

GRAL MSc RESEARCH SCHOLARSHIP 2020-2021

RESEARCH INTERNSHIP PROPOSAL

Institute / Group

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Research Project Title

Borna disease virus replication: do N, P and X form a ternary complex?

Description of the project

Within the negative-strand RNA viruses group (influenza, measles, Ebola,...), the Borna disease virus (BoDV) constitutes a peculiar case. BoDV is a zoonotic agent and can either persist "asymptotically" (as seen for example in organ donors) or cause fatal encephalitis. Being part of the *Mononegavirales* order like measles or Ebola, BoDV replicates in the nucleus of the infected cells like influenza. Through its similarities with other members of the *Mononegavirales* order, BoDV genome encodes for the classical nucleoprotein (N), phosphoprotein (P), matrix (M), glycoprotein (G) and RNA polymerase (L). A sixth protein (X) is produced from an ORF that overlaps with the 5' end of the P gene (mRNA). X is specific to BoDV, predicted to be an intrinsically disordered protein and is known to negatively modulate the RdRp activity by interfering with P, the cofactor of L. The team has set up the expression/purification procedures to obtain individually all the recombinant partners (i.e. L, N, P and X) of BoDV replication machinery. The objectives of the M2 student will be to handle recombinant N, P and X proteins in order (i) to test their ability to form (or not) binary and/or ternary complexes in vitro and (ii) to characterize them using adequate structural biology technics (i.e. X-ray crystallography, NMR and/or EM). The corresponding proposal is part of a bigger project that aims by adding L, to characterize the whole replication machinery of BoDV. The candidate should have a strong background in biochemistry with good knowledge in each structural biology technics (i.e. X-ray crystallography, NMR and EM).

Keywords

Borna disease virus, viral replication, protein assembly, biochemistry, structural biology

Relevant publications of the team

Ashraf U, Tengo L, Le Corre L, Fournier G, Busca P, McCarthy AA, Rameix-Welti M-A, Gravier-Pelletier C, Ruigrok RW, Jacob Y, Vidalain P-O, Pietrancosta N, Crépin T and Naffakh N (2019) Destabilisation of the human RED-SMU1 splicing complex as a basis for host-directed anti-influenza strategy. *Proc Natl Acad Sci USA*, 116:10968-10977. doi: 10.1073/pnas.1901214116.

Donchet A, Oliva J, Labaronne A, Tengo L, Miloudi M, Gérard CA, Mas C, Schoehn G, Ruigrok RW, Ducatez M and Crépin T (2019) The structure of the nucleoprotein of Influenza D shows that all Orthomyxoviridae nucleoproteins have a similar NPCORE, with or without a NPTAIL for nuclear transport. *Sci Rep*, 9:600. doi: 10.1038/s41598-018-37306-y.

Labaronne A, Milles S, Donchet A, Jensen MR, Blackledge M, Bourhis, J-M, Ruigrok RW and Crépin T (2017) Structural analysis of the complex between influenza B nucleoprotein and human importin- α . *Sci Rep*, 7:17164. doi: 10.1038/s41598-017-17458-z.
