GENE EXPRESSION AND METHYLATION PROFILES AS A BIOMARKER FOR HUMAN RADIATION EXPOSURE

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Introduction. Taking into account the fact that Kazakhstan is one of the world's leaders in uranium mining, and given the extent of the damage suffered as a result of the work on the Semipalatinsk nuclear test site, the general background radiation in some regions came under the influence of additional effects of chronic exposure to low doses of radiation, the study and search for new methods of dosimetry, as an integral part of the radiological protection of the population, is a priority for the state. The purpose of this study is the search for and development of potential biomarkers by assessing the impact if ionising radiation on gene expression and quantification of global methylation and hydroxymethylation of uranium industry workers.

Materials and methods. Peripheral blood samples were collected from uranium industry workers (N=93) whose average annual received radiation doses were different: Group A (<25mSv) and Group B (<5() mSv) from Shyntobe village (N=40) and Stepnogorsk city (N=53). To examine global methylation and hydroxymethylation levels capture and detection antibodies were used and then measured colorimetrically by reading the absorbance in a microplate spectrophotometer. Methylated DNA (5mC%) and Hydroxymethylated DNA (5hmC%) quantification kits (Qiagen,Hpigentek) were used according to manufacturer's standard protocol. To examine gene expression profiles of radiation exposed workers quantitative real-time PCR were used. The expression of LIG3,XPA genes were analysed and compared between two groups using RQ Manager Software.

Results and discussion. Global methylation and hydroxymethylation levels were examined and compared between two groups of uranium industry workers of Stepnogorsk city (A= 25 mSv, B= 50 mSv). The observed difference between sample means for %5mC was not statistically significant. However, the observed difference between sample means for %5hmC, on the other hand, was statistically significant. The relative gene expression analysis showed small difference between exposed individuals and control group. LIG3 and XPA genes were found to be upregulated in subjects with higher doses. Statistical analysis showed that due to High Standard Error, which indicates how well a sample represents each group, the obtained results are not statistically significant. This can be due to heterogeneity and small number of individuals in compared groups.

Conclusions. The results obtained in this pilot study indicate that the possibility of using hydroxymethylation relatively to the entire genome can act as a biological marker for dosimetry *in vivo.* The radiation level affects the level of gene expression reestablishment, which is carried by hydroxymethylation. It is important to note that for more reliable results the amount of samples should be increased.