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Transforming stem cell research to cardiovascular remodeling

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Cardiovascular diseases (CVDs) remain the foremost reason of mortality and debility accounting for 31% of deaths worldwide. Currently, regeneration of damaged cardiac tissue with functional cardiomyocytes via stem cell therapy represents an effective approach in CVDs treatment. In this study, differentiation of cardiosphere derived cells (CDCs) to cardiomyocytes was performed in search of enhanced cardiovascular regeneration therapeutics. Cardiac Progenitor Cells (CPCs) from rat heart were propagated by explant culture and CDCs were derived. Cardiac explant outgrowth cells (CEOCs) and CDCs were characterized by Immunofluorescence, flow cytometry and reverse transcriptase PCR. Further, CDCs were treated with an optimized concentration of 10µM 5-Azacytidine for 24 h followed by supplementation with 10-4M ascorbic acid for 14 days. Extent of differentiation was analyzed by immunofluorescence and quantitative real-time PCR (qRT-PCR). In the results, flow cytometric analysis has demonstrated that 30.23% of CEOCs were positive for the c-kit marker, specific to CPCs. Gene expression analysis showing high expression of *GATA4*, *Nkx2.5* and *CD90* markers suggested enhanced cardiac lineage commitment of CDCs in comparison to CEOCs. Immunofluorescence results confirmed that 5-Aza+AA treated CDCs expressed cardiomyogenic markers i.e. α-sarcomeric actinin and Nkx2.5. qRT-PCR analysis revealed relative up-regulation of Nkx2.5, *GATA4* and *α-MHC* markers in 5-Aza+AA treated CDCs while Wnt markers, Wnt 3a, β-catenin and cyclin D1 were down regulated. Generation of spontaneous beating of 5-Aza+AA treated CDCs further reinforces that 5-Aza+AA efficiently differentiated CDCs. The cardiomyogenic potential of CDCs indicates that they can serve as an effective cellular therapeutic as well as an ideal candidate for the treatment of cardiovascular disorders.

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