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Mesenchymal stromal cells stimulate C2C12 myoblast cell proliferation: potential relevance in skeletal muscle regeneration

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Skeletal muscle tissue harbors of a population of resident myoblastic stem cells which are capable of regenerating the damaged tissue. However, in case of extended injury, their myogenic potential is compromised by excessive inflammatory response and collagen deposition which hamper the environmental conducivity to muscle regeneration. Therefore, the identification of new strategies aimed at potentiating the proliferative attitude of myoblasts may have potential therapeutic application for muscle repair. In this line, we have previously demonstrated in a co-culture system, that adult mouse bone marrow-derived mesenchymal stromal/stem cells (MSCs) stimulate mouse neonatal cardiomyocyte proliferation. On these premises, in the present study, we searched whether MSCs were also able to influence C2C12 myoblast cells proliferation. We found that myoblast proliferation was significantly enhanced in co-culture as compared with the single culture, and that this response involved the activation of Notch-1 signalling in the myoblastic cells. These data were confirmed by the finding that Hes1 transcriptional regulator, the major downstream effector of Notch-1, was also upregulated in C2C12 cells cultured in the presence of MSCs or their derived conditioned medium. In particular, MSCs were able to release growth factors, including FGF and VEGF, thus underscoring potential paracrine mechanisms involved in the regulation of myoblast proliferation and Notch-1 expression by MSCs. In conclusion, the results of the present study provide strong evidence for a role of MSCs in stimulating myoblast cell proliferation and suggest that the functional interaction betweeen the two cell types may be exploited to the development of new and more efficient cell-based skeletal muscle repair strategies.

Keywords: mesenchymal cells, myoblasts, cell proliferation, Notch-1 signalling