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PREPARATION FOR RADIOBIOLOGY RESEARCH AT ELI-ALPS WITH SECONDARY IONIZING RADIATION SOURCES

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Introduction: ELI-ALPS will provide laser accelerated electron and ion beams with unique, ultra-short pulses and ultra high dose rate parameters to examine the effects of different ionizing radiations on cells, zebrafish and rodent models.
Aims: Our aims are to develop the appropriate dosimetry system and to validate preclinical models for Relative Biological Effectivity (RBE) investigations, in order to prepare future radiobiological experiments focused on healthy tissue reactions. After the establishment of an accurate control and verification of the delivered radiation dose, cancer and normal cell lines, zebrafish embryos and rodents will be exposed to escalated doses of accelerator based photons, electrons, protons, carbon ions, photon-neutron mixed beam of a nuclear research reactor and laser driven very high energy electron-, and hadron beam.
Materials and methods: In our previous and ongoing investigations we used different cell lines to measure the dose-dependent cell survival by clonogenic, colorimetric assays, and by impedance-based label-free technology. We irradiated zebrafish embryos of wild type-, and different tissue-specific transgenic lines in the presence of radiation modifier agents and by different radiation qualities (photon, neutron). In addition, we set up two rodent models (rat and mouse) to investigate the acute and late consequences of focal brain irradiation.
Results: We observed higher sensitivity at earlier stages of the zebrafish embryogenesis and dose-, and radiation type-dependent organ damages macroscopically (e.g. shortening of the body length, spine curvature, microcephaly) and microscopically (marked cellular changes in skin, cardiac, gastrointestinal system) as well. Furthermore, we detected the irradiation-caused overexpression of proinflammatory cytokines (IL-1β, IL-6, NF-κB) in this protocol. Regarding the rat model, we found evidence for acute inflammatory activation in the peripheral circulation, and significant memory deficits and histological damages after irradiation.
Conclusion: Our vertebrate models proved to be appropriate models for preclinical examinations on different radiation quality, and especially, to test possible protective agents that can theoretically increase the therapeutic index, and provides the prospect of an improved outcome of radiation, and consequently to an improved quality of life of patients who undergo radiotherapy.
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Author: Dr TOKES, Tunde (ELI-ALPS, ELI-HU Non-Profit Ltd., Szeged, Hungary)

Co-authors: Dr UGHY, Bettina (ELI-ALPS, ELI-HU Non-Profit Ltd., Szeged, Hungary); Ms SZABO, Emilia Rita (ELI-ALPS, ELI-HU Non-Profit Ltd., Szeged, Hungary); Dr HIDEGHETY, Katalin (ELI-ALPS, ELI-HU Non-Profit Ltd., Szeged, Hungary); Mr POLANEK, Robert (ELI-ALPS, ELI-HU Non-Profit Ltd., Szeged, Hungary); Mr SZABO, Zoltan (ELI-ALPS, ELI-HU Non-Profit Ltd., Szeged, Hungary)

Presenter: Dr TOKES, Tunde (ELI-ALPS, ELI-HU Non-Profit Ltd., Szeged, Hungary)

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