Cell Research (2008) 18:s62.

www.nature.com/cr

Co-culture with cardiomyocytes induces mesenchymal stem cells to differentiate into cardiomyocyte-like cells and express heart development-associated genes

Junyi Zeng[1], Yang Wang[2], Yunfeng Wei[1], An Xie[2], Yuanlei Lou[2], Mei Zhang[1]

[1]Department of Cardiology, [2]Institute of Urological Surgery, the First Affiliated Hospital of Nanchang University, NanChang 330006,China

Recent studies have demonstrated that bone marrow mesenchymal stem cells (MSCs) have the potential to transdifferentiate into cardiomyocytes(CMs) under an appropriate condition either *in vivo* or *in vitro*, and our previous studies also confirmed it. However, there exists a controversy among a variety of studies about whether MSCs can differentiate into CMs without physical contacts with CMs, and the molecular signals that underlie this process are not fully understood. In the present study, MSCs isolated from adult rats were cocultured with CMs obtained from neonatal rat ventricles at 1:5 ratio in a dual chamber dish separated by a semipermeable membrane for 2 weeks. During this non-direct contact coculture procedure, cardiomyogenic differentiation and relative genes expression in MSCs were evaluated. After having been cocultured with CMs, MSCs showed a stick-like or elliptical morphology, connected with adjoining cells and aligned in a striated pattern. Immunofluorescent stain results revealed that α-actin and cardiac troponin T(cTnT) positive cells were found in MSCs at 5 days after coculture with CMs, and these positive cells reached the peak (29.63% for α-actin, 27.38% for cTnT) at 14 days. Results from RT-PCR demonstrated the expression level of TGF-β, Nkx-2.5, GATA-4 and MEF-2C genes, which are known to play a crucial role during heart development, began to increase at 1 day and reached the peak at 7 days after coculture. In conclusion, non-direct contact with CMs (1:5) is conducive for MSCs to differentiate into CMs *in vitro*, and TGF-β, Nkx-2.5, GATA-4 and MEF-2C genes may play a critical role during the transdifferentiation. Therefore, our findings may help to understand the mechanisms that induce MSCs to undergo cardiomyogenic differentiation within the myocardial environment.

***Keywords*:** bone marrow mesenchymal stem cells, non-direct contact, coculture, differentiation, genes, cardiomyocytes
Cell Research (2008) **18**:s62. doi: 10.1038/cr.2008.152; published online 4 August 2008

Correspondence: Yunfeng Wei
E-mail: weiyunfeng2007@126.com
Supported byNatural Science Foundation of Jiangxi province (No. 0640189)