LIFETIME STUDY IN LOW-DOSE IRRADIATED MICE FOCUSING ON MARKER FOR CARDIOVASCULAR AND INFLAMMATORY DISEASE

(Presentation at the 2016 annual meeting of the GBS Gesellschaft für Biologische Strahlenforschung, Erlangen)

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Introduction:

Male and female mice were acutely whole-body irradiated at the adult age of 10 weeks (0, 0.063, 0.125 and 0.5 Gy). Wild-type hybrid mice (C57BL/6 x C3H F1) were compared to virtually healthy heterozygous Ercc2 mutant mice of the same strain background. ERCC2 (also known as XPD, xeroderma pigmentosum group D; OMIM 278730) is a DNA repair helicase. We hypothesize that heterozygous mutants might show increased radiation-sensitivity due to a deficient DNA repair mechanism. Mice were sacrificed at various time points (4, 24 hours, 12, 18, 24 months post-irradiation) for blood and organ collection to investigate in vivo the underlying mechanisms of radiation-induced effects.

Objectives and Methods:

1) Inflammatory markers in plasma: Radiation effects on the immune and cardiovascular system are examined by using a highly standardized multiplex immunoassay for cytokines/chemokines.

2) Validation of candidate proteins for radiation sensitivity in spleen: Differentially expressed proteins after irradiation were identified in previous projects (ZiSS, DoReMi). These candidate proteins in spleen protein extracts will be quantified e.g. by Western blotting in order to verify radiation-induced alteration on protein level.

3) Mouse liver proteome and phosphoproteome analysis: Liver enzymes for detoxification and stress response (ROS) may be affected by radiation. By 2D-DIGE (Difference Gel Electrophoresis) analysis of liver cell extracts followed by MALDI MS/MS proteins deregulated by low dose irradiation and the involved pathways will be analysed.

Acknowledgement: This work is supported by the German Federal Ministry of Research and Technology (FKZ 02NUK045A).