ALLIANCE

Biomarkers of exposure and effects in living organisms, as operational outcomes of a mechanistic understanding of intra- and inter-species variation of radiosensitivity under chronic low dose exposure situations

Challenge

The issue of biological effects of low doses of ionising radiation (environmentally relevant) is still of major concern for both human and environmental radiation protection, as highlighted after the Fukushima accident, especially with the aim of quantifying (and reducing if needed) the magnitude of risk to individuals (human and endangered species) and populations (human and biota) health at such low doses/dose rates. The present moving of ICRP towards an integrated system of protection of both human and the environment urges to complement the knowledge and associated tools to be able to face the wide biodiversity and biological responses to radiation (from molecules to ecosystems) in a credible and robust way. A key for success is to explore intra- and inter-species causes of radiosensitivity variation. This requires reliable quantification of radiosensitivity *in vitro* and ideally also *in vivo*. This will help to screen out candidates for biomarkers of exposure and effects to be used as early warning tools after *ad hoc* validation. Identification of such biomarkers will be relevant to radiation protection.

Scope

Proposals will contribute to the identification of the principal mechanisms of radiation induced effects at the molecular level and their propagation up to the individual level, including consequences for physiological functions (e.g. reproduction) with potential population level impact. This will be evidenced by evaluating suitable biomarkers of exposure and biomarkers of effects. A comparative and "lab-field-modelling"-combined approach for a number of exposure conditions and/or a number of species will enhance the understanding of the toxicity profiles as a response to exposure conditions. When relevant, dose-response relationships will be established making the best use of "omics" analytical methods, possibly combined with the use of a system biology approach, to provide evidence of linkage between metabolic pathways and associated biomarkers of effects. Research could expand to the use of genetic and epigenetic changes as potential biomarkers by implementing innovative approaches to test changes in the genome (*e.g.,* mutation rates and types) and the epigenome (*e.g.,* epigenetic tags) through generations. The research will need accurate biodistribution and accurate dosimetry as a prerequisite for any robust dose-response relationships. The proposed research should provide the basis for the development of biologically-based extrapolation models which are the key to tackle the wide species diversity and would be useful for risk assessors by helping reducing uncertainty in predictions of exposure and/or effects (and ultimately risk). The implications of the research results on the perception and communication of risks from low doses of ionising radiation should be evaluated and addressed.

The topic is relevant for any exposure situations where flora and fauna, and humans, may be chronically exposed to environmentally relevant levels of radionuclides from various sources

(e.g., radiocontaminated territories after a major accident, NORM-sites, legacy sites) in that biomarkers potentially also useful in health surveillance, are looked for.

Expected impact

The study will contribute to answer an issue of concern which is the long-term biological effects of low radiation doses and alleviate part of the existing controversy.

The identification of robust biomarkers of exposure and effect and of radiation sensitivity and associated acquired knowledge will highlight and feed the various extrapolations needed when assessing radiological risk to humans or non-human species, and will provide robustness in decision making. Outcomes will support emerging policy in the field of radioprotection of the environment, mentioned in the EURATOM Basic Safety Standards through the statement that "*While the state of the environment can impact long-term human health, this calls for a policy protecting the environment against the harmful effects of ionising radiation. For the purpose of long-term human health protection, environmental criteria based on internationally recognised scientific data (….) should be taken into account*".

By encouraging openness to other disciplines and innovative hypothesis-driven approaches to understand underlying mechanisms, this research topic will contribute to increasing acceptability of the radiation protection system and aid in risk prediction, management and communication.

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