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Study shows how bacteria evolve in the lungs of cystic fibrosis patients

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Burkholderia pseudomallei colonies on a Blood agar plate. Image credit: CDC/Courtesy of Larry Stauffer, Oregon State Public Health Laboratory (PHIL #1926), 2002.

The bacterium *Burkholderia multivorans* evolves and adapts in bursts to survive in the lungs of cystic fibrosis patients, according to a study published this week in *mSystems*, an open access journal from the American Society for Microbiology. The work, believed to be the first retrospective look at the evolution of this microorganism, indicates that *B. multivorans* directly or indirectly targets adherence, metabolism and changes to the cell 'envelope' to stick around and evade antibiotics.

B. multivorans is the most commonly isolated *Burkholderia* species from chronic infections of the airways of CF patients worldwide, with an overall prevalence in the U.S. of 0.68%, said senior study author Leonilde M. Moreira, PhD, an assistant professor at the Instituto Superior Técnico in Lisbon, Portugal. "Yet our understanding of the traits required for bacterial colonization and persistence, as well as the molecular mechanisms underlying this adaptation, are limited."

To study how the bacteria adapts in CF patients, Moreira and colleagues analyzed the genomic and functional evolution of *B. multivorans* by studying sputum samples collected from a female CF patient in a Vancouver clinic over a 20-year period. The patient was hospitalized once due to CF-related respiratory illness, but had been treated on multiple occasions with antibiotics.

They sequenced and analyzed the genomes of 22 *B. multivorans* isolates taken from the patient and compared their results with the patient's medical records to look for correlations, finding that several distinct bacterial lineages coexisted at any given time but evolved at different rates. One family quickly diversified into three others. The new lineages evolved mainly by mutations in genes with regulatory/signaling roles, and in genes whose proteins are involved in lipid, amino acid and carbohydrate metabolism. A slow and steady population-wide rate of genetic changes occurred over the course of infection, at a rate of about two single nucleotide polymorphisms per year.

The evidence suggests that mutations in several of these genes were adaptive to allow the bacteria to survive, Moreira said: "These mutations corresponded to what was happening physically with the patient, so we could see that those mutations were not just random—they were specific targets that affected the physiology of the bacteria."

B. multivorans was first isolated from the patient in 1993 and recovered periodically until 2013. She was initially infected by *Staphylococcus* *aureus*, *Haemophilus influenzae* and *Pseudomonas aeruginosa* in 1989-1993, followed by a period of co-infection of these microorganisms with *B. multivorans* from 1993-1996. Overall, the evolution was marked by periods of strong diversification followed by periods of relative stability. The period of the most diversification within the *B. multivorans* infection was associated with more rapid deterioration of the patient's lung function, Moreira said.

The work not only sheds new light onto *Burkholderia* evolution but "this dynamic suggests that monitoring these evolutionary and molecular patterns could be used to design responsive therapies designed to limit population diversity and disease progression," Moreira said. "Altogether, our observations suggest that *B. multivorans* populations, during long-term colonization of the CF lungs, either directly or indirectly target adherence, metabolism, and changes in the cell envelope related to adaptation."

Because the study analyzed just one patient, results would need to be repeated, Moreira said. Her team is continuing studies of the bacteria in an additional 10 CF patients.

Provided by American Society for Microbiology

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