# A Lifetime Study in whole-body irradiated mice focusing on markers for radiation-induced DNA damage and inflammatory processes


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**Introduction:** Higher doses of ionizing radiation are well known to inflict damage on tissue, such as cataracts and radiation-induced fibrosis. Nevertheless, discussions are ongoing about the dose limit or threshold for radiation-induced effects after low-dose exposure (below 0.5 Gy). In this study the *in vivo* effects of single doses between 0 Gy and 0.5 Gy on protein expression in liver and spleen as well as cytokine concentrations in plasma were investigated up to 24 months after irradiation. Wild type mice of both sexes were compared to virtually healthy mice bearing a heterozygous mutation in the *Ercc2* gene, coding for a DNA helicase involved in transcription and DNA repair.

**Methods:** Hybrid mice (C57BL/6 x C3H F1) at the adult age of 10 weeks were submitted to whole-body irradiation with doses of 0.063, 0.125 and 0.5 Gy using a \(^{60}\)Co source (0.063 Gy/min) (Dahlke et al. 2018). Over the following 24 months animals were sacrificed at different time points (4 and 24 hours, 12, 18, 24 months after irradiation) for sampling of blood, liver and spleen. A panel of 32 cytokines as well as C-reactive protein (CRP) were analyzed with a multiplex immunoassay. Analysis of the hepatic proteome was conducted using two-dimensional difference gel electrophoresis (2D-DIGE). In spleen extracts Western blot was used to screen protein expression.

**Results:** 2D-DIGE results showed only marginal effects of the radiation treatment in the liver proteome at 0.5 Gy 24 h and 18 months after irradiation without an obvious time-dependency. Differences in protein abundance between male and female irradiated mice indicated a different reaction to radiation between sexes. An experimental setup for Western blotting of spleen tissue was established for 13 protein markers of radiosensitivity. Measurement of 10 cytokines in plasma of male mice of both genotypes after a freeze-thaw-cycle was well reproducible. Wild type mice 4 h after irradiation showed a significant dose-dependent negative trend for eotaxin. Concentration of CRP showed a dose-dependent increase for the time points 24 h, 12 and 18 months after irradiation.

**Conclusion:** First results still have to be validated. Overall, observed effects in the respective dose-range were small and might be masked by interindividual variation. Future experiments should include doses above 0.5 Gy as positive controls and larger number of biological replicates.

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