RADIATION-SPECIFIC GENE EXPRESSION CHANGES IN HUMAN PBL AFTER *EX VIVO* IRRADIATION SUITABLE FOR RADIATION BIODOSIMETRY

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Introduction: In case of a large-scale radiation accident with involvement of individuals without physical dosimeters it is important to identify individuals who have received a moderate to high radiation dose to ensure proper medical care. As current methods are time-consuming, a fast and reliable method based on gene expression alterations is developed.

Methods: Human blood of 3 male and 3 female healthy donors, belonging to 3 different age classes, was irradiated *ex vivo* with 0, 0.02, 0.1, 0.5, 1, 2 and 4 Gy (γ-rays, Cs-137). Peripheral blood lymphocytes (PBL) were isolated and cultured for 6, 24 and 48 h in the medium- and high dose range (0.5 – 4 Gy) and for 24 and 48 h after low dose irradiation (0.02 and 0.1 Gy). At these times RNA and proteins were isolated and RNA was applied for processing whole human genome DNA-microarrays to analyse expression profiles. In the medium- and high dose range the most robust altered genes were selected for further qRT-PCR and protein expression analysis. To examine the radiation-specificity of the candidate genes, PBL were exposed to the DNA-damaging agents Paracetamol (25 and 200 µg/ml) and Mitomycin C (0.1 and 0.4 µg/ml) for 6, 24 and 48 h and gene expression was accordingly analyzed.

Results: By a p-value and fold-change driven gene selection 9 genes were identified in the low dose range and 16 genes in the medium- and high dose range allowing a radiation dose prediction accuracy of 96% independently on the time-point post irradiation up to 48 h. For 6 predictive genes in the medium- and high dose range qRT-PCR measurements based on pooled and non-pooled irradiated samples additionally validated the observed radiation-induced gene expression alterations. Furthermore, qRT-PCR analysis showed that the strong up-regulation of these genes is highly radiation-specific as the up-regulation after irradiation was much more pronounced when compared to exposure with Paracetamol or Mitomycin C. Protein expression analysis showed only for two genes a weak correlation between gene and protein expression after irradiation.

Conclusion: In vitro gene expression analysis in human PBL based on whole human DNA-microarray data allowed identifying a rather small set of radiation dose predictive and radiation-specific genes with a high potential for biodosimetric applications *in vivo* after low-, medium and high dose exposure.

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