Genetic Instability induced by tritium contamination

Y. Saintigny[a,*], F. Di Giacomo[a], D. Laurent[a], J.-B. Lahaye[a], B. Lopez[a] and P.-H. Roméo[a]

[a]*Commissariat à l'Energie Atomique, Institut de Radiobiologie Cellulaire et Moléculaire, 92265 Fontenay aux Roses, France*

Because of it's low disintegration energy, tritium biological effects cannot come from external exposure but from integration of organically bound (OBT) tritium into tissue. This results in an *in situ* chronic auto-irradiation. Consequently, radioactive compounds incorporated in tissues can have biological effects resulting from energy deposition in subcellular compartments. We addressed the genetic consequences of ^{3}H- or ^{14}C-thymidine incorporation into mammalian DNA on cell survival, DNA double-strand breaks (DSB), cell cycle, mutagenesis and homologous recombination (HR).

While γ-rays induced measurable DNA double strand breaks repair only at toxic doses and high dose rate, sublethal contamination with ^{3}H-thymidine strongly induced DNA double strand breaks repair. Moreover, we found oxidative stress induced by low doses of ^{3}H-thymidine responsible for mutagenesis induction.

We then analyzed genetic instability induced by tritium contamination of haematopoietic stem cells. Hematopoietic stem cells are stem cells that give rise to all the blood cell types including myeloid (monocytes and macrophages, neutrophils, basophils, eosinophils, erythrocytes, megakaryocytes/platelets, dendritic cells), and lymphoid lineages (T-cells, B-cells, NK-cells). The hematopoietic tissue contains cells with long-term and short-term regeneration capacities and committed multipotent, oligopotent, and unipotent progenitors. One final goal is to compare the impact of an OBT, ^{3}H-thymidine which target tritium to the DNA, with triated water. We evaluate in our animal models the haematopoietic consequences of contamination by tritium doses consistent with human accidental exposition.

Our results emphasize that the biological impact of tritium is conversely proportional to the isotope emission energy but correlate to the energy transferred to the nucleus. Taking together, the data presented here show that cell contamination with non-toxic doses of tritium may be hazardous for genetic stability. Thus, the remarkable survival of these contaminated cells associated to genetics alterations may increase the risk of: 1 - transmission of genetic modifications to the next generation and 2 - increase the risk of cancer (cancer cell should accumulated mutations and be viable to generate a tumour). Our work emphasizes the strong differences between an external ionizing radiation exposure and an internal radioactive contamination on biological consequences.