Regenerating Organs Using Stem Cells and Biomaterials

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Abstract

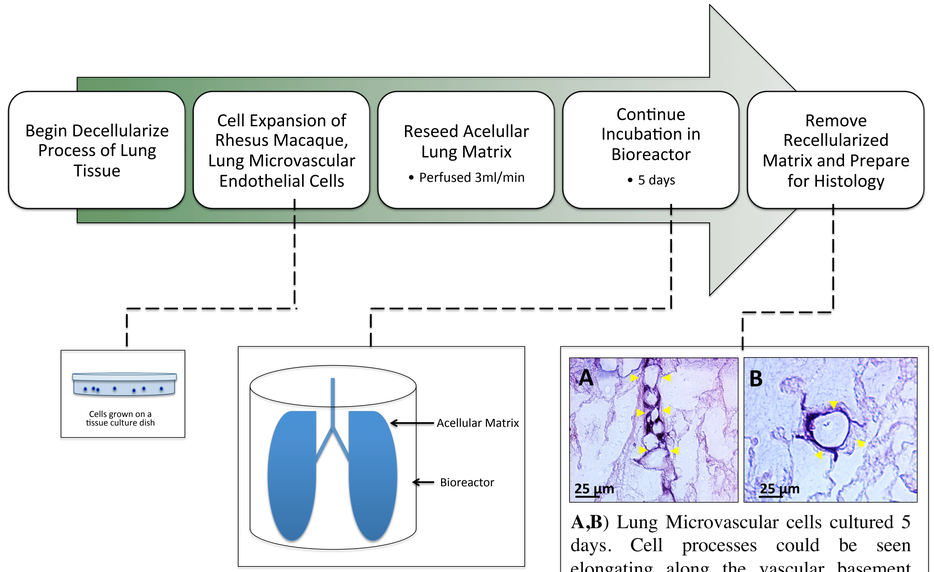
The goal of regenerative medicine is to provide novel solutions by which body tissues and subsequent organs can be repaired or replaced. An important aspect of this research is its highly translational value. The IGERT Bioinnovation program at Tulane University focuses on translational research, in which regenerative medicine is one approach to provide applicable scientific research to the medical market. Two innovative projects at Tulane University's Center for Stem Cell Research and Regenerative Medicine, involve regenerating the lung and esophagus by using specialized stem cells in unique biomaterials, both biological and synthetic biomaterials. Critically, there is a dire need to regenerate both organs: there is a high demand for lung transplantations with a low number of suitable donors, and a high rate of esophageal cancers that destroy the esophagus. The regenerative approach for the lung requires autologous (self) stem cells implanted in a decellularized lung biological material, while for the esophagus both allogeneic (non-self) and autologous stem cells are implanted in a synthetic biodegradable material. Both approaches are unique and provide applicable ways in which the target organ can be regenerated and then implanted into the body.

Significantly, both regenerative models not only provide a schematic to specifically reconstruct the lung or esophagus, but the approaches from each application can elucidate the regeneration of other damaged organs as well. Therefore, using unique stem cells and biomaterials to robustly regenerate organs will hopefully translate to novel medical therapies and will successfully satisfy the current need for hard to find donor organs.

Regenerating Lung Using Acellular Biological Matrices

Problem/Focus: According to the Organ Procurement and Transplantation Network, the average time an individual remains on the lung transplant waitlist is over 3 years. There is a need for an alternative to organ transplantation due to the low number of usable donor tissue relative to the high recipient demand. To alleviate this unmet need, an individualized tissue engineering approach for lung replacement is highly desirable.

Solution: Whole-organ decellularization is a technique used to obtain an acellular native organ scaffold by instillation/ perfusion of detergents, salts, and enzymes, effectively removing all of the cellular components while leaving the natural extracellular matrix intact. These scaffolds can be seeded with autologous cells toward the goal of reconstituting functional tissue. This technology can be potentially applied to lung.



A,B) Lung Microvascular cells cultured 5 days. Cell processes could be seen elongating along the vascular basement membrane (yellow arrows)

Regenerating Damaged Esophageal Tissue

Problem/Focus: An advanced stage of Barrett's Esophagus can destroy esophgeal tissue and lead to a lethal esophageal cancer (adenocarcinoma). Barrett's Esophagus affect 5-16 million people in the U.S. [1] and adenocarcinoma affects 18,000 – 30,000 people annually in the U.S. [2].

Solution: Implement induced human mesenchymal stem cells (MSCs) that can attenuate inflammation at the injury site, while also incorporating human endothelial progenitor cells (EPCs) in a biodegradable scaffold.

1.Hayeck, T.J. & *et al*. The prevalence of Barrett's esophagus in the US: estimates from a simulation model confirmed by SEER data. *Diseases of the Esophagus* (2010) **23**, 451-457; 2.Hur, Chin & *et al*. Development, Calibration, and Validation of a U.S. White Male Population-Based Simulation Model of Esophageal Adenocarcinoma. *PLoS one*. (2010) 5(3)