RISC-RAD Radiosensitivity of Individuals and Susceptibility to Cancer induced by Ionizing Radiations

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The purpose of RISC RAD integrated project, funded by the European Commission (FP6), is to provide fundamental scientific information needed to test the key assumptions of current radiation protection standards. A key foundation to the project strategy is the knowledge that ionising radiation (at least at high doses) causes genetic damage in somatic cells and that certain of these genetic changes are causally related to the development of cancer. Consortium members believe that a sound understanding of the mechanisms and processes that drive spontaneous and radiation-induced carcinogenesis is needed to understand and quantify radiation cancer risk at low doses ($\leq$100 mSv),. New genes involved in radiosensitivity have been identified. Significant results have been obtained concerning the specific structure of radiation-induced DNA damage ; the processing of complex DSBs by specific proteins like the Artemis endonuclease ; the dose dependence of IR-induced DNA damage response (chromosome aberrations, cell cycle checkpoints, transcriptome and stress response, apoptosis, senescence and emergence, telomere related genome instability) ; the telomeres as sites of DNA repair gene sequestration and drivers of phenomena such as gene amplification, non reciprocal translocations and LOH ; the impact of genetic variation in nonhomologous end joining processes may on the in vivo radiation response of mice ; the development of a number of (transgenic) animal models to provide experimental evidence for genetic risk factors ; the identification of five specific radiation cancer systems for experimentation in the mouse: osteosarcoma, skin basal cell carcinoma, intestinal adenoma, medulloblastoma and myeloid leukaemia. Moreover it has been demonstrated that carcinogenesis can be induced in tissue at distance from the radiation. It is encouraging that within RISC-RAD experimentalists and mathematical modellers are developing close working relationships, particularly for multi-step cancer modelling and for detailed biophysical modelling of chromosome aberration formation after irradiation

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