SENSITIVITY OF CELLS WITH VARIOUS LEVELS OF *Ppm1d* EXPRESSION TO CLASSICAL COMBINATION OF CHEMOTHERAPEUTIC DRUGS IN COLORECTAL CANCER TREATMENT

E. Yu. Kochetkova[a, *], B. B. Grigorash[a, b], and O. N. Demidov[a, b]

[a] *Institute of Cytology, Russian Academy of Science, Saint-Petersburg, 194064 Russia*
[b] *INSERM UMR 1231, University of Bourgogne, Dijon, France*
**e-mail: lena.linnaea@gmail.com*

Various malignant tumors were shown to exhibit mutations and amplifications of *Ppm1d* gene that encodes the Wip1 phosphatase. Recent studies show that presence of mutated Wip1 isoform after chemotherapy implies that dysregulated Wip1 activity favors chemoresistance of cancer cells. The aim of this study was to investigate the role of Wip1 in response of DLD1 colorectal cancer cells to treatment with 5-fluorouracyl and oxaliplatin. We used lentiviral transfection method to construct cell lines with overexpression of *Ppm1d* gene. We obtained that Wip1 overexpression is linked with increased resistance to oxaliplatin treatment, while Wip1 deletion decreases cellular viability and clonogenic survival upon both agents. Data acquired show that Wip1 overexpression may favor chemotherapy resistance of cancer cells. Development of strategies, aimed on decreasing Wip1 activity, is required to increase effectiveness of treatment of colorectal cancers.

Keywords: Wip1, *Ppm1d*, 5-fluorouracyl, oxaliplatin, chemotherapy