

- the IKCa1 potassium channel during T-cell activation. Molecular mechanism and functional consequences. *J. Biol. Chem.* 275 : 37 137—37 149.
- Dornand J., Favero J., Bonnafous J. C., Mani J. 1986. Mechanism whereby ouabain inhibits human T lymphocyte activation: effect on the interleukin-2 pathway. *Immunobiology.* 171 : 436—450.
- Duran C., Thompson C. H., Xiao Q., Hartzell H. C. 2010. Chloride channels: often enigmatic, rarely editable. *Annu. Rev. Physiol.* 72 : 95—121.
- Frantz C. N., Stiles C. D., Pledger W. J., Scher C. D. 1980. Effect of ouabain on growth regulation by serum components in Balb/c-3T3 cells: inhibition of entry into S phase by decreased protein synthesis. *J. Cell. Physiol.* 105 : 439—448.
- Fridlyanskaya I. I., Alekseenko L. L., Nikolsky N. N. 2015. Senescence as a general cellular response to stress: a mini-review. *Exp. Gerontol.* 72 : 124—128.
- Grinstein S., Dixon S. J. 1989. Ion transport, membrane potential and cytoplasmic pH in lymphocytes: changes during activation. *Physiol. Rev.* 69 : 417—481.
- Hoffmann E. K., Lambe I. H., Pedersen S. F. 2009. Physiology of cell volume regulation in vertebrates. *Physiol. Rev.* 89 : 193—277.
- Hoffmann E. K., Pedersen S. F. 2011. Cell volume homeostatic mechanisms: effectors and signalling pathways. *Acta Physiol.* 202 : 465—485.
- Karitskaya I., Aksenov N., Vassilieva I., Zenin V., Marakhova I. 2010. Long-term regulation of Na,K-ATPase pump during T-cell proliferation. *Pflügers Arch.* 460 : 777—789.
- Klausen T. K., Preisler S., Pederse, S. F., Hoffmann E. K. 2010. Monovalent ions control proliferation of Ehrlich Lettre ascites cells. *Amer. J. Physiol. Cell. Physiol.* 299 : C714—C725.
- Lang F., Föller M., Lang K. 2005. Ion channels in cell proliferation and apoptotic cell death. *J. Membr. Biol.* 205 : 147—157.
- Lang F., Föller M., Lang K., Lang P., Ritter M., Vereninov A., Szabo I., Hube S. M., Gulbins E. 2007. Cell volume regulatory ion channels in cell proliferation and cell death. *Meth. Enzymol.* 428 : 209—225.
- Lang F., Ritter M., Gamper N., Huber S., Fillon S., Tanneur V., Lepple-Wienhues A., Szabo I., Gulbins E. 2000. Cell volume in the regulation of cell proliferation and apoptotic cell death. *Cell. Physiol. Biochem.* 10 : 417—428.
- Ledbetter M. L., Lubin M. 1977. Control of protein synthesis in human fibroblasts by intracellular potassium. *Exp. Cell Res.* 105 : 223—236.
- Lin V. J. T., Zolekar A., Shi Y., Koneru B., Dimitrijevich S., Di Pasqua A. J., Wang Y.-C. 2017. Potassium as a pluripotency-associated element identified through organic element profiling in human pluripotent stem cells. *Sci. Rep.* 7 : 5005.
- Lopez-Rivas A., Adelberg E. A., Rozengurt E. 1982. Intracellular K<sup>+</sup> and the mitogenic response of 3T3 cells to peptide factors in serum-free medium. *Proc. Nat. Acad. Sci. USA.* 79 : 6275—6279.
- Marakhova I. I., Ivanova A. E., Toropova F. V., Vereninov A. A., Vinogradova T. A. 1999. Functional expression of the Na/K pump is controlled via a cyclosporin A-sensitive signaling pathway in activated human lymphocytes. *FEBS Lett.* 456 : 285—289.
- Marakhova I. I., Vereninov A. A., Toropova F. V., Vinogradova T. A. 1995. Long-term enhancement of Na,K-ATPase pump during blast transformation of human lymphocytes is controlled first by translational, then by transcriptional mechanisms. *FEBS Lett.* 368 : 110—112.
- Marakhova I. I., Vereninov A. A., Toropova F. V., Vinogradova T. A. 1998. Na,K-ATPase pump in activated human lymphocytes: on the mechanisms of rapid and long-term increase in K influxes during the initiation of phytohemagglutinin-induced proliferation. *Biochim. biophys. acta.* 1368 : 61—72.
- Noh H. V., Ahn Y. J., Lee W. J., Kwack K., Do Kwon Y. 2010. The molecular signature of in vitro senescence in human mesenchymal stem cells. *Genes Genomic.* 32 : 87—93.
- Orlov S. N., Hamet P. 2006. Intracellular monovalent ions as second messengers. *J. Membr. Biol.* 210 : 161—172.
- Pardee A. B., Dubrow R., Hamlin J. L., Kletzien R. F. 1978. Animal cell cycle. *Annu. Rev. Biochem.* 47 : 715—750.
- Pedersen S. F. 2006. The Na/H exchanger NHE1 in stress-induced signal transduction: implications for cell proliferation and cell death. *Pflügers Arch.* 452 : 249—259.
- Stutzin A., Hoffmann E. K. 2006. Swelling-activated ion channels: functional regulation in cell-swelling, proliferation and apoptosis. *Acta Physiol. (Oxford).* 187 : 27—42.
- Tosteson D. C., Hoffman J. F. 1960. Regulation of cell volume by active cation transport in high and low potassium sheep red cells. *J. Gen. Physiol.* 44 : 169—194.
- Tupper J. T., Zorgniotti F., Mills B. 1977. Potassium transport and content during G<sub>1</sub> and S phase following serum stimulation of 3T3 cells. *J. Cell. Physiol.* 91 : 429—440.
- Vereninov A. A., Goryachaya T. S., Moshkov A. V., Vassilieva I. O., Yurinskaya V. E., Lang F., Rubashkin A. A. 2007. Analysis of the monovalent ion fluxes in U937 cells under the balanced ion distribution: recognition of ion transporters responsible for changes in cell ion and water balance during apoptosis. *Cell Biol. Int.* 31 : 382—393.
- Wonderlin W. F., Strobl J. S. 1996. Potassium channels, proliferation and G<sub>1</sub> progression. *J. Membr. Biol.* 154 : 91—107.
- Yurinskaya V. E., Rubashkin A. A., Vereninov A. A. 2011. Balance of unidirectional monovalent ion fluxes in cells undergoing apoptosis: why does Na<sup>+</sup>/K<sup>+</sup> pump suppression not cause cell swelling? *J. Physiol.* 589 : 2197—2211.

