



Linear and Non-linear Dose-effect Relationships at Low Dose Ionizing Radiation

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Ionizing Radiation (IR) provokes several cellular responses, including DNA repair, transcriptional changes and cell cycle checkpoints. Some of these responses are linear to quite low doses (e.g. formation of chromosomal abnormalities and micronuclei), but some other responses can differ significantly from the linear no threshold model. Unexpectedly, we found that IR stimulated integration of extrachromosomal DNA was only linear in the low dose range (up to approximately 200 mGy) and that stimulation of random integration is probably the most sensitive assay, with 2-fold stimulation at 10 mGy. Unexpectedly, this did not depend on functional NHEJ, suggesting that low dose IR may stimulate another form of DNA repair.

Furthermore, we also studied transcriptional responses upon low dose IR. We discriminated between DNA double strand break (DSB) induced and other transcriptional changes by using DSB repair mutant mice. In this way we determined a low dose IR expression profile dependent on DSBs and a profile independent of DSBs in mouse liver. We are currently extending this analysis to other organs, other time points and other doses.