growth factor-beta-mediated chondrogenesis of human mesenchymal progenitor cells involves N-cadherin and mitogen-activated protein kinase and Wnt signaling cross-talk. J. Biol. Chem. V. 278. P. 41227. https://doi.org/10.1074/jbc.M305312200

- Ushakov R.E., Skvortsova E.V., Vitte M.A., Vassilieva I.O., Shatrova A.N., Kotova A.V., Kenis V.M., Burova E.B. 2020. Chondrogenic differentiation followed IGFBP3 loss in human endometrial mesenchymal stem cells. Biochem. Biophys. Res. Commun. V. 531. P. 133. https://doi.org/10.1016/j.bbrc.2020.07.064
- Yin W., Park J.I., Loeser R.F. 2009. Oxidative stress inhibits insulin-like growth factor-I induction of chondrocyte proteoglycan synthesis through differential regulation of phosphatidylinositol 3-Kinase-Akt and MEK-ERK MAPK signaling pathways. J. Biol. Chem. V. 284. P. 31972. https://doi.org/10.1074/jbc.M109.056838
- Zemelko V.I., Grinchuk T.M., Domnina A.P., Artzibasheva I.V., Zenin V.V., Kirsanov A.A., Bichevaia N.K., Korsak V.S., Nikolsky N.N. 2012. Multipotent mesenchymal stem cells of desquamated endometrium: Isolation, characterization, and application as a feeder layer for maintenance of human embryonic stem cells. Cell Tiss. Biol. V. 6. P. 1. https://doi.org/10.1134/S1990519X12010129
- Zha K., Sun Z., Yang Y., Chen M., Gao C., Fu L., Li H., Sui X., Guo Q., Liu S. 2021. Recent developed strategies for enhancing chondrogenic differentiation of MSC: Impact on MSC-based therapy for cartilage regeneration. Stem Cells Int. V. 2021. P. 8830834. https://doi.org/10.1155/2021/8830834
- Zhang Y., Pizzute T., Pei M. 2014. A review of crosstalk between MAPK and Wnt signals and its impact on cartilage regeneration. Cell Tissue Res. V. 358. P. 633. https://doi.org/10.1007/s00441-014-2010-x

Involvement of the PI3K/Akt/mTOR Pathway in Controlling Chondrogenic Differentiation of Endometrial Mesenchymal Stromal Cells

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The present work describes ability to chondrogenic differentiation of human mesenchymal stromal cells (MESCs) derived from desquamated endometrium in menstrual blood. Neither MESCs chondrogenic capacity nor related signaling pathways have been studied yet. MESCs monolayer culture cultivated in chondrogenic medium within 11–14 days demonstrates chondrogenesis markers such as positive staining with Safranin O and with Alcian blue as well as the increased *COL2A1* expression level. We studied linkage between expression of chondrogenic markers and activation status of PI3K and MAPK pathways by cultivating MESCs in chondrogenic medium in the presence of PI3K inhibitor LY294002; we found that PI3K/Akt/mTOR signaling negatively regulates *COL1A1* expression and positively regulates *COL2A1* during differentiation and that it is also involved in regulation of Raf/MEK/ERK kinase activity. These results suggest that PI3K/Akt/mTOR pathway plays significant role in regulation of MESCs chondrogenesis.

Keywords: chondrogenic differentiation, endometrial mesenchymal stromal cells, PI3K/Akt/mTOR pathway, qRT-PCR

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