THE HARTWELL FOUNDATION

2017 Individual Biomedical Research Award

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Application of Cellular-Derived Therapies for the Regeneration of Lung Structure and Function

Premature birth results in persistent abnormalities of lung structure and function that increases the risk for developing emphysema, heart disease, asthma and decreased life expectancy. Premature birth occurs in 12.5% of live births (>500,000 infants/yr) and up to 20-50% of infants born less than 28-weeks gestation will die. The problem is that these infants sustain lung injury in the first few weeks of life that results in the development of bronchopulmonary dysplasia (BPD), which is characterized by a undeveloped lung tissue structure, abnormal growth of blood vessels in the lung and decreased lung function. In addition, there are many recognized negative respiratory outcomes of premature birth including higher incidence of asthma, emphysema and cardiopulmonary disease. Unfortunately, there are no definitive therapies to treat and recover lung tissues injured or underdeveloped from BPD. A therapy is needed to enhance lung growth to allow survivors of prematurity to develop normal lungs. Recently, Vivek demonstrated the potential of mesenchymal stromal stem cells (MSC) conditioned media to prevent lung injury and recover normal lung structure and cardiovascular function. Interestingly, the MSC secrete extracellular vesicles (EV) including exosomes known to contain proteins, lipids and RNA. Based on these observations, he hypothesized that the exosomes enter the tissue and cells of the developing lung, stimulating pathways that would otherwise be impaired in the premature lung, representing a potential therapy. To determine the effectiveness of such exosomes to prevent lung dysfunction and repair normal lung growth, he will use an established rodent model of neonatal lung injury that mimics the arrest of lung development seen in premature infants exposed to high oxygen therapy (hyperoxia). To understand the regeneration of lung structure and function following neonatal hyperoxia-induced lung injury, he will determine the temporal effects of exosome treatment delivered by intraperitoneal injection using non-invasive PET imaging for spatial and temporal tracking their distribution. He will also determine the exosome payload composition. If Vivek is successful in demonstrating the use of exosomes for the protection and/or restoration of lung structure and function in infancy, translation of his research will provide longlasting health benefits to children who survive premature birth and who are at risk to develop BPD or already have been diagnosed with BPD.