CELLION Report Summary

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Final Activity Report Summary - CELLION (Studies of cellular response to targeted single ions using nanotechnology)

The human population is constantly exposed to charged particle radiation from cosmic radiation, natural radioactivity, medical diagnostics and treatment of cancer, and industrial applications (including the nuclear energy generation). However, our understanding of the biological effects of radiation exposure is still far from being complete in spite of the tremendous progress achieved in recent years. While there is a general agreement in the area of the risk associated with high radiation doses, the low doses region is still a field of vivid scientific discussion.

In case of particle radiation the radiobiological effect is a result of direct interactions of biological matter with primary particles traversing the cell, of interactions with positive ions and secondary electrons produced along the track, and of subsequent chemical reactions with reactive oxygen and nitrogen species. The direct interactions occur in a discrete region along the track with a radius comparable to the radius of a chromosome or even of a single DNA strand. Therefore, the investigation of the cellular response to the particle radiation requires a good definition of the ion traversal through the cell. This is not possible in traditional experiments with a broad beam of ions bombarding the biological sample randomly. Only after introduction of ion microprobes, working in the single hit (SIH) mode, many topics from this area could be successfully studied. This is particularly true for subtle, non-direct effects of irradiation like bystander effect (damage transfer from directly hit cells to neighbouring (bystander) ones), hypersensitivity, or adaptive response.

The CELLION RTN was formed to coordinate European efforts in these studies by creation of a critical mass of experimental, theoretical and clinical scientists, working on a border between physics and biology in the field of targeted irradiation of cells.

In development of new SIH facilities, many topics of common interest were investigated and developed by the network. Ion beam targeting, dose control, design of irradiation end stations were the most important experimental issues. Much effort was put into the development of efficient detection systems for single ions of different mass and energy. New methods and approaches in microscopy, image processing, and analysis were required for fast, automatic recognition and positioning of cells. The ambitious goal was imaging of unstained cells, in order to avoid potential burden related to cells staining and the use of UV light.

Biological effects of ion irradiation were studied as a function of energy and atomic number of primary ions, ion track location within the cell, number of ion tracks, and cell species (human keratinocytes, fibroblasts, etc.). One of the most studied topics was the investigation of Double-Strand Breaks (DSBs) formation and their subsequent repair kinetics. Comparison studies of the effect of different irradiation qualities on the DSBs formation and micronuclei assay have been performed. In non-targeted effects area, the bystander effect was the mostly studied topic, with the emphasis on one possible mechanism involved in the bystander phenomenon, i.e. the creation of reactive oxidative species (ROS) in cell colonies exposed to radiation. The biology programme included also studies of the calcium response to ionising radiation in mammalian cells. Finally, in order to deepen the knowledge of the non-targeted effects, bystander effect and the low dose hyper-radiosensitivity, a computer model of a population of cells irradiated was proposed, taking into account the phenomena in the low dose domain.

CELLION network employed over 20 young researchers, early-stage and experienced ones, who not only acquired multidisciplinary skills and scientific degrees but produced also a significant scientific output. After the RTN end, their career has been linked mostly to science, however some of them moved to hi-tech industry and medicine.

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