Editorial

Transdifferentiation: A novel technology to advance cell regeneration
Q & A with Professor Lijian Hui, principle investigator at Shanghai Institute of Biological Sciences, China Academy of Science

This story begins with the discovery of induced pluripotent stem (iPS) cells, which won the Nobel-prize in Physiology or Medicine in 2012. The discovery of iPS has allowed regeneration scientists to bypass the endless discussion on ethics and push forward the functional regeneration of damaged tissues, and even organs. It has also inspired many cutting-edge studies including those accomplished by Professor Hui and his team. In the hope of inspiring more young scientists in this field, we have invited him to share his findings.

Q: iPS cells allow scientists to bypass the controversy regarding the source of stem cells during cell regeneration, but your idea is actually more ambitious—it does not even involve ‘stem cells’.
How did you come up with the idea and what’s ‘behind’ the story?
A: Inspired by these findings, we are wondering if all cell types are convertible. Also, we are curious if cell plasticity can be achieved in vivo. Could we then use cells from a particular organ or system, rather than the stem cells, for regeneration? To accomplish this, we need to understand the inter- and intracellular regulatory mechanisms behind the control of conversion, in other words, when do the cells stop differentiating or proliferating? Will these mechanisms facilitate the development of regenerative medicine? We aim to answer these questions in future studies. In collaboration with Dr. Wei-Fen Xie at the Chang Zheng Hospital, we managed to convert the bile cells into hepatocellular cells which then repaired the damaged liver. We have also obtained hepatic stem-like cells in vitro by dedifferentiating primary hepatocytes. These hepatic stem-like cells can proliferate in vitro and can be used as seed cells in cell transplant.

My team and I have always been interested in tumor research. Several steps in carcinogenesis are similar to those in the regeneration induced by injury. However, injuries do not necessarily induce tumorigenesis. We wonder if the dedifferentiation during injury facilitates tumor progression due to cell identity infidelity of the dedifferentiated cells. If normal cells can have plasticity, so may cancer cells. Theoretically, it is possible to cure cancer by converting the cancer cells back into normal cells. Our team has just obtained evidence that hepatic cells can be converted into bile duct cancer cells by introducing oncogenes into the hepatic cells. That is something worth looking into in future cancer research.

In summary, we focus on the conversion among different cell lineages and the underlying regulatory mechanisms. We are also interested in the relationship between cell/tissue regeneration and carcinogenesis. We hope to translate these discoveries into approaches that can mediate conversions among different cell lineages, which can be used to treat patients.

Q: So, what’s next?
A: Of course. We first converted the fibroblast cells into hepatocellular-like cells and then searched for ways to proliferate these cells. After getting sufficient functioning liver cells, we were able to eventually regenerate the liver in model animals such as mice and pigs; the liver cells were functional and could secret and excrete bile. This work led to the development of the bioartificial liver system. In 2016, this system was used to successfully treat a patient who developed acute liver failure 40 years after HBV infection. This technique has been handed over to a professional team that specializes in translating lab-based technologies to commercially-available products in clinical practice.

Can you share more on that?
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Q: It is truly amazing what you and your team have accomplished and will achieve in the near future. It seems that all these mind-blowing findings we have discussed so far were inspired by the birth of iPS cells—one single discovery.

As a well-respected expert in this field, could you please share some tips on finding ideas in research with young scientists who are working their ways through a career in academia?

A: I think one should always be aware of what’s on the spotlight, in other words, what’s the hot topic in the field? However, it’s equally important to line up the research objectives according to your own expertise. Being open-minded to the new discoveries and hot topics will help you identify those that match your interests and experiences. That is my two cents.