Press Release (プレスリリース)

東京薬科大学
Tokyo University of Pharmacy and Life Sciences
(TUPLS)

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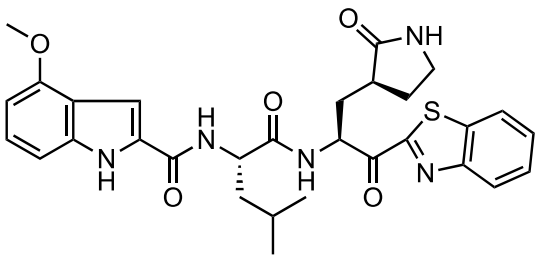
Good inhibitory activity of selective SARS-CoV protease inhibitor **YH-53** was confirmed against new coronavirus SARS-CoV-2

A research group led by Professor Yoshio Hayashi and Assistant Professor Sho Konno of School of Pharmacy, Tokyo University of Pharmacy and Life Sciences (TUPLS), in collaboration with Professor Wataru Kamitani of the Graduate School of Medicine, Gunma University, have confirmed a potential treatment for new coronavirus (SARS-CoV-2). **YH-53**, which was developed in 2013 as a 3CL protease inhibitor against severe acute respiratory syndrome coronavirus (SARS-CoV), strongly inhibits the growth of SARS-CoV-2.

The new coronavirus disease (COVID-19) that appeared at the end of last year caused a pandemic in many countries. The number of people infected and killed is currently about 14 million and 600,000 worldwide, respectively. To overcome the continually spreading disease, the development of therapeutic agents targeting SARS-CoV-2 is imperative and urgent. Viral protease inhibitors are generally known to be miracle drug in the treatment of AIDS and hepatitis C. SARS-CoV-2 also has 3CL protease (3CL-Pro), which is also called main protease (M-Pro). Since it is essential for virus replication in infected cells, selective inhibitors targeting the enzyme are considered to be typical COVID-19 therapeutic drug candidates based on a clear mechanism of action. In addition, 3CL-protease inhibition may have a potential to reduce the severity of COVID-19 by suppressing the growth of the virus.

Professor Hayashi's group is one of the few research groups in the world for SARS-CoV 3CL-Pro inhibitors. Since the occurrence of SARS in 2002, they have been developing SARS-CoV 3CL-Pro inhibitors. Recently, another research group reported that the homology of 3CL-Pro in SARS-CoV and SARS-CoV-2 is extremely high (99%), so that their enzyme inhibitors were expected to be effective against SARS-CoV-2. Experiments led by Professor Kamitani confirmed that multiple inhibitors including **YH-53**, showed a good antiviral effect against SARS-CoV-2. The result will be published in academic papers as early as possible.



TUPLS's SARS CoV 3CL-Protease Inhibotor
YH-53

This SARS-CoV-2 3CL-Pro inhibitor study was funded by the Japan Agency for Medical Research and Development (AMED) Research Program to Promote the Development of Innovative Drugs for Emerging and Re-

emerging Infectious Diseases in FY2020 (2nd phase). Professor Kamitani is the research representative and Prof. Hayashi and Prof. Masaki Kojima (Computer Molecular Design), Schools of pharmacy and life sciences from TUPLS, participated as co-workers. They will continue to conduct further creative research on new selective inhibitors of SARS CoV-2 3CL-Pro.

As for **YH-53**, since it has been confirmed that **YH-53** has good anti-SARS-CoV-2 activity, Hayashi group will conduct the in vivo anti-viral evaluation using animal models to pursue its potential as a drug, including safety and pharmacokinetics evaluations. For this purpose, his group is seeking a collaboration research worldwide. Furthermore, since the synthetic method for **YH-53** has already been established, TUPLS plans to provide **YH-53** worldwide to the research groups interested. Additionally, **YH-53** is useful for studying the pathophysiology and function of SARS-CoV-2 and structural biology of 3CL-Pro. Moreover, **YH-53** will be an important common tool to verify the effectiveness of protease inhibitor strategy against COVID-19. TUPLS hopes that this will accelerate the research and development of COVID-19 therapeutic agents. If you are interested in this project, please contact us for further information.

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YH-53 is a low molecular weight compound with the chemical structure shown on the right, and it is a potent and selective enzyme inhibitor created in 2013 targeting SARS-CoV 3CL-Pro. It has been featured in a recent review of COVID-19 therapeutic candidates[2]. **YH-53** potently inhibits SARS-CoV-2 3CL-Pro at low concentrations[3]. Furthermore, Professor Kamitani's recent experiment with SARS-CoV-2 infection in cells revealed that **YH-53** has a strong antiviral effect. On the other hand, due to its low cytotoxicity, **YH-53** is considered to be a promising development candidate for COVID-19 therapeutic agents.

1) Thanigaimalai, P., Konno, S., Hayashi, Y., et al., Eur. J. Med. Chem., 2013, 68, 372-384. 2) Ghosh, AK, et al., ChemMedChem, 2020, 15, 907–932.

3) Enzyme inhibitory activity against SARS-CoV-2 3CL-Pro was studied in collaboration with Professor Christa E. Müller, University of Bonn (Germany).