Whole genome expression analysis in human Jurkat cells after exposure to I-123-iododeoxyuridine, γ-rays and α-particles

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Introduction: In order to develop a gene expression profile-based method for biodosimetry purposes we used the human p53-deficient T-lymphoma Jurkat cell line to study whether gene signatures exist allowing the discrimination of radiation quality.

Methods: Equi-effect doses, i.e. radiation doses and exposure conditions causing the same biological effect level, were determined with regard to micronucleus formation, γ-H2AX foci intensity and apoptosis induction for the radiation qualities of γ-rays (Cs-137) and α-particles (Am-241) as well as for the Auger electron emitter I-123. Prior to the DNA-microarray based gene expression experiments, Jurkat cells were either irradiated with 0.8 and 5 Gy γ-rays, respectively with 0.1 and 0.5 Gy α-particles or were exposed to 4 - 200 kBq I-123-iododeoxyuridine (I-123-UdR) per 10E6 cells. I-123-UdR was incorporated into the DNA for 20 h. After quantification of cellular uptake and calculation of accumulated decays the absorbed radiation dose was assessed based on the 3-D geometry of the cells. RNA-isolation was performed 6 h and 24 h post-exposure. Whole human genome DNA-microarrays (Agilent) were processed and expression profiles were analyzed. Genes showing significant expression changes after irradiation were identified by one-way ANOVA and Tukey-HSD post-hoc testing. The biological functions of significantly regulated genes were further investigated.

Results: Preliminary results of the gene expression analysis indicate that the expression of more and different genes is significantly altered after exposure to I-123-UdR and α-particles when compared to γ-irradiation. The functional analysis of significantly changed genes reveals that apoptosis relevant genes are enriched after exposure to I-123-UdR and α-particles in comparison to γ-irradiation.

Conclusions: I-123-UdR and α-particles induce pronounced alterations in gene expression when compared to γ-rays. Changes in the gene expression of p53-dependent apoptosis-related genes were observed suggesting p53-independent back-up pathways for apoptosis signalling in Jurkat cells.

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