Introduction: Skeletal myoblast (SMB) transplantation is a promising strategy for treating end-stage heart failure. Formation of electrical and mechanical coupling with and transdifferentiation into cardiomyocyte (CMC) are essential for synchronized contraction and coordinated work between transplanted SMBs and host myocardium. We evaluated methods to utilize myocardial proteins and oscillating pressure in vitro and in vivo.

Subject and Methods: SMBs were obtained from Fisher 344 rats. Myocardial proteins were prepared from normal myocardium of rats. Applications of oscillating pressure and myocardial proteins were introduced to induce transdifferentiation of SMBs into CMC-like cells. Differentiated status of SMBs in vitro were evaluated with cardiac specific proteins such as troponin-I/T, connexin43, and N-cadherin by RT-PCR, immunocytochemistry, and western blot analysis. Additionally, normal SMBs or SMBs committed with oscillating pressure and myocardial proteins were transplanted into infarct myocardium to detect effects of individual therapeutic group on infarct myocardium. Cell transplantation was performed after one week of infarct formation in a rat heart. After eight weeks of cell transplantation, animals were sacrificed and the hearts transplanted with SMBs were harvested for further analysis. Echocardiography was performed at three stages: pre-infarction, after one week of post-infarction, and after eight weeks of cell transplantation.

Results: In simple culture condition of SMBs, cardiac specific proteins troponin-I/T were not expressed. In addition, N-cadherin and connexin43 expressions were decreased in accordance with differentiation into skeletal myobute. Myocardial proteins induced expressions of cardiac specific troponin-I/T, and increased expression of connexin43 in SMBs. However expression of N-cadherin was not changed in SMBs by myocardial proteins. Further augmentations in the expressions of connexin43 and N-cadherin were induced by the application of oscillating pressure in SMBs. The expression of troponin-I, however, was not induced in the same condition. Thus, synergistic effect of oscillating pressure and myocardial proteins was required for commitment of SMBs into CMC-like cells. In SMBs transplantation experiment, echocardiography indicated that SMBs committed with myocardial proteins and oscillating pressure had more potency to improve infarct myocardium than uncommitted SMBs. Furthermore, incorporated cell number and gap junction between transplanted cells and host myocardium were more abundant in infarct myocardium that received the committed SMBs than uncommitted SMBs. All of the incorporated cells expressed cardiac specific protein troponin-I and the difference in expression of troponin-I between committed SMB group and uncommitted SMB group was not shown.

Conclusion: Application of myocardial proteins and oscillating pressure on SMBs had a beneficial effect on SMBs transplantation for myocardial repair. These data show that the treatment of oscillating pressure and myocardial proteins helps SMBs to integrate with host myocardium in more rapid and efficient manner.

* Note: The text above is the abstract of the thesis.
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