Characterization of cell cycle perturbances after exposure to I-123-iododeoxyuridine

Marcus Unverricht-Yeboah, Dominik Oskamp, Ralf Kriehuber

Department of Safety and Radiation Protection, Radiation Biology Group,
Forschungszentrum Jülich, Jülich, Germany

Introduction: Due to the numerous short-range electrons ejected during a single decay of an Auger electron emitter (AEE), the biological effectiveness of AEE depends strongly on intracellular location. DNA-associated AEE possess the highest biological effectiveness per decay and are presumed to cause complex DNA lesions and cell cycle perturbances. The main goal of the study was to determine the average number of decay per cell necessary to induce a pronounced G2/M-arrest in human T-lymphoma Jurkat cells.
Material & Methods: Synchronized Jurkat cells were exposed to I-123-iododeoxyuridine (I-123-UdR, 1-50 kBq/ml) for 20 h and co-labeled with 5-ethynyl-2'-deoxyuridine (EdU). Cell cycle was subsequently analyzed by flowcytometry (FACSCanto II, FACSDiva software, BD). General cellular uptake and DNA-incorporation of I-123-UdR in isolated DNA (DNeasy Blood & Tissue Kit; QIAGEN) was determined by gamma-counting (Perkin Elmer).
Results: The percentage of G2/M-cells which are labeled with EdU increased 20 h after exposure to I-123-UdR/EdU from 26% in the control to 57%, 66% and 63% at 111, 417 and 3255 accumulated decays per cell, respectively. Simultaneously, the percentages of post-mitotic G1-cells which are fully labeled with EdU decreased from 38% in the control to 10%, 1% and 3% at 111, 417 and 3255 accumulated decays per cell, respectively. Approximately 93% of the cells were labeled with I-123-UdR/EdU after 20 h of exposure whilst ~ 90% of the I-123-UdR activity was located in the DNA.
Conclusions: On average one decay every ~180 seconds of I-123 occurring in the genome of a Jurkat cell induces a massive G2/M-arrest. This coincides very well with observations in I-125-UdR exposed SCL-II cells, showing massive and persistent G2/M-arrest at similar decay rates. Decay rates as low as one decay every 12 minutes per genome induce massive but transient G2/M-arrest suggesting different damage levels for induction and escape of the G2/M arrest in human cells.

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