Docket #: S19-280

iPSC-derived cardiac fibroblasts for in vitro modeling of cardiac fibrosis

Fibroblasts are known to be a source of the numerous pathologies associated with fibrotic diseases. However, drug development targeting the cell type has been impaired by poor in vitro models, where primary human fibroblasts are difficult to culture and expand, and murine models have limited translational value. This is particularly problematic for cellular models of cardiac fibrosis, where activated myofibroblasts can easily contaminate stem cell-derived cultures of quiescent cardiac fibroblasts.

Inventors at Stanford's Joseph Wu lab have developed a differentiation program for cardiac fibroblasts using induced pluripotent stem cells (iPSCs), offering a valuable tool for drug and target screening in cardiac diseases. The differentiated fibroblasts maintain a quiescent phenotype to enable mechanistic evaluation of cardiac fibrosis, and the inventors have used the platform to identify a novel fibrotic pathway impacting heart tissue.

The differentiation platform represents an unlimited source of cardiac fibroblasts that closely resemble primary human tissue genetically, morphologically, and functionally, and enables mechanistic exploration of pro- and anti-fibrotic pathways for drug and target discovery in cardiac diseases.

Applications

- Disease model for cardiac diseases, including
    - Myocardial infarction
    - Cardiomyopathy
    - Heath failure
- Evaluation of pro- and anti-fibrotic pathways impacting cardiac tissue
- Adaptable to patient-specific cardiac fibroblasts

Advantages

- Unlike existing iPSC-based differentiation protocols, results in limited production of smooth muscle cells, pericytes, or activated myofibroblasts
- Preservation of quiescent properties
- High cell uniformity and purity
- iPSC platform enables patient-specific drug and toxicity testing
- Amenable to co-culturing

Publications

- Generation of Quiescent Cardiac Fibroblasts From Human Induced Pluripotent Stem Cells for In Vitro Modeling of Cardiac Fibrosis Zhang et al., Circ. Res.

Patents

- Published Application: WO2020264308
- Published Application: 20220348877

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