European Integrated Project RISC-RAD

Radiosensitivity of Individuals and Susceptibility to Cancer induced by Ionizing Radiations

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In radiological protection, the risks of inducing stochastic health effects (largely cancer) by a radiation exposure are generally controlled on the assumption that there is a linear no-threshold (LNT) response with dose at dose levels below those that cause deterministic effects (Tissue Injury) and which are known from epidemiological studies to cause stochastic health effects. Despite significant improvements in understanding the mechanisms, genetics and modelling of spontaneous and of radiation carcinogenesis in FP5 and elsewhere, there remain several important areas of uncertainty in the current approach to quantitative radiation cancer risk estimation. The validity of all the assumptions that radiological protection standards rely upon is scientifically uncertain in the low dose and low dose rate region, where practical radiation protection usually operates. Therefore optimization of radiation protection for the public and workers and rational evaluation of radiation risks of low level exposures to ionizing radiation are not currently based on solid scientific knowledge but rather on internationally accepted conventions. Against a background of continued and possibly extended use of ionising radiation in nuclear power generation, increasing medical radiation exposures, the need to control exposures from Radon and fears of radioactive waste repositories and of radiological/nuclear terrorism, it is essential that these uncertainties are reduced.

RISC RAD has been designed to contribute towards this goal. The purpose of the RISC RAD project is to provide fundamental scientific information needed to test the key assumptions mentioned above and, thus, to improve the management of risks at low doses. In RISC RAD low doses are defined as those ≤100 mSv, low dose rates are those where the increment of dose in a relevant target volume by two or more independent radiation tracks is ≤ 1 mSv per hour. It is, however, recognised that higher doses will be used for specific experimental purposes as this is often required to test for qualitative differences in biological responses at different dose levels. 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. Given the present state of knowledge and the need to perform studies involving experimental irradiation, a significant number of experimental studies will be undertaken in rodent, generally mouse, systems. Human *in vitro* cellular studies are also undertaken in recognition of the biological differences between rodents and humans.

The RISC RAD research strategy will contribute significantly to **bridge the remaining gap of scientific knowledge about effects of lows doses of ionizing radiation.** To do so, the following **three Key Questions** have been identified to address specific needs :

A To evaluate the validity of current and new risk extrapolation models based on effects induced at higher doses:

Do the processes that drive carcinogenesis due to high dose exposures also contribute to low dose radiation carcinogenesis ?

B To judge on the distribution of radiation risks in populations:

To what extent do heritable factors affect individual radiation cancer risks ?

C Translation of the above into practical radiation protection measures:

Judgement on the most appropriate mathematical model for cancer risk projection and of the operational implications.

Funded by the European Commission in the framework of a dedicated programme supporting research in the Nuclear sector (Euratom), 30-million euros* project RISC-RAD started on 1st January 2004 for a duration of four years. It involves 11 european countries (Austria, Denmark, Finland, France, Germany, Ireland, Italy, the Netherlands, Spain, Sweden and the United Kingdom) and a consortium of 29 partners. Dr. Laure Sabatier from the French Atomic Energy commission is in charge of the coordination and overall management. Dr L.H.F Mullenders from Leiden University Medical Centre is the scientific manager of the project.

RISC-RAD research is organised in five closely interacting work packages as follows:

WP 1 : DNA damage response mechanisms, Prof. L. Mullenders

WP 2 : Genomic instability and epigenetic effects Dr. L. Sabatier

WP 3 : Mechanisms of tumorigenesis Dr. S. Bouffler

WP 4 : Genetic susceptibility to radiogenic tumours Dr. M. Atkinson

WP 5 : Modelling for improvement of risk assessment Prof. H. Paretzke

*estimated total scientific effort. EC contribution amount to 10 millions.

For more information about RISC-RAD please visit www.riscrad.org