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IIPS Japan Policy Commentary

Policy-Driven Science and Technology

—From iPS cells to science-and-technology diplomacy—

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Introduction

In 2012, Shinya Yamanaka became the first Japanese recipient of the Nobel Prize in Physiology or Medicine in 25 years. This splendid achievement makes him the nineteenth Japanese Nobel laureate in a line of succession stretching back to Dr. Hideki Yukawa, the nation's first prize recipient (if University of Chicago professor Yoichiro Nambu, who obtained US citizenship, is included in the list).

Professor Yamanaka's award represents a golden opportunity to restore Japanese self-confidence (as many Japanese have, of late, lost confidence in the nation's vitality). Many Japanese will undoubtedly have been reassured that Japan is still fighting-fit in terms of scientific and technological prowess.

In recent times, there has been debate in the mass media regarding the decline in Japan's power as a nation. The context for this has been the remarkable advances made by China and South Korea. However, in terms of science and technology, Japan's power as a nation is not declining at all—it is instead growing. For example, as there have been three Japanese winners—Dr. Kunihiko Kodaira, Dr. Heisuke Hironaka, and Dr. Shigefumi Mori—of the Fields Medal (which is nicknamed "the mathematician's Nobel prize"), Japan's scientific and technological research capability has become well-known throughout Asia and the entire world. Many will likely recall the splendid achievements of the Hayabusa, which recently shot photographs of far distant asteroids and returned to Earth on a single ion engine.

The significance of Professor Yamanaka's Nobel Prize

The Nobel Prize was awarded to Professor Yamanaka in recognition of the fact that he was the first person to establish a technique for creating iPS cells. Of even greater significance than this, however, is the fact that (as Professor Yamanaka himself recalls) the prize was awarded to him a mere six years after he had established this technique. How was it that he was able to win this prize after such a short interval? In the author's view, this represents a typical example of "policy-driven science and technology."

This most celebrated prize for science and technology is awarded to individual scientists and technologists, not to nations. However, although leading-edge scientific and technological research involves assiduous work over a long period of time and could conceivably be performed with nothing more than a pencil and paper (just like research in mathematics or theoretical physics), there has, in recent times, been a shift towards experimental research, which requires that researchers team up with research assistants, put forward original ideas, and then verify them experimentally. This trend is evident in physics and chemistry as well as in medicine and physiology. Super Kamiokande and the giant particle accelerator at CERN in Switzerland represent examples of this phenomenon in the field of elementary particles.

The outstanding nature of the research conducted by Professor Yamanaka's group on iPS cells was due to the fact that it was founded on experimental work. Their unique concept involved identifying four genes (from numerous possible candidates) which, when combined, would initialize the somatic-cell program. Experimental science was required to verify this unique idea. This, in turn, required a superb team of experimental assistants. There is no doubt that the impetus for Professor Yamanaka's Nobel Prize was provided by a highly talented group of research assistants led by Kazutoshi Takahashi, an early graduate student of Professor Yamanaka when he was an assistant professor at Nara Institute of Science and Technology. As a graduate of the Faculty of Science and Engineering at Doshisha University, Mr. Takahashi—who devised the idea of selecting the four genes—is an expert at logical, step-by-step experimentation. At the press conference held after he had been informed of his Nobel Prize, Professor Yamanaka acknowledged Kazutoshi Takahashi's achievements in this regard.

Experimental science requires numerous researchers and large amounts of experimental equipment. It is external public funding for research that makes such experimental research possible. If this research funding can be obtained, a certain percentage (normally 30%) is allocated for general and administrative expenses, and the university can use this to pay the salaries of research assistants. This money can also be applied to the purchase of experimental equipment. Thus, the government is becoming involved in the promotion of research. Aside from the construction of large research installations like Super Kamiokande, there is no need for the government to expend huge amounts of the national treasury in support of original research. A moderate degree of assistance—providing back-up support for small research teams and enabling them to continue their research—will be sufficient. In this case, a "moderate degree of assistance" means research funding of approximately 100 million yen per annum for a pre-determined period (normally around five years).

