## February 19, 2019 - Prof. Dr. Nicolas Foray

### Radiobiology Group, French Institute of Health and Medical Research, Lyon, France

### “The nucleoshuttling of the ATM protein: applications to defence, health and environment“

Dr. Foray’s group focuses on the understanding of biological consequences of high dose (used for radiotherapy) and lose dose (used for radiodiagnostic, industry, space) ionizing radiations. They particularly study the impact of individual factors in DNA damage repair signaling. Therefore, the radiobiology group is now an expert in human genotoxicology caused by every DNA-damaging agent, including metals and pesticides. The main goal of this group is to develop predictive means to specific complications to radiotherapy, and to evaluate the risk of radioinduced cancers.

In his talk he focused on the ATM kinase, which is a major stress response factor involved in the DNA double-strand breaks (DSB) repair and signaling. Ionizing radiation causes the monomerization of the cytoplasmic ATM dimers and the diffusion of ATM monomers in the nucleus. Once in nucleus, the ATM monomers phosphorylate the variant H2AX histone protein, which triggers the DSB recognition and their repair via non-homologous end-joining (NHEJ) pathway. Delay in the ATM nucleoshuttling may cause incomplete DSB repair and radiosensitivity. The ATM nucleoshuttling model is at the basis of a classification of human radiosensitivity in three groups depending simply on the rate of the ATM nucleoshuttling after 2 Gy. Furthermore, this model also provides a relevant biological interpretation of the famous linear-quadratic formula linking cell survival and radiation dose. The low-dose specific phenomena like the hyper-radiosensitivity to low dose, the adaptive response and hormesis can also be explained by this model. This model is also at the basis of new chemical approaches of radiation protection relevant to defence and space. More recently, the relationship between the lineal energy transfer and the relative biological efficiency was also shown to be predicted by this model. Lastly, some implications of the ATM protein in response to other DNA breaking agents (pesticides, metals) suggests a high potential of this model to understand the toxicity and carcinogenicity risks in the frame of environmental and occupational exposures.

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