



**THE CHINESE UNIVERSITY OF HONG KONG
FACULTY OF MEDICINE
SCHOOL OF BIOMEDICAL SCIENCES**

SBS PI Seminar Series 2023-2024

Prof. Bo FENG

Associate Professor

School of Biomedical Sciences, Faculty of Medicine,
The Chinese University of Hong Kong, Hong Kong SAR, China.

will present a seminar entitled

***“Continual Battle Against SARS-CoV-2: New Insights from a Study on
ACE2 Decoy”***

Abstract

SARS-CoV-2 exhibits rapid evolution and global circulation, evading neutralization by monoclonal antibodies and convalescent/vaccine sera. Soluble angiotensin-converting enzyme 2 (sACE2) has potential as a therapeutic strategy due to conserved binding property to SARS-CoV-2 spike, but its clinical application is limited. In this study, we aimed to develop sACE2 decoys for effective protection against SARS-CoV-2. By fusing sACE2 with human IgG1 Fc (sACE2-Fc) and introducing as few as two mutations, we generated sACE2-Fc mutants with enhanced neutralization potency and abolished enzymatic activity. These mutants were evaluated against SARS-CoV-2 pseudoviruses and authentic strains, demonstrating improved neutralization capacities. Furthermore, in mice, adeno-associated virus (AAV)-based overexpression of the mutants showed low immunogenicity and minimal disruption to the renin-angiotensin system. Intranasal administration of the most promising mutant (B5-D3) resulted in highly efficient prophylaxis, providing 100% protection, efficient virus clearance, and reduced neutralizing antibody titers in SARS-CoV-2-inoculated K18-hACE2 transgenic mice. Transcriptomic analysis revealed early interferon (IFN)- β responses and enhanced macrophage activities in lungs of B5-D3-treated mice. Notably, B5-D3 prophylaxis was effective in aged mice as well. These findings highlight the potential of simple sACE2-Fc mutants, particularly B5-D3, as a therapeutic approach for neutralizing SARS-CoV-2.

16 November 2023, Thursday, 4:00 – 5:00 pm

Room G02, Lo Kwee-Seong Integrated Biomedical Sciences Building,
Area 39, The Chinese University of Hong Kong