American Heart Association | American Stroke Association

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Top Ten Things to Know
Induced Pluripotent Stem Cells for Cardiovascular Disease Modeling and Precision Medicine

1. Human pluripotent stem cells provide an invaluable model for studying the genetic basis of human cardiovascular disease. iPSC is the most abundant and widely used type of human pluripotent (can be differentiated into any of the human body's somatic cell types) stem cells.
2. The key approaches to studying cardiovascular diseases by utilizing iPSCs involve either reprogramming somatic cells from individuals affected by the disease or by using gene editing tools to generate stem cells with specific genotypes.
3. Disease modeling represents the most productive use of iPSCs to date. A singular advantage of iPSCs is that they are genetically matched to the person from whom they were derived, making them ideally suited for the study of diseases that have a strong underlying genetic cause.
4. iPSCs helps better understand how disease genotypes at the genetic level are manifested as phenotypes at the cellular level with respect to an array of cardiovascular diseases including cardiomyopathies, rhythmic disorders, vascular disease, and metabolic factors associated with heart disease.
5. Some of the challenges on using iPSCs on cardiovascular disease modeling includes potential confounders such as differences in cellular sources of iPSCs, methodological differences used for induction of pluripotency, differences in the epigenetic states of the cell lines etc. The recent emergence of efficient genome editing tools provides alternative study designs that eliminate most of the confounders, and is an excellent approach for monogenic disorders.
6. Despite advances in cardiomyocyte differentiation, the lack of purity and lack of maturity of cardiomyocytes remain key obstacles. Many strategies have been attempted to obtain a pure population of the cardiomyocytes and to increase their maturity to make them like adult cardiomyocytes. A definitive solution to the problem remains a vigorously pursued goal in the field.
7. The statement is not intended to address the use of stem cells as regenerative therapy, such as transplantation into the body to treat ischemic heart disease or heart failure.
8. iPSCs offers opportunities to test the efficacy and safety of medications in vitro without exposing the patient to risk, and to understand mechanisms relevant to patient's mutation. Investigations of whether iPSCs models is predictive to warrant clinical decision making is still in infancy, but initial studies show promise.
9. Strategies for promoting the use of iPSC for biomedical application involves a) establishing and facilitating access to iPSC biobanks, b) fostering the development of technologies to produce and differentiate iPSCs at a large scale and c) Incorporating iPSCs as a complementary model into studies for assessment of toxicity.
10. The field of iPSCs is continuing to expand for cardiovascular disease modeling, and is important as clinically relevant findings can impact the health burden of cardiovascular diseases and streamline precision medicine therapies.

Musunuru K, Sheikh F, Gupta RM, Houser SR, Maher KO, Milan DJ, Terzic A, Wu JC; on behalf of the American Heart Association Council on Functional Genomics and Translational Biology; Council on Cardiovascular Disease in the Young; and Council on Cardiovascular and Stroke Nursing. Induced pluripotent stem cells for cardiovascular disease modeling and precision medicine: a scientific statement from the American Heart Association. *Circ Genom Precis Med*. 2018;11:e000043. DOI: 10.1161/HCG.0000000000000043.