Application – Microfluidic Cell Culture Devices (2)

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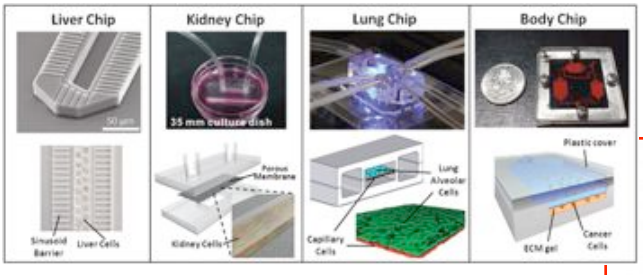
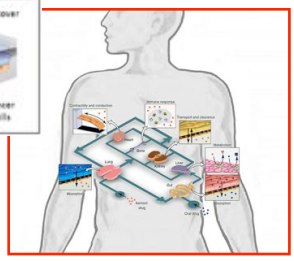
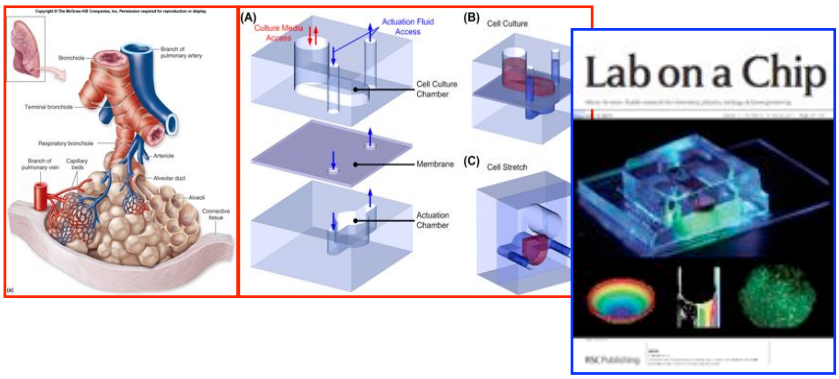
Cells to Tissues even Organs

- An ***Organ-on-a-Chip*** is a multi-channel 3-D microfluidic cell culture chip that simulates the activities, mechanics and physiological response of entire organs and organ systems.



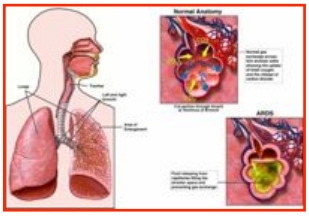


Microfluidic Alveolar Model for Studying Contributions of Fluid and Solid Mechanical Stresses to Cell Behaviors



Motivation - ARDS

- Acute Respiratory Distress Syndrome (ARDS)
- ARDS is Life-Threatening Lung Condition
  - It affects about 190,000 people in the US each year (NIH)
  - Swelling of tissues in the lungs
  - Build up fluid in the tiny air sacs
- Causes
  - Direct injury to the lungs (chest trauma, tuberculosis, etc.)
  - Indirect injury to the lungs (severe infection, shock, etc.)
- Treatment
  - Mechanical Ventilation
  - Oxygen via face mask



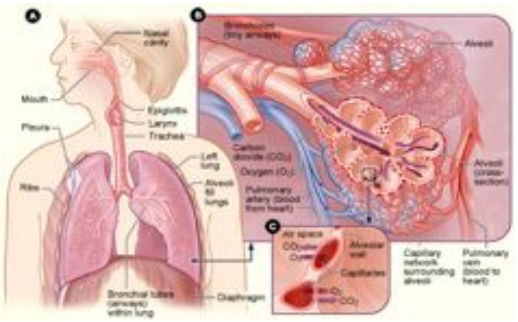
Motivation - VILI

- Mechanical ventilation has been used to support acutely ill patients for several decades. However, clinicians are aware for several potential drawbacks and complications – Ventilator Induced Lung Injury (VIL): pulmonary edema, alveolar spave collapse etc.
- Relative High Strain (~ 25%) in lung region due to large tidal volume (12-15 ml/kg)
- Stress Concentration due to the heterogeneity in lung impedance.
- Stress Concentration due to the moveme interfaces.

