In Vitro Improvements to lung-on-a-chip technology

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Background/purpose

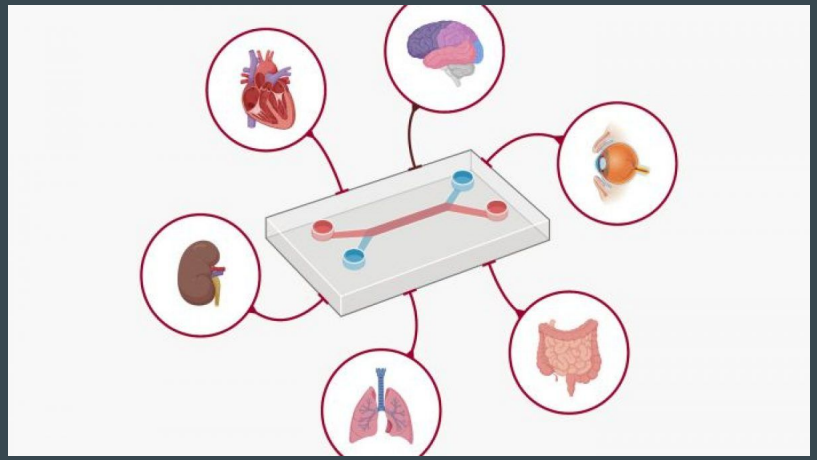
Organ on chip: Micro device simulates the physiological and mechanical activity of entire organ.

Acts like an artificial organ !

Used for .....

- faster
- Inexpensive
- Efficient

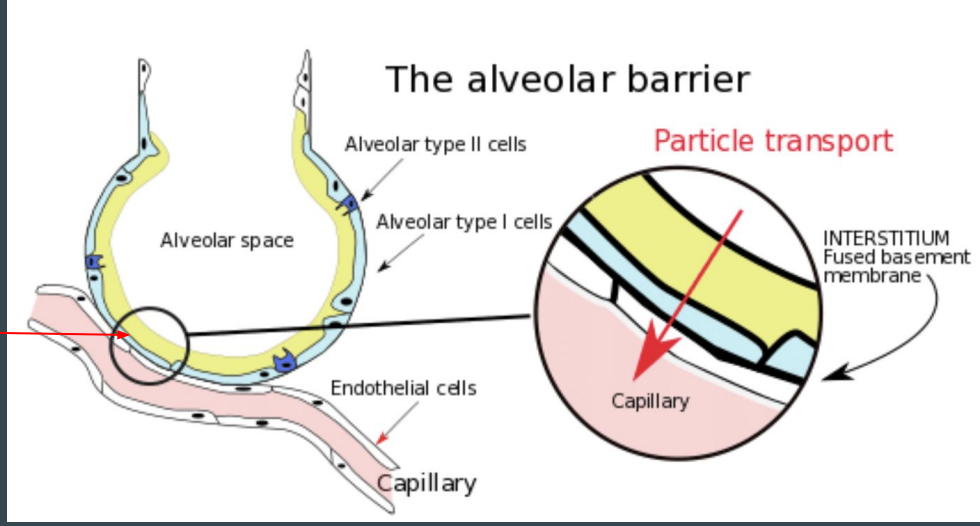
Testing.



