Docket #: S20-041

Igf1r Knockout to Increase Donor Cell Contribution in Interspecies Organ Generation

Researchers in the Nakauchi lab at Stanford University have shown that the contribution of human donor cells to tissues and organs can be increased in an interspecies host embryo by knocking out insulin growth factor 1 receptor (Igf1r).

Thousands of people around the world await lifesaving organ transplants. However, given the shortage of available organs and subsequent long wait times, not everyone on a transplant list will receive the organ they need to survive. The Nakauchi lab studies the interspecies organ generation using induced pluripotent stem cells (iPSC). Researchers inject donor iPSCs into host embryos that later develop into a fetus with cells derived from both the host and donor animals. They can then determine what portion of the fetus's cells derive from either the host or the donor.

Previously, researchers found that the organs of the chimeric animals had a mixture of both host and donor cells. However, they discovered that knocking out insulin growth factor 1 receptor (Igf1r) increases donor cell contribution to organs. In one model, the kidney of a chimeric animal was made up almost entirely of donor cells. This research has the potential to revolutionize organ transplantation therapy. Although their current models only involve mouse-mouse and rat-mouse interspecies organ generation, further research could lead to the generation of human organs for transplantation and basic research.

Proof of concept – *in vivo* rodent models

Applications

- Organ transplantation therapy

- Human organ regeneration
- Basic research: drug discovery, toxicology testing, and drug screening in engineered organs

Advantages

- Increases the number of human donor cells in animal-grown human organs and tissues
- Can help solve the issue of organ shortage for transplantation therapy

Publications

- Nishimura, T., Suchy, F.P., Bhadury, J., et al. "Generation of Functional Organs Using a Cell- Competitive Niche in Intra- and Inter-species Rodent Chimeras" Cell Stem Cell 28, 1-9 (2021).

Patents

- Published Application: WO2021207493
- Published Application: 20230180725

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