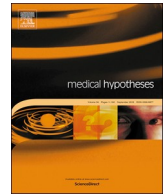




Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.



Letter to Editors

Biofabrication: An interesting tool to create *in vitro* model for COVID-19 drug targets



Dear editor,

Lung biofabrication is an emerging tool used in tissue engineering and regenerative development aimed at identifying new drug targets where the cells are seeded into an acellular organ scaffold and cultured in a bioreactor [1]. Bio-fabrication is used in drug discovery processes. Development of newer and better medicines requires a proper diseases modeling. Several research groups are working on the development of vaccines for COVID-19. There is an emerging need to develop Two-dimensional (2D) or Three-dimensional (3D) lung models to identify the drug targets for lung infection caused by COVID-19. 2D model cannot fulfill the study requisites due to the biological change in humans and animals. Non-alcoholic fatty liver disease has been examined

using such models. 3D printing can be used to target newer sites following *ex-vivo* pattern like diseased cells extracted from the patient's body. Better images can be developed by 3D bio-printing technology using tissue engineering tethered with multi-omics, single cell genomics. It produces cellular level data points to confirm specific gene triggering causes which confirm new drug targets. Thus, this model can detect disease progression *in-vitro*. This helps in drug development by target modulation [2]. 3D bio-printing model replaces both the animal models and 2D printing cell based screening. It also overcomes the inconvenience of imperfect animal model and reduces the chances of clinical trial failures. It facilitates the discovery of lead molecule by providing 3D multi-cell interactions, so that the best selected molecular candidate can put in bio-printed model for the optimization [3].

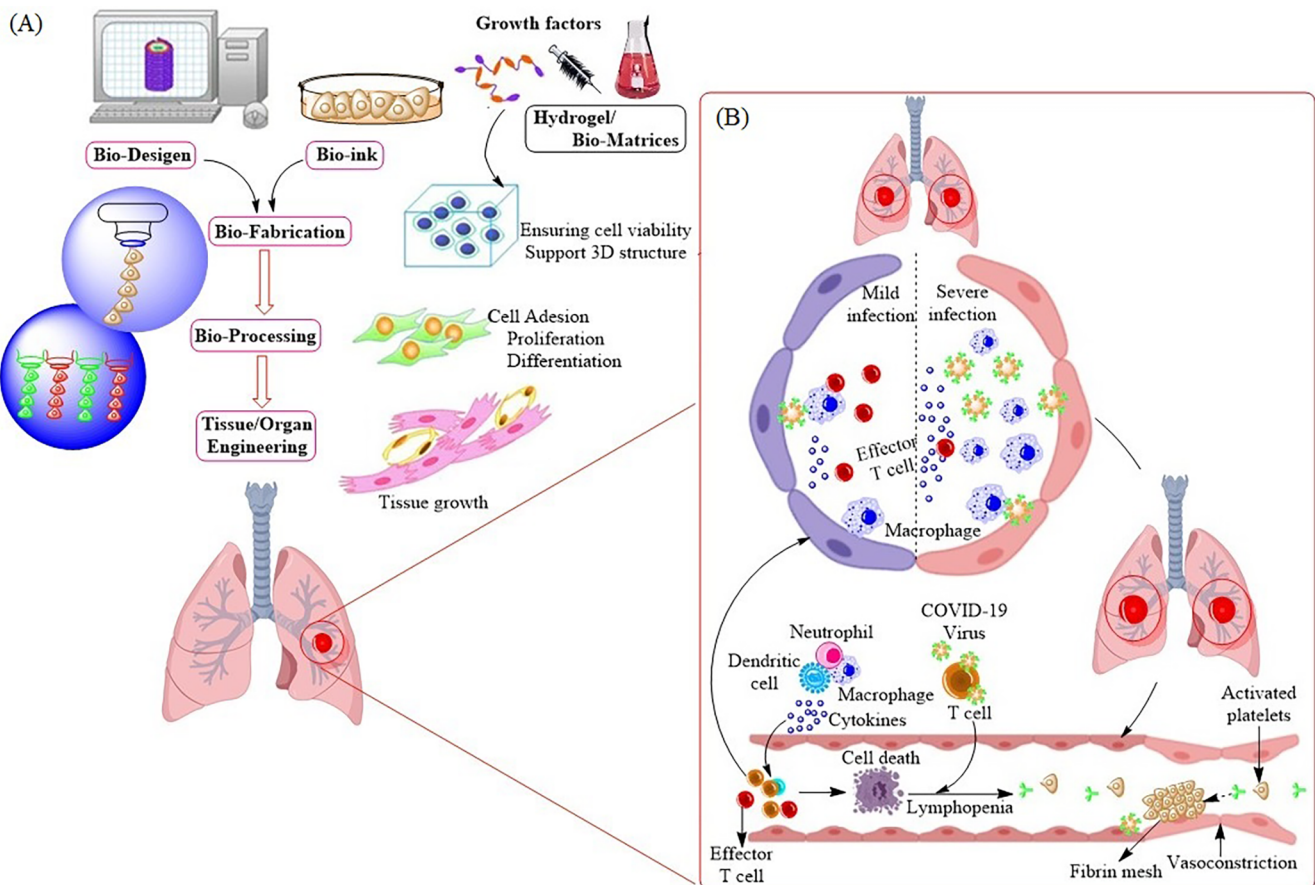


Fig. 1. Presentation of (A) biofabrication process to generate *in vitro* lung tissue model, and (B) the occurrence of COVID-19 infection in lungs.

