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Cystic Fibrosis Research News

Title:
Disruption of the extracellular polymeric network of *Pseudomonas aeruginosa* biofilms by alginate lyase enhances pathogen eradication by antibiotics

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What was your research question?
Will an enzyme secreted by marine bacteria, alginate lyase, be able to disrupt the alginate within *Pseudomonas aeruginosa* biofilm? Can we develop a combined therapy of alginate lyase and antibiotics to treat chronic *P. aeruginosa* infection?

Why is this important?
Pseudomonas aeruginosa is a bacterium that forms biofilms, clumps of bacteria, on the lungs. Because of the biofilms, it is difficult for the human immune system and antibiotics to attack *Pseudomonas* infections in the lungs of people with CF. *P. aeruginosa* biofilms are largely made of alginate, which is a substance that improves the stability of the biofilm. The enzyme alginate lyase breaks down alginate and therefore decreases the stability of biofilms. When used with the right antibiotics to disrupt *P. aeruginosa* biofilms (chosen for clinical reasons), alginate lyase and antibiotics are even more effective. Interestingly, alginate is present in many types of seaweeds. Alginate lyase is secreted by many marine bacteria to break down alginate. Our proposed research takes a new approach by using the enzyme alginate lyase to breakdown the alginate the *P. aeruginosa* biofilm.

What did you do? In this study, we purified alginate lyase from a marine bacterium. We then tested whether the purified enzyme could directly inhibit the growth of a biofilm of a strain of *P. aeruginosa* taken from a sample from someone with CF. We first determined whether there was a decrease in the amount of alginate in the biofilms treated with alginate lyase. We then examined the synergy of alginate lyase with antibiotics tobramycin and ciprofloxacin to eradicate biofilms.

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What did you find?

The strain of *P. aeruginosa* we used for this research was taken from a sample from a person with CF it was able to overproduce alginate to protect itself from the person's own immune system and antibiotics. We showed that our purified alginate lyase was able to break down alginate from this strain and that it was able to disrupt the biofilms. Interestingly, the alginate lyase became inactive when heated and lost its ability to destroy the biofilm. In addition, the effects on the biofilm were more obvious when a higher dose of alginate lyase was used. It is worth noting that alginate lyase is not an antibiotic because it does not directly kill bacterial cells. Our analysis of the images seen through the microscopic of the biofilms which we had grown showed a dramatic difference in the amount of bacteria killed when antibiotics were used alone or in combination with alginate lyase. When used on their own, antibiotics only affected the top layer of the biofilms and were not efficient in killing cells protected within the inner layers of the biofilms. The bacterial biofilms displayed a dramatic response to ciprofloxacin and tobramycin used together with alginate lyase, which resulted in bacterial cells deep within the biofilm being killed.

What does this mean and reasons for caution?

There has been some controversy about whether the effects of alginate lyases on biofilms were due to the enzyme activity. This is partly because the alginate lyases under investigation were from different sources, and therefore demonstrated different properties. In addition, the alginates within the biofilms of different *P. aeruginosa* strains are quite different, meaning they react very differently in terms of sensitivity to being broken down by enzymes from different sources. Our data suggest that alginate lyase purified from marine bacterial was the type needed to break down the biofilm of the alginate-overproducing strain CF27. However, we could not completely rule out the possibility that this enzyme disrupted the biofilm due to other unknown reasons.

What's next?

Further studies are needed to work out how the purified alginate lyase destroys *P. aeruginosa* biofilms. Future experiments in animals are needed to develop a combination therapy to treat *P. aeruginosa* infection in people with CF.

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