

- ian oat (*Avena sativa* L.) variety. Genet. Mol. Biol. 23: 681–684.
- Catalán J., Falck G.C.-M., Norppa H. 2000. The X chromosome frequently lags behind in female lymphocyte anaphase. Am. J. Hum. Genet. 66: 687–691.
- Crasta K., Ganem N.J., Dagher R., Lantermann A.B., Ivanova E.V., Pan Y., Nezi L., Protopopov A., Chowdhury D., Pellman D. 2012. DNA breaks and chromosome pulverization from errors in mitosis. Nature. 482: 53–58.
- Erenpreisa J., Huna A., Salmina K., Jackson T.R., Cragg M.S. 2012. Macroautophagy-aided elimination of chromatin: sorting of waste, sorting of fate? Autophagy. 8: 1877–1881.
- Fenech M., Kirsch-Volders M., Natarajan A.T., Surrallés J., Crott J.W., Parry J., Norppa H., Eastmond D.A., Tucker J.D., Thomas P. 2011. Molecular mechanisms of micronucleus, nucleoplasmic bridge and nuclear bud formation in mammalian and human cells. Mutagenesis. 26: 125–132.
- Foster H.A., Griffin D.K., Bridger J.M. 2012. Interphase chromosome positioning in *in vitro* porcine cells and *ex vivo* porcine tissues. BMC Cell Biol. 13: 30.
- Gernand D., Rutten T., Varshney A., Rubtsova M., Prodanovic S., Brüß C., Kumlehn J., Matzk F., Houben A. 2005. Uniparental chromosome elimination at mitosis and interphase in wheat and pearl millet crosses involves micronucleus formation, progressive heterochromatinization, and DNA fragmentation. Plant Cell. 17: 2431–2438.
- Gonzalo S. 2014. DNA damage and lamins. Adv. Exp. Med. Biol. 773: 377–399.
- Gozuacik D., Kimchi A. 2004. Autophagy as a cell death and tumor suppressor mechanism. Oncogene. 23: 2891–2906.
- Hatch E.M., Fischer A.H., Deerinck T.J., Hetzer M.W. 2013. Catastrophic nuclear envelope collapse in cancer cell micronuclei. Cell. 154: 47–60.
- Hoffelder D.R., Luo L., Burke N.A., Watkins S.C., Gollin S.M., Saunders W.S. 2004. Resolution of anaphase bridges in cancer cells. Chromosoma. 112: 389–397.
- Huang Y., Jiang L., Yi Q., Lv L., Wang L., Zhao X., Zhong L., Jiang H., Rasool S., Hao Q., Guo Z., Cooke H.J., Fenech M., Shi Q. 2012. Lagging chromosomes entrapped in micronuclei are not 'lost' by cells. Cell Research. 22: 932–935.
- Kopin B.P. 2000. Targets of oncogenes and tumor suppressors: key for understanding basic mechanisms of carcinogenesis. Biochemistry 5: 2–27.
- Lingle W.L., Ingle J.N., Maihle N.J., Salisbury J.L. 1998. Centrosome hypertrophy in human breast tumors: implications for genomic stability and cell polarity. Proc. Natl. Acad. Sci. USA. 95: 2950–2955.
- Medvedeva N.G., Panyutin I.V., Panyutin I.G., Neumann R.D. 2007. Phosphorylation of histone H2AX in radiation-induced micronuclei. Radiat. Res. 168: 493–498.
- O'Donovan P., Livingston D.M. 2010. BRCA1 and BRCA2: breast/ovarian cancer susceptibility gene products and participants in DNA double strand break repair. Carcinogenesis. 31: 961–967.
- Rao X., Zhang Y., Yi Q., Hou H., Xu B., Chu L., Huang Y., Zhang W., Fenech M., Shi Q. 2008. Multiple origins of spontaneously arising micronuclei in HeLa cells: direct evidence from long-term live cell imaging. Mutat. Res. 646: 41–49.
- Rello-Varona S., Lissa D., Shen S., Niso-Santano M., Senovilla L., Mariño G., Vitale I., Jemaá M., Harper F., Pierron G., Castedo M., Kroemer G. 2012. Autophagic removal of micronuclei. J. Cell Cycle. 11: 170–176.
- Sagona A.P., Nezis I.P., Stenmark H. 2014. Association of CHMP4B and autophagy with micronuclei: implications for cataract formation. Biomed. Res. Int. 974393.
- Shimizu N., Shimura N., Tanaka T. 2000. Selective elimination of acentric double minutes from cancer cells through the extrusion of micronuclei. Mutat. Res. 448: 81–90.
- Sun H.B., Shen J., Yokota H. 2000. Size-dependent positioning of human chromosomes in interphase nuclei. Biophys J. 79: 184–190.
- Terradas M., Martín M., Tusell L., Genesca A. 2010. Genetic activities in micronuclei: is the DNA entrapped in micronuclei lost for the cell? Mutat. Res. 705: 60–67.
- Terradas M., Martín M., Genesca A. 2016. Impaired nuclear functions in micronuclei results in genome instability and chromothripsis. Arch Toxicol. 90: 2657–2667.
- Utani K., Okamoto A., Shimizu N. 2011. Generation of micronuclei during interphase by coupling between cytoplasmic membrane blebbing and nuclear budding. PLoS One 6: e27233.
- Vargas J.D., Hatch E.M., Anderson D.J., Hetzer M.W. 2012. Transient nuclear envelope rupturing during interphase in human cancer cells. Nucleus. 3: 88–100.
- Vergnes L., Peterfy M., Bergo M.O., Young S.G., Reue K. 2004. Lamin B1 is required for mouse development and nuclear integrity. Proc. Natl. Acad. Sci. USA. 101: 10428–10433.
- Weaver B.A. 2014. How Taxol/paclitaxel kills cancer cells. Mol. Biol. Cell. 25: 2677–2681.
- Zhang C.Z., Spektor A., Cornils H., Francis J.M., Jackson E.K., Liu S., Meyerson M., Pellman D. 2015. Chromothripsis from DNA damage in micronuclei. Nature. 522: 179–184.

