CHROMOSOME ABERRATIONS INDUCED BY THE AUGER ELECTRON EMITTER ^{125}I

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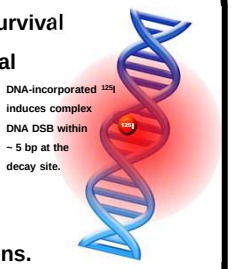
Introduction

- DNA-associated Auger electron emitters (AEE) induce cellular damage leading to high-LET type cell survival curves and possess enhanced relative biological effectiveness.
- DNA double strand breaks (DSB) induced by Iodine-125-deoxyuridine (^{125}I-UdR) decays are claimed to be very complex, thus efficiently leading to cell transformation and gene mutations.
- To elucidate the assumed genotoxic potential of DNA-associated AEE, chromatid aberrations (CA) were analyzed in ^{125}I-UdR-exposed human blood lymphocytes (PBL).

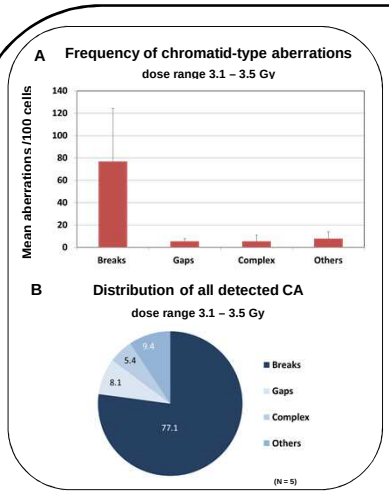


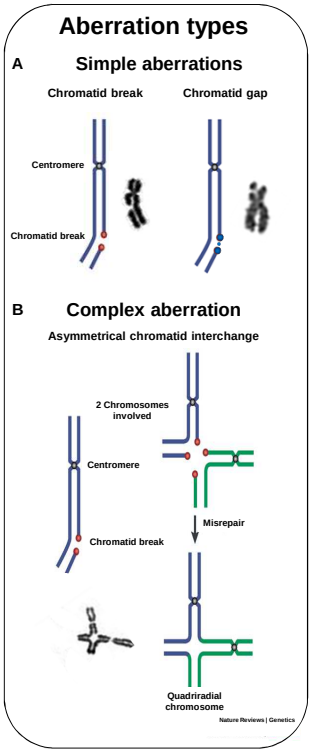
Summary

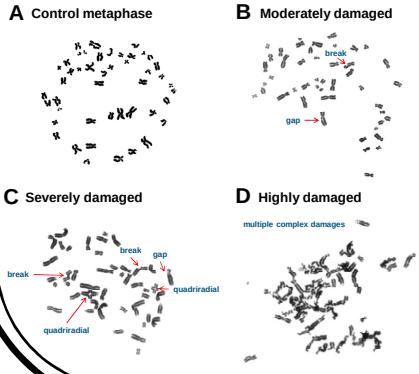
- ^{125}I-UdR has an explicit genotoxic capacity in human PBL, even at very low doses of about 0.2 Gy (29 decays/cell).
- Cells bearing a critical amount of unrepaired breaks, representing accumulated lethal damages due to high activity concentrations of ^{125}I-UdR, die due to apoptosis.
- Every fifth ^{125}I decay in the DNA gives rise to a single CA, which is in good agreement with data from Sedelnikova et al. (2002) and Yasui et al. (2004), stating that one decay gives rise to ~ 0.26 DSBs.
- **Each ^{125}I-UdR-induced DSB is converted into one CA.**

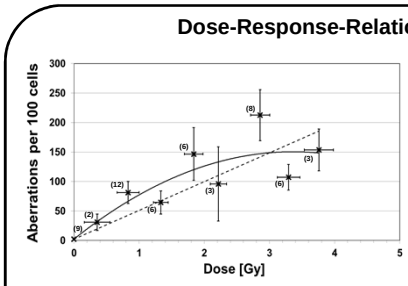
Results

Induction of chromatid aberrations in lymphocytes

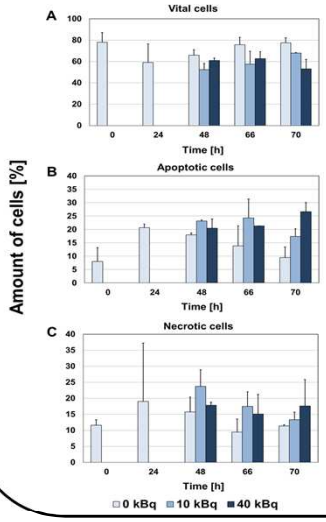








Dose-response relationship for chromatid-type aberrations induced by I-125-UdR (N= 9). The solid line represents the polynomial fit (Y= -13.11x² + 88.10x + 2.43; R^2 = 0.72) , whereas the dashed line shows the linear fit (Y = 48.72x + 2.43; R^2 = 0.58).



Percent of viable (A), apoptotic (B) and necrotic (C) cells at different time points: After isolation (0 h) of PBL, after stimulation with PHA and before incubation with I-125-UdR (24 h), after removing of I-125-UdR (48 h), immediately before addition of Colcemid (66 h), and before harvesting (70 h) of PBL. Error bars represent the SD.

Material and Methods

PBL were isolated from whole blood and stimulated with chromosome medium containing phytohaemagglutinin (PHA). After 24 h cultures were labelled with I-125-UdR for 18 h (1- 45 kBq) during the S-phase of the cell cycle. After removal of radioactive medium and washing steps, cells were cultured in stimulation medium for further 24 h. Colcemid was added 5.5 h before harvest of cells followed by fixation for aberrations at 71.5 h post-stimulation. All slides were stained with 10 % Giemsa, and at least 100 metaphases were analyzed microscopically for each activity concentration. Apoptosis was measured by Annexin V-FITC Assay using flow cytometry.

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