Grenoble Alliance for Integrated Structural & Cell Biology

INTERNSHIP PROPOSAL

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

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Research project title: Structure and function of Nipah C protein

5 Keywords to describe the project: RNA virus, Nipah virus, virus-host cell interactions, innate immune response

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

Nipah virus is among the deadliest viruses infecting humans and presenting a true risk of pandemic, but the underlying mechanisms of its pathogenicity remain poorly understood. Experimental evidences indicate that the non-structural C protein, expressed from a gene created *de novo* and overlapping the phosphoprotein (P) gene, is involved in the hijacking of several cellular machineries and in the escape of the host defense mechanisms. Several partners have been identified but no structural information is available

The objectives of the PhD thesis project are to determine the structure Nipah virus C protein alone or in complex with a cellular partner and to use this structural information to perform an integrative structure-function approach to decipher the roles of the non-structural C protein in the replication and pathogenicity of Nipah virus and to further investigate the paradigm of interdependence in expression of proteins coded within the Nipah virus P gene.

The main part of work will involve protein expression in different systems (bacteria, insect cells, mammalian cells), protein purification, biophysical characterization (SEC-MALLS, calorimetry, biolayer interferometry, …) and structural characterization (X-ray crystallography, SAXS/SANS). The project will also involve cell biology experiments using a minireplicon to probe the role of C in the activity of the polymerase complex. The project relies on collaboration with the Volchkov group in Lyon (CIRI), who has access to the Jean Mérieux BSL-4 laboratory and will carry out infection assays.

Justification that the internship's subject fits with the general theme of GRAL:

This project will lead to a better understanding of the evolution and adaptation of Nipah virus as well as of its abilities to adapt to new hosts and cross the barrier species. It will also pinpoint new potential therapeutic targets.

Relevant publications of the team:

(1) Ensemble structure of the modular and flexible full-length vesicular stomatitis virus phosphoprotein. Leyrat C., Schneider R., Ribeiro E.A. Jr, Yabukarski F., Yao M., Gérard F.C., Jensen M.R., Ruigrok R.W., Blackledge M. and Jamin M. (2012) J. Mol. Biol. **423**, 182-197.

(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. (2014). Nat Struct Mol Biol. **21**, 754-759.

(3) 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.