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Pseudomonas aeruginosa surface attachment studies for facilitating new drug development

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Abstract:

Pseudomonas aeruginosa (P. aeruginosa) is one of the most highly virulent and antibiotic-resistant opportunistic pathogens. *P. aeruginosa* uses multiple virulence mechanisms to infect and possess multiple strategies to tolerate or resist to antimicrobial treatment. Among them, surface attachment is one of the critical steps contributing to the virulence gene expression and biofilm formation. Our lab is taking an interdisciplinary approach to investigate *P. aeruginosa* infections. First, we developed a new *in vitro* model that replicates the biological and physical environments of the airway mucosal surface. We used tissue-engineering principles to design a novel airway model called AirGel. We grow AirGels from primary human lung cells in a tube-shaped hydrogel scaffold. With AirGels, we can visualize *P. aeruginosa* infections at high spatiotemporal resolution. This allowed us to observe that *P. aeruginosa* can actively compress the mucus layer covering on the host airway epithelium. This newly discovered mucus remodeling mechanism during the initial infection may further contribute to the following biofilm formation in the chronic infection. In addition to this new model, our lab is investigating the regulation of *P. aeruginosa* virulence in response to surface contact. We discovered that *P. aeruginosa* cells sense surface contact and respond by upregulating many virulence factors, including type III secretion systems. We will show that this response stimulates motility, primes the cells for pathogenicity and for the subsequent development of chronic virulence. From the drug development perspective, our results show that surface attachment is a potential therapeutic target. These studies reinforce our knowledge on this drug target and provide a more constructive direction for developing weapon tackling the antimicrobial resistance.