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Tribology Tackles Cancer and COVID-19

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Since the advent of the optical microscope, scientists and physicians have focused this tool on biology with the laudable goals of improving the diagnosis, prognosis, treatment, and prevention of disease. Over the past century, imaging and cell-culture have been locked in a coupled development pipeline limited by perceived constraints of two-dimensional culture plates, slides, and imaging dishes. In situ techniques and approaches pioneered in tribology offer the potential to break this constraint and provide new tools to biomedicine research.

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1. Introduction

The Coronavirus disease of 2019 (COVID-19) is a pandemic respiratory viral infection caused by the novel pathogen SARS-CoV-2. The trajectory of the outbreak is difficult to predict, but many hundreds of thousands of deaths are expected worldwide, overwhelming the capacity of some healthcare systems. Although the scale is daunting, focused scientific inquiry in such times of crisis has, in the past, contributed to ending disease outbreaks. Major impediments to unravelling the mechanisms of action and potential cure to COVID-19 include a lack of suitable 3D models with phenotypic heterogeneity (including tissue-dependent resident immune cells) and appropriate populations of human airway and peripheral lung cells. We developed, validated, and optimized a living 3D model of airway and peripheral lung microtissues that can be infected with SARS-CoV-2 viruses under controlled conditions that are amenable to studies of the progression and treatment of SARS-CoV-2 and the COVID-19 disease.

2. Methods

To address these impediments, we have followed a transdisciplinary approach, with investigators from Astronomy, Chemistry, Medicine, and Engineering, working together with professors with expertise in lung biology and Coronavirus virology to develop a model for COVID-19. The integrated suite of tools can 3D print microtissues collected from patient biopsies of at-risk patient populations into arrays for precision screening maintain the viability of these tissues under controlled perfusion of oxygenated liquid media, preserve phenotypic heterogeneity of the tissues, and retain the delicate features unique to pulmonary tissues. The 3D printing medium is made from a low friction bed of transparent soft granular hydrogel particles that we custom synthesize with molecular level control to provide a low modulus, charge neutrality, low adhesion, high permeability, and optimized dimensions to provide interstitial space for perfusion of viruses, drugs, and metabolites, while also facilitating immune cell movement.

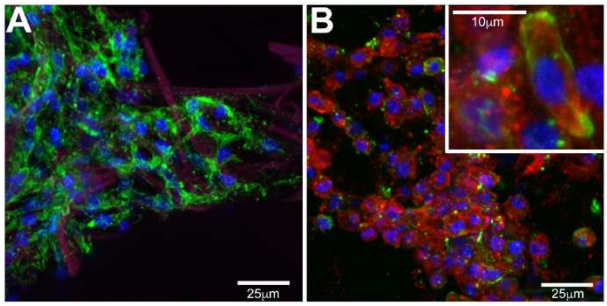

Figure 1: A) Living biopsy of peripheral lung after 48 under no viral infection, and B) living biopsy of peripheral lung after 48 post infection with HCoV-OC43. green: actin, blue nucleus, red: HCoV-OC43. Note the infected tissue (B) shows extensive blebbing and damage after 48 hours in stark contrast to the uninfected control (A).

3. Discussion

We generate 3D microtissue models from living patient-derived tissues capable of mimicking the biology of the disease and amenable to studies of the early stages of the disease and will be validated against existing pathogens and baseline transcriptome analysis. This model includes in-situ scanning fluorescence confocal microscopy, 3D cell-tracking, and controlled perfusion of viruses and metabolites. Uniquely, this system facilitates high resolution spatiotemporal studies of early infection and progression in a human microtissue model from donors that are of elevated risk for morbidity and mortality related to COVID-19 (e.g. COPD, >60, diabetes, lung cancer). These models will inform and contribute to the science of viral transmission.