Julius-Maximilians-
UNIVERSITÄT
WÜRZBURG

Lecture *via* Zoom
meeting ID: 995 4086 2444
login code: 909398

Genetics, Structural Biology, and Bioinorganic Chemistry of Coronaviruses

Ulrich Schatzschneider

Institut für Anorganische Chemie, Julius-Maximilians-Universität Würzburg,
Am Hubland, D-97074 Würzburg, Germany
eMail: Ulrich.schatzschneider@uni-wuerzburg.de

Since late 2019, the COVID-19 pandemic has spread to essentially all countries of the world, with close to 60 million confirmed cases and about 1.4 million deaths. The causative agent of the disease is severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2).[1,2] As the result of impressive global research efforts, the genetics, structure of key proteins, and pathophysiology of this new coronavirus is now known in significant detail.

In addition to the four structural proteins E (envelope), M (membrane), N (nucleocapsid), and S (spike), which make up the virus capsid, significant attention has also been directed at the 16 non-structural proteins (NSPs). As they help to colonize the host, organize and protect the replicative machinery, and synthesize the viral RNA genome,[3] NSPs are attractive targets for drug development.[4] Although not immediately obvious, there is also a significant bioinorganic chemistry component in coronavirus proteins, as a number of NSPs feature zinc fingers as an important structural element, while others rely on metal ions such as Mg^{2+} and Mn^{2+} for catalytic function. Furthermore, some peculiar genomic RNA secondary structures might serve as binding sites for nucleic acid recognizing metal complexes.

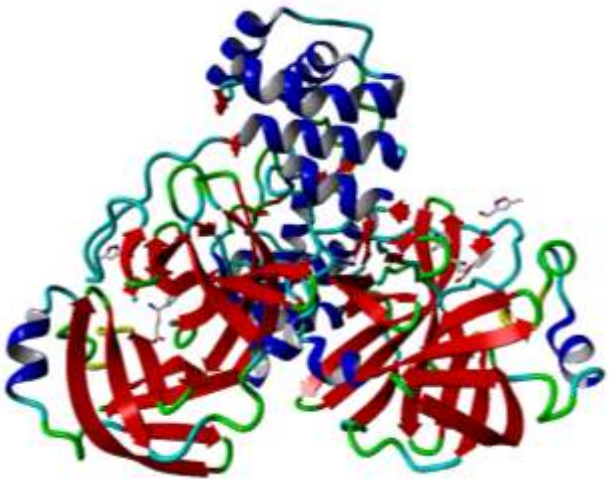

Figure 1. Schematic representation of $3CL^{pro}$, the main protease of SARS-CoV-2, and a major potential target for antiviral drugs. Figure created with Yasara based on PDB entry 7BQY (Z. Rao, H. Yang *et al.*, *Nature* **2020**, *582*, 289-293).

In the present seminar, I will give an overview of the genomic organisation of SARS-CoV and SARS-CoV-2, talk about the structural biology of key viral proteins, and present some very preliminary data on our own attempts to develop an assay as well as metal-based inhibitors for $3CL^{pro}$, the SARS-CoV-2 main protease.[5]

References

[1] Y.-Z. Zhang *et al.*, Nature, **579**, 265 (2020).
[2] J. Ziebhur *et al.*, Nature Microbiol., **5**, 536 (2020).
[3] B.W. Neuman, P. Chamberlain, F. Bowden, J. Joseph, Virus Res. **194**, 49 (2014).
[4] A.K. Ghosh, A.D. Mesecar *et al.*, ChemMedChem **15**, 907 (2020).
[5] N. Farn, M. Müller, D. Graf, I. Ott, U. Schatzschneider, unpublished results.