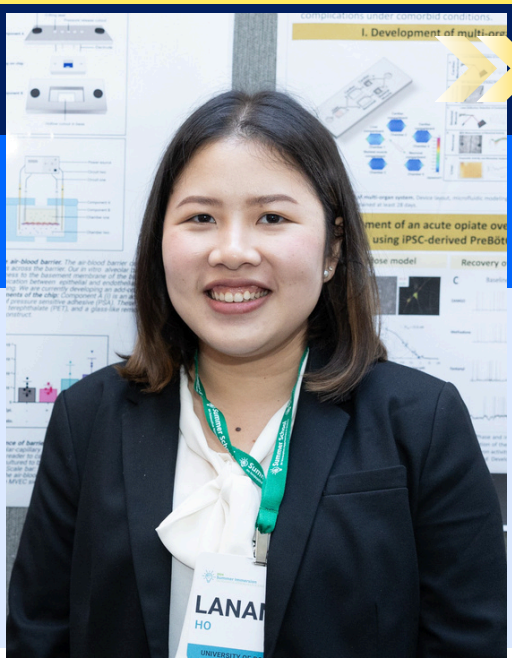
University of Rochester

BME PhD Defense Seminar



Lananh Whigham

SEPTEMBER 08

Supervised by
Drs. David Dean & Hani Awad

"A Lung-on-Chip Model of the Alveolar-Capillary Barrier for Studying Acute Respiratory Distress Syndrome and Evaluating Potential Therapeutic Strategies"

Seminar Abstract:
Acute respiratory distress syndrome (ARDS) is a severe inflammatory lung disease characterized by pulmonary edema, hypoxemia, and bilateral infiltration. ARDS can arise from both pulmonary (direct ARDS) and systemic (indirect ARDS) insults, including pneumonia, lung trauma, aspiration of gastric contents, inhalation of toxic irritators, and sepsis. While the development of advanced supportive care has eased the impact of the disease, ARDS remains associated with a high mortality rate, ranging from approximately 30% in mild cases to 40% in more severe cases. Despite decades of research, no pharmacological therapy has been developed for the treatment of ARDS. The heterogeneity of the disease and its underlying pathological mechanisms has limited a comprehensive understanding of its pathogenesis and hindered the development of effective treatments.

The objective of this project was to develop a biophysically relevant model of the alveolar-capillary barrier, the interface most affected during ARDS, to investigate disease mechanisms and evaluate potential therapeutic strategies. Primary rat alveolar epithelial cells and microvascular endothelial cells were co-cultured on a novel lung-on-chip platform incorporating an ultrathin silicon nitride nanoporous membrane to recreate the native alveolar-capillary interface. The platform was optimized to establish a stable, physically relevant barrier through optimization of relevant extracellular matrix coatings, cell seeding densities, and other culture parameters. The results demonstrated that barrier integrity is regulated by complex interactions among alveolar epithelial cells, endothelial cells, macrophages, and the extracellular matrix. Furthermore, inflammatory and coagulation-associated injury pathways disrupted barrier function through distinct mechanisms. Lipopolysaccharide (LPS), representing bacterial inflammatory injury commonly associated with direct ARDS, and thrombin, representing activation of the coagulation cascade commonly associated with indirect ARDS, produced different patterns of barrier dysfunction while both ultimately compromised alveolar-capillary integrity. Additionally, different approaches for direct genetic manipulations and pharmacological treatment of cells on the lung-on-chip were evaluated, including chemical and physical transfections, lentiviral transduction, and triiodothyronine (T3), to advance the platform toward disease mechanisms and therapeutic evaluation applications. Lastly, a human lung-on-chip was developed to create a human-relevant model. Collectively, this work establishes a physiologically relevant lung-on-chip model as a versatile platform for investigating ARDS pathogenesis and evaluating novel therapeutic strategies.

Tuesday, September 8, 2026 | 10:00am EST | K-207 (2-6408, Med Center)
https://rochester.zoom.us/j/94171989914

UNIVERSITY OF ROCHESTER, BIOMEDICAL ENGINEERING DEPARTMENT