UNIVERSITY of WASHINGTON

Undergraduate Research Symposium May 17, 2019 Mary Gates Hall

Online Proceedings

POSTER SESSION 1

Commons West, Easel 24

11:00 AM to 1:00 PM

Using ExoFlow to Assess Exosome Profiles of Cystic Fibrosis Patients with and without Chronic Lung Allograft Dysfunction after Lung Transplantation

Nihar Mahajan, Senior, Biology (Molecular, Cellular & Developmental), Biochemistry
Mentor: Billanna Hwang

Lung transplantation is currently the only treatment solution for end-stage lung disease in a large cohort of patients afflicted with a range of pulmonary issues including cystic fibrosis (CF) and idiopathic pulmonary disease (IPF). Despite the successes, a major setback is the development of chronic lung allograft dysfunction (CLAD). This is characterized by chronic inflammatory host responses towards the transplanted lung resulting in injury of the donor tissue. Currently, we are investigating the role of cell-derived vesicles or exosomes, in a range of immune responses such as chronic inflammation. The composition of exosome membrane components and internal signaling within exosomes depend on the cell type from where it was secreted and the current immune state. A major benefit is that unlike cells, exosomes do not change phenotype after being secreted by the parent cell due to environmental stimuli, making them ideal targets for biomarkers associated with immune responses. In these studies, we assessed exosome surface markers and investigated exosome function from retrospective patient serum, which provides insight into potential novel mechanisms in the development of CLAD. We developed a novel ExoFlow that qualitatively and quantitatively assesses exosomes at 1, 3, 6, and 12 months posttransplant using CFSE, traditional fluorescent antibodies for T cell and macrophage markers, and ImageStream to generate immune profiles. We then correlated these results to clinical outcomes. In a preliminary study, it appears that macrophage exosome profiles show significance in differentiating patients who develop CLAD, while T cell specific exosomes seem to be unremarkable. This could be attributed to the heavy course of immunosuppression posttransplant. Functional studies show insight in potential polarization capabilities of exosomes as immune modulators and provides another novel area of investigation into the complex pathogenesis of CLAD.

POSTER SESSION 1

Balcony, Easel 103

11:00 AM to 1:00 PM

Delivery of CRISPR Cas9 Using Mesenchymal Stem Cell-Derived Exosomes to Reduce Fibrosis and Promote Regeneration in Lung Tissue

Sean Anthony Hoeger, Senior, Biology (Molecular, Cellular & Developmental)
Mentor: Billanna Hwang

Pulmonary fibrosis is a disease marked by irreversible scarring and thickening of the lung tissue causing significant decline in lung function. Individuals afflicted will struggle to perform simple physical activities and often require mechanical assistance at some point in their lives. Currently, there are no permanent solutions for those with pulmonary fibrosis as most treatments only aim to slow down the progression of the disease. In these studies, we developed a novel therapeutic that could stop the progression through DNA modification of fibrotic gene targets using exosomes as a delivery vehicle. Additionally, regeneration of lung tissue is imperative for reinstating lung function and by using similar technologies we aim to target and overexpress critical regenerative genes. Using CRISPR Cas9 gene editing technology, we were able to knockdown key cytokine specific genes responsible for the development of fibrosis. We specifically targeted TGFß(Transforming Growth Factor ß) and Interleuken-6 (IL-6), both known to play a significant role in pro-inflammatory responses and fibrosis through exosome-mediated delivery mechanisms. CRISPR Cas9 vectors were designed to contain unique guide RNAs that could effectively target specific genes that the Cas9 complex could use to repress TGFßand IL-6. Cell lines were treated with the modified CRISPR Cas9 vectors and assessed for gene and protein expression. This study provides key insight into a novel therapeutic platform using a new delivery mechanism that mitigates and reduces fibrosis and promotes recovery of pulmonary function.

POSTER SESSION 1

MGH 241, Easel 141

11:00 AM to 1:00 PM

Last-Passage Charge Density Algorithm via Off-Centered Dipole Green's Function

Glenn Rui Zhang, Senior, Mathematics, Computer Science
Mentor: Chiok Hwang, Gwangju Institute of Science and Technology

First-passage and last-passage algorithms are two diffusion Monte Carlo methods that we can use to obtain the charge density distribution on a conducting surface. Usually, we use first-passage algorithms to obtain the capacitance and the overall charge distribution of the arbitrary-shaped conductor. On the other hand, the last-passage algorithms calculate the charge density at a point on a conducting surface by initiating the random walk at that point. The last-passage algorithm utilizes the dipole Green's function to expedite the diffusion process which starts from the point. Past results determine the initial sitting using the largest hemisphere around that point with a radius that is contained in the surface, which inefficiently starts the random walk if the point is near the edge of the surface. Here, we derive the dipole Green's function to start the diffusion process from a point on the hemisphere off-centered from the original point using weighted sampling to further expedite the computing process.