

- Vicente López Á., Vázquez García M.N., Melen G.J., Entrena Martínez A., Cubillo Moreno I., García-Castro J., Ramírez Orellana M., Zapata González A.G. 2014. Mesenchymal stromal cells derived from the bone marrow of acute lymphoblastic leukemia patients show altered BMP4 production: Correlations with the course of disease. *PLoS One*. V. 9. ID e84496.  
<https://doi.org/10.1371/journal.pone.0084496>
- Visnjic D., Kalajzic Z., Rowe D.W., Katavic V., Lorenzo J., Aguilera H.L. 2004. Hematopoiesis is severely altered in mice with an induced osteoblast deficiency. *Blood*. V. 103. P. 3258.
- Voorhees P.M., Chen Q., Kuhn D.J., Small G.W., Hunsucker S.A., Strader J.S., Corringham R.E., Zaki M.H., Nemeth J.A., Orłowski R.Z. 2007. Inhibition of interleukin-6 signaling with CNTO 328 enhances the activity of bortezomib in preclinical models of multiple myeloma. *Clin. Cancer Res*. V. 13. P. 6469.
- Wang J., Hendrix A., Hernot S., Lemaire M., De Bruyne E., Van Valckenborgh E., Lahoutte T., De Wever O., Vanderkerken K., Menu E. 2014. Bone marrow stromal cell-derived exosomes as communicators in drug resistance in multiple myeloma cells. *Blood*. V. 124. P. 555.
- Xu C., Gao X., Wei Q., Nakahara F., Zimmerman S.E., Mar J., Frenette P.S. 2018. Stem cell factor is selectively secreted by arterial endothelial cells in bone marrow. *Nat. Commun*. V. 9. ID 2449.  
<https://doi.org/10.1038/s41467-018-04726-3>
- Yang Y., Mallampati S., Sun B., Zhang J., Kim S.B., Lee J.S., Gong Y., Cai Z., Sun X. 2013. Wnt pathway contributes to the protection by bone marrow stromal cells of acute lymphoblastic leukemia cells and is a potential therapeutic target. *Cancer Lett*. V. 333. P. 9.
- Zhang G., Miao F., Xu J., Wang R. 2020. Mesenchymal stem cells from bone marrow regulate invasion and drug resistance of multiple myeloma cells by secreting chemokine CXCL13. *Bosnian J. Basic Medical Sci*. V. 20. P. 209.
- Zhang Q.Z., Su W.R., Shi S.H., Wilder-Smith P., Xiang A.P., Wong A., Nguyen A.L., Kwon C.W., Le A.D. 2010. Human gingiva-derived mesenchymal stem cells elicit polarization of M2 macrophages and enhance cutaneous wound healing. *Stem Cells*. V. 28. P. 1856.

## MESENCHYMAL STROMAL CELLS: ROLE IN THE FORMATION OF HEMATOONCOLOGICAL NICHE

A. V. Chubar<sup>a,\*</sup> and N. I. Enuakashvily<sup>a</sup>

<sup>a</sup>*Institute of Cytology, Russian Academy of Sciences, St. Petersburg, 194064 Russia*

<sup>\*</sup>*e-mail: annachubar95@incras.ru*

The bone marrow (BM) microenvironment is an important component of normal hematopoiesis support. Such components of the microenvironment as endothelial cells, osteoblasts, adipocytes, bone marrow mesenchymal stromal cells (BM-MSCs), and immune cells regulate the proliferation and differentiation of hematopoietic stem cells (HSCs) in the BM. However, in hematological diseases the BM microenvironment changes under the influence of tumor cells. Currently, the successful treatment of such diseases is complicated by the development of drug resistance that is associated with various mechanisms that reduce the effect of chemotherapeutic agents on the tumor. The altered microenvironment contributes to the development of drug resistance in tumor cells through cell contacts and produced cytokines. BM-MSCs are one of the main types of BM stromal cells capable of differentiating into various mesenchymal cells. In recent years, it has been shown that MSCs of the niche play a significant role in the formation, progression, and development of hematological tumors. The purpose of the review is to analyze data on the role of MSCs in the formation of the hematological niche and their contribution to the formation of drug resistance. The article defines the prerequisites for the effect of BM-MSCs (phenotype change, resistance to cytostatics) on tumor survival. Changes in the components of the hematopoietic niche in the development of leucosis and multiple myeloma and the key role of the altered BM-MSCs in the induction of the antiapoptotic factors synthesis in tumor cells are shown. Thus, for the successful treatment of hematological diseases, it is necessary to select the methods of treatment that affect not only the tumor cells themselves, but also the components of the niche, in particular, MSCs. It is especially necessary, among others, to develop approaches aimed at normalizing the hematopoietic niche, which will help prevent the development of relapses.

**Keywords:** hematological diseases, bone marrow, mesenchymal stromal cells, tumor microenvironment