2015 年度
日本再生医療学会

学会賞

（臨床）

自己筋芽細胞シートを用いた重症心不全に対する心筋再生治療

Development of Myoblast Cell-Sheet Transplantation Therapy for Advanced Cardiovascular Disease

澤　芳樹

Sawa, Yoshiki

大阪大学大学院医学系研究科 心臓血管外科
Department of Cardiovascular Surgery, Osaka University Graduate School of Medicine
E-mail : sawa-p@surg1.med.osaka-u.ac.jp

KEY WORDS
重症心不全　筋芽細胞シート　サイトカイン　多施設治験　トランスレーショナルリサーチ

Abstract

Heart failure is a life-threatening disorder worldwide, and the current end-stage therapies for severe heart failure are replacement therapies such as ventricular-assist devices and heart transplantation. Although these therapies have been reported to be useful, there are many issues in terms of the durability, complications, limited donors, adverse effect of continuous administration of immunosuppressive agents, and high costs involved. Recently, regenerative therapy based on genetic, cellular, or tissue engineering techniques has gained attention as a new therapy to overcome the challenges encountered in transplantation medicine. We focused on skeletal myoblasts as the source of progenitor cells for autologous cell transplantation and the cell-sheet technique for site-specific implantation. *In vitro* studies have reported that myoblast sheets secrete cytoprotective and angiogenic cytokines such as hepatocyte growth factor (HGF). Additionally, *in vivo* studies using large and small animal models of heart failure, we have shown that myoblast sheets could improve diastolic and systolic performance and enhance angiogenesis and antifibrosis as well as the expression of several cytokines including HGF and vascular endothelial growth factor (VEGF) in the tissues at the transplanted site. Based on the results of these studies, we performed clinical trials using autologous myoblast sheets in ischemic cardiomyopathy (ICM) and dilated cardiomyopathy patients. Some patients showed left ventricular reverse remodeling and improved symptoms and exercise tolerance. Recently, multiple medical institutions including our institution successfully conducted an exploratory, uncontrolled, open-label phase II study in subjects with ICM to validate the efficacy and safety of autologous myoblast sheets. Moreover, as a novel cell source for regenerative medicine, our recent studies demonstrated that induced pluripotent stem cell-derived cardiomyocyte sheets showed electrical and microstructural homogeneity with heart tissue *in vitro* and *in vivo*, thus establishing proof of concept in small and large animal models of heart failure.