Pseudomonas aeruginosa Breaches Respiratory Epithelia Through Goblet Cell Invasion in a Microtissue Model

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Presenter: Ni Made Teriyani **Date/Time:** 2024/10/03, 16:10 -17:00
Commentator: Dr. Po-Lin Chen **Location:** Room 601, Med College Building

Background:

Pseudomonas aeruginosa is a gram-negative bacterium that is a major cause of severe pneumonia acquired in hospitals, with infection mortality rates reaching up to 50% in patients on mechanical ventilation[1]. Moreover, the rise in multi-drug resistant strains of *P. aeruginosa* is concerning, as evidenced by an outbreak in the US in 2023[2]. This highlights the urgency to study *P. aeruginosa* infection mechanisms to find vulnerabilities that can be used as therapeutic targets. Some previous *in vitro* studies using monolayer cell lines have shown virulence factors in *P. aeruginosa* infection, such as bacterial apparatus for motility (flagella) and adhesion to surfaces (pili), secondary messengers, type III secretion system (T3SS), type VI secretion system (T6SS), and others. However, those *in vitro* studies cannot fully mimic human epithelial respiratory tissues. Therefore, it remains unclear how this bacterium spreads on mucosal surfaces and penetrates tissue barriers.

Objective/Hypothesis:

To investigate the infection mechanism of *P. aeruginosa* in the respiratory epithelium by using human respiratory epithelium organoids (microtissue models)

Results:

The authors found that after replicating on the surface of epithelial cells, *P. aeruginosa* adheres to the cell surface by using Type IV pili. It then colonizes the top surfaces of cells and spreads facilitated by flagella. The ability of *P. aeruginosa* to produce motile and sticky daughter offspring, which are modulated by c-di-GMP (a secondary messenger), also plays a role in colonization and spreading through the cell surface. After colonizing the cell surface, *P. aeruginosa* then invades the cell. The authors found that another secondary messenger-related gene, *cyaAB*, is involved in the invasion of *P. aeruginosa* into the cells. Moreover, it was shown that *Pseudomonas aeruginosa* preferentially invades mucus-secreting goblet cells. The authors also emphasized the role of T6SS in *P. aeruginosa* internalization into the goblet cell, and the T3SS function inside the cells causes goblet cells to die and be expelled. These mechanisms lead to epithelial rupture and increased bacterial dissemination by directly spreading through the basolateral side of the epithelium.

Conclusion:

These findings reveal that *P. aeruginosa* uses a coordinated set of virulence factors and behaviors to invade goblet cells and breach the epithelial barrier from within, providing new insights into how lung infections develop.

References:

1. Giantsou, E, and K I Manolas. “Superinfections in *Pseudomonas aeruginosa* ventilator-associated pneumonia.” Minerva anestesiologica vol. 77,10 (2011): 964-70.
2. Grossman, Marissa K et al. “Extensively Drug-Resistant *Pseudomonas aeruginosa* Outbreak Associated With Artificial Tears.” Clinical infectious diseases : an official publication of the Infectious Diseases Society of America vol. 79,1 (2024): 6-14. doi:10.1093/cid/ciae052