Funded PhD project in Integrated Structural & Cell Biology in Grenoble, France (2025-2028)

Title of the PhD project: Structure and role of a telomere-binding protein in the poxvirus genome telomere

PhD supervisor(s): Wim Burmeister contact: wim.burmeister@ibs.fr
Host laboratory (UMR): Institut de Biologie Structure (UMR 5075 UGA–CNRS-CEA)
Host laboratory website: https://www.ibs.fr
Host team/group: Viral Replication Machines (VRM)
Team website: https://www.ibs.fr/en/research/microbiology-infection-and-immunity/viral-replication-machines-group-m-jamin/

Project summary:
In early summer 2022, Mpox virus entered into the MSM community leading to a worldwide outbreak of Mpox clade 2b virus with 100 000 cases before it could be circumscribed by vaccination with vaccinia virus, which is very closely related and also the model system in our team. Again, in 2024, human cases caused by clade 1b in the Republic of Congo and neighbouring countries with about 700 dead led to new concerns, in particular as the existing antivirals showed little effect. The poxvirus genome is best described as a linear dsDNA, where the AT-rich extremities (called telomeres) show imperfect base pairing and are circularized with loops. We hope to be able to visualize the peculiar telomere structure with its bound proteins, principally by cryo-EM and to contribute to the understanding of different steps in poxvirus replication where the telomeres are involved: (1) Initiation of replication; possibly connected to the entry of the D5 helicase-primase and the E9-A20-D4 polymerase holoenzyme in order to establish the replication fork and (2) Genome packaging. In the PhD project, more specifically, we aim for the structure of one of the telomere-binding proteins and of its complex with the ~120 base telomere DNA and partner proteins or we may target subcomplexes of the system.

Student role:
The work of the PhD student will concentrate on the production and characterization of one of the proteins and of its complexes with DNA and other telomere-binding proteins and proteins of the DNA replication machinery. The interactions of the purified protein will be studied using several biophysical techniques, such as electrophoretic mobility shifts (EMSA), multi-angle light scattering (MALS), biolayer interferometry (BLI) and small-angle X-ray scattering (SAXS). When defined complexes are obtained, their structure will be studied by cryo-electron microscopy (cryo-EM) and macromolecular crystallography. Training and expertise in cryo-EM will be provided by the supervisors and in collaboration with the MEM group at IBS.

Keywords: Protein-DNA interactions, biophysical techniques, Cryo-EM, macromolecular crystallography, DNA replication

Relevant publications of the team:
Burmeister, W. P., Boutin, L., Balestra, A. C., Gröger, H., Ballandras-Colas, A., Hutin, S., Kraft, C., Grimm, C., Böttcher, B., Fischer, U., Tarbouriech, N. & Iseni, F. (2023). BioRxiv https://doi.org/10.1101/2023.09.03.556150.
Hutin, S., Ling, W. L., Tarbouriech, N., Schoehn, G., Grimm, C., Fischer, U. & Burmeister, W. P. (2022). Viruses 14, https://doi.org/10.3390/v14102206.
Bersch, B., Tarbouriech, N., Burmeister, W. P. & Iseni, F. (2021). Journal of Molecular Biology 167009. https://doi.org/10.1016/j.jmb.2021.167009.
Tarbouriech, N., Burmeister, W.P., Bersch, B. & Iseni, F. (2024).
Virologie 28 (1): 23-35. https://doi.org/10.1684/vir.2024.1033.
Tarbouriech, N., Ducournau, C., Hutin, S., Mas, P. J., Man, P., Forest, E., Hart, D. J., Peyrefitte, C. N., Burmeister, W. P. & Iseni, F. (2017). Nat Commun 8, 1455. https://doi.org/10.1038/s41467-017-01542-z

Skills/Qualifications: Recombinant protein production in *E. coli* or insect cells, basic biochemistry, knowledge of biophysical techniques (EMSA, BLI, etc.). Computer literacy (Linux) and some knowledge of protein crystallography or electron microscopy are an asset.