

- Solaini G., Sgarbi G., Baracca A. 2011. Oxidative phosphorylation in cancer cells. *Biochim. Biophys. Acta Bioenerg.* V. 1807. P. 534.
- Son J., Lyssiotis C.A., Ying H., Wang X., Hua S., Ligorio M., Perera R.M., Ferrone C.R., Mullarky E., Shyh-Chang N., Kang Y., Fleming J.B., Bardeesy N., Asara J.M., Haigis M.C. et al. 2013. Glutamine supports pancreatic cancer growth through a KRAS-regulated metabolic pathway. *Nature.* V. 496. P. 101.
- Spitz D., Simons A., Mattson D., Dornfeld K. 2009. Glucose deprivation-induced metabolic oxidative stress and cancer therapy. *J. Cancer Res. Ther.* V. 5. P. 2.
- Tang J.-C., An R., Jiang Y.-Q., Yang J. 2017. Effects and mechanisms of metformin on the proliferation of esophageal cancer cells *in vitro* and *in vivo*. *Cancer Res. Treat. Off. J. Korean Cancer Assoc.* V. 49. P. 778.
- Tran Q., Lee H., Park J., Kim S.H., Park J. 2016. Targeting cancer metabolism – revisiting the Warburg effects. *Toxicol. Res.* V. 32. P. 177.
- Valastyan S., Weinberg R.A. 2011. Tumor metastasis: Molecular insights and evolving paradigms. *Cell.* V. 147. P. 275.
- Varshavi D., Varshavi D., McCarthy N., Veselkov K., Keun H.C., Everett J.R. 2020. Metabolic characterization of colorectal cancer cells harbouring different K-RAS mutations in codon 12, 13, 61 and 146 using human SW48 isogenic cell lines. *Metabolomics Off. J. Metabolomic Soc.* V. 16. P. 51.
- Vaupel P., Multhoff G. 2020. Fatal alliance of hypoxia-/HIF-1 α -driven microenvironmental traits promoting cancer progression. *Adv. Exper. Med. Biol.* (Springer). P. 169.
- Vizan P., Boros L.G., Figueras A., Capella G., Mangués R., Basilian S., Lim S., Lee W.-N.P., Cascante M. 2005. K-ras codon-specific mutations produce distinctive metabolic phenotypes in NIH3T3 mice [corrected] fibroblasts. *Cancer Res.* V. 65. P. 5512.
- Wallace D.C. 2012. Mitochondria and cancer. *Nat. Rev. Cancer.* V. 12. P. 685.
- Warburg O. 1956. On the origin of cancer cells. *Science.* V. 123. P. 309.
- Weinberg F., Hamanaka R., Wheaton W.W., Weinberg S., Joseph J., Lopez M., Kalyanaraman B., Mutlu G.M., Budinger G.R.S., Chandel N.S. 2010. Mitochondrial metabolism and ROS generation are essential for Kras-mediated tumorigenicity. *Proc. Natl. Acad. Sci. USA.* V. 107. P. 8788.
- Wolvetang E.J., Johnson K.L., Krauer K., Ralph S.J., Linnane A.W. 1994. Mitochondrial respiratory chain inhibitors induce apoptosis. *FEBS Lett.* V. 339. P. 40.
- Xiao D., Powolny A.A., Singh S.V. 2008. Benzyl isothiocyanate targets mitochondrial respiratory chain to trigger reactive oxygen species-dependent apoptosis in human breast cancer cells. *J. Biol. Chem.* V. 283. P. 30151.
- Yang W., Lu Z. 2013. Nuclear PKM2 regulates the Warburg effect. *Cell Cycle.* V. 12. P. 3343.
- Yang D., Wang M.T., Tang Y., Chen Y., Jiang H., Jones T., Rao K., Brewer G., Singh K.K., Nie D. 2010. Impairment of mitochondrial respiration in mouse fibroblasts by oncogenic H-RAS (Q61L). *Cancer Biol. Ther.* V. 9. P. 122. <https://doi.org/10.4161/cbt.9.2.10379>
- Yang W., Zheng Y., Xia Y., Ji H., Chen X., Guo F., Lyssiotis C.A., Aldape K., Cantley L.C., Lu Z. 2012. ERK1/2-dependent phosphorylation and nuclear translocation of PKM2 promotes the Warburg effect. *Nat. Cell Biol.* V. 14. P. 1295.
- Ying H., Kimmelman A.C., Lyssiotis C.A., Hua S., Chu G.C., Fletcher-Sananikone E., Locasale J.W., Son J., Zhang H., Coloff J.L., Yan H., Wang W., Chen S., Viale A., Zheng H. et al. 2012. Oncogenic Kras maintains pancreatic tumors through regulation of anabolic glucose metabolism. *Cell.* V. 149. P. 656.
- Yu L., Chen X., Sun X., Wang L., Chen S. 2017. The glycolytic switch in tumors: How many players are involved? *J. Cancer.* V. 8. P. 3430.
- Yun J., Rago C., Cheong I., Pagliarini R., Angenendt P., Rajagopalan H., Schmidt K., Willson J.K.V., Markowitz S., Zhou S., Diaz L.A., Velculescu V.E., Lengauer C., Kinzler K.W., Vogelstein B. et al. 2009. Glucose deprivation contributes to the development of KRAS pathway mutations in tumor cells. *Science.* V. 325. P. 1555.
- Zambrano A., Molt M., Uribe E., Salas M. 2019. Glut 1 in cancer cells and the inhibitory action of resveratrol as a potential therapeutic strategy. *Int. J. Mol. Sci.* V. 20.
- Zhang Y., Yang J.M. 2013. Altered energy metabolism in cancer: A unique opportunity for therapeutic intervention. *Cancer Biol. Ther.* V. 14. P. 81.
- Zheng W., Tayyari F., Gowda G.A.N., Raftery D., McLamore E.S., Porterfield D.M., Donkin S.S., Bequette B., Teegarden D. 2015. Altered glucose metabolism in harvey-ras transformed MCF10A Cells. *Mol. Carcinog.* V. 54. P. 111.
- Zhong H., Chiles K., Feldser D., Laughner E., Hanrahan C., Georgescu M.M., Simons J.W., Semenza G.L. 2000. Modulation of hypoxia-inducible factor 1 α expression by the epidermal growth factor/phosphatidylinositol 3-kinase/PTEN/AKT/FRAP pathway in human prostate cancer cells: implications for tumor angiogenesis and therapeutics. *Cancer Res.* V. 60. P. 1541.
- Zhou H., Huang S. 2011. Role of mTOR signaling in tumor cell motility, invasion and metastasis. *Curr. Protein Pept. Sci.* V. 12. P. 30.

GLUCOSE METABOLISM OF CANCER CELL AS A TARGET IN ANTITUMOR THERAPY

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The alterations of cellular metabolism play a decisive role in malignant cell transformation. The review presents modern data on the mechanisms of development and the role of energetic reprogramming of cells during their malignant transformation. Attention is also focused on the role of Ras-dependent signaling pathways that induce metabolic reprogramming. The features of the energy metabolism of tumor cells expressing mutant Ras are discussed. Different approaches of the cancer therapy aimed at glucose metabolism in cancer cells are considered.

Keywords: glucose metabolism, cancer cells, Warburg effect, *ras*-oncogene, anticancer therapy