Docket #: S20-312

Methods enabling infection and differentiation of human distal lung organoids by SARS-CoV-2 and other pathogens

The distal lung functions in gas exchange essential for breathing and can be critically affected by infectious respiratory diseases, bacteria, and other pathogens which can lead to pneumonia and life-threatening respiratory failure. In vitro culture systems of primary human cell lines are invaluable to understand the pathologies that affect those same cells. Unfortunately, primary 3D tissue and organoid culturing of adult distal lung tissues, in particular long-term, feeder free culturing, remain challenging. Organoid cultures, for example, often grow as cystic structures with their apical surfaces oriented inwards toward a central lumen, rendering those surfaces inaccessible to the externally added pathogens or other agents in the culture media. Stanford researchers have developed a robust, long-term, feeder free, and chemically defined method for organoid culturing of tissues derived from human distal lung. This method allows for eversion of the organoids, enabling these organoid cultures to serve as critical tools for studying apical viral infection of human distal lung tissues.

Applications

- Long-term, feeder free, chemically defined human alveoli or distal broncholar organoid culturing
- Drug screening using human alveoli or distal broncholar tissue for SARS-CoV-2 or other pulmonary infectious pathogens (bacterial, viruses)
- COVID-19

Advantages

- Long-term, feeder free, chemically defined culturing of human distal lung tissue (alveoli, terminal bronchioles), which was not previously possible.
- Organoid cultures can be everted without mechanical shearing, enabling apical infection.

Publications

- Salahudeen, A.A., Choi, S.S., Rustagi, A. et al. Progenitor identification and SARS-CoV-2 infection in human distal lung organoids. *Nature* 588, 670–675 (2020).

Patents

- Published Application: WO2022016116
- Published Application: 20230257716

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