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The structural biology task force at Elettra to support drug discovery against Covid-19

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At the beginning of 2020 the Covid-19 pandemic emergency caused by a newly identified coronavirus universally known as SARS-CoV2 spread out all over the world, changing irreversibly our life style and wellness. In response to the crisis, while everybody was caught off guard by the rapid diffusion of the viral infection and the alarming of death toll worldwide, the global structural biology community has experienced an unprecedent "call-to-arms" to shed light on every step of the viral replication [1]. All x-ray diffraction beamlines at synchrotrons focused their efforts on the 3D structure determinations of the druggable proteome of SARS-CoV2. The Protein Facility, and the XDR2 beamline at Elettra, jumped on the opportunity to be involved in a huge drug discovery project, financed by the EC H2020 emergency call to counter the SARS-CoV2 Coronavirus pandemic. The project Exscalate4Cov (E4C, https://www.exscalate4cov.eu), brought together 18 European institutions combining supercomputing resources and AI with state-of-art experimental facilities up through clinical validation. Goal of the project was to identify the most promising and safe in man drugs for immediate treatment of the infected population.
Elettra group has been part of the structural biology task force focusing on the 3D structure determination of the two SARS-CoV2 proteases: 3CLpro/Mpro and PLpro. We applied classical crystallographic techniques to validate the binding mode of several compounds coming from the virtual and biochemical High-Throughput Screening performed by the partnership [3, 4]. A number of repurposed and de-novo designed molecules were co-crystallized with Mpro and PLpro respectively. A large amount of crystals was screened and collected on XRD2 resulting in different ligand-bound and unbound structures. Here we will describe the complete workflow of Elettra's activities; from protein production to crystal structure determinations. The highlighting will be on the most relevant results [4] as well as on the strategies applied to maximize our knowledge when crystallisation did not prove to be on our side.

[1] D. R. Littler, B. J. MacLachlan, G. M. Watson, J. P. Vivian, and B. S. Gully, Biochemical Society Transactions. 2020, 48, 2625.
[2] M. Kuzikov, E. Costanzi, J. Reinshagen, F. Esposito, L. Vangeel, M.Wolf, B. Ellinger, C. Claussen, G. Geisslinger, A. Corona, D. Iaconis, C. Talarico, C. Manelfi, R. Cannalire, G. Rossetti, J. Gossen, S. Albani, F. Musiani, K.Ye,Y. Herzog, B. Giabbai, N. Demitri, D. Jochmans, S.D. Jonghe, J. Rymenants, V. Summa, E. Tramontano, A.R. Beccari, P. Leyssen, P. Storici, J. Neyts, P. Gribbon, A. Zaliani, ACS Pharmacol. Transl. Sci., 2021, 4, 1096.
[3] J. Gossen, S. Albani, A. Hanke, B.P. Joseph, C. Bergh, M. Kuzikov, E. Costanzi, C. Manelfi, P. Storici, P. Gribbon, A.R. Beccari, C. Talarico, F. Spyrakis, E. Lindahl, A. Zaliani, P. Carloni, R.C. Wade, F. Musiani, D.B. Kokh, G. Rossetti, ACS Pharmacol. Transl. Sci., 2021, 4, 1079.
[4] E. Costanzi, M. Kuzikov, F. Esposito, S. Albani, N. Demitri, B. Giabbai, M. Camasta, E. Tramontano, G. Rossetti, A. Zaliani, P. Storici, Int J Mol Sci, 2021, 22, 11779.

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