THE HARTWELL FOUNDATION

2013 Individual Biomedical Research Award

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Surfactant-Enhanced Delivery of Silencing Ribonucleic Acid to Prevent Bronchopulmonary Dysplasia

Bronchopulmonary dysplasia (BPD) is the most common cause of chronic lung disease in premature infants. It is the consequence of birth before the development of the lung is completed and prepared for exposure to air, and commonly occurs in infants who receive prolonged exposure to high levels of oxygen (hyperoxia) and mechanical ventilation to treat respiratory distress. BPD is characterized by inflammation and development of large abnormal air sacs in the lungs. For infants, obstruction of the weakened, pliable airways results in difficulty in breathing, lowered blood oxygen levels, and low heart rates. Up to 50% of babies with BPD require hospitalization in the first year, and 36% in the second year. Sequelae include poor physical growth and delayed mental development, accompanied by significant respiratory and cardiac deficiencies that persist into adulthood. Despite medical advances in the treatment of premature infants, the incidence of BPD has not decreased, with an estimated 10,000 - 15,000 new cases reported each year. To date, there is no specific and effective prevention or treatment. In a hyperoxia-induced mouse model of BPD that Vineet developed in 2011, he recently discovered a novel role for a small RNA molecule called miR34a that is known to control gene expression involved in lung injury and repair, including tumor growth and metastasis. He found that the levels of miR34a in lung secretions and lung tissue of human babies who had respiratory distress syndrome and subsequently developed BPD were significantly increased. Vineet hypothesizes that counteracting miR34a activity in the premature infant lung with a specific antagonist could provide a novel and potentially highly effective strategy to prevent BPD. In seeking to understand the cellular functions and mechanism of action of miR34a in BPD, he will develop an innovative method to deliver a miR34a-inhibitor to the periphery of the lung using an FDA-approved surfactant (detergent-like substance). If Vineet is correct, blocking the deleterious effects of miR34a in the immature lung will prevent the development of BPD in those babies at risk for the chronic disease, thus improving their lifetime health.