Cellular Radiobiological Studies

TG91 Workshop

Radiation Risk Inference at Low-Dose and Low-Dose-Rate Exposure for Radiological Protection Purposes

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Background

- Previous reports from UNSCEAR, EPRI and SENES drawn upon to identify relevant endpoints
- Notably the 2020/2021 UNSCEAR Annex C, *Biological mechanisms relevant for low-dose and low-dose-rate radiation cancer risk inference*
- These indicate that most secure data which to consider in terms of relevance to low-dose and low-dose-rate risk inference relate to DNA damage, its repair and the induction of gene mutations and chromosomal aberrations. [Broadly similar to conclusion of Brooks et al., 2016 Int. J. Radiat. Biol. 92, 405–426]

Primary endpoints considered

- DNA damage induction and repair assayed *in vitro* and *in vivo*
- Induction of gene mutations
- Induction of chromosomal aberrations
- Induction of cell cycle checkpoints and apoptosis

Potential modulators considered

- Non-targeted effects – transmissible genomic instability, bystander phenomena, adaptive response
- Differential gene/protein expression
- Immune modulation
- Tumour invasion/metastasis
- Tumour vascularization

Main conclusions - I

- Chromosomal aberration studies indicate LDEF and DREF values in the range 3-5
- Little evidence for dose thresholds from chromosomal aberration data
- Few data pose a significant challenge to the central role of DNA damage and mutation in radiation carcinogenesis
- However, a number of potential risk modulating processes that might serve to increase or decrease risk are identified
- The role of such processes in radiation carcinogenesis *in vivo* is presently insufficiently defined to bring them into considerations of health risk assessment
- Evidence from potential risk modulators is not yet sufficient to allow firm conclusions to be drawn on their impact on the evaluation of DREF/LDEF/DDREF

Main conclusions - II

- In general terms cellular and molecular data tend to support the application of a DDREF to estimate risk at low doses and dose rates
- The magnitude of DREF/LDEF values is not large - chromosomal studies, which include some of the largest data sets, indicating around 4
- Sound data indicating that DNA damage responses and mutational processes operate at low doses (down to 20 mGy) and dose rates (down to 20 mGy day^{-1} and 1 mGy day^{-1}) as they do at higher doses/dose rates
- Many processes are likely to modulate DNA damage responses, and while poorly defined could together have a significant influence on the magnitude of DREF/LDEF values

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