Discrimination of Radiotoxic and Chemotoxic Effects of Uranium on Mouse Embryo Fibroblasts

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Uranium (U) is a natural radioactive heavy metal used in the nuclear industry, in different forms with different isotopic compositions (natural, depleted or enriched in 235U) and solubilities. Uranium internal exposure is a major risk for the nuclear workers. Uranium uptake can occur accidentally after inhalation, ingestion, or absorption through intact or injured skin. Due to these physical and chemical properties, U toxicity results from both chemical and radiological toxicity. The aim of this work was to find biological markers of internal contamination able to discriminate between chemotoxic and radiotoxic effects of U.

The study was carried out in vitro on mouse C3H10T1/2 embryo fibroblasts contaminated either with 0.3% depleted uranium in isotope 235U (DU) or with 12% enriched uranium in isotope 235U (EU). In our experimental conditions, EU has a specific activity 20 times higher than DU. Fibroblasts were grown in culture medium containing various concentrations of DU or EU (0μM, 5μM, 50μM, 500μM and 1000μM). Genotoxic effects of both DU and EU were assessed with the cytokinesis-block micronucleus assay in combination with the fluorescent in situ hybridization of centromeric DNA probes. Binucleated cells with one micronucleus (BN-1MN), binucleated cells with centromere-negative micronucleus (BN-MNC-), mononucleated cells with one MN (Mono-1MN) and nucleoplasmic bridges (NPBs) were scored. Moreover ?-H2AX immunostaining was achieved to detect DNA double-strand breaks (DSB).

The percentage of BN-1MN increased with both DU and EU concentration. The percentage of BN-MNC- was significantly higher when cells were contaminated with EU compared to DU for all concentrations (for example, 1,2% and 0,4% for a 50μM EU and DU concentration, respectively), this result confirms clastogen effect of EU. The frequency of NPBs increased with the U concentration. However EU induces more NPBs than DU (for example, 1,35% and 0,25% for a 50μM EU or DU concentration, respectively). In addition, the percentage of Mono-1MN is higher after a contamination with EU compared to DU (for example, 5,5% and 4,5% for a 50μM EU and DU concentration, respectively). The percentage of cells with DSB increased with U concentration.

As a conclusion, our experiments show that BN-1MN and DSB seem to be a marker of U genotoxicity (chemical + radiological). The BN-MNC-, NPBs, and to a lesser extent Mono-1MN seem to be a marker of a radiotoxic effect. A microdosimetric calculation is in process and will consolidate these results.

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