

Position: Postdoctoral Fellow in Integrated Structural Biology in the Viral Infection and Cancer (VIC) Group at the Institut de Biologie Structurale (IBS) under the supervision of Dr. Joanna Timmins

Title: Study of the hNTH1/YB1 Complex: a new anti-cancer drug target

Project summary: The most prevalent non-surgical cancer treatments function by generating DNA damage. Such therapies generate dose-limiting toxicities in normal tissues, but are often efficacious since cancer cells often display impaired DNA repair systems and proliferate more rapidly than most normal cells. Nonetheless, in such cells, functional DNA repair pathways provide a common mechanism for cancer-therapy resistance. The development of resistance to cytotoxic therapy that was initially effective is extremely common and is a major clinical issue. Drugs targeting repair pathways thus exhibit a promising potential as new anti-cancer agents. This project aims at characterising a complex formed between a human DNA repair enzyme (the DNA glycosylase hNTH1) and a transcription factor (Y-box binding protein, YB1) that is implicated in resistance of tumour cells to the chemotherapeutic drug, cisplatin. More specifically, our objectives are to: (i) determine the structures of hNTH1 alone and in complex with either lesion-containing DNA or YB1, (ii) characterise the N-terminal extension of hNTH1 and its role in regulating DNA repair activity and interaction with YB1 and (iii) gain further structural information regarding YB1. Structural information will be obtained using a combination of X-ray crystallography, small-angle X-ray scattering and NMR. The project is funded by the French Labex GRAL and involves the collaboration between three partners: the teams of J. Timmins and M. Blackledge at IBS and the CMBA screening platform at CEA/BIG Grenoble.

Laboratory: The IBS is located on the European Photon Campus (alongside EMBL, ILL and ESRF) in Grenoble, France. The IBS performs interdisciplinary research at the interface of biology, physics and chemistry and benefits of a privileged access to the EMBL High Throughput Crystallization (HTX) platform to explore crystallization conditions and to the Synchrotron Radiation source, ESRF, to collect diffraction data.

Qualification requirements: The applicant should hold a PhD degree in Structural Biology or in Biophysics obtained in 2015, 2016 or 2017. Prior experience with X-ray crystallography and/or NMR would be a strong asset.

Terms of employment: 18 months contract with the Université Grenoble Alpes. Gross salary ~2500€/month.

Applications: Please send a detailed CV (including degrees, grades, ranks and other completed courses, work experience and a list of publications), a cover letter and two recommendation letters (one of which should be from your PhD supervisor) to: Joanna.timmins@ibs.fr. Deadline for sending applications: 31st July 2017.

Expected start date: October/November 2017

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