Genotoxicity of the Auger electron emitter I-123-iododeoxyuridine in comparison to high- and low-LET radiation

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The biological effectiveness of Auger electron emitters (AEE) is attributed to the numerous short-range electrons released during the decay of these radionuclides. Damage on cellular level depends largely on their intracellular distribution. AEE located exclusively in the cytoplasm produce low-LET type cell survival curves, whereas DNA-associated AEE cause high-LET type survival curves. To determine whether AEE induce high-LET type genotoxic effects, micronucleus induction and γ-H2AX formation were analyzed after exposure to I-123-iododeoxyuridine (I-123-UdR) in comparison to high- and low-LET radiation.

Human T-lymphoma Jurkat cells were either exposed to I-123-UdR for 20 h or irradiated with different doses of low-LET γ-rays (Cs-137, 0.7 Gy/min) or high-LET α-particles (Am-241, 0.032 Gy/min). Cells were assayed for micronucleus formation (Cytochalasin B assay) employing automated image analysis (MetaSystems, Germany). The γ-H2AX foci were quantified by measuring the mean signal intensity of γ-H2AX foci per cell using flow cytometry and by counting the number of γ-H2AX foci with a fluorescence microscope.

In contrast to γ- and α-irradiation the numbers of γ-H2AX foci per cell showed a much more pronounced increase after exposure to I-123-UdR. However, the mean intensity of γ-H2AX signals 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 appear to be smaller and/or less intense stained than those after α-irradiation and resemble γ-H2AX foci induced by γ-rays. Micronucleus induction was almost identical for all three investigated radiation qualities.

Due to the fact that most of the ionizing events of I-123-UdR occurred within the DNA, γ-H2AX foci are very efficiently induced by I-123-UdR when compared to γ- and α-radiation. Taken into account the very low dose rate of I-123-UdR exposure, the effect is even more pronounced. The presumed complexity of the DNA-lesions caused by DNA-associated AEE is not reflected in the size and the intensity of γ-H2AX foci.

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