BIOMEDICAL ENGINEERING
Carnegie Mellon University

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10:30 – 11:30 a.m.
Posner Hall A35

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Exosomes and Tissue Engineering: Developing Novel Therapies for Lung Disease

Abstract: This talk will discuss two research directions in an active industry R&D laboratory. The first focus area is secreted exosomes, which are bioactive particles that elicit profound responses in target cells. Using targeted metabolomics and global microarray analysis, we identified a role of exosomes in promoting mitochondrial function in the context of pulmonary arterial hypertension (PAH). While chronic hypoxia results in a glycolytic shift in pulmonary artery smooth muscle cells (PASMC), exosomes restore energy balance and improve O_2 consumption. These results were confirmed in a hypoxia-induced mouse model and a semaxinib/hypoxia rat model of PAH wherein exosomes improved the mitochondrial dysfunction associated with disease. Importantly, exosome exposure was linked to improved flux through the TCA cycle and evidence of an improvement in mitochondrial function. The application of exosomes to lung diseases will be discussed, with a focus on PAH as well as bronchopulmonary dysplasia.

The second research area that will be reviewed is the recellularization of decellularized lung scaffolds as a strategy to increase the supply of lungs available for transplant. Decellularized porcine lung scaffolds were recellularized by perfusion of epithelial cells and/or endothelial cells into the airway or vasculature and allowed to culture in a bioreactor. Strategies for lung decellularization and recellularization will be discussed, including functional analysis of engineered tissues using metrics that include vascular resistance, dynamic compliance (Cdyn) and gas exchange (ΔPO2/FIO2). This work reports positive progress toward production of functional bioengineered lung grafts with perfusable vasculature and gas exchange capability. Through improved culture paradigms iterating upon the top performing strategies, we will move closer towards generating functional engineered lungs.