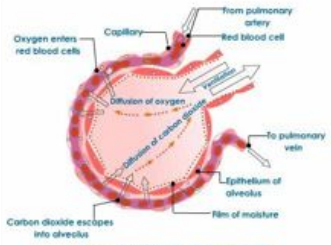
Objective – Alveoli on a Chip

- Development of a microfluidic device capable of simulating the mechanical microenvironments in an alveoli.

Branching of Airways



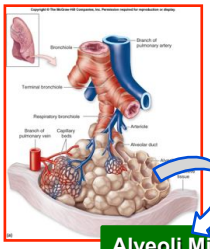
Alveoli



Type I Cell for Gas Exchange

Type II Cell Synthesizes Surfactant

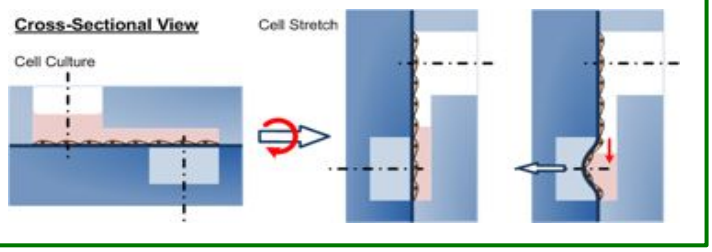
Device Design



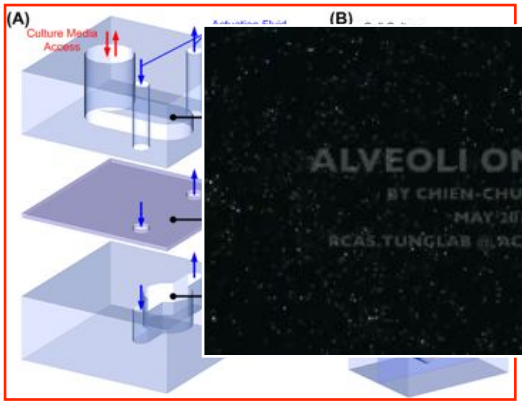
Mechanical Strain

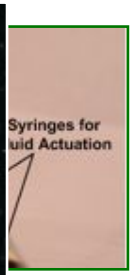
Air/Liquid Interface

