Radiobiology with accelerated heavy ions: a new radiobiology

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High-energy heavy charged particles are an *effective tool* of solving fundamental problems of radiobiology. Classics of quantitative radiobiology pointed out the necessity and fruitfulness of using different types of ionizing radiation with different physical characteristics for studying the mechanisms biological action of ionizing radiation. In recent decades, a number of important practical tasks have emerged, the answers to which require a detailed study of the mechanisms of biological action of accelerated heavy ions. These tasks are associated, first of all, with *space radiobiology* problems related to working out the measures of radiation protection of the crews on long missions beyond the Earth's magnetosphere; using accelerated heavy ions in the treatment of oncological diseases; and resolving the problems of *standardizing the radiation exposure* of the staff working in mixed fields of different kinds of radiation.

At the Laboratory of Radiation Biology (LRB), versatile research into the regularities and mechanisms of the biological action of heavy charged particles of different energies is performed at heavy ion accelerators. The research is aimed at studying the specifics of the damaging action of the heavy charged particles on the cellular DNA in different organisms and studying the mechanisms of the lethal and mutagenic action of multi-charged ions. Using accelerated heavy ions, one of the *central problems* of radiobiology was solved – the problem of relative biological efficiency of different radiation types; the mutation mechanisms in pro- and eukaryotic cells were determined; and the cellular DNA damage character and reparation regularities were found. The specific features of the interaction between high-energy heavy ions and biological object allow charged particles to be considered a unique tool for resolving a number of fundamental and practical problems of modern biology.

For solving the problem of the biological effects of heavy charged particles, the data on the regularities and mechanisms of their genetic action on cells with different genome organization levels seem to be extremely important. The character of the DNA damage caused by heavy charged particles is substantially different from that caused by gamma-rays. Accelerated heavy ions, unlike gamma-rays, induce mainly the cluster-type damage in the DNA. These kinds of lesions are the combination of simultaneous disorders of a DNA part with the formation of single-strand breaks, modification of bases, and sugar modification. The events of this kind result from a local energy deposition which happens when a heavy charged particle travels through a DNA thread. The cluster-type damage determines the specifics of the lethal, mutagenic (induction of gene and structural mutations in prokaryotes and formation of chromosome aberrations in higher eukaryotic cells), and transforming action of radiation on cells with different genome organization levels. The LRB has acquired ample experimental material regarding the genetic action of heavy charged particles.

Among the topical but still poorly studied issues of the biological action of heavy charged particles is their cataractogenic effect. The available data on the cataract formation regularity in experimental animals irradiated by high-energy heavy ions (argon and iron) show that the doses as low as 0.01 cGy cause a cataract in the distant future. At the LRB, both in vivo and in vitro detailed studies of the cataract formation mechanism under the effect of high-energy heavy ions are underway.

The issues of the damaging action of heavy charged particles on the central nervous system are important and remain unresolved in many ways. Research in this field seem to be extremely topical for solving space radiobiology problems as there is evidence that behavioral functions of the experimental animals irradiated with heavy ions have been disordered. Low doses of accelerated iron ions cause an irreversible disorder of the cognitive and other functions in an irradiated organism. Research in this important field has also been started at the LRB.

Thus, versatile studies of the biological action of heavy charged particles of different energies are performed at JINR's accelerators. The main fields of research include the mechanisms of the genetic action of accelerated heavy ions; regularities and mechanisms of this type of radiation acting on the crystalline lens and retina; high-energy heavy ion action on the central nervous system; and mathematical modeling of radiation-induced effects of charged particles. The special features of the interaction between high-energy heavy ions and biological objects allow such ions to be considered a unique tool for resolving many fundamental issues. This all gives us a ground to regard high-energy heavy charged particle radiobiology as a new radiobiology different from the "classical" one.