Chapter 11
Cell Transplantation Therapy for Myocardial Repair: Current Status and Future Challenges

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Abstract  Recent experimental studies and clinical trials have demonstrated that cell transplantation therapy has the potential to improve cardiac function after myocardial infarction. However, the mechanisms responsible for the observed therapeutic effects remain unknown. Different mechanisms have been proposed to explain the beneficial effects, including regeneration of contractile myocardial tissue, therapeutic neovascularization, prevention of left ventricular remodeling, release of paracrine growth factors, induction of nerve fiber regeneration, and potential influences on the cardiac stem cell niche. Furthermore, the clinical application of stem cell transplantation therapy still faces many challenges, such as tumor formation and unexpected differentiation, immunogenicity, arrhythmogenesis of engrafted stem cells, as well as how to prevent cell loss after transplantation. In this chapter, we review the current status of cell transplantation therapy, and discuss future challenges for its application in treating ischemic heart disease.

Keywords  Cell transplantation therapy, myocardial infarction, stem cell

Abbreviations  ESC Embryonic stem cell; MSC Mesenchymal stem cell; SCID Severe combined immunodeficient; MMP Matrix metalloproteinase; TIMP Tissue inhibitor of matrix metalloproteinase; TK Herpes Simplex Virus; GCV Ganciclovir; FGF Fibroblast growth factor; TGF Transforming growth factor; IGF Insulin-like growth factor; G-CSF Granulocyte-colony-stimulating factor

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Y. Shi, D.O. Clegg (eds.) Stem Cell Research and Therapeutics, 193
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11.1 Introduction

Myocardial infarction results in the irreversible loss of cardiac muscle, thinning and stretching of the necrotic area referred to as infarct expansion, eccentric hypertrophy of the nonischemic myocardium with global dilation of the left ventricle – phenomena which in toto make up the concept of ventricular remodeling. The progressive cardiac remodeling ultimately leads to heart failure, and left ventricular dilation correlates with death. Currently, pharmacological and interventional procedures are not able to regenerate functional cardiomyocytes. Therefore, there is a need to seek new approaches to address this pathophysiological condition resulting from the loss of cardiomyocytes and viable blood vessels caused by the ischemic insult.

Over the past 15 years, cell transplantation therapy for cardiac regeneration has been extensively investigated in both experimental studies and clinical trials. In this chapter, we focus on the underlying mechanism of benefits of cell transplantation, and related side effects and problems.

11.2 Underlying Mechanism and Potential Strategies of Cell Transplantation Therapy in Heart Disease

A wide range of cells, including immature cardiomyocytes (such as fetal or neonatal cardiomyocytes), stem cells from various sources (embryonic or adult somatic tissue) and other non-myogenic cell types, have been transplanted into infarcted myocardium in animal laboratory studies and early clinical trials. Experimental and clinical data have demonstrated that cell transplantation therapy results in an improvement in ventricular function. However, the underlying mechanism remains unclear. The major controversy in interpretation is whether cell transplantation therapy truly replaces the damaged myocardium with newly formed cardiac cells.

11.2.1 Regeneration of Contractile Myocardial Tissue

The aim of cell transplantation is to restore the cardiac function after myocardial infarction by regeneration of healthy myocardial tissue. Transplanted fetal [1] and neonatal rat cardiomyocytes [2] exhibited long-term survival in a rat myocardial infarct model, developed sarcomeric structures and other morphological features of mature cardiomyocytes, thickened the infarcted left ventricular wall, and enhanced left ventricular ejection fraction. Engrafted rat neonatal cardiomyocytes formed cell junctions with the host cardiomyocytes at the border zone of rat myocardial infarction demonstrated by immunohistochemistry and confocal micros-