Поступила 12 VII 2018

## ION HOMEOSTASIS DURING THE GROWTH OF HUMAN MESENCHYMAL STEM CULTURE. II. AGE-RELATED CHANGES IN CELL K<sup>+</sup> CONTENT

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Ion homeostasis as determined by intracellular K<sup>+</sup> and Na<sup>+</sup> contents has been examined in long-term cultures of human mesenchymal stem cells (MSCs). The intracellular K<sup>+</sup> content was found to be dependent on the age of cultivated MSCs, namely, in the early-passaged MSCs (at 2<sup>nd</sup>—4<sup>th</sup> passages), K<sup>+</sup> content per 1 g cell protein was by almost 40 % higher than in late-passaged (12<sup>th</sup>—15<sup>th</sup> passages) cells. Under the same conditions, cell Na<sup>+</sup> content per 1 g cell protein was unchanged being independent on the MSCs culture age. In late-passaged MSCs cultures the decline in K<sup>+</sup> content per g cell protein was correlated with the accumulation of G<sub>1</sub> cells in the population. Based on the data on monovalent ion transport in permanent cell lines of different origin, hu-

man stem cells as well as in activated human lymphocytes, the mechanism of potassium ions participation in cell proliferation has been discussed. It is assumed that changes in cell K<sup>+</sup> content per 1 g cell protein which accompany the onset or inhibition of cell proliferation are related to the K<sup>+</sup> involvement in cell volume regulation. The high intracellular K<sup>+</sup> content is important for successful hMSCs proliferation and cell K<sup>+</sup> content per cell protein is an informative test for assessing the functional status of stem cells *in vitro*.

**Key words:** cell potassium content, cell sodium content, potassium fluxes, Na<sup>+</sup>,K<sup>+</sup> pump, proliferation, human mesenchymal stem cells