Groundbreaking Research Sheds Light on Organ Regeneration

By YAN Fusheng (Staff Reporter)

Scientists successfully transformed human pluripotent stem cells into bona fide 8-cell totipotent embryo-like cells for the first time, paving the way for advances in organ regeneration.

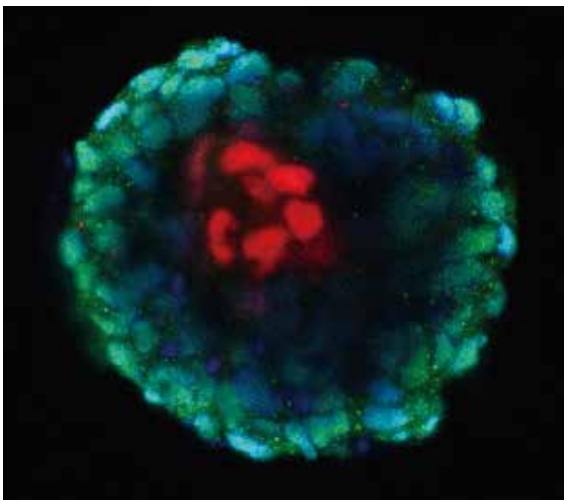
In the May 18 issue of *Nature*, an international team, led by scientists from the Guangzhou Institutes of Biomedicine and Health (GIBH) of the Chinese Academy of Sciences, announced the discovery of a transgene-free, rapid and controllable method to convert pluripotent stem cells into totipotent eight-cell embryo-like cells (8CLCs), providing valuable resources for studying early human embryogenesis.

Moreover, the researchers demonstrated for the first time that these converted cells could create placental cells *in vivo*, paving the way for individualized organ regeneration.

The researchers used a chemical cocktail to convert human pluripotent stem cells into 8CLCs. Using single-cell analysis, they identified DPPA3, a master regulator of DNA methylation in oocytes, and TPRX1, a eutherian totipotent cell homeobox (ETCHbox) family transcription factor, as two critical landmarks in the roadmap of 8CLC conversion. DPPA3 induces DNA demethylation throughout the 8CLC conversion process, whereas TPRX1 is a key executor of 8CLC gene networks.

The totipotency of 8CLCs allows the generation of all the tissues and organs, which is undoubtedly valuable in regenerating human organs for patients who are in the long waiting line for a donated organ. In addition, these converted cells capture human zygotic genome activation (ZGA) and provide a resource to elucidate the molecular process of early human embryogenesis.

"Totipotent 8-cell stage embryo-like cells recreate the embryonic state of a fertilized egg after only three divisions. Compared to the reported pluripotent stem cells, these cells can not only differentiate into placental tissue but also potentially develop into more mature organs, bringing good news to the millions of patients in need of organ transplants around the world," said the corresponding authors of the paper.



A self-organized blastoid was generated from 8CLCs. (Image credit: GIBH)

"Single-cell omics technologies are advancing our understanding of early human developmental processes, including ZGA, but the scarcity of embryos and relevant ethical considerations hinder progress," said the authors in the article. "These converted cells may provide a unique experimental model to study early human placental development and related diseases in a dish."

Reference

Mazid, M. A., Ward, C., Luo, Z., et al. (2022). Rolling back human pluripotent stem cells to an eight-cell embryo-like stage. *Nature, 605*(7909), 315-324. doi:10.1038/s41586-022-04625-0