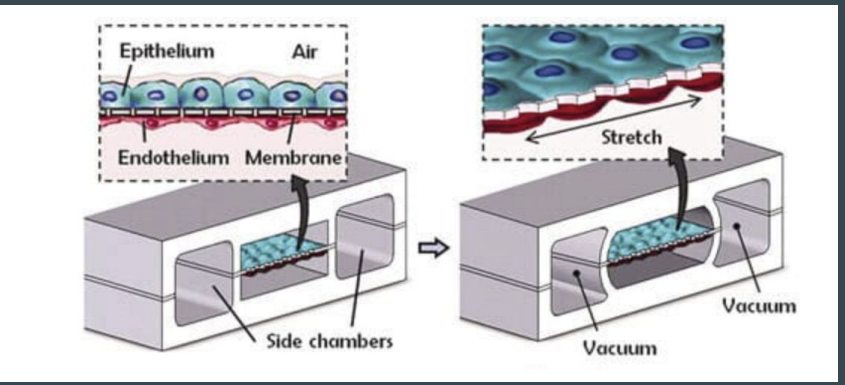
Background/purpose

Lung on a chip

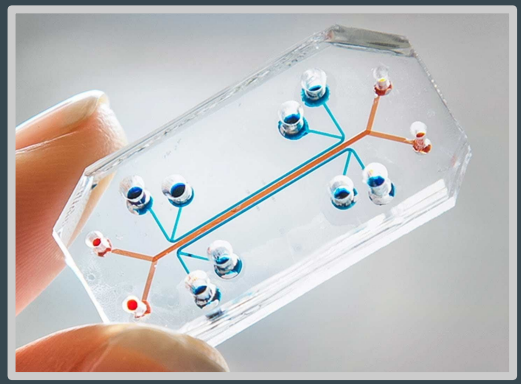
- unable to mimic an entire lung on a microfluidic chip
- Mimics an alveolo-capillary membrane
  - smallest functional unit in the lung
- Two compartments
  - Upper [epithelial cells in contact with the air}
  - Lower endothelial cells in contact with a fluid made of nutrients in lieu of blood
- PDMS used for the membrane



Cross section



The entire device



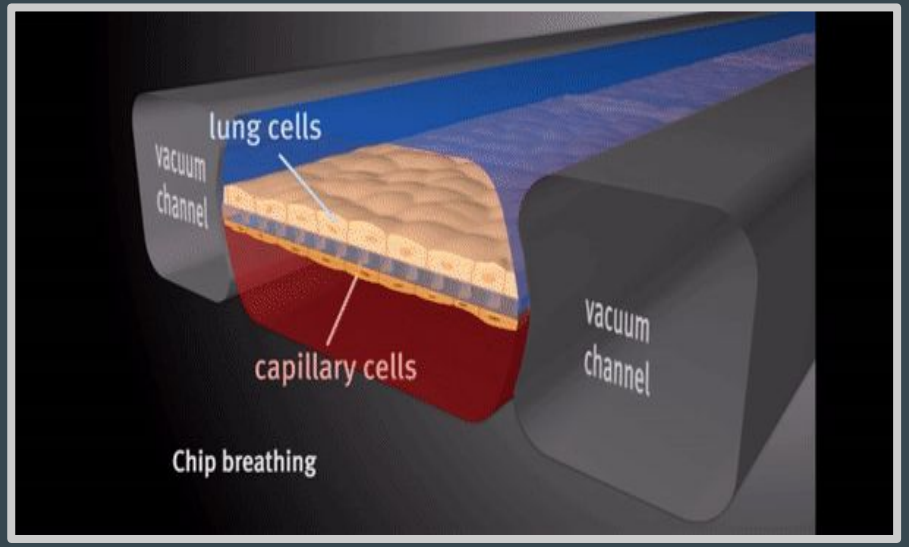
Background/purpose

PDMS

- Pros
  - Biocompatible
  - Flexible
  - easy to manufacture at small scale
- Cons
  - *Uncontrolled absorption of small molecules*
  - unstable surface treatment
  - high evaporation

Alternatives!

