

INTERNSHIP PROPOSAL

Institute and Group: Institut de Biologie Structurale – Group Viral Replication Machines

Supervisor: JAMIN Marc

Phone: 04 76 20 94 62

Email: marc.jamin@ibs.fr

Research project title: Mechanism of assembly of rabies virus replication machine- understanding the fundamental principles and discovering new drug targets

5 Keywords to describe the project: Pathogen, rabies virus, viral polymerase, protein-protein interactions, drug discovery

Description of the project (aims, experimental techniques, recommended background):

The objectives of the project are to understand the mechanism of rabies virus nucleocapsid assembly with a particular focus on the role of the viral polymerase and to discover new drug targets in this machinery. More specifically, the M2 internship will aim at (1) establishing the expression and purification of rabies virus RNA polymerase and unassembled nucleoprotein (N⁰) in complex with the phosphoprotein, (2) at characterizing the interaction between the polymerase and the phosphoprotein alone or in complex with N⁰ and (3) at building a model of the polymerase by molecular modelling. This project is challenging in terms of protein production and purification and will set-up the stage for a functional and structural characterization of the replicative complex of one of the deadliest virus infecting human.

The experimental work will involve protein expression in bacteria and eukaryotic cells, protein purification, biophysical characterization including SEC-MALLS, ITC, bio-layer interferometry, fluorescence anisotropy and SAXS.

Candidates should have a background in biochemistry and show an interest in biophysical and molecular modelling methods.

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

The project aims at understanding the fundamental mechanisms of the replication of a major human pathogen for which we still lack efficient drug and treatment and at identifying new drug targets. The long-term goal is to extend our current static view of the replication complex to a more dynamical view of the interplay between its components.

Relevant publications of the team:

- 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. (2014). Nat Struct Mol Biol. 21, 754-759.
- 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. (2016) J Mol Biol. 428:2671-2694.
- Yabukarski, F., Lawrence, P., Volchkov, V. and Jamin, M. (2014) Peptides including a binding domain of the viral phosphoprotein (P) subunit to the viral RNA free nucleoprotein (N⁰). Patent number: PCT/EP2015/066419