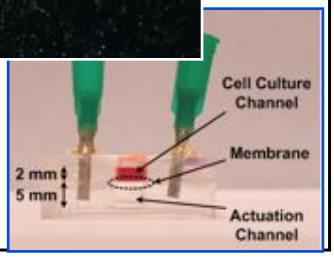
Alveoli Microfluidic Device



Device Fabrication





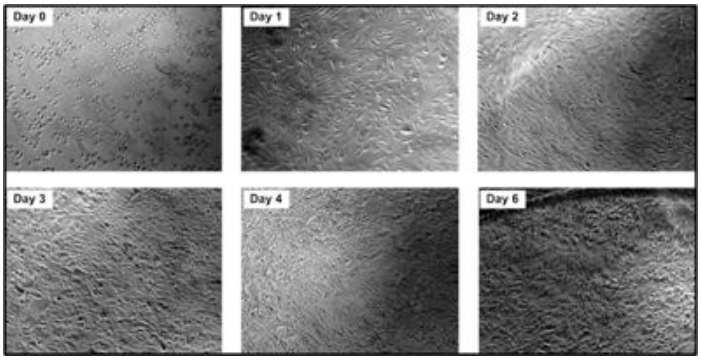


Mechanical Strain → Circular Pattern

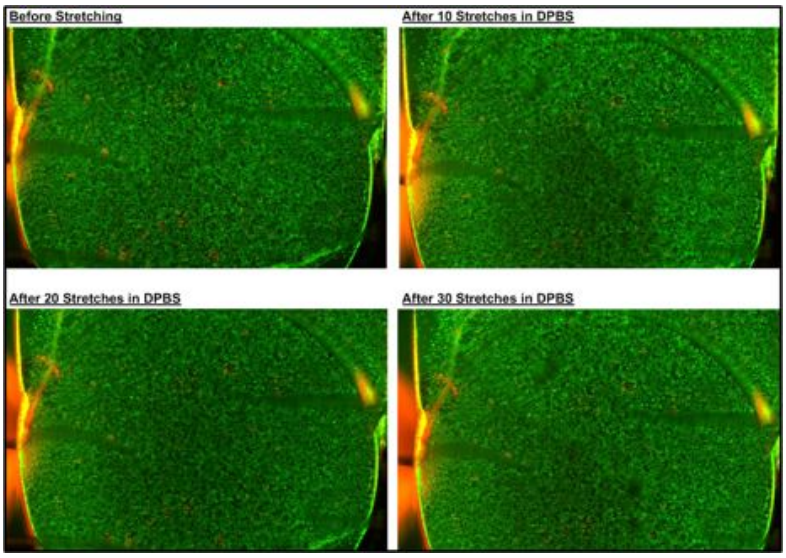
Air/Liquid Interface → Linear Pattern

Cell Culture

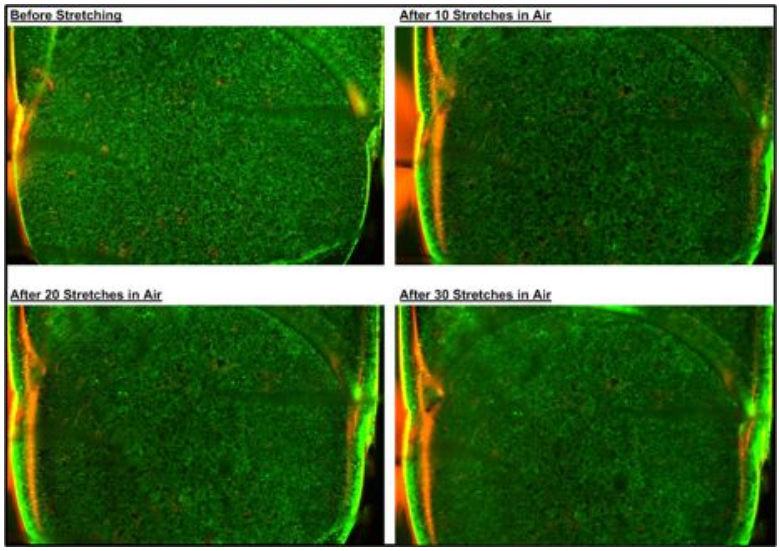
- A549 – Human Alveolar Basal Epithelial Cell
- Device Coating: 50 μg/ml fibronection
- Cell Density: ~ 200 cells/μl, 200μl
- Growth Medium: F-12K + 10% FBS (exchange everyday)



