CHINESE-AMERICAN LUNG ASSOCIATION

CALA Happy Friday Seminar

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Time: EST 10:30 am; PST: 7:30 am; Beijing time: 11:30pm

Zoom: 849 9682 9273 (Password: 654321)

Engineered ACE2 Decoy Mitigates Lung Injury and Death Induced by SARS-CoV-2 Variants

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Bio: Dr. Zhang received her M.D. from Medical School of Fudan University and Ph.D. in Pharmacology from University of Rochester. Dr. Zhang's research interests have been focused on exploring the mechanisms of inflammatory endothelial injury and repair using acute lung injury mouse model and developing novel mechanism-based regenerative strategies. Her scientific training began with her graduate work under the instruction of Dr. Alan Smrcka at the University of Rochester to dissect signal pathways of cardiac hypertrophy. Dr. Zhang's postdoctoral training in lung vascular biology was with Dr. Jalees Rehman and Dr. Asrar Malik in the Department of Pharmacology at the University of Illinois at Chicago. She just started to set up her own laboratory. Dr. Zhang is supported by NIH RO1. She has published in high impact journals such as, Nature Chemical Biology, Nature Communications, Circulation, Cell, etc.

Abstract: Vaccine hesitancy and emergence of SARS-CoV-2 variants of concern escaping vaccine-induced immune responses highlight the urgency for novel COVID-19 therapeutics. Engineered ACE2 proteins with augmented binding affinities for SARS-CoV-2 Spike (S) protein may prove to be especially efficacious against multiple variants. Using molecular dynamics simulations, we show that three amino acid substitutions in an engineered soluble ACE2 protein markedly augmented the affinity for the S protein of the SARS-CoV-2 WA-1/2020 isolate as well as multiple variants of concern: B.1.1.7 (Alpha), B.1.351 (Beta), P.1 (Gamma), and B.1.617.2 (Delta). In humanized K18-hACE2 mice infected with SARS-CoV-2 WA-1/2020 or P.1 variant, prophylactic and therapeutic injections of sACE22.v2.4-IgG1 prevented lung vascular injury and edema formation, essential features of CoV-2 induced SARS, and above all improved survival. These studies demonstrate broad efficacy in vivo of an engineered ACE2 decoy against SARS-CoV-2 variants and point to its therapeutic potential.