

PLOS Science Wednesday: Hi Reddit, we're Hui and Jessica, and we recently discovered that oral streptococci may protect the lungs of cystic fibrosis patients from the deadly pathogen, *Pseudomonas aeruginosa*. – Ask Us Anything!

PLOSScienceWednesday¹ and r/Science AMAs¹

¹Affiliation not available

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Abstract

Hi Reddit, My name is Hui Wu, a Professor at the University of Alabama at Birmingham. My research focuses on microbial molecular mechanisms that contribute to oral infectious diseases, such as dental caries and periodontal disease. Specifically, I am interested in protein glycosylation pathways and using novel small molecules to inhibit bacterial biofilms. And I'm Jessica Scofield, a Postdoctoral Fellow at the University of Alabama at Birmingham. My research examines competitive interactions between commensals (“friendly bacteria”) and pathogens that occur in polymicrobial infections. I am particularly interested in discovering unique antimicrobial mechanisms used by commensal bacteria to inhibit pathogenic bacteria. We recently published a study titled A commensal streptococcus hijacks a *Pseudomonas aeruginosa* exopolysaccharide to promote biofilm formation, in PLOS Pathogens. The purpose of the study was to characterize the two-species biofilm of *Pseudomonas aeruginosa* (a pathogen) and *Streptococcus parasanguinis* (a commensal), which are two bacteria that are present in the lungs of cystic fibrosis patients. Our study revealed that *S. parasanguinis* can utilize products made by *P. aeruginosa* to promote its own biofilm, while simultaneously restricting the incorporation of *P. aeruginosa* into the biofilm. Our findings suggest that commensals, such as *S. parasanguinis*, may be able to inhibit the persistence of *P. aeruginosa*. We will be answering your questions at 1pm ET – Ask Us Anything!

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PLOSSCIENCEWEDNESDAY [R/SCIENCE](#)

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Wednesday: Hi Reddit, we're
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streptococci may protect the
lungs of cystic fibrosis patients

Hi, as someone with Cystic Fibrosis and *P. aeruginosa*. Now you've made this finding during your research, how likely will this turn into an actual medication I could take?

[Draig](#)

Jessica: Hello, thanks for your question! Further studies need to be completed to determine whether the commensal used in our study, (*Streptococcus parasanguinis*), could serve as a therapeutic to treat cystic fibrosis. Our hope is that *S. parasanguinis* could potentially be developed into a probiotic that inhibits *Pseudomonas aeruginosa* in the lung. Interestingly, some probiotics have been shown to reduce the number of flare ups in some cystic fibrosis patients.

Greetings from NYC! Pulmonologist here, but lung cancer focused. Still, I manage a handful of complex bronchiectasis patients who could benefit from this line of ID work. Currently, one of my patients is sitting in an ICU waiting for a new pair of lungs.

from the deadly pathogen, *Pseudomonas aeruginosa*. – Ask Us Anything!, *The Winnower* 4:e149562.26677, 2017, DOI: [10.15200/winn.149562.26677](https://doi.org/10.15200/winn.149562.26677)

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So...s. *parasanguinis* is a jerk that looks out for itself.

Are you planning to look at these bugs in relation to other elements/pathogens/flora of the amazingly complex CF patients? Its surely not one to one!

And what do you see as the relation between something like a CFTR limitation in managing biofilms vs in a patient with non-CF bronchiectasis?

Thanks for the AMA!

[frogtoosh](#)

Jessica: Hello and thanks for your question! Yes, we are planning to look at the interaction between *Streptococcus parasanguinis* and other microbes that commonly infect the cystic fibrosis lung. *S. parasanguinis* does have the ability to inhibit pathogens other *Pseudomonas aeruginosa*, either planktonically or within a biofilm, therefore, *S. parasanguinis* could potentially be used to treat not only patients with cystic fibrosis, but also patients with non-CF bronchiectasis.

As someone who has several family members with CF, thank you so much for your work!!

Here's my question: don't they use really strong antibiotics to get rid of *Pseudomonas Aeruginosa*? Wouldn't that also kill the streptococcus? Are you guys proposing that they should give all CF patients the streptococcus bacteria to prevent *P. Aeruginosa*, as a preventative? One of my cousins has *P. A.* (which is managed from time to time with rounds of strong antibiotics), so I'm highly intrigued by your work!

