

## Master thesis advertisement

### Structural and functional characterization of alphavirus – receptor interactions

Prof. Dr. Dietmar Manstein, PD Dr. Roman Fedorov, Prof. Dr. Gisa Gerold

The research groups “Macromolecular Mechanisms” and “Molecular and Cellular Infectiology” at the Hannover Medical School (MHH) and the Research Center for Emerging Infections and Zoonosis (RIZ), University of Veterinary Medicine in Hannover, Germany, are recruiting a Master student in biochemistry to pursue a project aiming at elucidating and characterizing protein complexes relevant for alphavirus entry into human cells.

#### Research Topic

Alphaviruses are enveloped RNA viruses, which reside in animal reservoirs and cause arthritis or encephalitis in humans after transmission by mosquitoes. Among the re-emerging alphaviruses is Venezuelan equine encephalitis virus (VEEV), which causes neurological symptoms in humans and horses. Recently, LDLRAD3 was identified as a receptor for VEEV in humans (Ma et al. ,Nature, 2020). The nature of the interaction between the viral envelope proteins and the LDLRAD3 molecule remains elusive to date.

The planned project aims at generating expression systems for the ectodomains of the VEEV glycoproteins and the LDLRAD3 receptor from humans and horses. The ectodomains will subsequently be purified and characterized biophysically (e.g. by microscale thermophoresis, dynamic light scattering, native gel electrophoresis, isothermal titration calorimetry). To assess the biological activity of the ectodomains, competition assays will be performed, i.e. we will assess if the ectodomains can block VEEV cell entry in readily available infection assays (at RIZ). Ultimately, the protein complex of virus envelope and receptor ectodomains will be used for crystallization screens with the goal of resolving the structure and interfaces of the protein complex. In addition, structural modeling tools will be applied to predict the tertiary protein complex structure (at MHH).

This work will help understand how an important re-emerging pathogen enters human cells and whether similar mechanisms apply for other host species such as horses.

#### Your role

You will be responsible for carrying out research in the Federov and Gerold research groups ([AG Fedorov](#), [AG Gerold](#)) at MHH and RIZ. You will learn and apply expression construct design, protein expression techniques (in insect and mammalian cells), cell culture techniques, immunoblotting, virus infection assays (BSL2), biophysical analyses and protein crystallization techniques. You will work closely with researchers in both laboratories and actively participate in institute seminars.

#### Responsibilities

- Design of expression constructs for virus envelope and receptor ectodomains
- Protein expression in insect and mammalian cells
- Protein expression analysis by immunoblot
- Protein characterization by DLS, ITC
- Virus infection assays in mammalian cell culture and competition assays
- Communicate data in weekly team meetings
- Report at least once on the project at the institute-wide seminar
- Contribute to the publication of research findings.
- Comply with the University's Equal Opportunities and Data Protection policies

## **Selection criteria**

- B.Sc. in biology or similar discipline
- Good written and oral English communication skills
- Ideally experience in protein expression techniques
- Interest in studying the protein structure and function of virus-receptor complexes
- Ability to work as part of a team as well as independently
- Ability to deliver results to required standard and organize and prioritize own work

## **Research environment**

We are international teams based at the MHH and RIZ. Our groups have access to state-of-the-art equipment and techniques for protein expression, structural analysis and infection assays. We offer an international, stimulating and collaborative research environment, in which your scientific career development is fostered.

## **Application**

Please apply via email to

[fedorov.roman@mh-hannover.de](mailto:fedorov.roman@mh-hannover.de); [gisa.gerold@tiho-hannover.de](mailto:gisa.gerold@tiho-hannover.de)

with the following documents:

1. short 1-page CV
2. Copy of BSc certificate
3. Copy of high school certificate