

Background Cardiotrophin-1 (CT-1) is a cytokine involved in the growth and survival of cardiac cells that stimulates cardiomyogenesis in pluripotent murine embryonic stem (ES) cells. But it is not known whether CT-1 is responsible for the fate of differentiated bone marrow mesenchymal stem cells (BMMSCs).

Methods We investigated the effects of CT-1 on differentiation and maturation of BMMSCs in vitro induced with 5-azacytidine. After 4 weeks of induced culturing, we observed the levels of α -cardiac actin and troponin-I by immunohistochemical staining, the ultrastructure of induce-cultured BMMSCs, and the expression of GATA-4, NKx2.5, beta-myosin heavy chain (beta-MHC) and α -cardiac actin mRNA by real time RT-PCR analysis.

Results Differentiated BMMSCs cultured with CT-1 distinctly showed formations of myofilaments-morphological characteristics of myocyte like cells. The protein levels of α -cardiac actin and troponin-T were significantly higher than control. Furthermore, mRNA expression of GATA-4, NKx2.5, α -cardiac actin and beta-MHC was increased remarkably.

Conclusions This study suggests that induced culturing of BMMSCs in the presence of 5-azacytidine combined with CT-1 can enhance cardiomyocytic characteristics. CT-1 upregulates the expression of GATA-4, NKx2-5, α -cardiac actin and beta-MHC mRNA, and rapidly promotes the differentiation and maturation of cardiomyocyte-like cells differentiated from BMMSCs induced with 5-azacytidine.

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**EFFECTS OF CARDIOTROPHIN-1 ON
DIFFERENTIATION AND MATURATION OF RAT
BONE MARROW MESENCHYMAL STEM CELLS
INDUCED WITH 5-AZACYTIDINE IN VITRO**

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