代謝機構に基づく心筋細胞の大量製造と再生医療への応用

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Metabolism-Based Production of Cardiomyocytes from Human iPSCs for Regenerative Therapy

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Cardiac regenerative therapy using human induced pluripotent stem cells (hiPSCs) is a potentially promising strategy for patients with heart failure, but the inability to eliminate residual hiPSCs and generate a massive amount of purified hiPSC-derived cardiomyocytes (hiPSC-CMs) has been a barrier to realizing this potential.
We previously developed an innovative method for efficiently eliminating residual undifferentiated pluripotent stem cells (PSCs) and non-cardiac cells and producing a large number of highly purified cardiomyocytes based on metabolic profiles in hiPSCs and hiPSC-CMs (1-5). Moreover, we revealed that tryptophan supplementation promoted the proliferation of hiPSCs for large-scale culture (6).
We also developed an efficient transplantation system using pure hiPSC-CM spheroids (7-8). Transplanted pure hiPSC-CM spheroids also improved cardiac function in rat, pig, and monkey models (9). These technologies will facilitate the clinical application of purified hiPSC-CM spheroids-mediated regenerative therapy for heart failure patients.

Keywords : iPSCs; Cardiomyocytes; Regenerative Therapy; Metabolism; Heart Failure

ヒト iPS 細胞を用いた心臓再生医療は、心臓移植治療における極度のドナー不足を補う新たな治療法として注目を集めているが、分化後に未分化幹細胞が混入し腫瘍化を引き起こすリスクを抱えているため、安全性の高い心筋細胞を効率よく作製する手法の確立が求められていた。
そこで、我々はヒト iPS 細胞および分化心筋細胞における代謝プロファイルの差異を明らかにし、その性質を利用した革新的培養法を開発することにより、ヒト iPS 細胞から安価かつ簡便に心室筋細胞を大量選別する方法を確立することに成功した (1-5)。また、トリプトファン代謝を理解することで簡便にヒト iPS 細胞の増殖を促進させる培養環境を同定した (6)。
さらに、我々は移植後の生着率を高めるためにスフェロイド移植法を開発した (7-8)。非臨床試験において安全性および有効性を確認し (9)、現在は臨床グレードのヒト iPS 細胞を用いて心室筋細胞の大量作製を行っている。本シンポジウムでは臨床応用目前に迫ったヒト iPS 細胞を用いた心臓再生医療の現状を紹介したい。

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