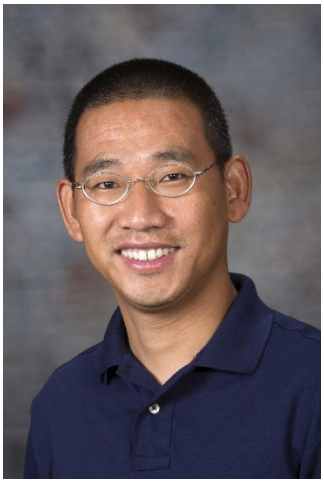
NEURAL ENGINEERING SEMINAR SERIES

Modulate inflammation and NF-kB pathway with anti-inflammatory cells and proteins

https://psu.zoom.us/j/92405373420

September 27, 2023

12:15 -1:15 p.m. (ET)
W306 Millennium Science Complex



Yuguo Lei

Associate Professor of Biomedical Engineering and Graduate Program Coordinator

Penn State University

ABSTRACT:

Trauma, surgery, and infection can cause severe inflammation. Both dysregulated inflammation intensity and duration can lead to significant tissue injuries, organ dysfunction, mortality, and morbidity. Conventional anti-inflammatory drugs such as steroids and immunosuppressants have drawbacks, including derailing inflammation resolution, compromising normal immunity, and having significant adverse effects. The natural inflammation regulator mesenchymal stromal cells (MSCs) have high therapeutic potential because of their unique capabilities to mitigate inflammation intensity, enhance normal immunity, and accelerate inflammation resolution and tissue healing. Furthermore, clinical studies have shown that MSCs are safe and effective. However, they are not potent enough, alone, to completely resolve severe inflammation and injuries. In this study, we investigated the synergistic effect of combining MSCs with alpha-1 antitrypsin (A1AT), a plasma protein with excellent safety and clinical use, to mitigate inflammation and promote resolution. We evaluated the effectiveness and synergy of MSCs and A1AT through in vitro inflammatory assay and in vivo mouse acute lung injury model. The in vitro assay measured cytokine releases, inflammatory pathways, reactive oxygen species (ROS), and neutrophil extracellular traps (NETs) production by neutrophils and phagocytosis in different immune cell lines. The in vivo model monitored inflammation resolution, tissue healing, and animal survival. We found that the combination of MSCs and A1AT was much more effective than each component alone in i) modulating cytokine releases and inflammatory pathways, ii) inhibiting ROS and NETs production by neutrophils, iii) enhancing phagocytosis and, iv) promoting inflammation resolution, tissue healing, and animal survival. At molecular mechanism, MSCs and A1AT synergistically turn off the NF-KB signaling. These results support the combined use of MSCs, and A1AT is a promising approach for managing severe, acute inflammation including inflammation accompanied to various neurological disorders.

BIOGRAPHY:

Dr. Lei had a B.S. in chemistry from Peking University, an M.Phil. in polymer science from Hong Kong University of Science and Technology, a M.S. in pharmacology and a Ph.D. in Chemical Engineering from UCLA, and a postdoctoral training in stem cell manufacturing at UC Berkeley. His research falls into two major areas: biotherapeutics design and biomanufacturing. His lab looks for natural proteins and cells (e.g., existing in human bodies) that have high therapeutical potential and develop engineering approaches to scale up their production and boost their potency and safety. He has a high interest in treating severe inflammation and injuries. A significant challenge with biotherapeutics is producing them at large scales and at affordable cost. This is particularly true for complicated biologics such as cells and viral vectors. Dr. Lei's lab develops technologies that enable the manufacturing of high-quantity, high-quality, consistent, and affordable cells, viruses, and proteins.