



A Funded PhD position is available for studying intrinsically disordered proteins by NMR at the Département de Chimie Moléculaire (DCM, Grenoble), in collaboration with Institut de Biologie Structurale (IBS, Grenoble).

The thesis will start on the 1st of October 2023.

PhD context and objectives:

The goal of the project is to determine the mechanism of interaction between hAPE1, which is a key player in the DNA repair process, and the hPrP prion protein. hAPE1 acts as a master regulator of cellular responses to oxidative stress and contributes to the maintenance of genome stability. The human prion protein is mainly known to be involved in neurodegenerative diseases. Both proteins possess an intrinsically disordered region (IDR) at their N-terminal extremity. It has been shown that under genotoxic stress, hPrP stimulates hAPE1 repair activity, thus playing a protective role against genotoxic agents, and that the IDRs are crucial for this stimulation. However, how the two proteins interact to stimulate the hAPE1 repair activity remains elusive.

NMR spectroscopy will be used to obtain a structural model of the hAPE1/hPrP complex and to determine the molecular basis for stimulation of hAPE1 by hPrP. In addition, biophysical techniques such as Surface Plasmon Resonance (SPR) and Microscale Thermophoresis (MST) will be performed to obtain complementary thermodynamic insight. More generally, understanding the structural details of the hAPE1/hPrP interaction would enable the design of therapeutics to fight the resistance of neuroblastoma to antitumour therapy.

The PhD student will express and purify the proteins, characterize the proteins by NMR and determine the mutually interacting regions in hAPE1 and hPrP, perform biophysical experiments (SPR and MST) of the protein/protein complex and solve its structure.

Host laboratory & research environment

The project will take place in Grenoble, at the Département de Chimie Moléculaire (DCM), within the I2BM team (<https://dcm.univ-grenoble-alpes.fr/research/i2bm-team>) under the supervision of Dr. Muriel Jourdan involved in the study of DNA repair processes, in collaboration with the team of Dr. Malene R. Jensen at the Institute of Structural Biology (IBS) (www.jensen-nmr.fr) expert in NMR of intrinsically disordered proteins.

The selected candidate is funded by the IRGA-Université Grenoble Alpes grant, in the framework of innovative project initiatives.

He/she will benefit from all the equipment available at the DCM for cell cultures and protein expression and purification. The DCM is also part of the ICMG (Institut de Chimie Moléculaire de Grenoble) providing access to biophysical platforms (<https://icmg.univ-grenoble-alpes.fr/>). The IBS houses six high-field NMR spectrometers (3 x 600, 700, 850 and 950 MHz). Access is available to biochemistry facilities and to a number of state-of-the-art research platforms through the ISBG (www.isbg.fr).

Candidate background:

Applicants should have a master degree in chemistry or biochemistry or structural biology with an interest in the study of proteins and biophysics. Practical knowledge in protein expression and purification is recommended. Knowledge in NMR spectroscopy would be appreciated.

Application:

Interested and motivated candidates can apply by email to muriel.jourdan@univ-grenoble-alpes.fr before the 26th of June. Please provide your CV, a motivation letter, copies of M1 and M2 marks and ranking, as well as names and contacts of two professional references.