

- stem cells causes a myeloproliferative disorder. *J. Exp. Med.* V. 205. P. 585.
- Palma C.A., A Sheikha D., Lim T.K., Bryant A., Vu T.T., Jayaswa V., Ma D.D.* 2014. MicroRNA-155 as an inducer of apoptosis and cell differentiation in acute myeloid leukemia. *Mol. Cancer.* V. 13. P. 79.
- Redner R.L.* 2002. Variations on a theme: The alternate translocations in APL. *Leukemia.* V. 16. P. 1927.
- Salvatori B., Iosue I., Djodji Damas N., Mangiavacchi A., Chiarretti S., Messina M., Padula F., Guarini A., Bozzoni I., Fazi F., Fatica A.* 2011. Critical role of c-Myc in acute myeloid leukemia involving direct regulation of miR-26a and histone methyltransferase EZH2. *Genes Cancer.* V. 2. P. 585.
- Saumet A., Vetter G., Bouttier M., Portales-Casamar E., Wasserman W., Maurin T., Mari B., Barbry P., Valla L., Friederich E., Arar K., Cassinat B., Chomienne C., Leceilier C.H.* 2009. Transcriptional repression of microRNA genes by *PML-RARA* increases expression of key cancer proteins in acute promyelocytic leukemia. *Blood.* V. 113. P. 412.
- Sharifi M., Salehi R., Gheisari Y., Kazemi M.* 2014. Inhibition of microRNA miR-92a induces apoptosis and necrosis in human acute promyelocytic leukemia. *Adv. Biomed. Res.* V. 3. P. 61.
- Titov S.E., Ivanov M.K., Karpinskaya E.V., Tsivlikova E.V., Shevchenko S.P., Veryaskina Y.A., Akhmerova L.G., Poloz T.L., Klimova O.A., Gulyaeva L.F., Zhimulev I.F., Kolesnikov N.N.* 2016. MiRNA profiling, detection of BRAF V600E mutation and RET-PTC1 translocation in patients from Novo-
- sibirsk oblast (Russia) with different types of thyroid tumors. *BMC Cancer.* V. 16. P. 201.
- Trino S., Lamorte D., Caivano A., Laurenzana I., Tagliaferri D., Falco G., Del Vecchio L., Musto P., De Luca L.* 2018. MicroRNAs as new biomarkers for diagnosis and prognosis, and as potential therapeutic targets in acute myeloid leukemia. *Int. J. Mol. Sci.* V. 19. P. 460.
- Vandesompele J., De Preter K., Pattyn F., Poppe B., Van Roy N., De Paepe A., Speleman F.* 2002. Accurate normalization of real-time quantitative RT-PCR data by geometric averaging of multiple internal control genes. *Genome Biol.* V. 3. <http://genomebiology.com/2002/3/7/research/0034>.
- Weiss C.N., Ito K.* 2017. A Macro View of MicroRNAs: The Discovery of microRNAs and their role in hematopoiesis and hematologic disease. *Int. Rev. Cell Mol. Biol.* V. 334. P. 99.
- Xiao Y., Su C., Deng T.* 2016. miR-223 decreases cell proliferation and enhances cell apoptosis in acute myeloid leukemia via targeting *FBXW7*. *Oncol. Lett.* V. 12. P. 3531.
- Zheng Y.S., Zhang H., Zhang X.J., Feng D.D., Luo X.Q., Zeng C.W., Lin K.Y., Zhou H., Qu L.H., Zhang P., Chen Y.Q.* 2012. MiR-100 regulates cell differentiation and survival by targeting *RBSP3*, a phosphatase-like tumor suppressor in acute myeloid leukemia. *Oncogene.* V. 31. P. 80.
- Zhou B., Wang S., Mayr C., Bartel D.P., Lodish H.F.* 2007. MiR-150, a microRNA expressed in mature B and T cells, blocks early B cell development when expressed prematurely. *Proc. Natl. Acad. Sci. USA.* V. 104. P. 7080.

PROFILING KARYOTYPE-DEPENDENT PATTERNS OF miRNA EXPRESSION IN ACUTE PROMYELOCYTIC LEUKEMIA

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Acute promyelocytic leukemia (APL) is a subtype of acute myeloid leukemia (AML), with a balanced reciprocal translocation t(15; 17) (q24.1; q21.1) detected in most cases. Acute leukemia progression is accompanied by the occurrence of genetic and epigenetic modifications, including microRNA. The aim of the work is to analyze the role of differential miRNA expression in APL, depending on the cytogenetic properties of tumor cells. The study used cytological specimens containing bone marrow smears: APL with t(15; 17) (q24.1; q21.1) ($n = 7$), normal-karyotype APL ($n = 8$) and benign tumors (BT) ($n = 20$). Analysis of expression levels of miR-128, miR-150, miR-155, miR-26a, miR-181b, miR-29b, miR-20a, miR-223, miR-92a, miR-100, miR-126, miR-451, miR-103a, miR-191, and miR-378 was performed by RT-qPCR. The markers differentiating between BT and APL, no matter which karyotype, are miR-150, miR-26a, miR-29b, miR-20a, miR-223, miR-126, and miR-451a ($P < 0.05$). Expression levels of miR-128 ($P = 0.020513$) and miR-155 ($P = 0.013986$) are statistically different between APL with t(15; 17) (q24.1; q21.1) and normal-karyotype APL. The results obtained confirm the epigenetic regulation of APL; however, the miRNAs in question lie beyond t(15; 17) (q24.1; q21.1), suggesting the presence of more complex, staged regulatory pathways underlying APL.

Keywords: microRNA, acute promyelocytic leukemia, acute myeloid leukemia, t(15; 17) (q24.1, q21.1), *PML-RARα*