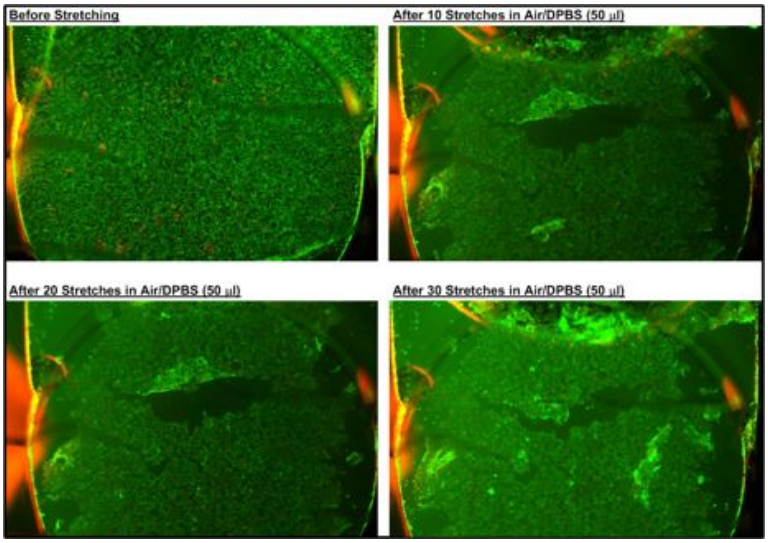
Cell Experiments – Stretch in DPBS



Cell Experiments – Stretch in Air

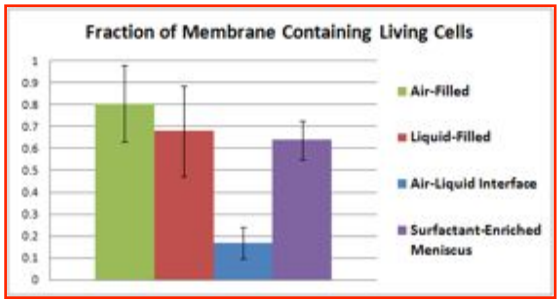


Cell Experiments – Stretch in Air/DPBS

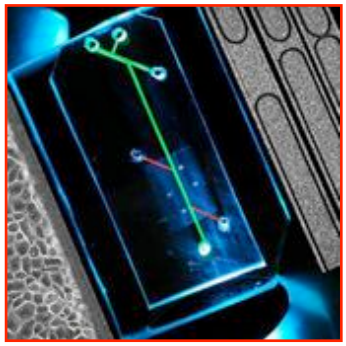


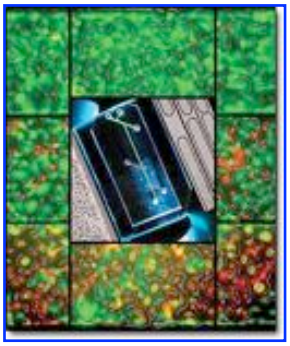
Experimental Results

- 60 cycles of stretch, the percentage of a total area containing living cells (stained by Calcein AM)
- Air-Filled: 80.6±17.5%
- Liquid-Filled: 68.0±20.8%
- Air-Liquid Meniscus: 16.8±7.3% (w/o Survanta)



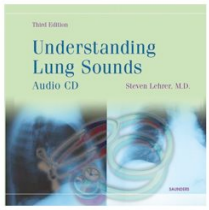
Acoustically Detectable Cellular-Level Lung Injury Induced by Fluid Mechanical Stresses in Microfluidic Airway Systems

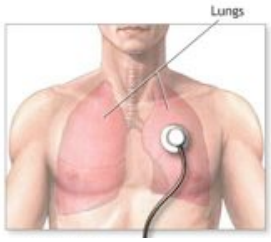




Motivation – Symptom or Cause?

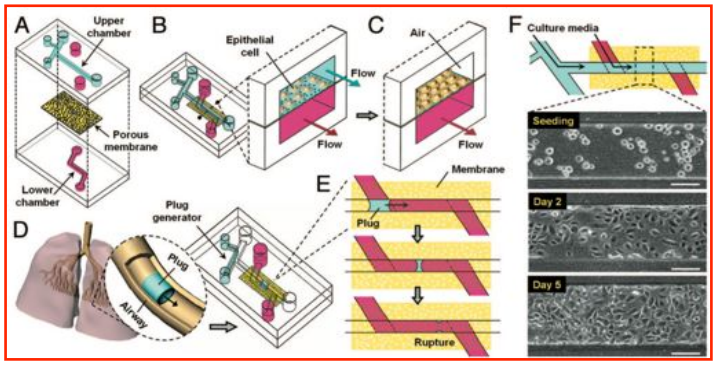
- Scientists have modeled the lungs' tiniest airways on a microchip device a little larger than a quarter, providing new insight into lung diseases like pneumonia and cystic fibrosis.
- By scientifically reproducing the real crackling sound diseased lungs make when clogged with fluid, the lung-on-a-chip showed that the crackles aren't just a symptom of trouble, they're also a cause.





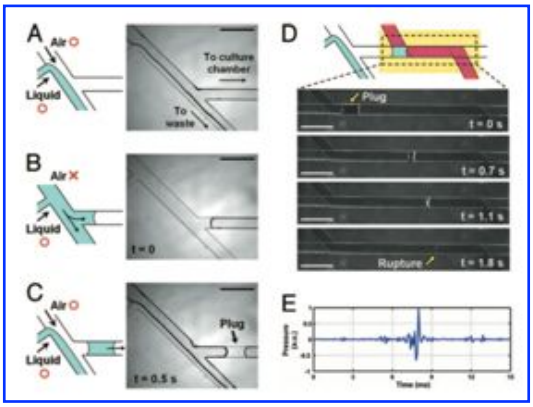
Device Design

- Compartmentalized microfluidic airway systems. The microfabricated small airways are comprised of PDMS upper and lower chambers sandwiching a porous membrane.



