

# Chapter 11

## Evolving Concepts for Use of Stem Cells and Tissue Engineering for Cardiac Regeneration

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### **ABSTRACT**

*The incidence of cardiovascular disease (CVD) in adults are increasing worldwide with impaired repair mechanisms, leading to tissue and organ failure. With the current advancements, life expectancy has improved and has led to search for new treatment strategies that improves tissue regeneration. Recently, stem cell therapy and tissue engineering has captured the attention of clinicians, scientists, and patients as alternative treatment options. The overall clinical experience of these suggests that they can be safely used in the right clinical setting. Ultimately, large outcome trials will have to be conducted to assess their efficacy. Clinical trials have to be carefully designed and patient safety must remain the key concern. At the same time, continued basic research is required to understand the underlying mechanism of cell-based therapies and cell tissue interactions. This chapter reviews the evolving paradigm of stem cell therapy and tissue engineering approaches for clinical application and explores its implications.*

### **INTRODUCTION**

Cardiovascular diseases (CVDs) are prevalent worldwide among all age groups (Mann, Zipes, Libby, & Bonow, 2014). In adults, with increasing age repair mechanisms get impaired, leading to tissue and organ failure, which is a significant risk factor for progression of CVD (Kalyani, Corriere,

DOI: 10.4018/978-1-4666-9530-6.ch011

& Ferrucci, 2014; Zethelius et al., 2014). With the advancements in the cardiovascular medicine and surgery, life expectancy of the elderly population with CVD has improved and this has led to the search for new treatment strategies that reduces the surgical risk and improves tissue repair and regeneration. Despite the advancements, mortality rates have nevertheless remained virtually unchanged in the last twenty years among patients with rheumatic and degenerative heart diseases (Ray et al., 2014). In recent years, stem cell therapy and tissue engineering has captured the attention of clinicians, scientists, and patients as alternative treatment options (Fuh & Yeghiazarians, 2014). When the heart is injured, stem cells in the adult body gradually migrate to the site of injury and aid in repair. In aged population, the majority of these cells becomes dormant with a rise in levels of age related cellular damage and signaling mechanisms. Hence, cell-based therapies have raised the possibility that may regenerate the heart, which provides an alternative to conventional treatments (Van Den Berg et al., 2014). Cells that have the potential to generate cardiomyocytes and vascular cells have been identified in both the adult heart and peripheral tissues, and in vivo experiments suggest that these cardiovascular stem cells and cardiovascular progenitor cells, including endothelial progenitor cells, are capable of replacing damaged myocardium and vascular tissues with improved tissue perfusion and contractile performance (Fox et al., 2014; Tung et al., 2014). But, these cell-based therapies appear to be insufficient to protect against CVD in older individuals due to age associated changes that impair their function. These changes may contribute to the dysregulation of endogenous cardiovascular repair mechanisms in the aging heart and vasculature (McCance & Huether, 2014). Tissue engineering is another approach that is used to generate cardiac patches that can replace damaged tissue or organ along with different types of cells. Scaffolds made of polymeric and natural decellularized tissues along with the stem cells have been used so far to provide a natural environment for cellular growth, differentiation, and angiogenesis of tissue-engineered grafts (Ghasemi-Mobarakeh et al., 2014). They aid in the restoration of the structure and function (Georgiadis et al., 2014). The overall clinical experience of cell based therapies and use of tissue-engineered grafts suggests that they can be safely used, if the right type is used in the right clinical setting ([www.clinicaltrials.gov](http://www.clinicaltrials.gov); Doppler et al., 2013). Ultimately, large outcome trials will have to be conducted to assess their efficacy. We need to proceed cautiously with carefully designed clinical trials and keep in mind that patient safety must remain the key concern. At the same time, continued basic research is required to understand the underlying mechanism of cell-based therapies and cell tissue interactions. Preliminary efficacy data indicates that stem cells have the potential to enhance myocardial perfusion and/or contractile performance in patients with acute myocardial infarction, advanced coronary artery disease, and chronic heart failure. This chapter reviews the evolving paradigm of stem cell therapy and tissue engineering approaches for clinical application and explores its implications. Specifically, we discuss various types of stem cells used for repair and regeneration of adult cardiac tissue; mechanisms of stem cell and diseased tissue interactions; potential of various tissue engineering approaches for the development of cardiac patches to either replace/repair the damaged cardiac tissue and clinical outcome of so far used stem cell based therapies and tissue engineered materials to repair damaged tissue in aging population. The need for research and clinical translation are highlighted.

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