Lung dECM bioink-based 3D-bioprinted lung-on-a-chip for testing therapeutic responses

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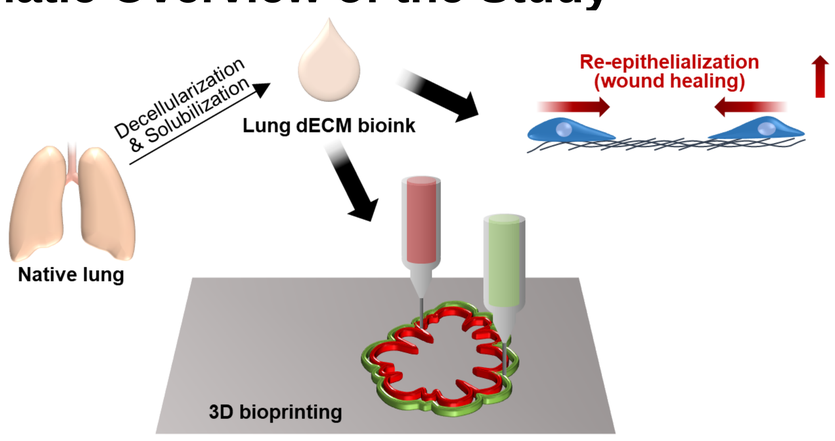
Abstract

The objective of this study was to develop a physiologically relevant lung model by leveraging the biochemical fidelity of lung-derived decellularized extracellular matrix (LudECM) and to explore its therapeutic applicability in fibrotic lung disease. To achieve this goal, lung tissues were subjected to an optimized decellularization protocol that effectively removed cellular components while preserving essential ECM constituents. The resulting LudECM was processed into a printable bioink and systematically characterized for its rheological properties, biochemical composition, and cytocompatibility.

Using this bioink, lung-specific cells were spatially organized through 3D cell printing to reconstruct key features of the alveolar–capillary architecture. The printed tissue was integrated into a microfluidic lung-on-a-chip system that enabled controlled perfusion and physiological microenvironmental cues. Fibrosis was induced by applying pro-fibrotic growth factors, generating characteristic pathological phenotypes associated with fibrotic lung disease. Therapeutic assessment using LudECM demonstrated measurable improvements, including the restoration of epithelial barrier function and attenuation of fibrosis-related phenotypes. These findings highlight both the functional relevance of the lung-on-a-chip model and the therapeutic potential of LudECM.

Materials and Methods

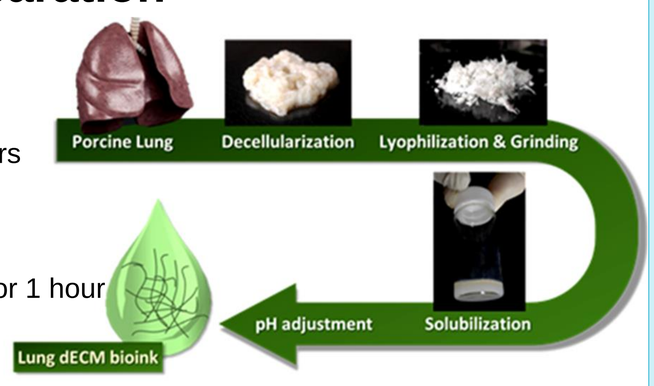
Schematic Overview of the Study



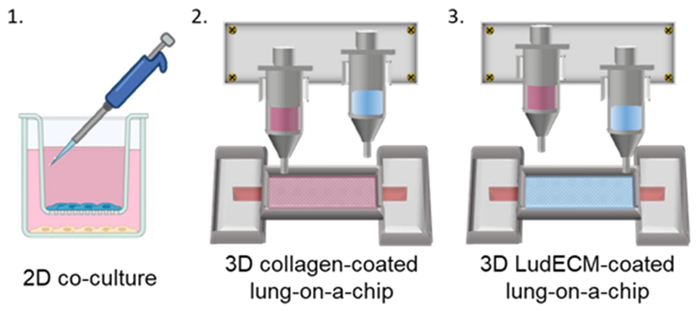
- Schematic illustration of lung dECM bioink fabrication and its application in 3D bioprinting to regulate cellular behavior.

Lung dECM Bioink Preparation

1. Slicing native tissue (thickness > 0.5mm)
2. Washing with DW for 3 hours
3. Treating 2 % Triton X-100 in PBS for 36 hours
4. Washing with DW for 12 hours
5. Treating 1M NaCl for 2 hour
6. Washing with DW for 24 hour
7. Sterilizing with 0.1% peracetic acid in PBS for 1 hour
8. Washing with DW for 2 hour



Comparative Analysis of Bioprinted Constructs

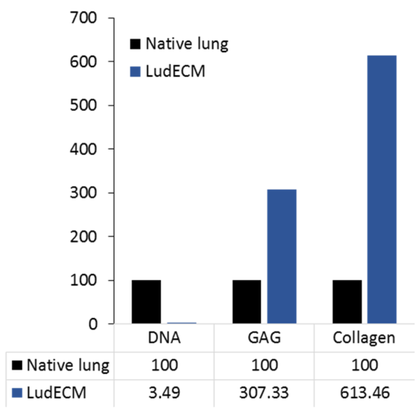


- Schematic illustration comparing 2D co-culture, 3D collagen-based, and dECM-based lung-on-a-chip environments for evaluating cellular responses.

