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DNA DSB repair pathways in mammalian cells – measurements and simulations

The GEANT4 Monte Carlo simulation toolkit for radiobiology, GEANT4-DNA, developed earlier [Belov et al., 2015; 2017] is to be improved and extended. The stages of DNA double strand break (DSB) repair in mammalian cells will be verified by the reconstruction of the repair time courses of radiation induced foci, which are suited to specific repair processes.

The model shows a possible mechanistic explanation of the basic regularities of DSB processing through the non-homologous end-joining (NHEJ), homologous recombination (HR), single-strand annealing (SSA) and two alternative end-joining pathways.

New experimental data produced in the field will be incorporated during further development of the model. The new radiation modalities suggested for introduction into the model are protons, neutrons and alpha particles. The cells under investigation range from healthy fibroblast to cancer cells.

The cell survival and repair mechanisms will be assessed, and results will be compared to those obtained from the extended GEANT4-DNA. Geant4-DNA will be applied for DSB repair in a wider range of human cell lines, ranging from healthy fibroblast to cancer cells. The cell culturing, radiation exposure, immunohistochemical staining of different DNA repair proteins and microscopic evaluation of the cells will be performed in the radiobiology laboratory at iThemba LABS using the Metafer automated microscope from Metasystems. The cells will be exposed to 222Rn as well as alpha particles, protons and neutrons. The dose accumulated due to 222Rn will be estimated by using a RAD7 detector from SU.

The developed model would be a more comprehensive version that incorporates recent findings and reconstructs DSB repair outcomes, induced by different radiation modalities. The cell survival and repair process will be assessed in the radiobiology laboratory at iThemba LABS and results compared to those obtained by the model.

The improved model will enhance our predictive capabilities and significantly contribute to the fields of medicine, radiation protection as well as space exploration

Primary authors: Ms BAILEY, Tarryn (Student); Prof. NEWMAN, Richard; Dr VANDEVOORDE, Charlot; Dr BELOV , Oleg; Ms BELOCOPITOVA, Ksenia

Presenter: Ms BAILEY, Tarryn (Student)

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