Engineering a Heterogeneous Tissue from Pluripotent Stem Cells
Technology #16205

Applications

Engineering heterogeneous tissue from autologous pluripotent stem cells has huge potential in regenerative medicine and could potentially address shortage of donor organs and tissues. In addition, heterogeneous tissue could yield more predictive in vitro models compared to homogeneous organoids for functional genetics and drug screening.

Problem Addressed

Human embryonic stem cells (hES) and human induced pluripotent stem cells (hiPSCs) have opened up the field of developmental biology and regenerative medicine with access to in vitro model system for understanding development and differentiation, and developing organoids of different cell types. However, most of the technologies so far have focused on generating homogeneous population of specialized cells from a single germ layer, or mixing cells to generate a mimic of complex tissue. This technology utilizes genetic engineering to induce cells of all germ layers that co-develop to form heterogeneous tissue similar to the embryogenesis process.

Technology

The aim of the technology was to co-differentiate hiPSCs into cells of all germ layers, such that they can co-develop into a heterogeneous tissue mimicking the process of embryogenesis. Since ectoderm fate is the default pathway for differentiation, a symmetry break was induced by engineering a system to pulse the expression of Gata6, a master transcription factor that guides cell fate towards endoderm and mesoderm lineage. Gata6 was encoded under an inducible promoter and a lentiviral system was used to deliver the transgene in order to achieve heterogeneity in respect to the number of transgene copies received per cell, and consequently, expression level of Gata6. Since a threshold level of Gata6 is required to induce endoderm and mesoderm lineage, the system effectively creates a heterogeneous population of all three germ layers. With sufficient time in culture, paracrine signaling from cell populations results in an organized and heterogeneous tissue.

Advantages

- This technology describes a method of generating complex homeostatic heterogeneous tissues from hiPSCs that co-develop, mimicking the process of embryogenesis.
- Heterogeneous tissues provide a better system for functional genetics and drug screening.
- Heterogeneous tissues derived from autologous hiPSCs could potentially be used for regenerative medicine.

Categories For This Invention:
**Intellectual Property:**

Engineering a heterogeneous tissue from pluripotent stem cells

*Issued US Patent 9,677,085*

Generation of specialized, high value cells and tissues from human induced pluripotent stem cells by recapitulating early embryogenesis using gata factor 6

*US Patent Pending 2017-0306351*

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**Publications:**

Genetically engineering self-organization of human pluripotent stem cells into a liver bud-like tissue using Gata6  
Nature Communication  
2016 Jan 6;7:10243. doi: 10.1038/ncomms10243.

**External Links:**

Weiss Lab  
http://groups.csail.mit.edu/synbio/

**Image Gallery:**