School of Biomedical Engineering, Science and Health Systems

Biomedical Technology Showcase, 2006

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Engineered Tissue Models for Drug Development: The Lung as a Paradigm

Mark J. Mondrinos[1], Sirma Koutzaki[2], Christine M. Finck[2], and Peter I. Lelkes[1]

1 - School of Biomedical Engineering, Drexel University, Philadelphia, PA

2 - St. Christopher's Hospital for Children, Philadelphia, PA

Clinical and Research Needs

In addition to the development of functional tissue equivalents, tissue engineering holds the promise of revolutionizing the pharmacological industry by providing novel venues for high throughput drug testing.

Goals

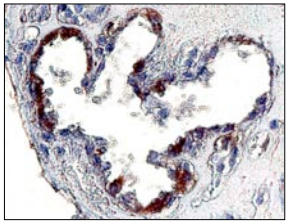
1. Generate functional tissue equivalents.
2. Demonstrate physiological responses.
3. Induce pathological conditions.
4. Test therapeutics in disease models.

Research Approach

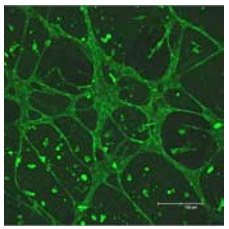
Utilize tissue engineering methods to develop functional tissue equivalents, via optimization of cell sourcing and engineering of the tissue culture microenvironment in terms of ECM composition and growth factor milieu.

1. **Cell Sourcing:** Testing various stem cell populations including embryonic stem cells, fetal cells, and adult stem cells.
2. **Scaffold Engineering**: Design and implement extracellular matrix scaffolds that support optimal tissue development.
3. **Growth Factor Biology**: Optimize the growth factor stimulation required to stimulate functional tissue development.

Functional Lung Tissue Constructs



Epithelial Branching Morphogenesis



Vascularization

Optimization

We must engineer these constructs to reflect both the organotypic lung architecture and differentiative status of the lung alveolus. Upon development of a suitable construct, the potential is vast for application in the realms of clinical medicine and drug development.

Physiological Responses

-surfactant production and secretion

Therapeutic Testing

-utilize engineered physiological and disease condition models to accelerate drug development.

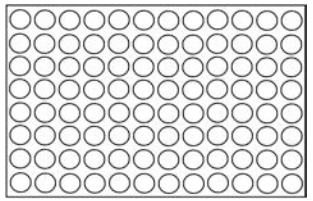
Pathological Responses

Potential Models of pulmonary disease:

1. **Pulmonary hypertension models, i.e. chronic hypoxia, can be generated by culturing lung tissue constructs under chronic hypoxic conditions.**
2. **Emphysema disease models can be generated by exposing lung constructs to known destructive agents.**

High Throughput Drug Screening

Process Scale Up:96-well plate format



Outcome Parameters:

-Biochemical tests for changes in cellular metabolism, proliferation, apoptosis, etc.

-Genomic/Proteomic profiling to examine global changes in cellular physiology in response to molecular stimuli.

In such a system, a large number of compounds could be tested in suitable replicates in parallel. This is of great need due to the laborious and variable nature of animal experiments and inability of standard cell culture models to approximate either normal or disease tissue conditions.

Deliverables

1. High throughput systems for drug development and screening as well as patient specific gene expression profiling and pharmacogenomics.
2. Therapeutic translation of engineered tissues, i.e. surgical implantation.