Title of the thesis	Computer Simulation and Experiments of Radio-Induced Cell Senescence
Acronym	SENESIMEX
Reference number	037

Hosting institution	**Employer**
Université de Lille Website: https://www.univ-lille.fr/home/	CNRS Website: http://www.dr18.cnrs.fr/
Hosting research unit 1	**Hosting research unit 2**
Name: Institut d'Electronique Microelectronique et Nanotechnologies Acronym: IEMN Identification number: UMR 8520 Address: Université de Lille Campus Cité Scientifique Avenue Henri Poincaré - CS 60069 59 652 Villeneuve d'Ascq Cedex, France Website: https://www.iemn.fr/	Name: Hétérogénéité, Plasticité et Résistance aux Thérapies des Cancers Acronym: CANTHER Identification number: UMR 9020 CNRS – 1277 Inserm Address: Institut de Biologie de Lille 1 Rue du Professeur Calmette CS 50447 59021 Lille Website: www.canther.fr
Principal supervisor	**Co-supervisor**
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Thesis information

Keywords	Ionizing radiations; DNA damage; Cell senescence; Multicellular models; Metabolic and repair pathway simulations
Abstract	Medical use of radiations for treating cancers and other diseases rests on a vast amount of empirical knowledge, accumulated over the past century. However, rather little attention is yet paid to the biological specificity of the individual cell response to ionizing radiation. Computer modelling of DNA damage and repair aims to give quantifiable depictions of the DNA damage response following therapeutic irradiation. Notably, a severe complication of radiation therapy is identified in the development of secondary sarcomas around the irradiated field, a very rare, difficult to predict, but often lethal pathology. According to a number of experimental indications, accumulated by our groups and others, it is supposed that normal cells around the treated primary cancer might be affected by scattered ionizing radiation, which diffuse in uncontrolled way from the irradiated main volume, and that the peculiar type of damage accumulated in this way could induce these cells into senescence; upon exiting from this state at much later times, defects latently accumulated in some such cells could evolve the secondary sarcoma. We propose to develop a complete computer model of the cell treatment, starting from the detailed description of the irradiation source by Monte Carlo dosimetry and micro-dosimetry; include a multicellular, evolutive description of the irradiated tissue; radiation damage and repair will be treated in full details at the scale of each single cell, including competitive pathways for different types of DNA and cell damage; dedicated high-resolution biology experiments will define ranges of values for fitting the model parameters, and provide benchmarks to test and improve the computer simulations.

	The candidate PhD student will work at the mathematical and computer developments, and take part in the biology experiments, in our two laboratories of IEMN (UMR8520) and CanTher (UMR9020 CNRS – 1277 Inserm) in Lille. Part of the model development will take place in the Cancer Sciences Division at the University of Manchester, UK. The resulting computational/experimental protocol would represent an important step forward into the domain of high-precision, personalized healthcare, by defining a general approach by which the detailed biological effects of different types of cell damage could be predicted by mathematical modelling.
Expected profile of the candidate	The successful PhD candidate should have a background in physics, chemistry, mathematical modelling, and a basic knowledge of biophysics; candidates with a more biology-oriented background will be considered, provided they demonstrate a solid competence in applied mathematics. Computer programming skills (Fortran90, C, C++ , Python, MatLab) and fluency in Unix/Linux OS are highly desirable.
Application procedure & eligibility criteria	The application procedure is detailed on the programme PEARL website www.pearl-phd-lille.eu. The funding is managed by the I-SITE ULNE foundation which is a partnership foundation between the University of Lille, Engineering schools, research organisms, the Institut Pasteur de Lille and the University hospital. The application file will have to be submitted before March 31, 2021 (10:00 AM Paris Time) and emailed to the following address : international@isite-ulne.fr.
Net salary and Lump Sum	A net salary of about €1,600 + €530 per month to cover mobility, travel and family costs.