Molecular-biological survey at occupational exposure

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The validity of the linear non-threshold model at very low doses (<50 mSv) is still a subject of investigation and discussion. There are a number of factors affecting such approach, including low-dose-hypersensitivity, adaptive-dose response, genomic instability and more recently bystander effect. New knowledge, especially on subcellular level, might contribute to the clarification of this problem.

The report presents some main results aimed at finding_appropriate biomarkers applicable in molecular epidemiological surveys of occupationally exposed individuals and/or population so that to prove low dose effects. The spontaneous and induced DNA repair and protein synthesis in leucocytes, the level of DNA damage by single cell gel-electrophoresis in lymphocytes and the concentration of malonedialdehyde in blood serum of occupationally exposed persons, were analyzed. A significant decrease of potentially lethal damage in persons with "mean annual dose" lower or equal to 5 mSv/a was found, compared to the control group. The highest repair capacity after a challenging dose of 2,0 Gy gamma rays as well as a significant decrease in the level of oxidative stress determined in the blood plasma was evaluated for persons from the same group. The annual doses not higher than twice the natural radiation background exert positive effects on DNA damage and repair increase cellular resistance and decrease oxidative stress. Some attention was paid to the establishment of individual radio-sensitivity and specific to radiation exposure proteins.

Our preliminary investigations are connected with bystander effect in human whole blood because of its practical importance for radiotherapy and risk assessment. The results support the hypothesis that potentially lethal damages in unirradiated cells are transformed into lethal by molecular signals produced by their irradiated neighbors. Also, the stimuli secreted in the blood plasma increase sensitivity to consecutive irradiation, and reaction oxygen species (ROS) possibly take part in this process.

We have initiated studies on the combined effects of proteasome inhibitors and ionizing radiation on HSP70 synthesis, which might be of potential interest for the radiation response as well as for the development of new strategies in radioprotection, radiotherapy and prophylaxis. In order to characterize the protein-protein network-like interactions in non-homologous end joining DNA repair, we carry out quantitative mechanistic studies using intermolecular FRET between fluorescence labeled couples of proteins that are considered potential partners in a DNA repair process.

Results obtained so far need further investigation to find molecular endpoints, which will increase the sensitivity of studies and make it possible to search effects of low radiation exposures.