- PMMA
- PC
- PS

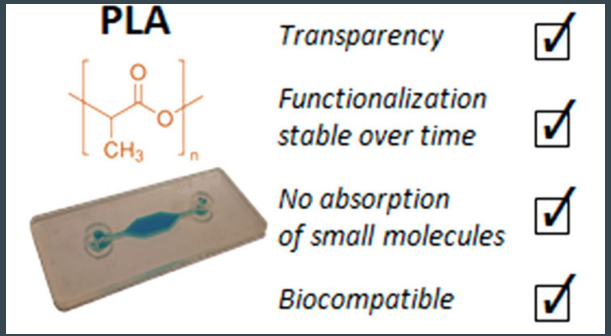


Theory

PLA (Polylactic Acid)

Why Polylactic Acid (PLA)

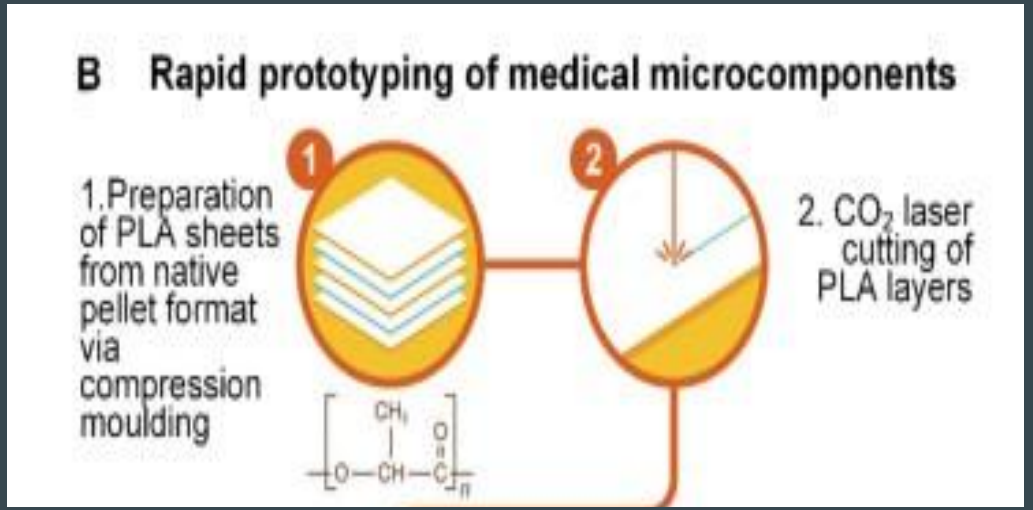
- **Does not absorb small molecules**
- **Transparent (92% transparency)**
- **Stability over time**
- **Biocompatible**



PLA Sheet Fabrication

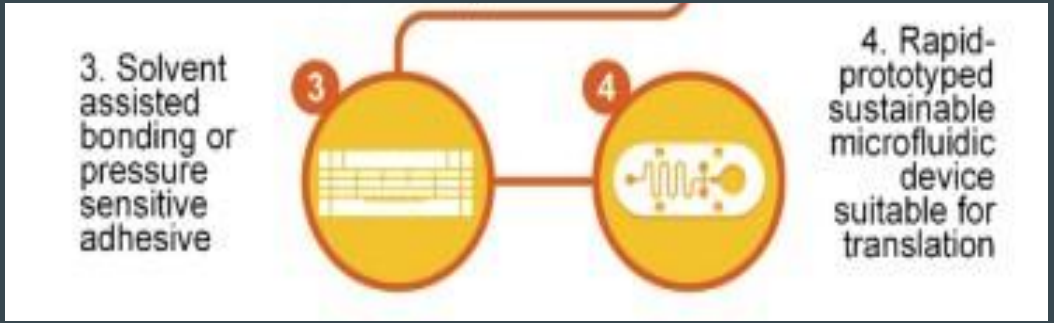
- Preparation of PLA Sheets From Pellet Form

