GENE EXPRESSION ANALYSIS AFTER EXPOSURE TO I-123-IODODEOXYURIDINE, GAMMA-RAYS AND ALPHA-PARTICLES

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Gene expression analysis was carried out in human p53-deficient T-lymphoma Jurkat cells in order to identify robust candidate genes showing significant gene expression alterations allowing the discrimination of radiation qualities.

Equi-effect radiation doses, i.e. radiation doses and exposure conditions causing the same biological effect level, were determined with regard to micronucleus formation, γ-H2AX foci signal intensity and apoptosis induction after γ-irradiation (Cs-137; dose range: 0.8-10 Gy), α-particle exposure (Am-241; dose range: 0.1-1 Gy) and exposure to the Auger electron emitter I-123 as I-123-iododeoxyuridine (I-123-UdR; activity range: 4-200 kBq per 10E6 cells).

I-123-UdR was incorporated into the DNA for 20 h. Absorbed radiation dose was assessed based on accumulated decays, point-kernel calculations and the 3-D morphology of the cells. Gene expression analysis was performed employing whole human genome DNA-microarrays (Agilent) after exposure to equi-effect radiation doses of all three investigated radiation qualities. RNA for gene expression analysis was isolated 6 and 24 h post-exposure. Only genes showing a >1.5-fold change of expression vs. non-irradiated control were further analyzed for significance. Potential candidate genes for the discrimination of radiation quality have to show (i) a significant expression change after exposure to a specific radiation quality and (ii) display no altered gene regulation (1-fold ± 0.1) or even a conversely (>1.1-fold) regulation in response to exposure to the other radiation qualities investigated. Gene expression of all selected candidate genes was validated via qRT-PCR. Biological processes and pathways of significantly regulated genes were subsequently analyzed.

At equi-effect doses the results of the gene expression analysis showed that 359, 598 and 1339 genes are significantly regulated after exposure to I-123-UdR, α-particles and γ-rays, respectively. Applying our stringent requirements for candidate genes, we identified only 4, 1 and 1 gene(s) allowing the reliable and robust discrimination between γ- vs. I-123-UdR-exposition, γ- vs. α-radiation and α- vs. I-123-UdR-exposition, respectively.

γ-rays induce pronounced alterations in gene expression in Jurkat cells when compared to I-123-UdR and α-particles at equi-effect radiation doses. In vitro gene expression analysis in Jurkat cells might suggest that the discrimination of different radiation qualities by means of gene expression is possible.

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