The government is faced with the problems of how best to unearth research that is likely to bear fruit and of how to determine the size of the research support subsidy. In empirical terms, its only recourse is to rely on the judgments of senior researchers who have a research track record. Naturally, such arbiters can be wrong. These senior researchers might also reject research that conflicts with their own ideas and principles. For these reasons, it is standard practice for research to be reviewed by several such arbiters. The external funding for Professor Yamanaka's initial research came from a program administered by the Japan Science and Technology Agency (JST) that is known as CREST (the full name for which is "JST Strategic Basic Research Programs"). Dr. Tadamitsu Kishimoto, the former president of Osaka University who discovered interleukin 6, a key substance in the field of immunology, has played a major role in this arbitration. Dr. Kishimoto, who served as an arbiter in the area of advanced medical technology to combat infectious diseases and serious immune diseases, made the following comments after the awarding of the Nobel Prize to Professor Yamanaka:

"At the time, Professor Yamanaka was an assistant professor at Nara Institute of Science and Technology and was conducting his research on a shoestring, with just two graduate students to help him. There were some who said that the proposition—that, if genes that characteristically appear in embryonic stem cells were to be inserted into mature cells, the mature cells might possibly return to an immature state—was outside the scope of my fields, which are infectious diseases and serious immune diseases. At the time, everyone believed that—although it was an interesting idea—mature cells

would be very unlikely to revert to normal, and no one had bothered to start any research work based on this premise. However, since this was an original and bold idea that had been the subject of an article in the well-known magazine *Cell*, and, since Professor Yamanaka's research was well organized, his proposal was accepted on the strength of the consensus view that it would not hurt to have one researcher pursuing this avenue. The upshot of this was that Kyoto University, which was impressed by the award of CREST program funding for Professor Yamanaka's work, offered him a professorship at its Institute for Frontier Medical Sciences. With increased manpower, as well, in the shape of more graduate students, his research was able to proceed at a faster clip, resulting in the discovery of iPS cells."

(Excerpt from the journal to commemorate the 12th anniversary of the CREST program)

A misconception regarding the Council for Science and Technology Policy

The body established by the Cabinet Office to promote policy-driven science and technology is known as the Council for Science and Technology Policy (CSTP).

The CSTP remained in existence during the administration of the Democratic Party of Japan (DPJ). Indicative of the DPJ administration's inability to execute policy, however, there was no evidence of any notable achievements during this period. The reason for this would seem to be that neither the DPJ nor the members of the CSTP fully understood that the Liberal Democratic Party (LDP) administration had founded this body for the purpose of implementing policy-driven science and technology.

At the time that this author belonged to the CSTP, it was comprised of top-class specialists in science and technology, including Dr. Tadamitsu Kishimoto, the former president of Osaka University, who was mentioned above; Professor Hiroyuki Abe, the former president of Tohoku University; and presidents and vice presidents of several major companies. Following a simple process, this group accomplished much in the way of implementing policy-driven science and technology. In other words, we simply determined—from a policy standpoint—which of the many scientific and technological fields ought to be strengthened and funded.

Naturally, funding required political backing, without which it would have been impossible to sway the powerful Ministry of Finance. Accordingly, we enjoyed close links with the Investigative Committee on National Development Based on Science and Technology, part of the LDP's Policy Research Council, and crossed swords with the director general of the Ministry of Finance's Budget Bureau. This was the process by which we promoted policy-driven science and technology.

The CSTP Bioethics Committee

In order to establish key policies, meetings known as "special investigative committees," which brought together numerous experts, were held under the umbrella of the CSTP. One of these—the Bioethics Committee—proved highly contentious and extremely difficult to manage.

The Bioethics Committee can be traced back to June 6, 2001, when the Act on Regulation of Human Cloning Techniques came into effect. This law stipulated that it is legal to create cloned sheep like Dolly but illegal to clone human beings. A supplementary provision to this law required the government to review the handling of

human fertilized embryos (somatic cell nuclear transfer embryonic stem cells, or SCNTES) and take necessary measures within three years. The fast-approaching deadline for this was June 2004.

When the author was a member of the CSTP, the Bioethics Committee was chaired by Professor Hiroo Imura, the former president of Kyoto University. Since Professor Imura was a doctor, it was mistakenly assumed that he was an advocate of human-embryo research. Despite the fact that the deadline for reaching a decision was looming, under his chairmanship, the Bioethics Committee turned into a dogfight between supporters and opponents of human-embryo research, and this atmosphere completely precluded any conclusion from being reached. On January 6, 2004, Professor Imura resigned as chairman of the committee, saying as he departed that a committee like this would be better off with a political scientist like Mr. Yakushiji as chairman. The author was utterly astounded by this stunning statement.

