

Super Innovation

The Japan Journal's Osamu Sawaji reports on the progress of three projects currently being implemented as part of Japan's Super Special Consortia for supporting development of cutting-edge medical care.

In November 2008, twenty-four projects were selected to become part of the Super Special Consortia for supporting development of cutting-edge medical care, which aims to develop and commercialize advanced pharmaceuticals, medical equipment and regenerative medicine.

The Super Special Consortia are a mechanism for returning the fruits of fundamental research in the life sciences back to the people as soon as possible.

“In Japan, new pharmaceuticals and medical treatments have to clear all kinds of regulatory requirements before they can be commercialized, to prevent harmful side effects and medical accidents,” says Dr. Tasuku Honjo, an executive member of the Council for Science and Technology Policy. “This was a problem because it meant that the fruits of fundamental research could not be made available immediately.”

The following areas of research and development have been selected for the Super Special Consortia, which are to be carried out over a five-year term: (1) applications using iPS cells, (2) regenerative medicine, (3) development of innovative medical equipment, (4) development of innovative, biotechnology-based pharmaceuticals, and (5) R&D of phar-

maceuticals and medical equipment used in treatment and diagnosis crucial to general public health.

The projects that have been selected as part of the Super Special Consortia are being given institutional and financial assistance to boost development and commercialization.

“If researchers can receive advice from government agencies, for example, about what kind of tests will be required, it allows them to proceed with their research more efficiently.”

Evaluating Toxicity Using iPS

One of the projects in the Super Special Consortia for which it is hoped that commercialization is not too far away is a project, led by Dr. Hiroyuki Mizuguchi of the National Institute of Biomedical Innovation, to create a system for evaluating the toxicity of phar-



Dr. Hiroyuki Mizuguchi

maceuticals using human iPS cells (induced pluripotent stem cells).

When pharmaceutical companies develop a new drug, they study its toxicity using animals or human liver cells. However, liver cells extracted from human bodies are extremely expensive, and another drawback is that the quality of such cells is not consistent. There are also cases where toxicity is found with humans even though no problems had been detected in trials using animal liver cells. Around 30% of cases where the development of a new drug is canceled are caused by toxicity being found in animal experiments or at the human clinical trial stage.

“In April 2010, we successfully completed an experiment where 80–90% of the iPS cells differentiated into liver cells. We can now see the way forward to cheaply creating liver cells with consistent quality,” says Dr. Mizuguchi. “If we can accurately assess the toxicity and efficacy of new drugs during the early stages of development, then the time required to develop a new drug can be reduced dramatically. Several major pharmaceutical companies have already indicated that they want to use liver cells created from iPS cells in toxicity trials, and we plan to proceed with further joint research in the future.”

Dr. Mizuguchi’s research team is aiming to establish methods for evaluating the toxicity of drugs using iPS cells within the next two or three years.

“Being selected as a Super Special Consortia project indicates the government’s positive assessment of the future potential of the research. This completely changes the level of interest that other researchers and companies

show with regards to our project,” says Dr. Mizuguchi. “Cooperation with private companies is essential for commercialization, and so in that sense the benefits of the Super Special Consortia are huge.”

Personalized Artificial Joints

The Super Special Consortia also include projects that have been advanced mainly by private companies. One such project is that by Nakashima Medical to extend the lifespan of artificial joints and to create a system for producing personalized artificial joints.

As the population ages, in recent years there have been more and more people in Japan using artificial joints. However, existing artificial joints typically only last about fifteen

years, and so some people need to have replacement surgery. Also, artificial joints are not always created to match the shape of the skeleton of each individual patient, and so problems can occur, such as pain developing or the joints slipping during use.

Although metallic artificial joints are more durable than other artificial joints, they have had a weakness whereby the moveable part where the leg joins the hip (known as the “caput”) is worn away by friction as the artifi-



Koichi Kuramoto, executive director of Nakashima Medical



COURTESY OF NAKASHIMA MEDICAL

An artificial hip joint developed and commercialized by Nakashima Medical

cial joint is used.

“In the future, as developing nations become more affluent and the global population continues to age, we are certain that there will be a higher demand for long-lasting, order-made artificial joints where the size and functions have been customized to fit the needs of each individual patient,” says Koichi Kuramoto, executive director of Nakashima Medical.

The product that has been developed as part of the Super Special Consortia project is still made of metal, but it has been designed to last much longer by covering the surface of the caput with ultra-fine cavities that can store

the body fluids that act as lubricants, in imitation of the surface of real joints.

“The approval of the relevant government agencies is required in order for the new product to be used in actual human bodies. It normally takes three or four years to receive approval, but thanks to the Super Special Consortia mechanism we hope to be able to gain approval in one or two years,” says Kuramoto.

Nakashima Medical is also making progress in developing a machine that can create custom artificial joints to order. The idea is that by inputting data relating to the patient’s body type and so on, the machine will be able to create an artificial joint that is optimized for that patient, by automatically shaping the parts like an industrial product.

“At the moment we need to stock a range of artificial joints of various sizes and types, but by shifting to an order-made process we will no longer need to keep such large inventories, and we will be able to reduce costs and produce artificial joints efficiently without waste,” says Kuramoto. “We are aiming to perfect the system within the next three years.”

Regenerative Medicine Using Cell Sheets

One of the groundbreaking projects selected for the Super Special Consortia in the area of medical health care research—a “project to initiate and promote regenerative medicine using cell sheet engineering” led by Dr. Teruo Okano, a professor at Tokyo Women’s Medical University (TWMU)—has already advanced to the stage of clinical applications. Cell sheet engineering, the skillful use of layers of cultured cells, was introduced in 1990, and Professor



Dr. Teruo Okano

Okano was the first person in the world to do so.

One of the benefits cell sheet engineering offers is that the transplanted cells, as a sheet of cells, stick precisely to the

target tissues and organs without the need for stitches, and the cell sheets then express and restore the functions of those affected areas.

In 2007, the world's first successful operation was carried out at the Osaka University Hospital, where a patient with a serious heart condition was treated by attaching a cell sheet, made from muscle cells in his foot, to his heart. There have also been successful clinical trials where eyesight was restored using a cell sheet for the damaged cornea and where esophageal tissues were regenerated by transplanting cell sheets after a cancerous tumor had been removed. There are also plans to conduct clinical trials involving cell sheets grown from lung, periodontal and cartilage cells in the near future.

Until recently, restrictions on the use of cell sheet engineering therapy at medical institutions

other than TWMU, to which Professor Okano belongs, were in place because this new therapy was still in the process of development. But selection as a Super Special Consortia project means that this type of therapy is now allowed to be practiced at different associated hospitals and research facilities, and this has accelerated the progress of cell sheet engineering technology significantly.

“The commercialization of regenerative medicine using cell sheet engineering will lead to the creation of a new industry,” says Professor Okano. “I expect that the global market for cell sheet based therapies will be worth about 20 trillion yen in the next ten to twenty years.”

Professor Okano's research team at TWMU is the only group in the world with the knowledge and technology to create cell sheets. Because of this, researchers from around the world are coming to Japan to work under Professor Okano.

“My dream is that Japan's advanced science and technology will be used to heal patients all over the world.”



In trials, cell sheets from the cornea (pictured) have been used to restore eyesight.