

HALRIC Research Internship Programme

Internship Proposal

Project Title:

Unravelling HCMV Immune Evasion: Validation of Predicted Protein-Protein Interactions

Name of Institution/Country:

Centre for Structural and Systems Biology: Hamburg
University Hospital Hamburg-Eppendorf (UKE)
Leibniz-Institute for Virology, Hamburg

Name of internship provider:

Dr. Matthias Pfeifer & Prof. Dr. Maya Topf

Contact details:

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Proposed timeframe:

3-6 month

Application deadline:

30.11.2025

Administrative contact person at the organisation:

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Scientific research questions

Human cytomegalovirus (HCMV) employs diverse strategies to evade and manipulate the host immune system, often through direct interactions with host immune factors. This project aims to validate computationally predicted protein-protein interactions between HCMV proteins and key components of the host immune system. We combined protein structure prediction (AlphaFold) and protein structure similarity searches (FOLDSEEK) to identify and evaluate novel immune-modulatory interactions between HCMV and host proteins. As a result, we have formulated several hypotheses that require functional validation. Using co-immunoprecipitation assays, we will experimentally test these interactions, while site-directed mutagenesis based on computational modelling will elucidate their molecular mechanisms. Flow cytometry will assess the impact of these interactions on immune factor presentation and activation, and advanced confocal microscopy will provide spatial insights into their localization within infected cells. The findings will contribute to a deeper understanding of HCMV immune evasion strategies and may identify potential targets for antiviral intervention.

Experimental approach

Initially, gene expression systems are developed and tested for their ability to express functional recombinant proteins. Interactions between HCMV proteins and host immune factors are validated through co-immunoprecipitation assays. Confirmed interactions are further analysed at the molecular level using site-directed mutagenesis. These approaches will be guided by structural predictions and interface evaluation. Flow cytometry will assess immune factor presentation and activation upon interaction, while advanced confocal microscopy will localize and visualize HCMV-host interactions within cells. Biophysical and functional methods, such as BRET assays and CreoptixWAVE, will be employed to measure protein-protein interactions and their kinetics.

Tasks of the intern

The intern will work in the interface between structure prediction and classical lab-based molecular and cellular biology.

- Cloning of viral and host proteins; site-directed mutagenesis
- Recombinant expression of proteins in human or bacterial cells; expression validation
- Co-immunoprecipitation experiments
- Flow cytometry for immune factor analysis
- Confocal microscopy for protein localization
- Setup of Bioluminescence Resonance Energy Transfer (BRET) assays
- Interaction kinetics analysis using Grating-Coupled Interferometry (Creoptix WAVE)
- Utilization of structural modelling and visualization tools, such as ChimeraX
- Independent literature research
- Documentation of experimental progress and results
- Presentation in internal meetings
- Attendance to institute seminars

General information about the work group, the university and the region

Professor Maya Topf leads the Integrative Virology research group at the Centre for Structural Systems Biology (CSSB) in Hamburg, Germany. Her research focuses on developing integrative structural methods that combine experimental data with bioinformatics and modelling techniques to elucidate the structures of macromolecular assemblies in viruses and their interactions with host cells. This approach aims to provide critical insights for guiding experimental design and the development of potential antiviral inhibitors.

The Centre for Structural Systems Biology (CSSB) in Hamburg is a research institution dedicated to understanding the molecular mechanisms behind infectious diseases, with a focus on structural biology. It combines experimental techniques, such as cryo-electron microscopy and X-ray crystallography, with computational modelling to study host-pathogen interactions and develop potential therapeutic strategies.

Hamburg is a vibrant life science hotspot, home to cutting-edge research institutions, biotech companies, and a collaborative environment that fosters innovation in areas like molecular biology and infectious diseases research. Beyond its scientific prowess, Hamburg is a dynamic city known for its rich history, cultural scene, and picturesque harbour, making it a great place to live and work.

Eligibility and qualification of the applicant.

- Eligible applicants need to be enrolled at a HALRIC partner institution
- Applicants should have a strong command of the English language
- Solid foundation in basic molecular techniques such as PCR, cloning, gel electrophoresis, or Western blotting
- Familiarity with cell culture techniques, recombinant protein expression or basic microscopy
- Ability to think critically and design experiments to test hypotheses
- Eagerness to learn and a keen interest in virus-host interactions and structural biology