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 group, Burmeister team

Title of the M2 research internship:
Structural and functional study of the telomere-binding proteins of vaccinia virus

Project summary:
With the recent epidemic outbreak of Mpox, poxviruses got into the headlines. A safe model system is vaccinia virus, which is 98 % identical to Mpox at the amino acid level regarding the proteins involved in DNA replication. Its genome is best described as a linear dsDNA circularized by loops at the extremities. These loops are surrounded by the ≈60 bp telomere region with imperfect base-pairing. Three proteins are associated with the telomere: I1, I6 and K4, where K4 has a nicking and nick-sealing activity. These proteins are packaged together with the viral DNA into the viral particles. It is likely that viral DNA replication, which proceeds through a still unknown mechanism combining rolling circle replication with leading and lagging strand DNA synthesis and nick-based priming, starts in the telomere region as there is no other known origins of replication. The aim of the M2 internship is to produce the telomere-binding proteins in the baculovirus-insect cell system for the in vitro reconstitution of the telomeres for structural and functional studies. We hope that this project will provide the missing information on replication initiation consolidating the current work of the team on the polymerase holoenzyme and the helicase-primase directly involved in DNA replication.

Keywords:
Baculovirus expression system, DNA-binding proteins, structural biology

Relevant publications of the team:

Hutin, SL, Ling, W.L., Tarbouriech, N., Schoehn, G., Grimm, C., Fischer, U. & Burmeister, W.P. The Vaccinia Virus DNA Helicase Structure from Combined Single-Particle Cryo-Electron Microscopy and AlphaFold2 Prediction. Viruses 14 (10). https://doi.org/10.3390/v14102206.(2022).

Bersch, B., Tarbouriech, N., Burmeister, W.P, & Iseni, F. Solution structure of the C-terminal domain of A20, the missing brick for the characterization of the interface between vaccinia virus DNA polymerase and its processivity factor. J. Mol. Biol., 167009. https://doi.org/10.1016/j.jmb.2021.167009 (2021).

Tarbouriech, N., Ducournau, C., Hutin, S., Mas, P. J., Man, P., Forest, E., Hart, D.J., Peyrefitte, C. N., Burmeister, W. P., & Iseni, F. The vaccinia virus DNA polymerase structure provides insights into the mode of processivity factor binding. Nat. Comm. https://doi.org/10.1038/s41467-017-01542-z (2017).