- Creating microchannels in the PLA sheets for Organ-on-a-Chip Function

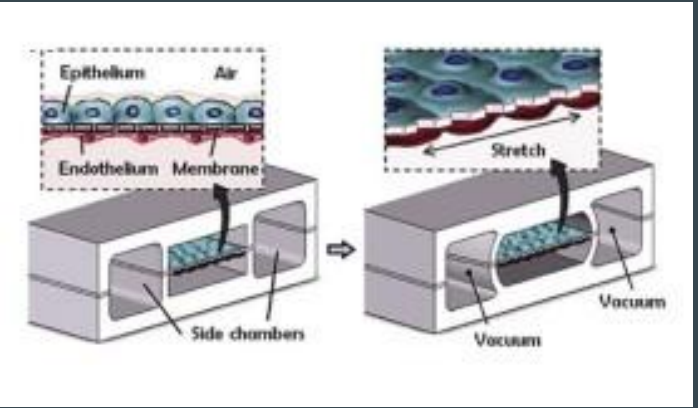


Creating OOC From PLA Layers

- Lasered PLA stacking to create OOC channel structure

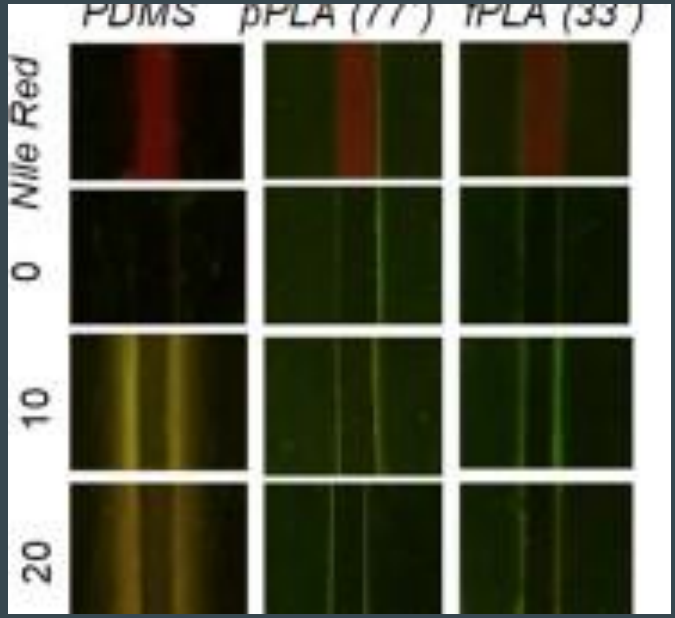


- Replicating the lungs architecture and function



Testing

- Tests to confirm the proof of principle of the PLA Lung-on-Chip device includes:
  - Biocompatibility testing
  - Absorption testing



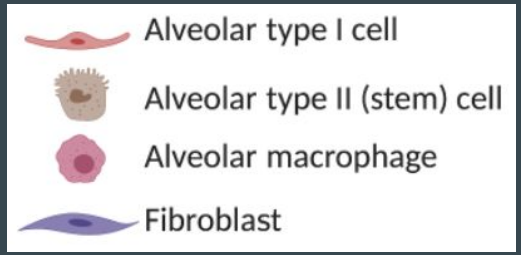
Biocompatibility

Cell viability of lung cells include

- Alveolar epithelial cells
- Respiratory endothelial cells
- Microvascular endothelial cells

