Cellular Radiobiology

Genotoxicity of Iodine-123 labeled 5-Iodo-2´-deoxyuridine in comparison to high- and low-LET radiation

Marcus Unverricht-Yeboah[1], Ulrich Giesen[2], Ekkehard Pomplun[1], Ralf Kriehuber[1]

[1]Department of Safety and Radiation Protection, Forschungszentrum Jülich, D-52425 Jülich, Germany,[2]Physikalisch-Technische Bundesanstalt (PTB), Bundesallee 100, D-38116 Braunschweig, Germany
Corresponding author's email: r.kriehuber@fz-juelich.de

To determine the genotoxic effects after exposure to Iodine-123 labeled 5-Iodo-2´-deoxyuridine (I-123-UdR) in comparison to α- and γ-irradiation, micronucleus (MN) induction and γ-H2AX formation were analyzed.

Jurkat cells were either exposed to I-123-UdR for 20 h or irradiated with different doses of γ-rays (Cs-137, 0.7 Gy/min) or α-particles (Am-241, 0.032 Gy/min). Cells were assayed for MN formation employing automated image analysis (MetaSystems, Germany). The γ-H2AX foci, as a measure of DNA double-strand-breaks (dsb), were quantified by measuring the mean overall signal intensity of foci per cell using flow cytometry and by counting the number of individual foci with a fluorescence microscope.

γ-H2AX foci number per cell showed a much more pronounced increase after exposure to I-123-UdR per dose unit when compared to γ- and α-irradiation. However, the mean intensity of total foci signal per cell, as measured by flow cytometry, was very similar for exposure to I-123-UdR and α-particles. Single γ-H2AX foci induced by I-123-UdR appeared to be smaller and/or less intense stained than those after α-irradiation and resembled foci induced by γ-rays. The distribution of the cellular γ-H2AX fluorescence signals showed that the dose distribution of single cells was more heterogenous after exposure to I-123-UdR and α-particles when compared to γ-irradiation. MN induction was almost identical for all three investigated radiation qualities.

γ-H2AX foci are very efficiently induced by I-123-UdR per unit dose when compared to γ- and α-radiation, probably because almost every I-123 decay occurred within the DNA. The presumed complexity of DNA-lesions caused by DNA-associated AEE is neither reflected in size nor intensity of individual foci. The microscopic quantification of γ-H2AX foci indicates that I-123 induced dsb are less prone to be transferred into an MN. The MN induction after exposure to I-123-UdR and α-particles could be underestimated because highly damaged cells within the heterogenous exposed cell population are not adequately represented in the MN assay. As α-particle-induced foci are aligned along the track, individual foci are hard to count, we suggest that flow cytometry is a more appropriate analysis tool to quantify LET-dependent γ-H2AX foci induction.

Funded by Bundesministerium für Bildung und Forschung (BMBF), Grant No.: 02NUK005A