

Creativity for a cure

Takanori Takebe is an assistant professor at the Cincinnati Children's Hospital Medical Center and a professor at Tokyo Medical and Dental University, Japan. His research aims to develop mini organ technologies derived from human stem cells and use those in patients with rare congenital metabolic disorders.

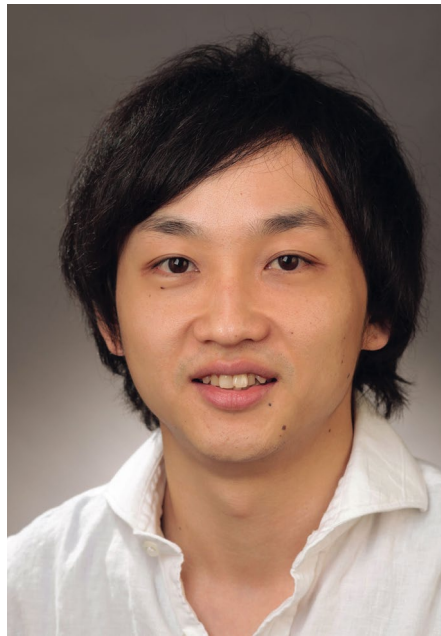
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What if someone dear to you had a condition for which there was no existing cure? There would be a feeling of desperation to find a remedy. This is what has driven me to become a scientist — the desire to challenge paradigms and create new prototypes.

I was born into a working-class family in Yokohama, Japan. When I was in elementary school, my father had a pontine stroke, which can be life-threatening. But, as he happened to be near a hospital when the stroke happened, he miraculously recovered and was eventually able to go back to work. As a young child, I was awed by the power of medicine.

Later, I decided to enter medical school at my 'home' university, Yokohama City University. In my early years in medical school, I was bothered by the fact that most doctors did not deviate from standard, accepted protocols. I started volunteering in a laboratory focused on stem cells every night after my classes for four years. I learned lab skills from many people and was excited when I identified in the human and mouse ear a progenitor population specific to elastic cartilage tissue.

While on a two-month exchange as a medical student in a surgical division at Columbia University, one of the world's largest liver transplant centers, I was struck forcibly by patients dying from liver failure owing to the organ shortage crisis. I was faced with many such patients, and my aspiration moved towards the establishment of an alternative approach to transplantation. After obtaining my MD, I accepted a research position at Yokohama City University in Japan and decided to initiate studies on the then-emerging field of induced pluripotent stem cells, which are adult cells reprogrammed to behave like embryonic stem cells. In the embryo, liver-forming cells rely on an elaborate communication system involving nearby cells to develop into the three-dimensional organ, and I suspected that these supportive cells would also be necessary to develop a liver in a dish. In 2011, I developed liver-



Credit: Cincinnati Children's Hospital Medical Center

cell precursors, or hepatoblasts mixed with mesenchymal and endothelial cells, almost serendipitously. I used a petri dish that was not meant for cell culture, but found a surprising degree of self-organization among the precursors into miniature 3D tissues. I still remember coming into the lab and visualizing these mind-blowing spheroid formations while my less-than-impressed co-workers thought these structures were 'contamination'. Fortunately, I proved that these formations were not a contamination issue, and thus my team managed to create 'miniature livers' (or organoids) that resemble the liver of a six-week-old human embryo.

In 2015, at age 28, I became an assistant professor (currently an associate director of Center of Stem Cell and Organoid Medicine) at Cincinnati Children's Hospital Medical Center, and, in 2018, I accepted a joint position as a full professor at

Tokyo Medical and Dental University. In 2017, I also started a unit focused on highly translational research at Takeda Pharmaceuticals in partnership with Kyoto University (Takeda-Center for iPS Cell Research and Application, or T-CiRA) under Nobel laureate Dr Shinya Yamanaka's directorship, for organoid-based drug safety and development applications. These three labs operate with a unified aim of bringing a difference to current medical care by fully utilizing organoids for real-world medical applications, namely organoid medicine.

Another of my life's works is to employ design and art in medicine. After 8 years of work with artistic creators, most of whom are in the advertising field, on design projects that ranged from fashion to space design to promote well-being, I recently founded a state-of-the-art design center, the YCU-Communication Design Center (YCU-CDC) (<http://y-cdc.org/portfolios/>), at my alma mater medical school. Recruited faculty and staff include designers, copywriters, web editors and educators, and we locally collaborate with design firms and advertising agencies.

The advice I give to those entering research is to (1) constantly ideate and share your thoughts with others, (2) interact with people with extremely different backgrounds and expertise, and (3) make a conscious, risky decision that is unique to human beings. □

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