conjugates after binding to the surface of tumor cells. Cancer. V. 73. P. 787.

Mitchell J.B., McIntosh K., Zvonic S., Garrett S., Floyd Z.E., Kloster A., Di Halvorsen Y., Storms R.W., Goh B., Kilroy G., Wu X., Gimble J.M. 2006. Immunophenotype of human adipose-derived cells: temporal changes in stromal-associated and stem cell-associated markers. Stem Cells. V. 24. P. 376.

Nassiri S.M., Rahbarghazi R. 2014. Interactions of mesenchymal stem cells with endothelial cells. Stem Cells Dev. V. 23. P. 319.

Planat-Benard V., Silvestre J.-S., Cousin B., André M., Nibbelink M., Tamarat R., Clergue M., Manneville C., Saillan-Barreau C., Duriez M., Tedgui A., Levy B., Pénicaud L., Casteilla L. 2004. Plasticity of human adipose lineage cells toward endothelial cells: physiological and therapeutic perspectives. Circulation. V. 109. P. 656.

Rüster B., Göttig S., Ludwig R.J., Bistrian R., Müller S., Seifried E., Gille J., Henschler R. 2006. Mesenchymal stem cells display coordinated rolling and adhesion behavior on endothelial cells. Blood. V. 108. P. 3938.

Saleh F.A., Whyte M., Genever P.G. 2011. Effects of endothelial cells on human mesenchymal stem cell activity in a three-dimensional *in vitro* model. Eur. Cell. Mater. V. 22. P. 242.

Sanz-Rodriguez F., Guerrero-Esteo M., Botella L.M., Banville D., Vary C.P.H., Bernabéu C. 2004. Endoglin regulates cytoskeletal organization through binding to ZRP-1, a member of the Lim family of proteins. J. Biol. Chem. V. 279. P. 32858.

Seon B.K., Matsuno F., Haruta Y., Kondo M., Barcos M. 1997. Long-lasting complete inhibition of human solid tumors in SCID mice by targeting endothelial cells of tumor vasculature with antihuman endoglin immunotoxin. Clin. Canc. Res. V. 3. P. 1031.

Smirnov I.V., Gryazeva I.V., Samoylovich M.P., Terekhina L.A., Pinevich A.A., Shashkova O.A., Krutetskaia I.Y., Sokolov D.I., Selkov S.A., Nikolskiy N.N., Klimovich V.B. 2016. Different pairs of monoclonal antibodies detect variable amounts of soluble endoglin in human blood plasma. Immunochem. Immunopathol. V. 2. P. 1–5.

Takahashi N., Haba A., Matsuno F., Seon B.K. 2001. Antiangiogenic therapy of established tumors in human skin/severe combined immunodeficiency mouse chimeras by anti-endoglin (CD105) monoclonal antibodies, and synergy between anti-endoglin antibody and cyclophosphamide. Canc. Res. V. 61. P. 7846.

Zuk P.A., Zhu M., Ashjian P., De Ugarte D.A., Huang J.I., Mizuno H., Alfonso Z.C., Fraser J.K., Benhaim P., Hedrick M.H. 2002. Human adipose tissue is a source of multipotent stem cells. Mol. Biol. Cell. V. 13. P. 4279.

Zuk P.A., Zhu M., Mizuno H., Huang J., Futrell J.W., Katz A.J., Benhaim P., Lorenz H.P., Hedrick M.H. 2001. Multilineage cells from human adipose tissue: implications for cell-based therapies. Tissue Engin. V. 7. P. 211.

Endoglin Expression and Surface Renewal in Mesenchymal Stem Cells and Endothelial Cells

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Endoglin (CD105) is one of the main positive markers expressed on the surface of both mesenchymal stem cells (MSC) and endothelial cells. While the functions of CD105 in endothelium have been widely declared, little is known about its role in stem cell biology. The current work is a comparative study of CD105 expression, internalization, and shedding by human EA.hy926 endothelial cells and adipose-derived human MSC from various sources. More than 97% of cells in EA.hy926 and all MSC cultures were CD105-positive, though MSC from visceral and subcutaneous adipose tissue differed in CD105 density on the cell surface. The total level of endoglin mRNA expression in MSC and endothelial cells was similar, while the contribution of mRNA that determines synthesis of the short CD105 isoform was higher in endothelial cells. With the help of monoclonal antibodies (mAbs) against various endoglin epitopes, significant differences in the dynamics of CD105 exchange on the membrane of endothelial cells and MSC were revealed. On EA.hy926 endothelial cells, CD105 bound with antibodies was internalized and remained in the perinuclear space. In MSC cultures, CD105-mAbs complexes were not subjected to endocytosis and remained on the cell membrane for a long time. It was shown that MSC similar to endothelial cells performed shedding of an extracellular fragment of endoglin into the environment to form a soluble CD105 molecules. Shedding in MSC was significantly less compared with endothelial cells. Taken together, it was shown for the first time that in contrast to endothelium endoglin persists on MSC cell surface for a long time and does not undergo internalization after binding with antibodies. For the first time it was found that MSC perform endoglin shedding to generate its soluble form.

Keywords: endoglin, CD105, mesenchymal stem cells, EA.hy926 endothelial cells, internalization, shedding, monoclonal antibodies