Results

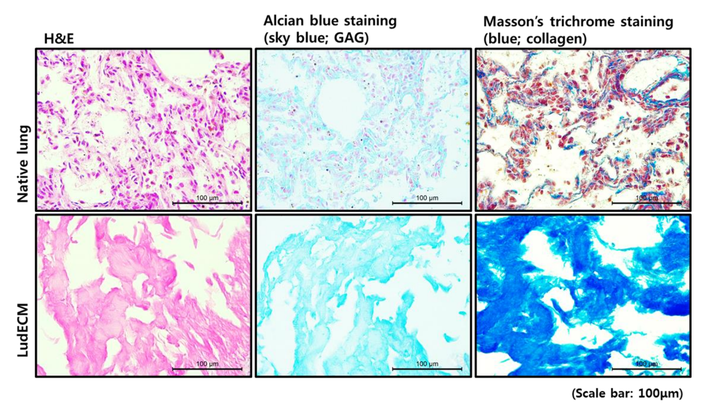
Characterization of LudECM

Biochemical Analysis

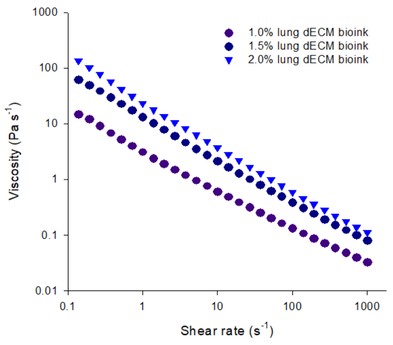


	DNA	GAG	Collagen
Native lung	100	100	100
LudECM	3.49	307.33	613.46

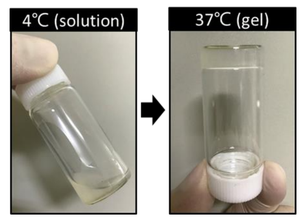
Histology



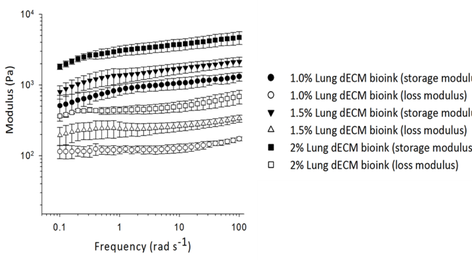
Viscositv



Sol-Gel Transition



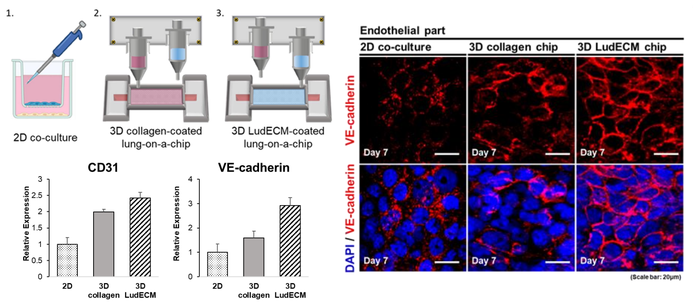
Dynamic modulus



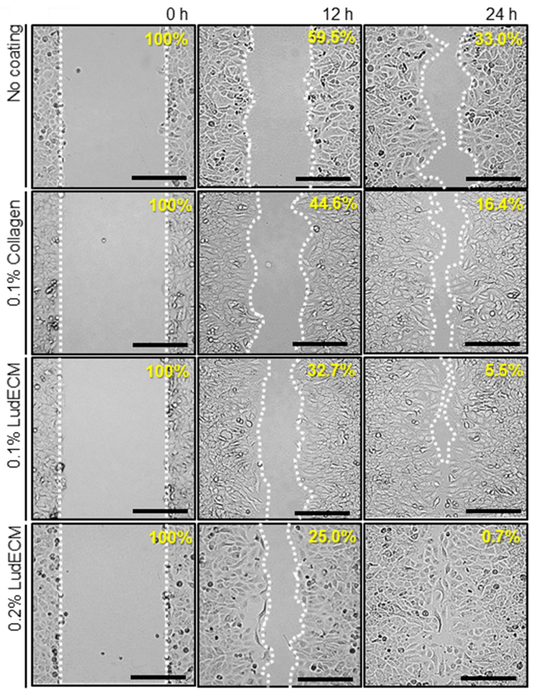
	Storage modulus (Pa)	Loss modulus (Pa)
1.0% Lung dECM bioink	938.9 ± 171.4	129.4 ± 16.8
1.5% Lung dECM bioink	1527.4 ± 290.5	255.1 ± 49.2
2.0% Lung dECM bioink	3373.8 ± 574.3	489.8 ± 71.5

Functional Enhancement in Lung-on-a-chip

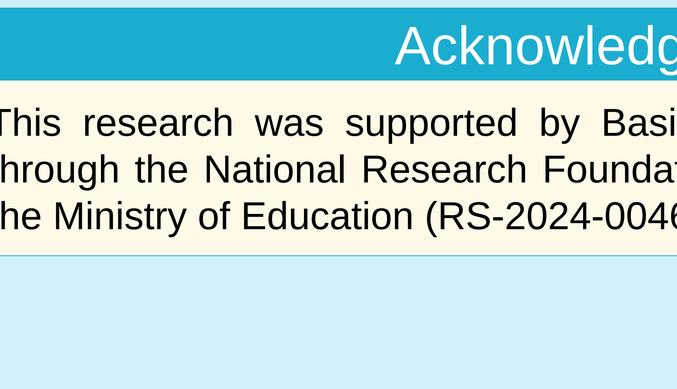
Enhanced Endothelialization



Wound Healing Assay



Evaluation of Dynamic Culture Effects



Conclusion

This study establishes a LudECM-based, 3D-bioprinted lung-on-a-chip as a robust and human-relevant platform for disease modeling and therapeutic evaluation. The integration of native ECM signals, multicellular architecture, and microfluidic control represents a significant advancement over conventional in vitro or animal models and supports future applications in drug screening and regenerative medicine.

Acknowledgment

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