

Cystic Fibrosis Research News

Title:

Multilocus amplicon sequencing of *Pseudomonas aeruginosa* cystic fibrosis airways isolates collected prior to and after early antipseudomonal chemotherapy

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What was your research question?

When the bacterium, *Pseudomonas aeruginosa* (*P. aeruginosa*), first colonizes the airways of an individual with cystic fibrosis (CF), there is a high chance of eradicating the bacterium using early antimicrobial treatment. However, early treatment may fail to eradicate *P. aeruginosa* on some occasions. Therefore, in this study we wanted to determine whether such treatment failure is associated with the emergence of mutations (i.e. changes in the DNA sequences) in certain *P. aeruginosa* genes.

Why is this important?

Chronic airway infections with *P. aeruginosa* are the most frequent co-morbidity associated with a high treatment burden and impaired quality of life for people with CF. Early antimicrobial treatment is a successful strategy to prevent or at least delay chronic *P. aeruginosa* infection. Investigation of *P. aeruginosa* recovered from treatment failures could teach us how to improve our early treatment regimens.

What did you do?

Over 10-years, we collected the first and subsequent *P. aeruginosa* airway isolates (pre- and post- treatment isolates) from previously negative for *P. aeruginosa* patients who were cared for at the CF center Hannover since the age of diagnosis. Of 54 patients who became positive for *P. aeruginosa* for the first time, 15 patients remained positive for *P. aeruginosa* after the first round of early antimicrobial treatment. A total of 34 genes that are known to

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affect antibiotic resistance and adaptation (i.e. how the bacteria changes to survive better in the airways) of *P. aeruginosa* to the CF lungs were analysed in the post-treatment *P. aeruginosa* isolate compared to the pre-treatment *P. aeruginosa* isolate for each of the 15 patients, who failed treatment.

What did you find?

We detected a total of 50 mutations in 12/34 target genes in post-treatment isolates compared to pre-treatment isolates of eleven patients. More than 60% of mutations emerged in *P. aeruginosa* genes that control the transport of antibiotics across the cell wall and another 20% of mutations emerged in genes that are responsible for the production of biofilms. Numerous pre- and post-treatment *P. aeruginosa* isolates contained mutations in a gene called *lasR*. *lasR* is a central control element of cell to cell communication and pathogenicity of *P. aeruginosa*.

What does this mean and reasons for caution?

Early antimicrobial treatment selects for mutations in genes that affect biofilm formation and drug resistance (also known as pathoadaptive traits) in *P. aeruginosa*. These mutations are typical of chronic infections with *P. aeruginosa* in CF lungs.

What's next?

These results are from a single CF center and should be backed up by the investigation of early treatment *P. aeruginosa* isolates from other CF centers.

Original manuscript citation in PubMed

<https://www.ncbi.nlm.nih.gov/pubmed/?term=Multilocus+amplicon+sequencing+of+Pseudomonas+aeruginosa+cystic+fibrosis+airways+isolates+collected+prior+to+and+after+early+antipseudomonal+chemotherapy>