

Bacterium infecting cystic fibrosis patients genetically evolves to live in lungs and evade antibiotic treatments

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This is Nicolas Rodrigue, University of Calgary professor of statistics in the Department of Mathematics and Statistics in the Faculty of Science. Credit: Riley Brandt, University of Calgary

The bacterium that's the most important pathogen in patients with cystic fibrosis (CF) has genetically evolved and adapted to survive in CF-infected lungs and evade antibiotic treatments, scientists from the University of Ottawa and the University of Calgary have shown.

Pseudomonas aeruginosa is called an "opportunistic pathogen." While the microorganism is widespread in the environment and is harmless to healthy people, it infects those who are ill or have compromised immune systems.

The team of scientists performed the first systematic analysis of entire genomes (the full genetic 'blueprint') for multiple "epidemic and nonepidemic" strains of *P. aeruginosa*.

Their analysis showed that the main drivers for the evolution and adaptation of the bacterium are the

CF-lung environment itself and the presence of antibiotics.

"Many of the genes and pathways implicated in adaptive evolution within the host had obvious roles in the pathogenic lifestyle of this bacteria," says their study, published this week in the *Proceedings of the National Academic of Sciences* of the United States of America.

Lead author is Jeremy R. Dettman, from the Centre for Advanced Research in Environmental Genomics at the University of Ottawa.

Better understanding of how the pathogen evolves will help advance more effective treatments for infected cystic fibrosis patients, says co-author Nicolas Rodrigue, University of Calgary professor of statistics in the Department of Mathematics and Statistics in the Faculty of Science.

"If we can devise a multi-pronged treatment approach that addresses all or most of the different ways that the bacteria can adapt to different treatments, then the bacteria will be out of luck," Rodrigue says.

Approximately 4,000 people have [cystic fibrosis](#) in Canada, and one person in the country dies from the disease each week, according to Cystic Fibrosis Canada.

The unique aspect of the new study is that "we looked at a large number of strains. Instead of looking at just a few genes here and there, we looked at the entire genomes of all these 32 strains," Rodrigue says.

The scientists also found that an epidemic strain of *P. aeruginosa* has spread between clinics in the United Kingdom and North America – likely through

international air travel.

As a statistician, Rodrigue's key role was to devise and implement the computational and statistical approaches used to analyze a massive amount of data.

He used computer programs – including some he wrote himself – to assemble "millions of little snippets" of DNA into the genomes for each bacterial strain. "It's like a huge jigsaw puzzle that we have to put together," he says.

Rodrigue also performed a "statistical inference of the evolutionary relationships" among all 32 strains. This included identifying which genes had been gained or lost during evolution, which underwent genetic recombination and which were the target of selection.

Rodrigue, who joined the University of Calgary in September, says a multidisciplinary research approach increasingly will be needed given the growing richness of scientific data. "Statisticians will have to know a lot about the science in which they're working. And the scientists are going to have to become more statistically sophisticated and knowledgeable."

Provided by University of Calgary

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