Interprotein

Publication of The Research Paper on Drug Repurposing Study for COVID-19 Treatment with Orally Active Drugs

January 7th, 2022 – Interprotein Corporation is pleased to announce that the research paper on drug repurposing study for COVID-19 treatment with orally active drugs has been published as follows:

Journal title:	Journal of Biomolecular Structure and Dynamics (peer-reviewed journal)
Research article:	Identification of SARS-CoV-2 main protease inhibitors from FDA-approved drugs by artificial intelligence-supported activity prediction system
Authors:	Hirotsugu Komatsu, Takeshi Tanaka, Zhengmao Ye, Ken Ikeda, Takao Matsuzaki, Mayo Yasugi & Masato Hosoda
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We conducted a drug repurposing study to identify small molecule compounds that bind to 3-chymotrypsin-like protease (an essential enzyme for SARS-CoV-2 replication; also known as $3CL^{pro}$, main protease and M^{pro}) and inhibit SARS-CoV-2 replication from FDA-approved drugs aiming at contribution to COVID-19 treatment.

Binding activity to M^{pro} was predicted by Interprotein's "AI-guided INTENDD®", a unique artificial intelligence (AI)-introduced activity prediction system and finally 20 potential binders to M^{pro} were proposed from 1741 approved drugs. SPR analysis revealed that 13 compounds (65%) of the 20 selected drugs showed positive M^{pro}-binding signals. Vorapaxar, one of the verified M^{pro} binders, exhibited a K_d value of 27 μM to M^{pro} in the SPR assay and inhibited virus replication with an EC_{50} value of 11 μM in SARS-CoV-2-infected cells as well. Although the potency of vorapaxar itself was not sufficient for the immediate application to COVID-19 patients, it would become a good lead compound to identify a novel potent M^{pro} inhibitor because the proposed binding pose of vorapaxal was much different from those of current M^{pro} inhibitors including α-ketoamide 13b.

Importantly, AI-guided INTENDD®-proposed 12 drugs (60%) had been not reported precedential to the present study and 6 drugs (30%) were verified to bind to M^{pro} for the first time to the best of our knowledge. It is strongly suggested that this result is brought by the unique machine learning methodology that is differentiated from current docking simulation/molecular dynamics (MD)-based technologies.

We believe the findings of the present study demonstrate that AI-guided INTENDD® can practically contribute to identification of active compounds for new drug targets through drug repurposing as well as drug discovery approaches.

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