

**Master 2 internship project
Year 2026-2027**

Laboratory/Institute: IBS

Team: Virus Replication Machines (VRM) group

Director: W. Weissenhorn

Head of the team: Darren Hart

Name and status of the scientist in charge of the project: Darren Hart, CNRS

HDR: yes ☒ no ☐

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Program of the Master's degree in Biology:

- ☐ Microbiology, Infectious Diseases and Immunology ☒ Biochemistry & Structure
☐ Physiology, Epigenetics, Differentiation, Cancer ☐ Neurosciences and Neurobiology

Title of the project: Characterising new peptide-based inhibitors of influenza virus designed by AI

Objectives :

We use phage display and new AI tools to discover high affinity peptide inhibitors of influenza virus replication. Hits are analysed by biophysical and structural methods. This represents a possible future therapeutic approach.

Abstract :

In collaboration with G. Uguzzoni (BGE, CEA), this interdisciplinary project integrates AI, structural biology, and protein engineering to develop inhibitors of influenza polymerase assembly. The viral polymerase is a heterotrimeric complex essential for viral replication. We have identified key contact regions between influenza polymerase subunits and are targeting these with high-affinity synthetic peptides by combining phage display-directed evolution and AI-based computational design. The proposed project will characterize new sets of AI-predicted peptides for target binding and inhibitory potency.

Methods :

Molecular biology, protein biochemistry, computational analysis, biophysical characterisation.

Relevant publications of the team:

1. Reich S et al. (2014) Structural insight into cap-snatching and RNA synthesis by influenza polymerase. Nature 516:361–366.
2. Thierry E et al. (2016) Influenza Polymerase Can Adopt an Alternative Configuration Involving a Radical Repacking of PB2 Domains. Mol. Cell 61:125–137.
3. Camacho-Zarco et al. (2020) Molecular basis of host-adaptation interactions between influenza virus polymerase PB2 subunit and ANP32A. Nat Comm. 11:3656
4. Fernandez-de-Cossio-Diaz J, et al. (2024) Inference and design of antibody specificity: From experiments to models and back. PLOS Computational Biology 20(10): e1012522
5. Florez et al. (2026) Calculation of sequence space coverage in a mutagenesis library. Biorxiv 10.64898/2026.06.15.729752

Requested domains of expertise :

Protein purification, SDS-PAGE, computer skills, good English level.