MS02-2-5 Inhibitor screening and structural characterization of virulence factors from SARS-CoV-2 #MS02-2-5

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Abstract
Coronavirus induced zoonotic diseases can cause pandemics with unforeseeable consequences to human health and global economy. Our project aims to screen and develop effective therapeutics against SARS-CoV-2, targeting its replication-transcription complex (RTC). Following an interdisciplinary research approach, compound libraries of approved drugs are used for the discovery of potent inhibitors for proteins of the RTC and the binding mode of these enzyme-inhibitor complexes is studied by X-ray crystallography.
Our workflow includes the production of proteins involved in the coronavirus RTC, the high-throughput inhibitor screening with fluorescence-based assays using drug repurposing libraries and the structure/function analysis of the identified enzyme-inhibitor complexes. The advantages of this approach is that it is cost efficient, high-throughput, allows the direct identification of potent inhibitors and ensures optimal beamtime usage. Furthermore, such a platform can be successfully used in future viral outbreaks.
In this presentation we will give an overview of this project and the results achieved to date. We will focus on one of the target proteins, namely the uridine-specific endoribonuclease nsp15, and apart from the results from its inhibitor screening we will also present findings that allowed us to shed light on important activity determinants of this enzyme.

References
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