[Threwthelookinglass](#)

Jessica: Hello and thanks for your question and your interest in our work! *Streptococcus parasanguinis'* tolerance to antibiotics is quite different from that of *Pseudomonas aeruginosa*. Our ongoing studies will determine whether the traditional antibiotics used to treat cystic fibrosis will negatively impact *S. parasanguinis*. At this time, we are not suggesting all cystic fibrosis patients be treated with streptococci to prevent *P. aeruginosa*, as we have much more work to complete to determine the effectiveness and safety of using streptococci in humans in that manner. However, future studies will determine whether *S. parasanguinis* can be potentially used as a probiotic to treat CF infections.

Interestingly, another study (Filkins LM, Hampton TH, Gifford AH, Gross MJ, Hogan DA, Sogin ML, O'Toole G. (2012) Prevalence of streptococci and increased polymicrobial diversity associated with cystic fibrosis patient stability.) demonstrated that CF patients that are colonized with *S. parasanguinis* in the CF lung have improved lung function. We know that oral streptococci, like *S. parasanguinis* are already present in the CF lung and may be inhibiting *P. aeruginosa*.

Based on other studies we have completed, (Scofield JA, Wu H. (2015) "Oral streptococci and nitrite-mediated interference of *Pseudomonas aeruginosa*), we know that *S. parasanguinis* can kill *P. aeruginosa* using nitrite. Nitrite is present at different levels in patients that have CF. Overall, we believe several mechanisms exist by which *S. parasanguinis* can kill or inhibit *P. aeruginosa* and we hope to use these mechanisms to develop treatments for CF and other infections.

What makes a *Streptococcus* biofilm less pathogenic than a *P. aruginosa* biofilm? Sure, we see it as a commensal now, but most commensal can cause just as much harm as pathogens in the right conditions.

[Vibriofischeri](#)

Jessica: Hello and thanks for your question! *Pseudomonas aeruginosa* is multi-drug resistant, produces an arsenal of virulence determinants, and has the ability to alter its genome to continuously persist during a chronic infection. The ability to form a protective biofilm contributes to *P. aeruginosa*'s ability to cause chronic infections. These attributes make *P. aeruginosa* deadly. *Streptococcus parasanguinis* on the other hand, can restrict *P. aeruginosa* from making a biofilm and does not produce the harmful virulence determinants that *P. aeruginosa* does. In fact, studies have shown that CF patients that are colonized with *S. parasanguinis* have improved lung function. Our hope is to potentially develop therapeutics or probiotics based on the unique antimicrobial mechanisms exhibited by *S. parasanguinis*.

What kind of measures could we take to promote commensals and help them keep a competitive edge against opportunistic pathogens in vulnerable patients? Is the work being done on producing drugs which block QS messenger molecules that help co-ordinate biofilm formation a possible route to making the 'bad guys' less competitive inside the body?

Additionally - do you think enough is being done to ensure current antibiotic regimes do minimal damage to commensal species?

[Feather_Snake](#)

Jessica: Hello, thanks for your question. Studies are ongoing to determine how to maintain homeostatic conditions by promoting the colonization of commensals. Commensals like the one used in our study are actually oral commensals that can disseminate to the cystic fibrosis lung and have already been shown to be associated with improved lung function in cystic fibrosis patients.

As it pertains to blocking quorum sensing, there are studies (<https://www.ncbi.nlm.nih.gov/pubmed/24143808>) that have demonstrated that QS inhibitors can block both *P. aeruginosa* virulence and biofilm formation, which represents another avenue to potentially treat CF infections.

Thanks for a very interesting read and taking the time to do this AMA, you all have some really great findings. I have a few questions about the implications of increased biofilm formation in the lung. From what I understand, a lot of the damage seen in CF lungs comes from the persistent state of inflammation caused by bacterial infection. While the Streptococci are commensal, wouldn't they still negatively affect this inflammatory phenotype, potentially even increasing lung tissue damage? Additionally, how do you envision potential therapeutics that may come from this research? It seems as though the Streptococci are able to hijack alginate production for their own growth purposes and out-compete the *P. aeruginosa*. Do you think there is still a way to block *Pseudomonas* growth without a competing bacterial species, or would therapeutics be based on probiotic treatments?

[crazyjaney](#)

Jessica: Hello, thanks for your questions!

