BACTERIAL PATHOGENESIS

Axis of evil

DOI:
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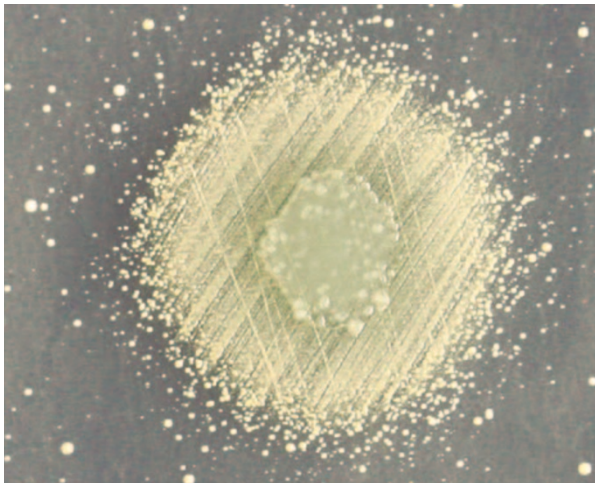
URLs

Pseudomonas aeruginosa
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=genomeprj&cmd=Retrieve&dopt=Overview&list_uids=12339

Staphylococcus aureus
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=genomeprj&cmd=Retrieve&dopt=Overview&list_uids=12304

Pseudomonas aeruginosa and *Staphylococcus aureus* are two of the more important bacterial pathogens of humans, and both are frequently isolated from the lungs of cystic fibrosis (CF) patients. A recent report in *Proceedings of the National Academy of Sciences USA* now shows that *P. aeruginosa* simultaneously suppresses the growth, and enhances the aminoglycoside resistance of *S. aureus* through the action of its exoproduct, 4-hydroxy-2-heptylquinoline-*N*-oxide (HQNO). Indeed, prolonged exposure of *S. aureus* to HQNO selects for small-colony variants (SCVs) of the pathogen and stable antibiotic resistance.



The photograph shows a colony of *Pseudomonas aeruginosa* (confluent colony in the centre) secreting HQNO. This product protects *Staphylococcus aureus* (haze surrounding the *P. aeruginosa* colony) from the antibiotic (tobramycin) included in the medium. Image courtesy of Lucas Hoffman, University of Washington, Seattle, USA.

Hospitalized patients, including those with CF, are frequently colonized with multiple pathogens, including *S. aureus* and *P. aeruginosa*. Interestingly, as CF patients acquire *P. aeruginosa*, *S. aureus* is cultured less frequently, although both pathogens are commonly found in respiratory cultures. Previous research showed that *P. aeruginosa* produces HQNO, an anti-staphylococcal molecule that suppresses the growth of many Gram-positive bacteria. Paradoxically, it was also shown that HQNO allowed some pathogens to grow in the presence of aminoglycoside antibiotics. As electron transport is required for aminoglycoside uptake, the authors reasoned that HQNO protects *S. aureus* from killing by inhibiting electron transport, and that the extent of *S. aureus* infection in the airways of CF patients represents a balance between the suppressive effects of HQNO produced by *P. aeruginosa* and the protection from antibiotics afforded by the exoproduct. To investigate these issues, the authors examined the effects of HQNO on the susceptibility of *S. aureus* to aminoglycoside under conditions that were clinically and physiologically relevant. They showed that the suppression of *S. aureus* growth by HQNO protected the pathogen from being killed by aminoglycoside antibiotics. Furthermore, the authors also demonstrated that prolonged growth of *S. aureus* with *P. aeruginosa* (or with physiological concentrations of HQNO) selected for *S. aureus* SCVs — SCVs of this pathogen can persist intracellularly and are notoriously difficult to detect, providing an explanation for the observation that *S. aureus* is cultured less frequently from CF patients following *P. aeruginosa* infection. Finally, the authors only detected HQNO in the sputum of CF patients that were infected with *P. aeruginosa*, providing evidence for the clinical relevance of HQNO production by *P. aeruginosa* and its subsequent effects on *S. aureus* within the environment of the CF lung.

As well as providing a fascinating example of pathogen interspecies interaction that impacts on virulence and the health of the host, the finding that *P. aeruginosa* selects for difficult-to-detect, antibiotic resistant *S. aureus* SCVs indicates that the role of this pathogen could be significantly underappreciated in all infections in which *P. aeruginosa* is present, a finding that also has practical implications for the treatment of CF patients.

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ORIGINAL RESEARCH PAPER Hoffman, L. R. *et al.* Selection for *Staphylococcus aureus* small-colony variants due to growth in the presence of *Pseudomonas aeruginosa*. *Proc. Natl Acad. Sci. USA* **103**, 19890–19895 (2006).

FURTHER READING
Proctor, R. A. *et al.* Small colony variants: a pathogenic form of bacteria that facilitates persistent and recurrent infections. *Nature Rev. Microbiol.* **4**, 295–305 (2006).