

GRAL Research proposal for PhD projects

Institute and Group: IBS- VRM

Supervisor I: JAMIN Marc
Co-Supervisor II: RUIGROK Rob

Contact information: marc.jamin@ibs.fr
Contact information: rob.ruigrok@ibs.fr

Title of the thesis project: Structure and operating principles of rabies virus RNA transcription/ replication machine

Keywords: Virus, viral replication, RNA polymerase, structural biology, mathematical modeling

Summary of the project:

The RNA replication complex of the nonsegmented negative-sense RNA viruses is composed of the template RNA covered by viral nucleoproteins (N) (this ribonucleoprotein complex is named nucleocapsids, NC), the phosphoprotein (P) and the RNA-dependent RNA polymerase (RdRp). This complex is highly specific to these viruses and thus a key target for developing much-needed antiviral drugs. Using rabies virus and a combination of biochemical, biophysical, structural and mathematical approaches, our project aims at reconstituting in vitro, from recombinant components, the NC and the tripartite functional complex involved in the replication and transcription of the genome and at unraveling some underlying molecular mechanisms.

The project relies on our preliminary results and on available tools and reagents. It is organized in three specific aims. (1) The assembly of uniform NC from long RNA molecules of well defined length and recombinant unassembled N. (2) The reconstitution and characterization of the tripartite NC/P/RdRp complex. (3) The quantification of interactions and modeling of the replication process to assess the mechanism of RdRp processivity. The work will generate unprecedented insights to decipher the mechanisms by which the replication machine of rabies virus, and of other NNVs, operates.