BUILDING A HUB FOR A CELL-THERAPY REVOLUTION

The old paradigm of giving the same drug to all patients is being supplanted by a new one that includes CO-OPTING INDIVIDUAL PATIENTS' OWN CELLS TO FIGHT DISEASE. Researchers at Kanazawa Medical University are spearheading the era of personalized medicine by developing treatments that harness the power of immune cells and stem cells.

The concept of repurposing a patient's own cells so that they become biologically optimized, rejection-proof vehicles for personalized therapy has immense appeal. That potential is now becoming a reality, with reprogrammed T-cells entering the clinical marketplace as a potent treatment for certain cancers, and a myriad of clinical trials underway around the world to test cell-based vaccines, drug-delivery systems and regenerative therapies.

In the past several years, Kanazawa Medical University (KMU) has placed itself at the forefront of this field, buoyed by substantial investment from the Japanese government — part of a broader government effort to accelerate clinical progress in cell therapy.

"Our mission is to conduct advanced research and development into technologies for producing easily accessible regenerative medicine and cutting-edge cancer immunotherapy," says Shigetaka Shimodaira (see upper left image on facing page), chair of the university's Department of Regenerative Medicine.

KMU has boosted its clinical capabilities in this realm by establishing the Regenerative Medicine Center at KMU Hospital, which will conduct trials of promising therapies and serve as a training facility for researchers and medical professionals across the country. "This is one of the first clinical departments in this field at a Japanese university," notes Shimodaira. Meanwhile, the university's researchers are leading a number of exciting cell-therapy-based programmes, several of which have advanced to readiness for clinical testing or commercial development. Led by KMU president, Tsugiyasu Kanda, this project is supported by the Private University Research Branding Project run by the Japanese government.

"THIS NEW TECHNOLOGY WILL ALLOW US TO MANUFACTURE A LOT OF DENDRITIC-CELL VACCINES"

Harnessing immune cells in the fight against cancer

Shimodaira's laboratory focuses on reprogramming patient-derived immune cells known as dendritic cells so that they can stimulate an aggressive immune response against tumours on being transplanted back to the donor. In contrast to the 'one size fits all' regimens of aggressive chemotherapy or radiation traditionally endured by patients, "this approach aims to provide personalized cancer therapy with an efficacy that offers both improved survival rates and maintenance of quality of life," Shimodaira says.

The aim with vaccines based on dendritic cells is to expose the immune cells to molecular markers found on tumour cells, but not on healthy cells. The work of Shimodaira's group has contributed to determining that a protein called Wilms' tumour 1 (WT1) fits the bill, serving as what he calls "a universal common antigen of cancer." They have also identified treatment regimens that can amplify the performance of dendritic-cell vaccines by boosting the anti-tumour immune response they elicit in the recipient, and by making it harder for tumours to evade destruction by concealing themselves from immune surveillance. Shimodaira's work is being facilitated by parallel research from his KMU colleague Nobuyuki Onai, who has identified a promising method for efficiently generating dendritic cells from other types of immune cells. "This new technology will allow us to manufacture a lot of dendritic-cell vaccines," says Shimodaira.

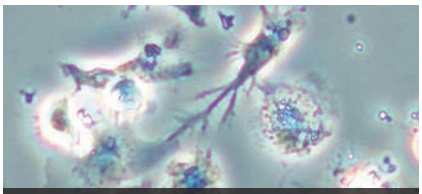
Realizing the promise of stem cells

On the regenerative medicine front, KMU researcher Yasuhito Ishigaki is exploring the tissue repair capabilities of adipose-derived stem cells, which can be extracted directly from a patient's own fat tissue. "We're conducting animal experiments using these cells to treat liver failure, oesophageal stricture, salivary gland disorders, olfactory disorders and anal atresia," explains Ishigaki. Clinical research groups at KMU have obtained promising animal data supporting the use of these cells as a potential treatment for knee osteoarthritis, and they hope to move into clinical testing in the near future. In parallel, Ishigaki's group is exploring the development of materials that can be used for culturing newly extracted stem cells and then transplanted to the site of injury, where they subsequently biodegrade, leaving only tissue behind.

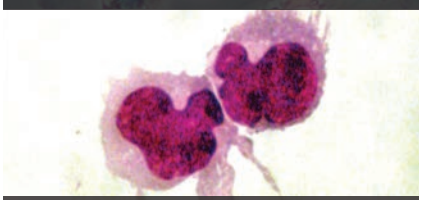
Into the real world

The fruits of some of these research projects are already moving out of the lab and into the real world. Shimodaira has teamed up with his colleague Haruo Sugiyama at Osaka University to conduct a phase 1 clinical trial of his WT1-based

Professor Shigetaka Shimodaira in front of a laboratory.



Dendritic cells



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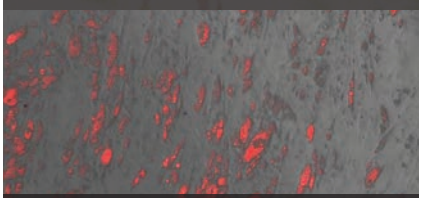

Adipose-derived stem cells

Kanazawa Medical University Campus on the Uchinada coast.

dendritic-cell vaccine in pancreatic cancer, and further trials, in collaboration with scientists in Taiwan, are planned for the near future. His team has also patented one of their techniques for producing dendritic-cell vaccines, and it will be employed at an entire network of cell-processing facilities that is now being established across Japan for manufacturing trial-ready cell therapies.

More generally, one of the objectives at KMU is to build excitement and awareness about such technologies and to transform the Hokuriku district into a regional powerhouse for the scientific, clinical and commercial development of cell-based medicines. Ishigaki notes that he is partnering with a number of external companies in the development of his biodegradable culture materials, and Shimodaira is looking into similar industry collaborations to help advance his vaccine work into late-stage trials.

"We're well positioned to raise the recognition of clinical regenerative medicine by researchers, educators, doctors, graduate students and other people who are looking to Japan to lead the way in this field," says Shimodaira. ■

Cell Therapy Project
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http://www.kanazawa-med.ac.jp/English/public_html/index.html