Efficient and cost-effective cardiomyocyte stem cell differentiation protocol

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Technology description

Summary

This technology is an optimized protocol to efficiently generate cardiomyocytes from human induced pluripotent stem cells (hiPSCs).

Unmet Need: Scalable cardiomyocyte production for pharmaceutical drug screens

Given the prevalence of cardiac diseases, there is substantial demand for new therapeutics and improved methods for screening drug toxicity. Generating cardiomyocytes from hiPSCs offers a unique opportunity to study cardiac disease. While protocols have been developed that improve differentiation efficiency, these often require the use of costly and unstable recombinant proteins, which has limited large-scale production of hiPSC-derived cardiomyocytes.

The Technology: Optimized protocols for low cost, efficient differentiation of hiPSCs into cardiomyocytes

This technology describes both serum-containing and serum-free protocols for generating human cardiomyocytes from healthy control or patient-derived iPSCs. The use of cheap, defined chemicals at a low dose eliminates the need for costly recombinant factors to produce human cardiomyocytes. Analysis of in vitro cultures demonstrates that this serum-free protocol offers higher yield than current methods. Further, this technology includes dual optical fluorescent reporters, administered through lentiviral infection, that record calcium and voltage simultaneously. This allows the cardiomyocytes to be characterized and monitored during extended time-course experiments, as well as during repeat experiments using the same cells. Taken together, the cost-effectiveness and absence of animal-derived products make this technology an important advance in generating human cardiomyocytes from iPSCs for use in screens for therapeutics and drug toxicity.

This technology has been used to generate cardiomyocytes from both control and patient-derived stem cells, with retention of the diseased phenotype.

Publications

Song L, Awari D, Han E, Uche-Anya E, Park S, Yabe Y, Chung W, Yazawa M. "Dual optical recordings for action potentials and calcium handling in induced pluripotent stem cell models of cardiac arrhythmias using genetically encoded fluorescent indicators" Stem Cells Transl Med. 2015 May; 4(5): 468-475.

Application area

Differentiation of control and patient-derived hiPSCs into cardiomyocytes

Large-scale production of cardiomyocytes

Therapeutic and drug-toxicity screening

Extended physiological experiments measuring excitation-contraction

Cardiac tissue engineering

Cardiac cell-based therapies

Advantages

Eliminates need for expensive and unstable animal-derived products to produce cardiomyocytes

Utilizes inexpensive, defined chemicals at low doses

Fluorescent reporters offer ability to monitor calcium and voltage levels

Protocols are applicable to both healthy control and fragile patient-derived cells

Increased yield of cardiomyocytes with serum-free protocol over other commonly used protocols

High convenience of feeder-free monolayer culture method

Institution

Columbia University

Inventors

Masayuki Yazawa