# Impact of various Poly(ADP-ribose)polymerase 1 level on DNA base excision repair status in human cells

P-02.5-35

**A.S. Kochetkova**[I], E.S. Ilina[I], S.N. Khodyreva[I], O.I. Lavrik[I,II]

[I]Institute of Chemical Biology and Fundamental Medicine SB RAS, Novosibirsk, Russia, [II]Novosibirsk State University, Novosibirsk, Russia

DNA repair systems exist to correct damage to the structure of DNA, thereby maintaining genome stability. Base excision repair (BER) is responsible for repair chemically modified bases, that are one of the most prevalent type of DNA lesions. It is considered that regulatory proteins are required for improving DNA repair efficiency and acceleration. Poly(ADP-ribose)polymerase 1 (PARP1) is a well-known protein involved in the repair processes regulation, including BER. Multiple studies have suggested that its function is being a "sensor" of damage and promote recruiting the complex for their removal by the ADP-ribose polymer synthesis, whereas others indicate that PARP1 can suppress activity of some key BER proteins. This work is aimed at studying the influence of various PARP1 level on the efficiency of BER steps and on expression of genes, encoding proteins involved in BER. For this purpose, we used mRNAs and the whole-cell extracts obtained from wild-type, PARP1 knockdown (via siRNA transfection) and PARP1 knockout (via CRISPR/Cas9) human cell lines: HEK-293T and HEK-293FT. RT-qPCR assay data has not show significant changes in the expression at levels of mRNA, encoding BER proteins: PARP1, PARP2, UNG, APEX1, Polb, Lig3 in both PARP1 knockdown and knockout cells in comparison with wild-type ones. We have performed functional tests with protein extracts and $^{32}$P-labeled DNA substrates mimicking BER intermediates and demonstrated that various PARP1 level in cell extracts has little impact on the efficiency of key BER steps: removal of uracil from DNA, abasic site processing, gap filling and ligation. Taking together, results of the work show that knockdown and knockout of PARP1 lead to negligible change in BER status as well as in the kinetics of the pathway. The data obtained is important for better understanding the real role of PARP1 in BER regulation.
The research was supported by RSF grant № 19-14-00204.