CHROMOSOME ABERRATIONS INDUCED BY THE AUGER EMITTER I-125

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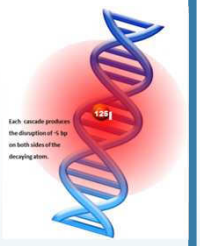
Introduction

- DNA-associated Auger-electron emitters (AEE) induce cellular damage leading to high-LET type cell survival curves and possess enhanced relative biological effectiveness.
- DNA dsb induced by Iodine-125-deoxyuridine (I-125-UdR) decays are claimed to be very complex, thus efficiently leading to cell transformation, gene mutation and induction of chromatid aberrations.



- To elucidate the assumed genotoxic potential of DNA-associated AEE, chromosomal/chromatid aberrations were analyzed in I-125-UdR-exposed human peripheral blood lymphocytes (PBL).

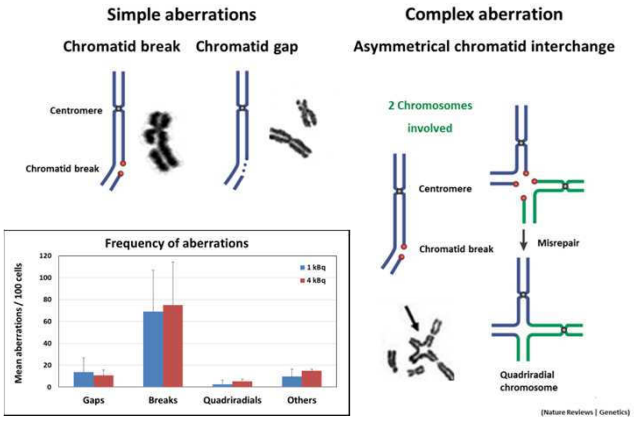
Conclusions

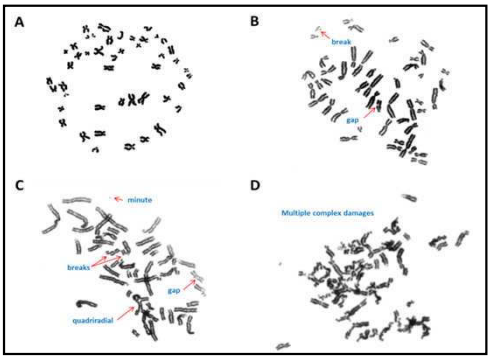
- I-125-UdR has a very strong genotoxic capacity in human PBL even at very low doses of about 0.2 Gy.
- Efficiently labeled cells displaying a prolonged cell cycle compared to moderate labeled cells, and cell death contribute substantially to the desynchronisation of the cell cycle.
- In summary, it can be concluded that every fourth intracellular I-125 decay give rise to a single chromosome aberration.
- Our data contradict former results (1 decay = 1 chromosome aberration) which overestimate the biological effectiveness of the AEE I-125.

Results

Induction of Chromatid aberrations in Lymphocytes

Aberration types

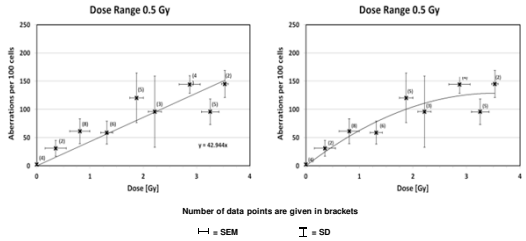




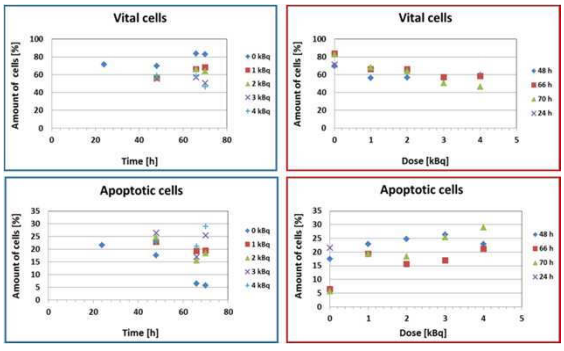
A: Control metaphase
B: Moderately damaged metaphase
C: Severely damaged metaphase
D: Highly damaged metaphase

Dose-Response-Relationship

Linear or polynomial?



Apoptosis



Materials and Methods

PBL were isolated from whole blood and stimulated with chromosome medium containing phytohaemagglutinin (PHA). After 24 h cultures were labeled with I-125-UdR for 18 h (0.25-4.5 kBq/ml) during the S-phase of the cell cycle. After removal of radioactive medium and washing steps, cells were re-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 100 metaphases were analyzed microscopically for each dose point.

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