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*Pseudomonas aeruginosa* is an opportunistic bacterial pathogen.

### **The effect of *Pseudomonas*-released quinolones on the mTOR pathway and phagocytic bacterial killing**

Cystic fibrosis (CF) patients are immunocompromised and often suffer from polymicrobial infections involving *Pseudomonas aeruginosa*, an opportunistic bacterial pathogen. *P. aeruginosa* pathogenicity is influenced by the secretion of bacterial compounds such as quinolones. *P. aeruginosa* secretes at least 50 different quinolone-based molecules. Although two of these, PQS and HHQ, are signals for a bacterial quorum sensing system, there are no known roles for the majority of the quinolones. A third quinolone molecule, HQNO, is secreted at high levels in culture. Preliminary data using macrophages suggest that HQNO inhibits respiratory burst, the process by which eukaryotic cells kill internalized bacteria with reactive oxygen. Respiratory burst is known to be regulated by the mammalian target of rapamycin (mTOR) pathway. We hypothesize that HQNO inhibits mTOR and thus macrophages' ability to kill bacteria such as *Burkholderia multivorans* and *P. aeruginosa*. We used western blotting to demonstrate that in HQNO-treated mouse embryonic fibroblasts (MEFs), phosphorylation of the mTOR inhibitor AMPK was upregulated, and phosphorylation of the mTOR downstream effector, S6 ribosomal protein was reduced, in a time- and dose-dependent manner. Next, we tested whether bacterial killing by RAW 264.7 macrophages depended on HQNO. We found that HQNO treatment decreased killing of *P. aeruginosa* and *B. multivorans* by RAW macrophage cells. HQNO more strongly suppressed macrophages' ability to kill *B. multivorans* than *P. aeruginosa*. Thus, the production of *P. aeruginosa* quinolones may protect secondary pathogens, such as *B. multivorans*, during polymicrobial infection in CF patients.