Grenoble Alliance for Integrated Structural & Cell Biology

GRAL MASTER 2 RESEARCH SCHOLARSHIP - Program 2018 - 2019

CALL FOR RESEARCH INTERNSHIP TOPICS

Deadline for proposal submission: **DECEMBER 15th, 2017**

Please fill in the template in English and send it back to manel.boumegoura@cea.fr

MASTER II University programs compatible with the scholarship program:

Master in biology: *Specialty biochemistry and structural Biology / Specialty cell Biology, Physiology and development / Specialty neurobiology and neurosciences / Specialty immunology, microbiology, infectiology/ Master Biology, Ecology, Environment*

Master in physics: *Specialty « Complex matter, living matter » (MCMV)*

Master in Nanosciences, nanotechnologies: ***S****pecialty Nanochemistry-Nano-objects / Specialty Nanobiology-Nanobiotechnology / Specialty Nanophysics – Nanostructures*

INTERNSHIP PROPOSAL

Institute and Group: IBS group VRM

Supervisor: Bourhis Jean-Marie **Phone: 044257**

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Research project title:

Structure-Function studies of the orthoreovirus de novo protein Sigma One S

5 Keywords to describe the project:

Structure, Virus, host-cell interaction, Cell cycle, *de novo* protein

Description of the project (aims, experimental techniques, recommended background): 10 to 15 lines:

The aim is to determine the 3D structure of the *de novo* protein sigma 1s of mammalian orthoreovirus. In order to acquire novel function, viruses create genes *de novo,* mainly by overprinting a new reading frame onto an existing (‘‘ancestral’’) frame. So far, few *de novo* proteins have been described meaning that their characterizations are very challenging. Sigma 1s has been shown to be one of these *de novo* proteins and is involved in the host cell cycle regulation upon infection by Mammalian orthoreoviruses. These latter are non-enveloped, icosahedral viruses that contain 10 segments of double-stranded RNA (dsRNA). Although infection in human can be associated with mild respiratory and enteric symptoms, the mammalian orthoreovirus have been recognized as an anticancer agent (more than 30 viruses are in clinical trials). Sigma 1s is known to block the cell cycle and therefore could be a key player in the oncolytic properties of Mammalian orthoreoviruses. The candidate will have to express, purify and crystalize Sigma 1s in order to solve the structure by X-Ray crystallography. As, there is no homologue

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in the Protein Data Bank, the high-resolution structure of sigma 1s could lead to a new fold and highlight the evolutionary origin of the protein.

Justification that the internship's subject fits with the general theme of GRAL (3 lines):

Structural characterisation will have an impact on the understanding of the evolution of these *de novo* proteins and will be the starting point to the identification host cell partners hat will explain the oncolytic properties of orthoreoviruses. Hence, the project is conceived as an integrated study from the atomic structure to the roles of the protein in cell arrest cycle.

Relevant publications of the team

1. Ensemble Structure of the Highly Flexible Complex Formed between Vesicular Stomatitis Virus Unassembled Nucleoprotein and its Phosphoprotein Chaperone.
   Yabukarski F, Leyrat C, Martinez N, Communie G, Ivanov I, Ribeiro EA Jr, Buisson M, Gerard FC, **Bourhis JM**, Jensen MR, Bernadó P, Blackledge M, Jamin M.
   J Mol Biol. **2016**
2. Structure of Nipah virus unassembled nucleoprotein in complex with its viral chaperone.
   Yabukarski F, Lawrence P, Tarbouriech N, **Bourhis JM**, Delaforge E, Jensen MR, Ruigrok RW, Blackledge M, Volchkov V, Jamin M.
   Nat Struct Mol Biol. **2014**
3. Procollagen C-proteinase enhancer grasps the stalk of the C-propeptide trimer to boost collagen precursor maturation.
   Bourhis JM, Vadon-Le Goff S, Afrache H, Mariano N, Kronenberg D, Thielens N, Moali C, Hulmes DJ.
   Proc Natl Acad Sci. **2013**
4. Production and crystallization of the C-propeptide trimer from human procollagen III.
   Bourhis JM, Mariano N, Zhao Y, Walter TS, El Omari K, Delolme F, Moali C, Hulmes DJ, Aghajari N.
   Acta Crystallogr Sect F Struct Biol Cryst Commun. **2012**
5. Structural basis of fibrillar collagen trimerization and related genetic disorders.
   Bourhis JM, Mariano N, Zhao Y, Harlos K, Exposito JY, Jones EY, Moali C, Aghajari N, Hulmes DJ.
   Nat Struct Mol Biol. **2012**