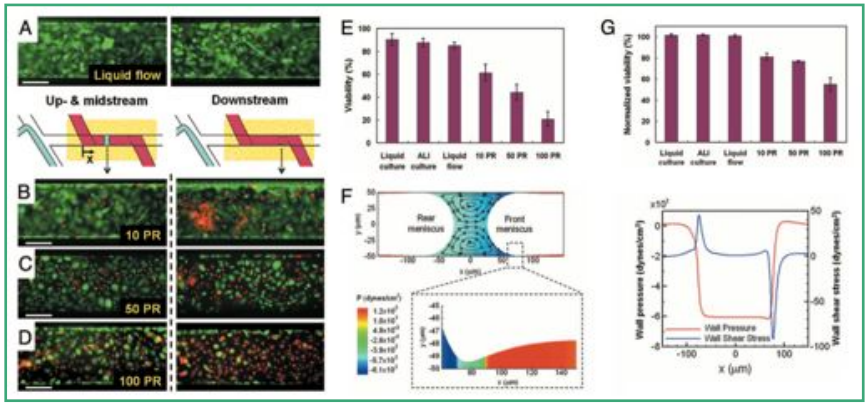
Experiments – Plug Formation

- Formation, propagation, and rupture of liquid plugs generated by dynamic fluidic switching in a microfabricated plug generator.

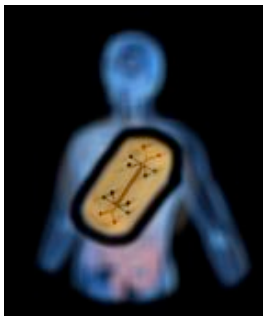


Experimental Results

- Cellular injury caused by propagation and rupture of liquid plugs.



Reconstituting Organ-Level Lung Functions on a Chip



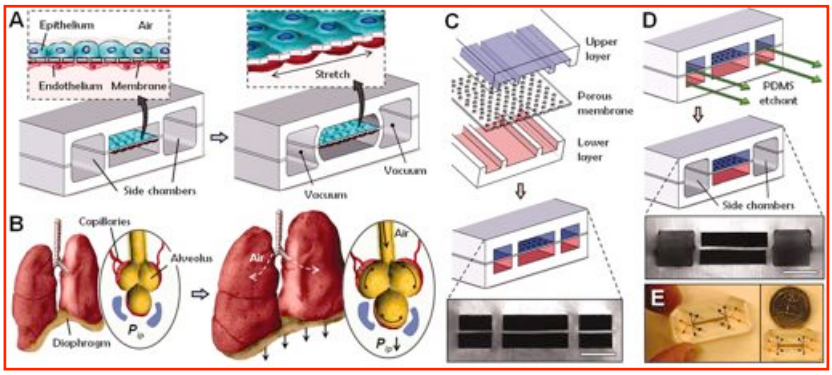
http://www.extremetech.com/extreme/131574-living-organ-on-a-chip-could-soon-replace-animal-testing

Motivation – A New Hope

- Microscale engineering technologies first developed to create microchips, such as microfabrication and microfluidics, enable unprecedented capabilities to control the cellular microenvironment with high spatiotemporal precision and to present cells with mechanical and biochemical signals in a more physiologically relevant context.

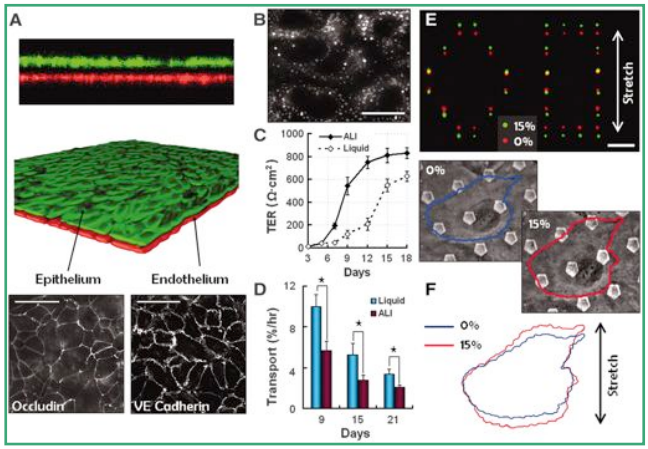
Device Design

- Biologically inspired design of a human breathing lung-on-a-chip microdevice.



Experiments – Plug Formation

- On-chip formation and mechanical stretching of an alveolar-capillary interface.



Experimental Results

- Reconstitution and direct visualization of complex organ-level responses involved in pulmonary inflammation and infection in the lung-on-a-chip device.