin cells, using just one bookmark did not work. It only took one bookmark to transform a fruit fly’s antenna into an eye, but this time using only one bookmark did not do the trick, possibly because humans are more complicated organisms. However, our members did not give up hope and tried even harder, until we learned that if we put four bookmarks into skin cells they would turn into ES-like cells. We named them induced pluripotent stem cells, or iPS cells, and subsequently announced the generation of mouse iPS cells in 2006 and human iPS cells in 2007 (Fig. 17).

I am speaking here today on behalf of my team, and I did not generate these iPS cells alone. Rather, thanks to the splendid service of the original members of my laboratory—Dr. Tokuzawa, Dr. Takahashi, and Ms. Ichisaka—we were fortunate enough to successfully generate iPS cells. Those three members are truly precious to me. They are like a part of my family, who mean as much to me as my two daughters.

At Kyoto University’s Center for iPS Cell Research and Application, or CiRA, we are generating iPS cells for many patients with cooperation from Kyoto University Hospital, Kitano Hospital, and many other medical institutions. We ask patients to offer a small piece of skin measuring several millimeters and adhere it onto a culture plate about ten centimeters in diameter. In two to three weeks, skin cells have multiplied to fill the plate (Fig. 18). However, that is the limit for skin cells, and they do not grow any further. Furthermore, skin cells will be skin cells no matter how much time has elapsed. However, if you put four kinds of “bookmarks” here, they will have turned into completely different cells—iPS cells—in about a month’s time (Fig. 19). Once they have transformed into iPS cells, they continue multiplying to fill ten, one hundred, and one thousand culture plates. If you stimulate them after multiplying them, you can generate many different cells from them. For example, a sufficient number of beating cardiac myocytes can be generated to fill several dozen culture plates (Fig. 20).

Potential of iPS cells—Regenerative medicine and drug screening

I would now like to talk about what we hope to do with this iPS cell technology. Suppose I were bedridden due to a cardiac disease. With our current medical technology, you cannot ask a patient with a heart disease to donate cardiac cells. If someone were to be asked for a few cardiac cells while still alive, they might be tempted to say, “Give me a break! Just wait until I die!” However, in this case, studying my cells after I die would
not do me any good. When using this iPS cell technology, however, I would only need to provide a small amount of my skin cells, and they could then be transformed into iPS cells and multiplied, eventually creating a large number of cardiac cells. Since the cardiac cells thus created would have the same blueprint as any of my other cells, we would end up with a large quantity of my own cardiac cells. My heart would be considerably weakened due to the disease, but the cardiac cells created from iPS cells would be just as new as those that I had when I was born, long before I had contracted any disease. What we could do is to either adhere or transplant my healthy cardiac cells onto my weakened heart so that it would recover and begin functioning as it did before.

Due to the shortage of organs, it is not easy to perform a heart transplant in Japan. With this technology, however, we may be able to generate as many cells as we want, and so expectations are running high for its application to regenerative medicine. Nevertheless, it is still technically difficult to create truly perfect cardiac cells, or a sufficiently large quantity of them. We also have to do more research to ensure that nothing will go wrong after the transplant and that cancer will not develop. We still have a long way to go before this technology can be put to practical use, but we expect that it will become possible in the future.

Before its application to regenerative medicine becomes a reality, there is one thing that we expect to see earlier, which is the reproduction of disease processes by culturing cells in vitro before disease has set in. Specifically speaking, by creating a disease model, we may be able to elucidate the causes of disease, and hopefully use the knowledge thus gained to develop drugs that will slow the progress of diseases, or completely cure them. Also, much is expected from applied research for drug screening, such as investigating adverse drug reactions when administering certain drugs (Fig. 21).

Actually, iPS cell research is expanding rapidly throughout the world (Fig. 22). The other day, I was surprised to find a Mini Cooper with a license plate that reads “iPS CELL” in San Francisco. Obviously, someone in the United States is working desperately on the development of iPS cells.

Thanks to the devoted efforts of Kyoto University President Hiroshi Matsumoto and generous support from the Ministry of Education, Culture, Sports, Science and Technology of Japan, we have this wonderful Center for iPS Cell Research and Application at Kyoto University, which stands on equal footing with its counterparts in the United States (Fig. 23). Here, more than 200 faculty and staff members are working with all their might on research and research support. I also have the privilege of having a small laboratory at the Gladstone Institute, where I spent time during my early days as a researcher. Having moved to a new building, the Gladstone Institute is
now regarded as one of the leading institutes of its kind in the United States (Fig. 24). Toward the goal of making the truly practical application of iPS cell technology a reality as soon as possible, young researchers both in Japan and the United States—many at CiRA and a few at the Gladstone Institute laboratory—are putting their heart and soul into their research work.

At the research institute in Kyoto we have some rather extraordinary students, but that is all right. We’re willing to put up with them since they are hard workers when it comes to research. With concerted efforts among our staff members, we hope to carry on with our endeavors (Fig. 25). And with the support of these fellow researchers and my family, I am determined to dedicate myself even further to my research work, taking to heart President Inamori’s personal belief and the Philosophy of the Kyoto Prize, which is, rather than seeking a mere research outcome, “striving for the greater good of humankind and society.”

Thank you all for coming and for your kind attention
Fig. 13

Fig. 14

Fig. 15

Fig. 16

Fig. 17

Fig. 18
Fig. 25