The Visicent's disease model provides high-quality information to identify new drug targets, uncover novel biology, and test disease-modifying (Fig. 1) drugs [3]. Scientists need to proceed for lung tissues for model development to investigate the potential of COVID-19 drug target. However, it is challenging due to the collapsing of lung parenchyma without ventilation and low tissue stiffness [2]. In contrast to the whole lobe or whole lung explants, lung samples eviscerated by means of thoracic surgery do not necessarily follow the anatomical segments and, therefore, require special preparation. Bio-printed 3D lung tissue models can be created to analyze the drug response. It has been well established that the 3D human lung tissue models are best fit model in viral infectivity than the regular cell culture [4].

The scope of novel discoveries in human disease is limited using currently available human tissue based models of disease. Thus, there is an emerging need to develop 3D models which could translate such discoveries to human disease. Precision-cut lung slices (3D lung tissue cultures) represent an elegant and biologically relevant 3D cell culture model. These slices resemble to the *in-situ* tissue due to their molecular composition, biomechanics and complexity. It helps in better understanding of functional effect and mechanisms of drug action in human tissues. Human precision-cut lung slices are prepared from resected soft elastic lung tissue of a patient experiencing lung lobectomy. These slices have better accessibility of diseased and peritumoral tissues [4]. Gerckens *et al.*, introduced agarose into the bronchoalveolar space of resectates to preserve lung structure and increase tissue stiffness. The precision-cut lung slices ensured comparable tissue sample size which can be used to study human lung biology at cellular to subcellular level and mechanisms of different diseases. The developed model was identical to *in situ* human lung with respect to its 3D structure and practicable to develop a novel strategy for precise medicine [4]. A computational lung model developed by the Technical University of Munich, Germany, can be used to reduce the damage caused by mechanical ventilation and could increase survival rates significantly in COVID19 patients [5].

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to

influence the work reported in this paper.

References

- [1] Farre R, Otero J, Almendros I, Navajas D. Bioengineered lungs: A challenge and an opportunity. *Arch Bronconeumol* 2018;54(1):31–8. <https://doi.org/10.1016/j.arbres.2017.09.002>.
- [2] Alsafadi HN, Staab-Weijnitz CA, Lehmann M, Lindner M, Peschel B, Königshoff M, et al. An *ex vivo* model to induce early fibrosis-like changes in human precision-cut lung slices. *Am J Physiol Lung Cell Mol Physiol*. 2017;312(6):L896–902. <https://doi.org/10.1152/ajplung.00084.2017>.
- [3] Using bioprinted tissue models to test drugs against diseases including COVID-19. Available from: <https://www.technologynetworks.com/drug-discovery/blog/using-bioprinted-tissue-models-to-test-drugs-against-diseases-including-covid-19-333489>. Accessed on 15.05.2020.
- [4] Gerckens M, Alsafadi HN, Wagner DE, Lindner M, Burgstaller G, Königshoff M. Generation of human 3D lung tissue cultures (3D-LTCs) for disease modeling. *J Vis Exp* 2019;144:e58437 <https://doi.org/10.3791/58437>.
- [5] Computational lung model for Covid-19 and ARDS. Available from: https://www.compamed-tradefair.com/en/Articles/Computational_lung_model_for_Covid-19_and_ARDS. Accessed on 15.05.2020.

Anurag Kumar Singh

Centre of Experimental Medicine and Surgery, Institute of Medical Sciences,
Banaras Hindu University, Varanasi, Uttar Pradesh, India

Gaurav Mishra

Institute of Medical Sciences, Faculty of Ayurveda, Department of Medicinal
Chemistry, Banaras Hindu University, Varanasi 221005, Uttar Pradesh,
India

Anand Maurya

Institute of Medical Sciences, Faculty of Ayurveda, Department of Medicinal
Chemistry, Banaras Hindu University, Varanasi 221005, Uttar Pradesh,
India

Giriraj T. Kulkarni

Amity Institute of Pharmacy, Amity University Uttar Pradesh, Noida
201303, Uttar Pradesh, India

Rajendra Awasthi*

Amity Institute of Pharmacy, Amity University Uttar Pradesh, Noida
201303, Uttar Pradesh, India
E-mail address: awasthi02@gmail.com.

* Corresponding author.