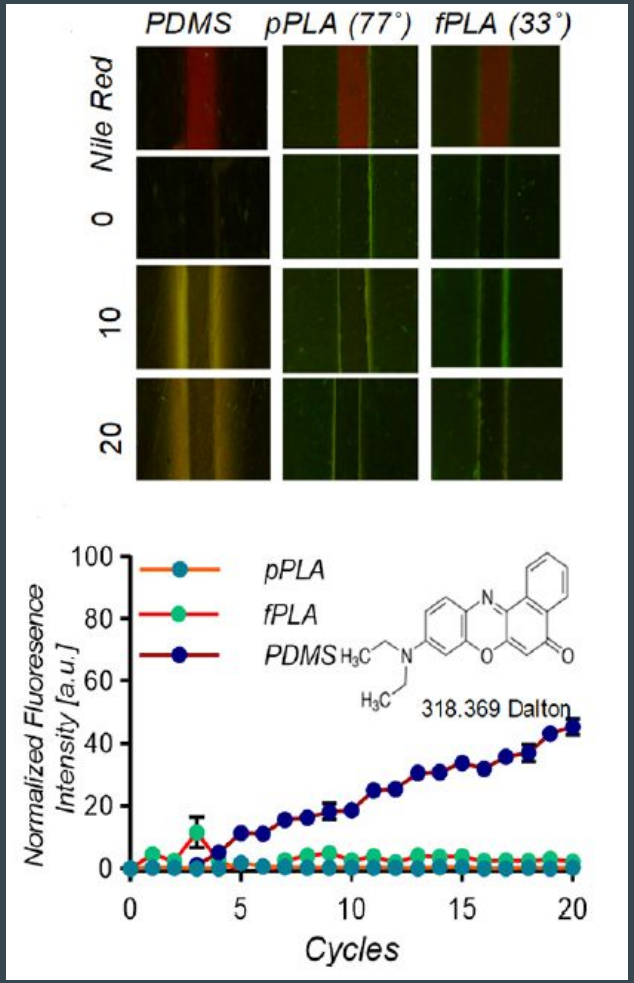
To assess biocompatibility of PLA

- Cytotoxicity
- Immune Response
- Irritation and Inflammation
- Chronic Toxicity



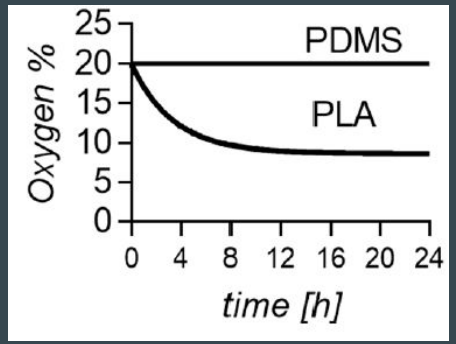
Adsorption Results

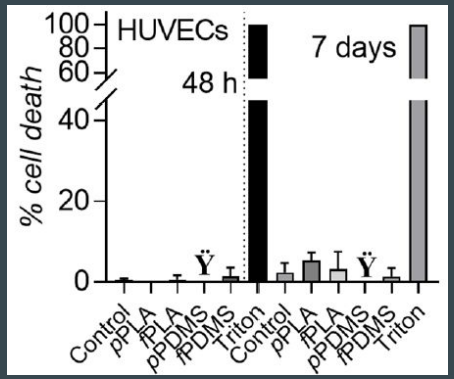
- The adsorption of small molecules was reviewed in Alfredo et al. where PLA and PDMS are compared using hydrophobic compounds
- Using nile red as a reference point, it can be seen how after many cycle, PDMS fluorescence intensity is much higher compared to both PLA types used



Limitations/Biocompatibility Results

- Due to the chemical composition of PLA, its hydrophobicity is a limiting factor, but it is not as hydrophobic as PDMS
  - Hydrophobicity affects cellular adhesion which is essential for cellular communication and regulation, this can result in different in behavior and function of the cells
    - The hydrophobicity can be reduced through modification methods which use oxygen plasma and ozone treatments
- Cell Death percentage is slightly higher than PDMS over time
- Oxygen levels reduce over time in PLA





Future Directions

- While drug testing and development is limited for lung on a chip due to the chemical properties of PDMS which cause adsorption of small hydrophobic coupons often found in newly developed pharmaceuticals, Future iterations of lung on a chip could include
  - A combination of both PDMS and PLA polymers for improved cell viability and decreased drug absorption
  - Inclusion of hydrophilic compounds like PEG to improve cellular adhesion
  - Replacement of polymers overall to use decellularized tissue to create the exact extracellular matrix and environment to mimic the lungs physiological conditions which would best replicat healthy and diseased states for pharmaceutical testing

Conclusion/Summary

- Overall, it was found that PLA is a sustainable biocompatible alternative to PDMS as it
  - Has lower adsorption rates
  - Has better cellular adhesion
  - Has lower hydrophobicity
  - Has high transmittance which is great for optical analysis

Sources:

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Thank You
Questions?