

Mesenchymal stromal cells exert a stimulatory effect on skeletal myoblast proliferation through the release of Sphingosine 1-phosphate (S1P)

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Bone-marrow-derived mesenchymal stromal cells (MSCs) have the potential to significantly contribute to skeletal muscle healing through the secretion of paracrine factors that support proliferation and enhance participation of the endogenous muscle stem cells in the process of repair/regeneration [1]. However, MSC-derived trophic molecules have been poorly characterized. The aim of this study was to investigate paracrine signaling effects of MSCs on skeletal myoblasts. It was found, using a biochemical and morphological approach that sphingosine 1-phosphate (S1P), a natural bioactive lipid exerting a broad range of muscle cell responses [2], is secreted by MSCs and represents an important factor by which these cells exert their stimulatory effects on C2C12 myoblast and satellite cell proliferation. Indeed, exposure to conditioned medium obtained from MSCs cultured in the presence of the selective sphingosine kinase inhibitor (iSK), blocked increased cell proliferation caused by MSC-conditioned medium, and the addition of exogenous S1P in the conditioned medium from MSCs pre-treated with iSK further increased myoblast proliferation. Finally, we also demonstrated that the myoblast response to MSC-secreted vascular endothelial growth factor (VEGF) involves the release of S1P from C2C12 cells. Our data may have important implications in the optimization of cell-based strategies to promote skeletal muscle regeneration.

References

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- [2] Meacci et al. (2012) Sphingosine-1-phosphate signaling in skeletal muscle cells. *Methods Mol Biol* 874: 155-165.

Keywords

Mesenchymal stromal cells (MSCs), sphingosine 1-phosphate (S1P), skeletal muscle cell, cell proliferation, paracrine factors, VEGF signaling.