



Cystic Fibrosis Research News

Title:

Identification of outer membrane Porin D as a vitronectin-binding factor in cystic fibrosis clinical isolates of *Pseudomonas aeruginosa*

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What was your research question?

We aimed to answer two questions. Firstly, when the bacteria *Pseudomonas aeruginosa* are becoming established in the lungs of people with cystic fibrosis (CF), is it important for the bacteria to become attached to the human protein vitronectin? Secondly, how does this attachment work?

Why is this important?

Pseudomonas aeruginosa is the most common bug that causes chronic or recurrent infections in the airway of people with CF. These infections are often difficult to treat because of antibiotic resistance and also because the bugs stick together and protect each other in a type of slime layer known as a biofilm. So, alternative treatments are needed.

Previous experiments have shown that vitronectin is involved in the interaction between bugs and human cells. It is thought that the bugs attach themselves to vitronectin, so they are able to stick to the walls of the airway, and to remain in the body. It is important to understand this kind of mechanism which causes disease in order to find new and alternative treatments.

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What did you do?

After testing of the samples of *P. aeruginosa* which we had collected to see if the bugs were attaching themselves to the vitronectin, we identified Porin D as the main vitronectin-binding protein on the surface of the bug which attached to vitronectin. Next, we checked the characteristics of the Porin D by modifying the bug's genes and using "mutated" bugs that had no Porin D.

What did you find?

By comparing *P. aeruginosa* from the airways of people with CF to *P. aeruginosa* grown from blood samples, we found that the strains of the bug taken from the airways of people with CF attached themselves to much more of the protein vitronectin. After this, we discovered that Porin D was the main protein on the surface of the bug which attached to the vitronectin. This was done in such a way that the bacteria were able to use vitronectin to stick to the walls of the airways.

What does this mean and reasons for caution?

Our results indicate that attaching to vitronectin is important for bugs to colonise the airways and that this is mainly done using the surface protein Porin D. Interestingly, Porin D has previously been studied for its importance for treatment with the antibiotic imipenem, and with the current study we show that Porin D has several roles.

What's next?

Not only does finding a surface protein with a defined role in the infection process increase our knowledge on the biological mechanisms leading to infections caused by *P. aeruginosa*, it also opens up a target for new vaccines and antimicrobial treatments.

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