MICRONUCLEI ELIMINATION IN HUMAN BREAST ADENOCARCINOMA CELLS MCF-7

O. I. Sutyagina^{a,*}, O. P. Kisurina-Evgenieva^a, G. E. Onishchenko^a

^aDepartment of Cell Biology and Histology, School of Biology, Lomonosov Moscow State University, Moscow, 119234, Russia

*e-mail: oksanasutyagina@yandex.ru

According to recent researches, cells are able to eliminate some of micronuclei. Micronuclei formation induced by using antimetabolic agents has widely use in antitumor chemotherapy, so micronuclei elimination could probably lead to micronuclear cells survival during therapy. Micronuclei elimination ways and mechanisms are still insufficiently studied. That is why investigation of micronuclei elimination has both fundamental and practical importance. In the present study, we show presence of two subpopulations of micronuclei: small single and large multiple micronuclei

in MCF7 cells (human breast adenocarcinoma cell line, p53+) both in control and after paclitaxel treatment. Each of these subpopulations obviously has individual way of formation. We identify ways of micronuclei elimination: lysosome-dependent degradation (for small single micronuclei) and structural destruction (for large multiple micronuclei). We show that micronuclei elimination is a rare process. Major part of micronuclear population persists, but micronuclei could have morphological defects. We describe different defects in micronuclear envelope: lack of peripheral heterochromatin, perinuclear space expansion, micronuclear membrane breaks, full or partial lack of nuclear lamina. We show presence of p53-negative micronuclei. Lack of p53 activation is more characteristic for small single micronuclei. Received data allow to conclude that micronuclei elimination is unable to change antitumor chemotherapy's results, however there is a danger of MN cell's progressing through the cell cycle (primary for cells with small single micronuclei).

Keywords: micronuclei elimination, nuclear envelope, nuclear lamina, p53