Post-Doctoral fellowship in cell and tissue scale alpha dosimetry

Radiopharmaceutical dosimetry group – INSERM U892, Nantes, France

Targeted radionuclide therapy taking advantage of alpha-emitters appears to be especially suitable for eradicating minimal residual disease, which represents the major cause for recurrence in cancer patients. A proposal entitled "Targeting Alpha-particle emitting Radionuclides to Cure Cancer" (TARCC) was recently approved by the EC. Within this proposal, our group is opening a post-doctoral fellowship position for 2 years.

The objective of the fellowship is to develop computational models to estimate radiation doses delivered by alpha emitters to tumours and healthy organs in order to establish correlations between therapeutic effectiveness, toxicity and dosimetry. This will require:

- Developing a microdosimetric approach to give account of energy delivery for cell experiments
- Developing an animal dosimetric model adapted to mice and rats for preclinal experiments
- Establishing a detailed tissue dosimetry model to study the dose-effect relationship for major risk organs (bone marrow, kidney, liver)

At the cellular level, dose calculations may seem easy, since homogeneous water equivalent medium may be assumed. However, the mean absorbed dose is probably not the relevant parameter to use, if statistical fluctuations of alpha particle irradiation should be considered. Monte-Carlo radiation transport codes for small-scale alpha dosimetry will be compared. Microdosimetric evaluations at the cellular level will be performed for the chosen radionuclides on isolated cells and heterogeneous cell clusters with variable radii and activity distributions. The relevance of microdosimetric modelling within the context of complex cell architecture will be studied.

Radiation transport modelling in rodents is complex since heterogeneous media have to be considered (soft, bone, lung and air equivalent tissues). This consideration often justifies the implementation of a refined Monte-Carlo based approach. We recently proposed a murine dosimetric model based on the 3D reconstruction of sequential slices obtained from a frozen nude mouse specimen. Monte-Carlo calculations were carried out for 16 beta-emitting radionuclides of interest. However, alpha emitters were not considered in the model. This murine dosimetric model will therefore be expanded to consider the alpha emitting radionuclides studied in TARCC. A similar approach will be used to define a rat model in order to give a dosimetric model for rat experiments conducted within other work packages. The specific configuration of tumour will be considered via small-scale imaging.

Detailed radionuclide distribution data will be obtained from autoradiography of tissue sections from animal models studied within the project by the different partners. Histological tissue samples will be used to geometrically describe the risk organs on a cellular level (tumour, risk organs, e.g. bone marrow, the kidneys and the liver). Critical target cells (e.g. stem cells in the bone marrow and proximal tubular cells and glomeruli in the kidney) will be defined. 3D reconstructions will provide the basis for specific dosimetric calculation using Monte-Carlo codes. Detailed dosimetric modelling will be done for the organs at risk: bone marrow, kidney, liver, taking into consideration the heterogeneous radionuclide distribution.

The applicant should have a background in physics and dosimetry, a good knowledge of scientific programming and preferably a previous experience in Monte-Carlo modelling.

Candidates should send a letter of purpose and a CV to:

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