COVID-19 research seminar

Philip Gribbon

Fraunhofer Institute for Translational Medicine and Pharmacology, Hamburg, Germany

Talk title:
Compound repurposing in COVID-19, target and phenotypic-based approaches.

Päivi Östling

Department of Oncology-Pathology,
Karolinska Institute

Talk title:
Exploring the morphology of the host cell to open new possibilities in drug repurposing

Wednesday June 1, 2022, at 15:15-16:45

Online via Zoom

Philip Gribbon is Head of Discovery Research, Fraunhofer Institute for Translational Medicine and Pharmacology, Hamburg, Germany

2014-2019: Assistant Head of Department, Fraunhofer Institute of Molecular Biology and Applied Ecology (IME), Hamburg, Germany.
2014-18 Coordinator of EU-OPENSCREEN, The European Infrastructure for Chemical Biology.
2008 - 2014 Chief Scientific and Operating Officer, European ScreeningPort GmbH., Germany.

Scientific interests: Development of technologies and methodologies for improving the practice of early stage drug discovery, in particular using disease relevant in-vitro models and biophysical methods for evaluation of target engagement.

Päivi Östling research expertise is within functional precision cancer medicine (fPCM) where drug libraries consisting of oncology drug with known mechanisms-of-action is used to profile disease cells. This approach provides for direct measurements of drug efficacy (or lack thereof) but also to identify drug repositioning opportunities. During the pandemic, she and the consortium linked to the project leveraged their existing expertise in drug repurposing, phenotypic screening, and drug target identification to focus on SARS-Cov-2. The team effort consisting of the teams of Charlotte Stadler, Ola Spjuth, the Chemical Biology Consortium Sweden (CBCS), the BSL3 facility, FIMM along with the virology expertise of postdoc Marianna Tampere in our own research group catalyzed a new approach to drug repositioning that will be presented.

ABSTRACTS

SciLifeLab

Philip Gribbon

Talk title:
Compound repurposing in COVID-19, target and phenotypic-based approaches.

The SARS-CoV-2 pandemic represents a severe and ongoing threat to worldwide health and economic systems. The development of multiple vaccines against SARS-CoV-2, based on a range of technologies, has improved the outcomes for infected individuals and will remain the primary strategy for protecting individuals going forward. As a complementary strategy to protection through vaccination, therapeutic interventions based on biological and small molecule have been developed by many organisations with several small molecule anti-viral therapeutics having already received emergency approval or in late stage development. The presentation will cover report on our collaborative efforts to identify antiviral compounds using repurposing screens in phenotypic formats as well as target based studies to identify inhibitors of SARS-CoV-2 viral protein function, including MPro one of the key enzymes of viral replication that is involved in maturation of the viral polyprotein. Deployment of COVID-19 related data to public platforms to ensure effective reuse of results will also be described.

Päivi Östling

Talk title:
Exploring the morphology of the host cell to open new possibilities in drug repurposing

New approaches are needed to find novel or repurposed drugs as antivirals. Most screening methods evaluate the drug activity on a given virus while neglecting the host mechanisms and responses to the virus infection. Here, we study host cell morphology changes by combining morphological profiling using the Cell Painting assay [1] with antibody- detection of infection and screened 5144 compounds from the SPECS drug repurposing library. We demonstrate how SARS- CoV-2 induced a specific phenotypic signature in Vero E6 cells, which was reversed by reference antivirals such as remdesivir. Our unbiased host-focused approach identified additional ~50 compounds that were able to revert SARS-CoV-2 infected host cells towards a healthy cell phenotype.
To further study the host response during infection, we quantified the subcellular localization and expression of 602 host proteins using antibodies from the Human Protein Atlas [2]. We identified phenotypic responses to SARS-CoV-2 infection in 97 proteins. Finally, to broaden the paradigm of how antiviral therapies are identified we aim to combine these host focused screening approaches.