

Infectious Diseases Labs

A*STAR IDL



Dr Xiao Tianshu

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Wednesday 14th May 2025 11:00 AM to 12:00 PM (SGT)

Venue: Cistron A & B, Matrix Level 5

Structural based development of broad-spectrum antiviral inhibitors

Virus envelope protein is responsible for interacting with host receptors and mediating membrane fusion and entry. This viral protein is targeted by the host immune system, and historically a focus in antiviral therapy development. My research focuses on antiviral inhibitor development based on insights gained from function and structure of flavivirus E protein and coronavirus S protein. Leveraging on different drug discovery strategies, we are developing small molecule and peptide-based inhibitors to block the membrane fusion process mediated by these proteins. For flavivirus, different from the traditional drug developments focusing on ligand pocket on the E protein, we develop inhibitors capturing a new target located at the center of E protein with the help of our antibody-guided platform and structure-based design. This platform allows us to apply such a critical, conserved but difficult target to drug discovery. S protein of coronavirus has been a major target of vaccine development, but rarely explored as a drug target because many conserved regions on S are not suitable for wet lab based drug discovery. Here, we utilize a variety of Al-facilitated approaches to design inhibitors capturing hotspots and hidden pockets on the S protein. With the inhibitor cocktail with a pancoronavirus potency. Collectively, with these efforts, we aim to find out broad-spectrum antiviral drug candidates with clear mechanisms and *in vitro/ in vivo* characterization.

Dr Xiao Tianshu is a structural virologist working on flavivirus and coronavirus. She was trained with protein NMR when she was a PhD student with Prof. Yang Daiwen at NUS department of biological sciences. After completing her PhD, Dr. Xiao moved to Boston Children's Hospital (BCH)/Harvard medical school in 2017, working with Prof. Chen Bing for her postdoctoral training. When she was in Prof. Chen's lab, she focused on the process of viral entry mediated by HIV-1 Envelope protein and SARS-CoV-2 Spike protein. Leveraging on an antibody-guided drug discovery strategy and NMR structural studies, she identified a new class of broad-spectrum HIV inhibitors to block entry and infection of HIV virus. During the COVID-19 pandemic, Dr. Xiao contributed significantly to understanding the structure and function of the Spike proteins from different variants. Based on the cryo-EM structure of ACE2-Spike complex, she developed a protein-based entry inhibitor with pan-COVID19 activity. In 2022, Dr. Xiao was awarded with Nanyang Assistant Professorship and started her own group in NTU School of Biological Sciences. Leveraging on her expertise in protein structure and antiviral inhibitor development, her lab now focuses on establishing different drug discovery platforms to interrogate conventionally challenging targets for broad-spectrum entry inhibitors against flavivirus and coronavirus.

Hosted by: Dr Stefan Oehlers

