Docket #: S22-080

Method to Vascularize Biological Organoids

Stanford inventors have developed a method to create spatially micropatterned vascularized structures that enable in vitro representation of human and animal biology in models such as cells, tissues, organs, and organoids. While tissue engineering techniques have yielded improvements to many in vitro systems, there remains a lack of robust vascularization in mammalian models that limits the usefulness of such models in many biomedical research contexts. Researchers in the Cardiovascular Institute have identified and optimized a regimen of growth factors and small molecules that can be applied to micropatterned human pluripotent stem cells (hPSCs), giving rise to a spatially organized and branched vascular network that is robust and scalable. To this end, the small molecules induce differentiation of micropatterned hPSCs first into the requisite germ layer(s), then into the desired progenitor cell types, finally into the terminal cell type(s). The tightly choreographed recipe has been demonstrated to create vascularized cardiac and hepatic organoids that recapitulate human development as determined by single cell sequencing, with current efforts aimed at creating vascularized neuronal organoids. This in vitro strategy offers an opportunity to build tools that better represent mammalian biology with significant implications for developmental biology, drug development, disease modeling, and regenerative medicine.

Stage of Development
Proof of Concept

Applications

- Developmental biology
- Drug efficacy and toxicity testing
- Disease modeling

- Regenerative medicine: grow vascularized organoids/tissue to replace lost or damaged tissue

Advantages

- More robust and representative 2D and 3D vascularized tissues or organoids
- Vasculature is created simultaneously with other tissue cell types
- Spatially organized and reproduceable
- Applicable to many organ, tissue, and cell types at different developmental stages
- Allows the growth of larger organoids
- Prevents death of cells inside the organoids that experience lack of oxygen
- Micrometer resolution of branching structures and hierarchical organization recapitulates that of in vivo structures

Publications

- Oscar J. Abilez, Huaxiao Yang, Lei Tian, Kitchener D. Wilson, Evan H. Lyall, Mengcheng Shen, Rahulkumar Bhoi, Yan Zhuge, Fangjun Jia, Hung Ta Wo, Gao Zhou, Yuan Guan, Bryan Aldana, Detlef Obal, Gary Peltz, Christopher K. Zarins, Joseph C. Wu Micropatterned Organoids Enable Modeling of the Earliest Stages of Human Cardiac Vascularization. bioRxiv 2022.07.08.499233

Patents

- Published Application: WO2023164242

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