CSC-RUB PhD Project Proposal

Title: Analysis of coronavirus immune control

Sector of research: Biomedical Science

Degree awarded: PhD

Keywords: coronavirus, SARS-CoV-2, interferon stimulated genes, immune control, immune evasion, reverse genetics, authentic cellular models

Supervisor of PhD project: Jun. Prof. Dr. Stephanie Pfänder, Department for Molecular and Medical Virology, e-mail: stephanie.pfaender@rub.de

Research focus of supervisor:

Our research group focuses on RNA viruses, with a particular emphasis on coronaviruses. We are interested in virus – host interactions to understand molecular processes during viral replication and pathogenesis. We study coronavirus immune control, coronavirus replication, and coronavirus transmission. Our group employs state-of-the-art molecular and cell biological methods, including authentic primary cell culture models, -omic-based approaches, genetic screening and virus reverse genetics. Within our state-of-the-art laboratories, we can study endemic and pathogenic coronaviruses, including SARS-CoV, MERS-CoV and SARS-CoV-2.

Publications:

1. Schuhenn J, [...] Sutter K#, and **Pfaender S#.** Differential interferon-α subtype immune signatures suppress SARS-CoV-2 infection. Proc Natl Acad Sci U S A. 2022 Feb 22;119(8):e2111600119. doi: 10.1073/pnas.2111600119.

2. Kratzel A, [...] **Pfaender S#**, Thiel V#. A genome-wide CRISPR screen identifies interactors of the autophagy pathway as conserved coronavirus targets. PLoS Biol. 2021 Dec 28;19(12):e3001490. doi: 10.1371/journal.pbio.3001490.

3. Meister TL, [...] Quast DR#, **Pfaender S#.** Low risk of SARS-CoV-2 transmission by fomites - a clinical observational study in highly infectious COVID-19 patients. J Infect Dis. 2022 May 5;jiac170.doi: 10.1093/infdis/jiac170. Online ahead of print.

4. **Pfaender S***, [...] Thiel V. LY6E Impairs Coronavirus Fusion and Confers Immune Control of Viral Disease. Nat Microbiol, 2020 Jul 23. doi: 10.1038/s41564-020-0769-y.

5. Thao TTN, [...] **Pfaender S**, [...] Thiel V. Rapid reconstruction of SARS-CoV-2 using a synthetic genomics platform. Nature. 2020 May 4. doi: 10.1038/s41586-020-2294-9.

* shared first author, # corresponding author

Number of Publications:

- Original Articles as First/Corresponding author: 24
- Original Articles as Co-author: 27
- Reviews: 7

H-index: 21

Second Supervisor of PhD project: Jun. Prof. Dr. Simon Faissner

Summary of research plan:

Background: Since the emergence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in China in late 2019, coronavirus disease 2019 (COVID-19) has caused >500 million confirmed infections and >6 million fatalities worldwide (data from May 2022). The host innate immune system is one of the first lines of defense against invading pathogens. Especially, the interferon (IFN) response plays a pivotal role in the host defense against infectious agent and interferon stimulated genes exert strong antiviral effects against coronaviruses. However, several lines of evidence indicate that systemic and local IFN responses are dysregulated during coronavirus infection, which could contribute to COVID-19 disease severity and pathogenesis.

Study objective: The goal of this project is to study the immune control of coronaviruses and elucidate factors that could contribute to a dysregulated IFN response. Therefore, we will utilize coronavirus reverse-genetics and authentic cellular systems to study the immune control and evasion of different endemic and pathogenic CoVs, including currently circulating variants of concern.

Expected Results: We aim to I) identify novel ISG restriction factors II) analyse the role of various cell types for viral immune control and II) dissect viral immune evasion strategies via reverse-genetics and genetic screenings. Several national and international collaborations will allow a transfer of our findings towards more authentic *in vivo* models to validate our *in vitro* results. All results obtained during this project will be published in peer-review journals.

Methods: Our methods include coronavirus reverse genetics, authentic cell culture systems, cellular methods including western blot, immunofluorescence analysis, qRT-PCR, CRISPR/Cas, lentiviral transduction, next generation sequencing (incl. Illumina and MinION sequencing), and biosafety level 2 and 3 experiments.

Candidate Requirements: We are looking for a highly motivated candidate with a Master's degree in the field of Biosciences/Biomedicine with a high capacity for teamwork. The candidate should have experience with molecular biology methods, preferably in the context of virus infection. The following knowledge is advantageous: Experience in culturing eukaryotic cells, experience in working with primary cultures, experience in working with RNA, experience with virological techniques (virus culture, infection experiments), and experience with immune cells. Fluency in written and spoken English language is mandatory.

Motivation for CSC application: We offer a medically relevant research topic, state-of-the-art methodologies, inter-disciplinary cooperations, flexible working-hours and work within a young and motivated team. Candidates will be enrolled in the structured PhD programmes of the Ruhr University Bochum and will get the opportunity for interdisciplinary skills development. National or international lab exchanges with collaboration partners (e.g., to learn new methods) could be initiated upon request and need.