

GRAL MSc RESEARCH SCHOLARSHIP 2020-2021
RESEARCH INTERNSHIP PROPOSAL

Institute / Group

IRIG / IBS – LEM

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Research Project Title

Structural characterization of bunyavirus replication complexes by single particle cryo-electron microscopy and tomography

Description of the project

Hantaviruses are negative stranded RNA viruses belonging to the Bunyavirales order. The Hantaviridae family encompasses several life-threatening viruses such as Hantaan virus that is causing haemorrhagic fever with renal syndrome. Neither vaccine or antivirals are currently available to counteract it. In this context, we focus our research on two critical steps of Hantaan virus cycle: replication and transcription. These reactions are carried out by the multifunctional viral polymerase which uses nucleocapsids as templates. Viral nucleocapsids are formed by viral RNA segments enwrapped with multiple viral nucleoproteins. We have significant preliminary results on the project, including high quality cryo-EM data of Hantaan virus nucleocapsid we are able to express and purify to homogeneity Hantaan virus polymerase. We have also access to Tula virus sample (Tula virus belongs to the Hantaviridae family but is non-pathogenic to humans).

The internship will consist in expression, purification and biochemical characterization of either the polymerase or the nucleocapsid/polymerase complex, followed by 3D structural determination by single-particle electron microscopy (negative stain and cryo-EM). Electron tomography will also be used for characterization of replication complexes in fixed Tula hantavirus particles.

The intern will benefit from the EM expertise in the group and will have access and training to the IBS state-of-the art EM facility, notably a Thermofisher Glacios microscope equipped with a Falcon II direct electron detector and a Gatan K2 direct electron detector. Students from either ISB, IMID and MCMV Masters have the requested background and are encouraged to apply if they are interested.

Keywords

electron microscopy, negative strand RNA virus, nucleocapsid, RNA polymerase, replication.

Relevant publications of the team

Arragain B, Reguera J, Desfosses A, Gutsche I, Schoehn G*, Malet H*. High resolution cryo-EM structure of the helical RNA-bound Hantaan virus nucleocapsid reveals its assembly mechanisms. *eLife* 2019;8:e43075

Gerlach P1, Malet H1, Cusack S, Reguera J. Divergent segmented negative strand viral polymerases have the same architecture and mode of regulation by vRNA. 2015. *Cell*. Jun 4;161:1267-79 1co-first author

Gutsche I, Desfosses A, Effantin G, Ling WL, Haupt M, Ruigrok RW, Sachse C, Schoehn G. Structural virology. Near-atomic cryo-EM structure of the helical measles virus nucleocapsid. *Science*. 2015 May 8;348(6235):704-7.