The deadline for reaching a decision was six months away. According to the learned opponents of human-embryo research on the committee, it would have been unwise to reach a decision before more safety information and up-to-date medical information were made available. Consequently, for the first three months, the committee summoned numerous doctors and held hearings. As a result of this, a certain level of confidence was built up among the faction opposed to human-embryo research as well, and it became apparent that there were different shades of opinion among the members of this opposition camp.

Thus it was that, with time running out, the author moved for a show of hands for or against in the afternoon session of the Bioethics Committee on June 23, 2004, in the belief that it would have been irresponsible to enter both sides of the argument into the official record. The details of the motion were as follows: (1) overall, this research shall be considered to be a social system program; (2) women shall not be used as experimental vehicles for this research; (3) the ban on research shall not be lifted unless the safety of research is guaranteed; and (4) research into the cloning of embryos (SCNTES) shall be restricted to one or two laboratories only. Thus, the proposal that we considered was one that also took into account the views of opponents of human-embryo research. The following day, however, banner headlines in four major newspapers proclaimed that the "Council for Science and Technology Policy lifts ban on research into cloning of embryos." This was the first and last time that the CSTP was featured on the front page of any major newspaper.

For the next few days, the author faced a barrage of questions from magazines and the mass media. The author was even attacked by committee members opposed to the decision who had gone along with it behind closed doors. (Strikingly, however, the only newspaper to report the matter accurately was the *Asahi Shimbun*, which had been consistently critical of the committee's work.) In addition, the author arranged and scheduled mass media interviews for opponents as well as supporters of the decision, thereby helping to disseminate also the opposing view. As the tide of events moved forward, both the opponents of the decision and the mass media subsequently moved on to consequential issues (such as the passing of the relevant legislation). A few years later, the author was even able to re-establish good personal relations with the decision's opponents.

The above-mentioned discovery of iPS cells by Professor Yamanaka in 2006 changed the dynamic. At the time that the author was holding external hearings of the Bioethics Committee, it was clear that the tide was swinging this way. Then, in 2005, UNESCO's General Conference adopted its Universal Declaration on Bioethics and Human Rights, and, in March 2006, the organization convened a general session of its International Bioethics Committee (IBC), which was held at Sophia University in the presence of Crown Prince Naruhito and to which the author was also invited. With this, the author's tumultuous term of service to the CSTP's Bioethics Committee came to an end.

Conclusion

As a member of the CSTP, the author was able to assist in the execution of a number of policy-driven science-and-technology initiatives, such as the draft of the Third Basic Plan for Science and Technology and the institutional reforms enshrined within it. One such initiative, which continues to this day, is science-and-technology diplomacy.

Japan has continued to overlook the fact that innovation is born of societal norms. Without social reforms, Japan will likely lapse into a state of deadlock from which no fresh innovation will emerge. In a sense, the act of grafting new ideas onto the things one has learned, in order to come up with completely new inventions, represents a form of betrayal of one's teachers. The more rigid the structure of teaching and learning, the fewer the people emerging who can graft on new ideas.

Henry Dyer, the Scot who created the Faculty of Engineering at the University of Tokyo during the Meiji era, was surprised at the skill with which his students were able to rapidly build new types of construction. As described in the novel *Clouds above the Hill*, societal norms during the Meiji era were characterized by a lack of constraints—society was fluid, and the rapid promotion of able personnel was common.

Shinichiro Ogaki, the president of the National Institute for Environmental Studies (NIES) (and a friend of the author) has recently said the same, relating how the students whom he taught almost 20 years ago at the Asian Institute of Technology in Bangkok are conducting environmental research which is more advanced than that presently being carried out at NIES. For this reason, he adds, NIES has concluded an umbrella contract with the AIT under which they will carry out joint environmental research.

Japan, too, will have to enter into cooperative programs in science and technology with developing nations on an equal footing. It was in line with this thinking that the author, at the end of his time on the CSTP, initiated a new policy-driven science-and-technology project with funding from the Overseas Cooperation Fund administered by the Japan International Cooperation Agency (JICA) and matching science-and-technology promotion funding from the JST. This was the Science and Technology Diplomacy Program (also known as SATREPS). The scale of the budget for this program is the same as that of the CREST program—100 million yen per annum per project, for three to five years. There are currently 66 projects underway in 34 countries in Asia, Africa, and South America, in fields such as the environment, disaster prevention, and infectious diseases.

The objective of this program is social implementation. In other words, the intention is that putting projects into effect in different countries with different societal norms will lead Japanese researchers and researchers from the countries in question to come up with innovations.