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Collective behavior of an opportunistic pathogen promotes colonization and breaching of the human respiratory epithelial barrier

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P. aeruginosa surface colonization entails complex behaviour including adherence, virulence induction and dissemination. Infection studies are hampered by the lack of experimental models that faithfully recapitulate the physiology of human tissue and, at the same time, offer the experimental power to investigate the infection process with high temporal and spatial resolution. We established an *in vitro* 3D lung infection model from human stem cells, with air-liquid interface in a Transwell. Immunocytochemistry- and histology staining confirmed that the architecture and cellular composition of the tissue closely resembles the human bronchial epithelium. Using live cell microscopy, we demonstrate that the tissue recapitulates lung functions such as production of mucus and cilia beating. We utilize the upper airway tissues to visualize and quantify *P. aeruginosa* lung infection with unprecedented spatial and temporal resolution. These studies provide a detailed mechanistic frame for how human pathogens overcome the mucus barrier and rapidly spread on mucosal tissue and how they combine internalization into specialized cell types and collective behavior to rapidly and effectively breach the barrier function of the lung epithelium. Our results establish lung Transwells as versatile *in vitro* model to study bacterial infections and drug response in a human-like environment.