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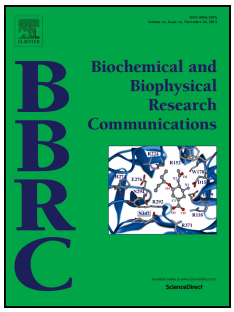

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The role of Wnt regulation in heart development, cardiac repair and disease: a tissue engineering perspective

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KEYWORDS

Pluripotent Stem Cells; Stem Cell Differentiation; Wnt Signaling; Cardiac Tissue Engineering; Engineered Cardiac Tissue; Cardiovascular Disease

ABSTRACT

Wingless-related integration site (Wnt) signaling has proven to be a fundamental mechanism in cardiovascular development as well as disease. Understanding its particular role in heart formation has helped to develop pluripotent stem cell differentiation protocols that produce relatively pure cardiomyocyte populations. The resultant cardiomyocytes have been used to generate heart tissue for pharmaceutical testing, and to study physiological and disease states. Such protocols in combination with induced pluripotent stem cell technology have yielded patient-derived cardiomyocytes that exhibit some of the hallmarks of cardiovascular disease and are therefore being used to model disease states. While FDA approval of new treatments typically requires animal experiments, the burgeoning field of tissue engineering could act as a replacement. This would necessitate the generation of reproducible three-dimensional cardiac tissues in a well-controlled environment, which exhibit native heart properties, such as cellular density, composition, extracellular matrix composition, and structure-function. Such tissues could also enable the further study of Wnt signaling. Furthermore, as Wnt signaling has been found to have a mechanistic role in cardiac pathophysiology, e.g. heart attack, hypertrophy, atherosclerosis, and aortic stenosis, its strategic manipulation could provide a means of generating reproducible and specific, physiological and pathological cardiac models.