Scientists uncover structure of key pneumonia virus enzyme, suggesting a route for new antiviral treatments
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As they infect human cells, HMPV and RSV commandeered the cell's machinery to make copies of themselves. To initiate the process, special proteins released by the virus interact with each other to make distinct protein complexes.

Writing in Nature, Dr. Julien Lescar from NTU's School of Biological Sciences and his team report that they have used cryo-electron microscopy to image the molecular structure of one of these large complexes, an enzyme called HMPV L:P polymerase.

Cryo-electron microscopy uses an advanced electron-scanning microscope, which can image a cryogenically frozen sample down to the sub-nanometer range. The NTU images captured the enzyme at a resolution of 3.7 Angstrom, or 0.37 nanometers. Based on these two-dimensional pictures, the team then built three-dimensional computer models of the proteins' L:P molecular structures.

Analysis of these model structures revealed key sites for molecules to interact, offering new targets for designing antiviral molecules against both viruses. Dr. Lescar, a principal investigator at the NTU Institute of Structural Biology, said that with this detailed structural knowledge, researchers can now develop inhibitors that disrupt the enzymatic activities of HPMV L:P protein and potentially block infection by the virus.

"We hope that our work will help researchers in pharma and academia around the world to design much-needed therapies for difficult viral infections that often lead to antibiotic-resistant bacterial infections," said Dr. Lescar.

Since the HMPV proteins they studied are essentially unchanged through evolution and very
similar to those of RSV and other virus species belonging to the Pneumoriviridae family, the scientists hope that inhibitors developed against HPMV could also work against a broad spectrum of viruses involved in respiratory diseases, and inform similar quests against other viral diseases.

Dr. Lescar and colleagues have founded a spin-off company named Epitoire that is actively engaged in designing DNA replication blockers as potential therapies against these viruses, and the company is currently seeking investors and clinicians to support it.


Provided by Nanyang Technological University