Organoids revolutionize research on respiratory infections

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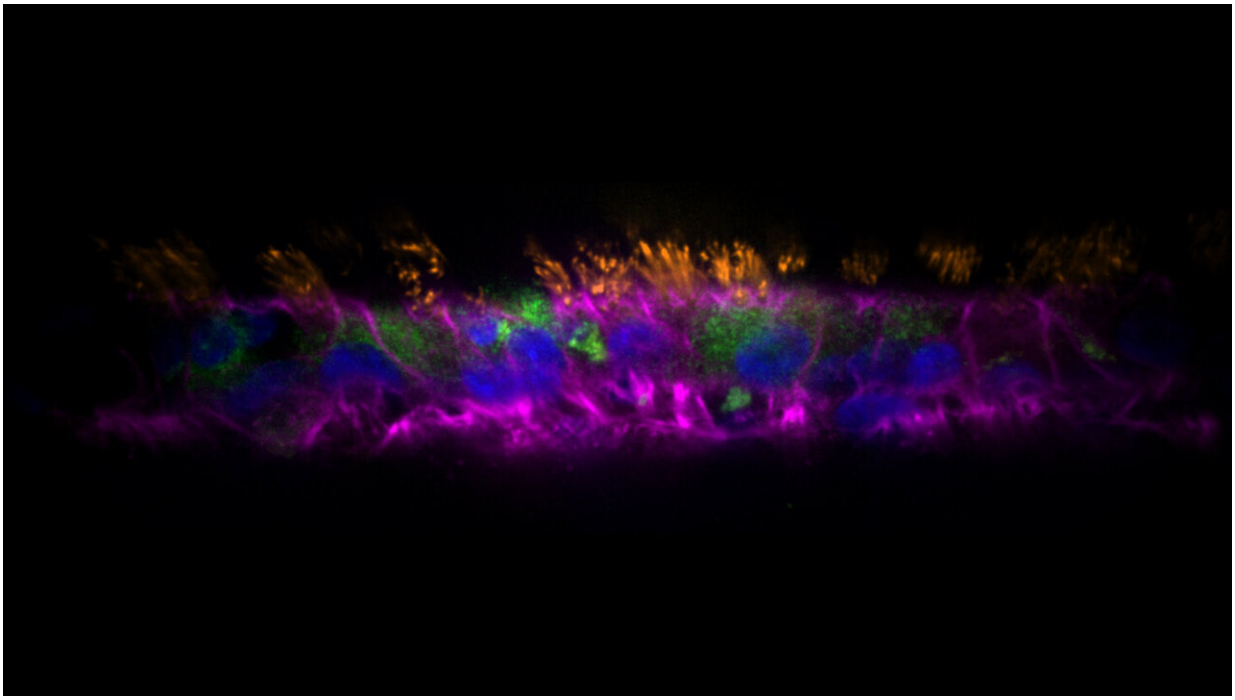

Human airway epithelial cells after growth and differentiation inside an AirGel tissue-engineered airway. Green: mucus; orange: cilia; pink: actin; blue: nuclei. Credit: Tamara Rossy (EPFL)

Biofilms are highly resistant communities of bacteria that pose a major challenge in the treatment of infections. While studying biofilm formation in laboratory conditions has been extensively conducted, understanding their development in the complex environment of the

human respiratory tract has remained elusive.

A team of researchers led by Alexandre Persat at EPFL have now cracked the problem by successfully developing organoids called AirGels. Organoids are miniature, self-organized 3D tissues grown from stem cells to mimic actual body tissues and organs in the human body. They represent a paradigm shift in the field, enabling scientists to replicate and study the intricate environments of organs in the laboratory.

Developed by Tamara Rossy and her colleagues, the AirGels are bioengineered models of human lung tissue that open up new possibilities in infection research. They revolutionize infection research by accurately emulating the physiological properties of the airway mucosa, including mucus secretion and ciliary beating. This technology allows scientists to study airway infections in a more realistic and comprehensive manner, bridging the gap between in vitro studies and clinical observations.

"There is a lot to say about this study, but the engineering of organoids for infection research has tremendous potential," says Persat. "It's a game changer."

In the study, published in *PLoS Biology*, the researchers used AirGels to investigate the role of mucus in the process of biofilm formation by Pseudomonas aeruginosa, a pathogenic bacterium that is commonly resistant to antibiotics. By infecting the AirGels with P. aeruginosa and studying them under high-resolution live microscopy, they were able to the bacterium form biofilms in real time.

Their observations revealed that P. aeruginosa actively induces contraction of its host's mucus using retractile filaments known as type IV pili (T4P). The T4P filaments generate the necessary forces to

contract the airway's mucus, which allows P. aeruginosa cells to aggregate and form a biofilm. The researchers validated their findings with follow-up simulations and biophysical experiments on selected P. aeruginosa mutants.

The study shows that the AirGel organoid model can provide unique insights into the mechanical interactions between bacteria and their hosts' environments, in this case uncovering a previously unknown mechanism that contributes to biofilm formation in the respiratory tract.

Being able to engineer organoids that faithfully replicate the mucosal environment opens up new avenues of exploration, enabling researchers to uncover overlooked aspects of infections, investigating the influence of additional physiological factors, such as temperature, humidity, drugs, and chemical stressors on the development and progression of infection, and develop targeted treatments against antibiotic-resistant pathogens.

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