GUEST COMMENTARIES

Bacterial Interactions and the Microevolution of Cytochrome bd: Implications for Pathogenesis

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In their article, “Microevolution of Cytochrome bd Oxidase in Staphylococci and Its Implication in Resistance to Respiratory Toxins Released by Pseudomonas,” Voggu et al. describe one mechanism whereby Pseudomonas aeruginosa pyocyanin and hydrogen cyanide act to reduce the viability of pathogenic but not benign species of staphylococci (13). In addition to interesting arguments concerning the evolution of antimicrobial resistance and competition among bacteria within an environmental niche, the results of Voggu et al. also reinforce studies on electron transport-dependent bacterial persistence.

As noted by Voggu et al., previous work has shown that Pseudomonas aeruginosa releases pyocyanin, hydrogen cyanide, and quinoline N-oxides into its surrounding milieu. While some of the toxic effects of pyocyanin have been attributed to the production of reactive oxygen species (4), the current article demonstrates that staphylococcal resistance to the toxic products of P. aeruginosa depends upon the cytochrome bd quinol oxidase. Interestingly, nonpathogenic staphylococci exhibit resistance to the effects of these compounds, while pathogenic staphylococci are susceptible. Voggu et al. have shown that the key to differences between these groups of bacteria is strongly associated with alleles of cydB that correspond to either resistant or sensitive cytochromes.

While an evolutionary argument can be made concerning the origin resistance of soil bacteria to P. aeruginosa respiratory toxins, the susceptibility of pathogenic staphylococci to these toxins hints at the complexity of multibacterial species infections within the host. On the skin of a host, P. aeruginosa and Staphylococcus aureus have different niches (P. aeruginosa is found intertigenous areas, while S. aureus is found in the anterior nares), but Staphylococcus epidermidis and P. aeruginosa appear to cohabitate within common niches. Thus, toxic P. aeruginosa products would be expected to exert little selective pressure on S. aureus cydB, and S. aureus remains sensitive to the toxic P. aeruginosa products. In the case of S. epidermidis, one would expect to see cydB mutants of S. epidermidis; however, S. epidermidis and P. aeruginosa have separate microchines within the host, and S. epidermidis is also sensitive to toxic P. aeruginosa products (7).

While all the questions concerning microevolution of staphylococci cannot be settled at this time, the work of Voggu et al. also has implications for the pathogenesis of pulmonary infections in patients with cystic fibrosis. These patients often become sequentially infected with S. aureus followed by P. aeruginosa (5, 6). The presence of Pseudomonas pyocyanin and hydrogen cyanide should select against normal S. aureus, especially since the bd-type cytochrome is important in microaerophilic and aerobic environments, conditions found in the infected lung (3, 12). However, entry of P. aeruginosa into the lungs does not clear S. aureus; rather, it is often associated with a greater chance of recovery of S. aureus strains that are defective in electron transport (i.e., small-colony variants [SCVs]) (6, 10). The electron transport type of SCV would be able to survive toxic P. aeruginosa products because they lack cytochromes (10). Therefore, P. aeruginosa products might select for staphylococcal SCVs. Alternatively, the low oxygen content of respiratory epithelial lung fluid (14) and the presence of host cationic proteins (11) might preselect for SCVs, thereby allowing S. aureus to coexist with P. aeruginosa.

There are other interactions between these lung pathogens and patients with cystic fibrosis. S. aureus may serve as an iron source for P. aeruginosa. Lysis of S. aureus by P. aeruginosa releases iron, thereby increasing its pathogenic potential (9). In addition, as cystic fibrosis progresses, there is a loss of pancreatic function, which can result in diabetes mellitus. The increased amount of sugars stimulates the growth of both P. aeruginosa and S. aureus (2). This is supported by the findings that patients with cystic fibrosis who have a dual infection with P. aeruginosa and S. aureus have more rapid progression of their disease (6) and that clearance of S. aureus improves clinical outcome in patients with either single or dual infections (1, 8).

In summary, the studies by Voggu et al. provide a molecular understanding of how pathogenic and commensal bacteria interact. Moreover, defining the molecular mechanisms of the interactions between P. aeruginosa and S. aureus is also shedding light upon pathogenesis as well.

REFERENCES

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