Master 2 research internship in Integrated Structural & Cell Biology in Grenoble

Supervisor(s):
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Host laboratory:
IBS, https://www.ibs.fr/

Host group/team:
VRM: Viral Replication Machines, team Crépin / Ruigrok

Title of the M2 research internship:
Toward the structure of Borna disease virus nucleocapsid

Project summary:
The group of negative-sense single-stranded RNA viruses (NSV) encompasses a large number of “human killers” such as rabies, Ebola, Lassa fever or influenza viruses. These enveloped viruses harbour a single-stranded RNA genome of negative polarity, encapsidated by the nucleoprotein (N/NP) to form the nucleocapsid. The Borna disease virus (BoDV) constitutes a peculiar case. BoDV is a zoonotic agent and can either persist "asymptomatically" (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. BoDV N was the first nucleoprotein structure solved, but unlike other Mononegavirales whose 3D structures were solved in complex with RNA (as nucleocapsid-like particles), this structure corresponds to a tetramer free of RNA. Nothing is known regarding the interaction between nucleic acids and BoDV N which was long expected to be unable to bind RNA in vitro.
From our recent work on BoDV phosphoprotein, we have identified conditions to destabilize the tetrameric BoDV N association and promote its interaction with synthetic RNA molecules in vitro. We now need to decipher the precise parameters to reconstitute BoDV nucleocapsid-like particle prior to structural characterization by cryo-electron microscopy. The objectives of the M2 student will be to handle the production/purification of recombinant BoDV N constructs and biophysics experiments (fluorescence anisotropy, biolayer interferometry, ...) as well as electron microscopy (negative staining) to establish the precise conditions to obtain homogeneous nucleocapsid-like particles for structural purposes. This proposal is part of a bigger project that aims, by adding both viral polymerase and phosphoprotein, to characterize the whole replication machinery of BoDV.
The candidate should have a strong background in biochemistry with good knowledge in all structural biology technics (i.e. X-ray crystallography, NMR and EM).

Keywords:
Borna disease virus, nucleoprotein-RNA complex, assembly

Relevant publications of the team:
Tarbouriech N, Chenavier F, Kawasaki J, Bachiri K, Bourhis JM, Legrand P, Freslon LL, Laurent EMN, Suberbielle E, Ruigrok RWH, Tomonaga K, Gonzalez-Dunia D, Horie M, Coyaud E and Crépin T (2022) Borna disease virus 1 phosphoprotein forms a tetramer and interacts with host factors involved in DNA double-strand break repair and mRNA processing. Viruses, 14(11), 2358; https:// doi.org/10.3390/v14112358.

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.

Chenavas S, Estrozi LF, Slama-Schwok A, Delmas B, Di Primo C, Baudin F, Li X, Crépin T and Ruigrok RW (2013) Monomeric nucleoprotein of influenza A virus. PLoS Pathog, 9:e1003275.