PhD position available at the Institut de Biologie Structurale in Grenoble

Laboratory: Institut de Biologie Structurale (IBS) in Grenoble, France - Integrated Imaging of Stress Response (I2SR) Group / Genome Organisation & Maintenance (GenOM) Team.
Web site: https://www.ibs.fr/research/research-groups/integrated-imaging-of-stress-response-group/genome-organisation-maintenance-genom-team/
PhD supervisor: Dr. Joanna Timmins (Head of GenOM team)
PhD co-supervisor: Dr. Jean-Luc Ravanat from CEA Grenoble (IRIG Institute / SyMMES group)
Funding: 3-year position starting October 1st 2021 (CEA grant)
Doctoral school: Chemistry & Life Sciences Doctoral School of the University Grenoble Alps

Keywords: DNA repair; Protein-protein interactions; Radiobiology; Clustered lesions; *Deinococcus radiodurans*; Biochemistry; Tandem mass spectrometry.

Project title: Deciphering the crosstalk between the base excision and nucleotide excision repair pathways in bacteria.

Project overview: Genomic DNA is subject to numerous attacks leading to the accumulation of DNA damage, which, if left unrepaired, generates mutations and genomic instability that ultimately threaten cell survival. In all kingdoms of life, organisms have developed multiple elaborate DNA repair pathways with distinct substrate specificities in order to preserve the integrity of their genomes. An emerging hypothesis is that efficient genome maintenance may be achieved by extensive crosstalk between different DNA repair pathways and notably between the base excision (BER) and nucleotide excision repair (NER) pathways, which together are responsible for eradicating bulky and non-bulky lesions occurring at the nucleobase level from the genome. The objective of this project is to evaluate the possible synergy between BER and NER in the repair of DNA lesions in the radiation resistant bacterium, *Deinococcus radiodurans*. The work will focus in particular on the repair of complex DNA lesions resulting from ionising irradiation. These include clustered and tandem lesions, that are indeed poorly repaired by BER or NER separately, and may require the synergistic intervention of both repair pathways. Our extensive work in recent years on DNA repair proteins from *Deinococcus radiodurans* places us in a unique position to initiate such a study. We have at hand all Uvr proteins involved in NER, 6 DNA glycosylases and several other BER enzymes, such as ligase or AP endonuclease (ExoIII) through a collaboration with Dr. Elin Moe (ITQB, Lisbon, Portugal), and have developed functional and efficient *in vitro* DNA repair assays.

Project objectives: (i) Explore possible protein-protein interactions between NER and BER factors, (ii) compare the repair kinetics of different DNA lesions by NER and BER proteins alone and then in combination to detect a possible synergy between the two pathways, and (iii) evaluate at the cellular level the involvement of each of these two pathways in the repair of radiation-induced lesions in collaboration with Jean-Luc Ravanat (IRIG/SyMMES).

Methodology: Expression and purification of DNA repair enzymes; *In vitro* DNA repair assays (basic biochemistry, electrophoresis etc.); Microbiology; Extraction of genomic DNA; Quantification of DNA lesions by HPLC-MS-MS.

Candidate profile: The candidates should hold a Master's degree in Biochemistry or Biophysics, with a good level in Chemistry, should possess excellent academic records and ideally should have a basic training in Microbiology. The candidates should be highly motivated and have experience in recombinant protein expression and protein chromatography techniques. Additional experience in analytical chemistry (in particular HPLC-MS) would be a bonus.

Application: To apply, please send your curriculum vitae, along with your Master degree transcripts (including grades and ranking), a letter of motivation and two recommendation letters to Joanna Timmins (Joanna.timmins@ibs.fr) by April 30th 2021.