Co-crystallization of hepatitis C virus NS3/4A inhibitors and SARS-CoV-2 main protease using high density acoustic droplet ejection (ADE)

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COVID-19 pandemic is a great threat to the general and global public health and economy. The rapid development of new antiviral compounds and vaccines is needed to control the current pandemic as well as to prepare for the emergence of new variants. Among the proteins encoded by the SARS-CoV-2 genome, M^{pro} is one of the primary drug targets due to its essential role in maturation of the viral polyprotein. In this study, we describe a high-density acoustic droplet ejection (ADE) method for co-crystallization of M^{pro}-ligand complexes using only 40 nL M^{pro} solution. Also, we will briefly describe crystallographic data from crystals obtained using ADE and other methods as evidence that three clinically approved anti hepatitis C virus (HCV) drugs are capable of covalent binding to the M^{pro} Cys145 catalytic residue in the active site (Fig. 1). Activities of the National Virtual Biotechnology Laboratory (NVBL) for the design and development of new antiviral inhibitors for SARS-CoV-2 is briefly discussed.

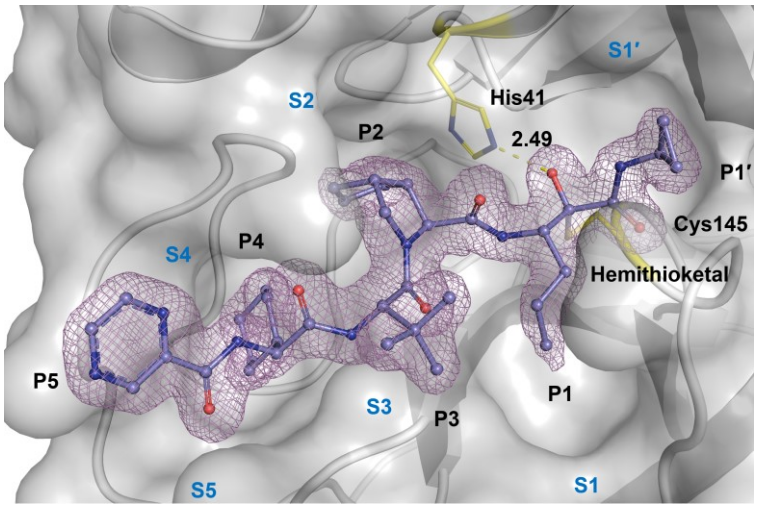

Figure 1. Crystal structure of SARS-CoV-2 main protease in complex with covalent inhibitor Telaprevir at 1.48 Å (PDB: 7K6D)

Keywords: SARS-CoV-2; main protease; acoustic droplet ejection; Telaprevir

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