WHOLE GENOME EXPRESSION ANALYSIS IN HUMAN JURKAT CELLS AFTER EXPOSURE TO I-123-IODODEOXYURIDINE, γ-RAYS AND α-PARTICLES

Unverricht-Yeboah, Marcus (1), Boldt, Sonja (2), Giesen, Ulrich (3), Pomplun, Ekkehard (1), Wolkenhauer, Olaf (2), Kriehuber, Ralf (1)

(1) Radiation Biology Unit S-US, Department of Safety and Radiation Protection, Forschungszentrum Jülich, D-52425 Jülich, Germany

(2) Department of Computer Science, Systems Biology and Bioinformatics Group, University of Rostock, D-18051 Rostock, Germany

(3) Physikalisch-Technische Bundesanstalt (PTB), Bundesallee 100, D-38116 Braunschweig, Germany

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 as well.

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 of synchronized cells for 20 h. After quantification of the cellular uptake the accumulated decays were calculated and the absorbed radiation dose was assessed after 3-D geometry analysis of the cells. RNA-isolation was performed always 6 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 after exposure to the three investigated radiation qualities indicate that the expression of more and different genes is significantly altered after exposure to I-123-UdR when compared to γ- and α-irradiation. The functional analysis of significantly changed genes reveals that apoptosis relevant genes are enriched after exposure to I-123-UdR in comparison to γ- and α-irradiation.

Conclusions: Changes in the gene expression of p53-dependent apoptosis-related genes were observed after I-123-UdR exposure suggesting p53-independent back-up pathways for apoptosis signalling in Jurkat cells.

Funded by Kompetenzverbund Strahlenforschung (KVSF), Bundesministerium für Bildung und Forschung (BMBF), Project No.: 02NUK005A and 02NUK005D

Kontakt: Unverricht-Yeboah, Marcus
Telefon:02461/615573
e-mail: m.unverricht@fz-juelich.de