Yes, the host immune response to the bacteria colonizing the cystic fibrosis causes damages. However, *Streptococcus parasanguinis* may not trigger the same type of inflammatory response as *Pseudomonas aeruginosa*. These are studies that we will have to perform. However, we do know that cystic fibrosis patients who are colonized with oral streptococci, such as *S. parasanguinis*, have better lung function compared to patients who are not colonized with these oral streptococci, which suggests their presence in the CF lung may not trigger a heightened inflammatory response. Ultimately, we hope to harness antimicrobial mechanisms displayed by *S. parasanguinis* to develop therapeutics. Also, it is possible to inhibit *P. aeruginosa* growth through non-bacterial mediated approaches, but these

approaches still require further improvement.

As a CF patient that has seen **literally hundreds** of lab research papers that could or might have either completely cured CF or at least solved one very big problem with it - which *P. Aeruginosa* is -, I unfortunately have to ask this. Don't take it personally.

Is this just another lab project done to get a research grant and something to write on your curriculum or are you actually going to further investigate and develop this? With the backing of who, in that case? Have you forwarded your research to the Cystic Fibrosis Foundation? What stage is this research at, is it something any pharma company might be interested in or is it too soon?

[Aremisio](#)

Jessica: Hello Aremisio, thanks for your questions! I have a good friend who has a child with cystic fibrosis and I have a niece that was diagnosed with Crohn's disease, so I understand how you feel when you read research papers that suggest their work may help treat CF. We do know that certain bacteria can mitigate the effects of these illnesses, therefore, our goal is to seriously push our research forward in a manner that generates improved health outcomes. Thankfully, there are currently ongoing clinical trials and drugs in the pipeline that show great promise in either correcting CFTR mutations or treating bacterial infections.

Hi Hui and Jessica, really cool work! Have you, or are planning to look at how *P. aeruginosa* change transcription in response to being grown in this dual-species biofilm? I think it'd be awesome to see what virulence pathways and QS systems are modified by the presence of *S. parasanguinis*

ELI5: Do the bad bacteria turn off genes that cause us to get sick when they're grown with the good bacteria?

[microbiololgy](#)

Hui: Thank you for the suggestions. Jessica actually has planned some studies to look at expression of *P. aeruginosa* genes in response to the presence of *S. parasanguinis* by RNA-sequencing. Hopefully we will see some interesting virulence pathways are modulated by *S. parasanguinis*. It is our hope that virulence genes of bad bugs got turned off when they encounter some powerful good bacteria such as *S. parasanguinis*.

CF patient here. I had a lung transplant 10 years ago. I had pseudomonas. Too late for me as I already have new lungs, but thank you for your work.

[kakbakalak](#)

Jessica: Hello, thanks for your response and glad to hear of your successful transplant!

There is a lot talk at the moment surrounding the gut microbiome. Some evidence suggests that gut microbes can impact many bodily systems, including the immune system, the nervous system and the liver.

Is there any evidence that commensal microbial populations in other areas of the body - the lungs, mouth, skin and urinary tract - are influencing the normal operations of distant organs in the body?

[AlexanderSupersloth](#)

As you are aware the microbiome studies have uncovered a new dimension of human health and disease, microbes are everywhere on our skin surface, and in our body. Commensal microbes are found in many parts of our body. A great deal of studies suggest there is a clear association between certain microbes and human health locally as well as remotely. However whether the commensal microbes directly impact the normal operations of distant organs awaits further investigation.

Every year during the summer i get pneumonia or bronchitis coupled with lost of blood flowing from my lungs i always wondered if the pneumonia vaccine works ? if yes i am gonna take that. Also every time the seasons change i get lung infections.

And will this new research help in my case.

I hate taking amoxicillin every summer for this :/

[Plerd](#)

Amoxicillin kills good and bad bacteria. When you don't have a balanced bacterial community to maintain health, infection occurs easily. Our research aims to develop selective anti-infection approaches

This is a more overall microbial question. Let's say someone is infected with a virus or bacteria that causes the person to be ill. The disease is new so antibodies are trying to get this new thing eliminated. Is it possible that another virus or bacteria or microbe enter the body through cut, inhaling, etc, and gets rid of the virus/bacteria causing the illness, but this helpful virus/bacteria/microbe doesn't cause harm to the body, but is eliminated by the antibodies?

[zatemxi](#)

Depends on what bacteria and virus you have, often antibodies are very selective, and do not cross react. Antibodies that recognize the microbes causing problems may not recognize good microbes