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Perfluorocarbon Based Intrapulmonary Drug Delivery to Enhance Alveolar Repair Following Acute Lung Injury

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Acute Respiratory Distress Syndrome (ARDS) is the sudden failure of the respiratory system after Acute Lung Injury from infection, sepsis, or major trauma. ARDS is characterized by severe inflammatory damage to the lung epithelium and microvasculature, resulting in fluid filling the alveoli and impeding this essential site for gas exchange. Approximately 190,000 Americans suffer from ARDS annually, with 30% mortality.

In order to address this shortcoming, a novel treatment is proposed in which the lungs are partially filled with perfluorocarbon (PFC) based emulsions containing growth factors intended to accelerate alveolar repair. This technique is built upon a previous technique, partial liquid ventilation (PLV) that was proposed as a means to lower ARDS mortality. During PLV, lungs are partially filled with liquid PFC and gas ventilated. PFC liquids have high O_2 and CO_2 solubility, low surface tension, density twice that of water, and anti-inflammatory properties. Thus, they are ideal for washing out lung fluid during ARDS, calming inflammation, and restoring normal gas exchange.

Despite these benefits, ARDSnet clinical trials have proven that ARDS survival requires both supporting the respiratory function of the patient as well as limiting further lung damage by improving alveolar repair. Thus, our proposed use of emulsions with a disperse phase of micron sized aqueous droplets allows drugs to be delivered via the PFC, while maintaining PFCs excellent gas solubility and low surface tension. Our lab has shown antibiotics delivered in this way have better maintained lung concentrations vs. identical inhaled doses. Our collaborator has shown the first proposed drug LPA (Lysophosphatidic Acid) to enhance pulmonary epithelial cell migration and barrier function. Delivered to the alveoli, we hypothesize LPA will be the first of several drugs in our pharmacological treatment to recover inflammatory-damaged alveolar cells, improve overall lung function, and decrease ARDS mortality rates.