

Radiosensitivity of male and female gametes: a decisive factor in radioinduced reprotoxicity?

Position Description - The environmental consequences of chronic exposure to low doses of radioactivity are still poorly understood. However, the impact of exposure to ionizing radiation on the organisms' reproduction, an essential biological function for population maintenance, has been demonstrated on several invertebrate species (Gilbin et al., 2008, Hertel-Aas et al. 2007, Knowles and Greenwood 1994). The results obtained in our laboratory on the *C. elegans* hermaphrodite roundworm show that chronic irradiation induces a reduction in the number of eggs from 3.3Gy (50mGy.h⁻¹) (IRSN theses C. Dubois, 2017, A. Buisset -Goussen, 2014) and effects on germ cells (spermatheca and oocyte precursor). Parallely, several molecular processes involved in development (including germline and embryo development) and reproduction are modulated from 0.5Gy (7.5mGy.h⁻¹). However, additional data are needed to understand, if any, the relationship between molecular regulation and reprotoxicity observed at 3.3Gy (50mGy.h⁻¹). This PhD project aims to analyze molecular mechanisms involved in germline radiosensitivity previously observed after chronic irradiation, and, to identify early molecular markers of radioinduced effects.

Particularly, the PhD project will focus on the radiosensitivity of the *C. elegans* male and female gametes after chronic exposure to several dose rates of gamma rays (0.1 - 100 mGy.h⁻¹), combined with the analysis of reproduction endpoints (number of offspring and hatching rate). The first part of the project deals with the study of the gamma ray effects on male and female gametes using i) morphological observations (via optical, confocal and electronic transmission microscopy) and ii) a molecular approach (RTqPCR and western blot for gene and protein expression analyses, respectively). The contribution of the most relevant genes or proteins identified, in the radioinduced reprotoxic processes, will be assessed using functional non-destructive analyses (GFP transgenes and RNAi methodology in collaboration with S. Galas, Montpellier University).

Finally, the most relevant and sensitive markers will be tested in response to environmental dose rates to determine their response threshold.

In fine, this project will enable to identify and validate a set of early and sensitive markers of effect. This would increase the knowledge on the mechanisms of toxic action of ionizing radiation, integrating both the response of proteins and genes, and working at different levels of organization, e.g. molecular, cellular and physiological (reproduction).

References:

Gilbin et al., Alonzo, F., Garnier-Laplace, J., Effects of chronic external gamma irradiation on growth and reproductive success of *Daphnia magna*. (2008) *Journal of Environmental Radioactivity* 99, 134-145

Hertel-Aas T., Oughton, D.H., Jaworska, A., Bjerke, H., Salbu, B., Brunborg, G. Effects of Chronic Gamma Irradiation on Reproduction in the Earthworm *Eisenia fetida* (Oligochaeta). (2007) *Radiation Research* 168, 515-526

Knowles and Greenwood. The effects of chronic irradiation on the reproductive performance of *Ophryotrocha diadema* (polychaeta, dorvilleidae), (1994) *Marine Environmental Research* 38, 207-224

Candidate experience (training, skills, restrictions): Biochemistry, physiology, cell and molecular biology; better if experience in genomic or proteomic analysis.

The candidate should be motivated by studies of biochemistry, molecular biology and should be interested in radiobiology.

Contacts:

FRELON Sandrine – 00 33 4 42 19 94 71 - sandrine.frelon@irsn.fr

LECOMTE-PRADINES Catherine – 00 33 4 42 19 96 64 - catherine.lecomte-pradines@irsn.fr

Places of work:

Main place: IRSN Cadarache - 13115 St. Paul lez Durance - France. Some movements will be expected for the analysis of markers not monitored in the laboratory.

Second experimental site (50% Occitanie grant is obtained) Faculty of Pharmaceutical and Biological Sciences - Faculty of Pharmacy - Laboratory of Toxicology - IBMM CNRS UMR 5247 - University of Montpellier

Field of expertise: Environment, Biology, Chemistry