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Worldwide, millions of people suffer daily from incurable lung diseases such as chronic obstructive pulmonary diseases (COPD), interstitial lung fibrosis (IPF) and genetically disordered lung diseases such as cystic fibrosis (CF). Although these refractory diseases are life threatening and have been studied, there has been little progress in realizing an innovative cure for end-stage lung diseases. The only viable option for patients with end-stage disease is lung transplantation. However, there is a definitive lack of donor lungs.

What if diseased lungs could be compensated immediately following pneumonectomy by transplanting new lung tissue derived from the patient's own induced pluripotent stem cells (iPS) cells? A personalized/precision medicine approach to tissue engineering using a patient's autologous cells could potentially optimize the surgical indications for the these patients by replacing the diseased, resected lung with healthy new tissue less likely to face immune response transplant rejection. Furthermore, this would provide an expanded patient-based approach for drug screening to achieve the most effective combination of drugs for a precision order-made therapy. Additional pathological analyses should contribute to the diagnostic aspects as well. Lastly the proposal for transplantable donor lungs is revolutionary and pertinent because of the definitive lack of available donor lungs. Though there are no world reports currently on the successful regeneration of functional lung organs in spite of an urgent need, this innovative approach, though challenging, would change the course of medical treatment for the patients with refractory lung diseases. Given the large number of pediatric and adult refractory pulmonary lung diseases, it is of great public concern to navigate the road leading to the regeneration of functional lungs, - "lung renewal".

How to regenerate transplantable lung organs...?

Recently, the field of regenerative medicine has shown promise by utilizing stem cells to repair and regenerate damaged tissues. Our goal in this proposal is to establish an experimental basis for the regeneration of lungs organs via BC bioengineering (in Aim1) and in utero progenitor injection (Aim2) in rodents (mice and rats). Notably our collaborators have had success in the regeneration of functional organs such as the pancreas and kidneys via a blastocyst complementation (BC) technique. In utero injection technology has developed in the field of neuroscience and dermatology, but has never been described in the lung literature. If successful in rodents, we will gain the knowledge to make use of BC in large animals, eventually with patient-specific, gene-corrected induced pluripotent stem cells (iPS). The proposed study would provide new knowledge in the area of stem cell research, particularly for the regulation of lung organ niches and stem cell competence. Our approach, for regenerating functional lungs via BC and gene correction though challenging, would pave a new road for the treatment of patients with a vast array of refractory lung diseases. If successful, this technology will allow us to model these diseases with patient-specific iPS cells in vivo, and ultimately will contribute to the diagnosis and treatment of refractory lung diseases. This concept would pave a new road for the treatment of incurable lung diseases. The development of a new regenerative tissue transplant surgery in large animals would expand surgery to a new patient population. Lung transplantation will evolve to lung renewal with gene-corrections. The success of this study would ultimately change the criteria for operable lung refractory diseases.