Bacterial airborne signal encourages fungal growth critical in lung infections

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Researchers in France have discovered that volatile compounds released by a bacterial pathogen stimulate the growth of a fungal pathogen found in lung infections in cystic fibrosis (CF). The findings, published this week in *mBio*, an online open-access journal of the American Society for Microbiology, show for the first time that one pathogen can emit a signal through the air that acts as a direct fuel for another pathogen to grow.

The bacteria *Pseudomonas aeruginosa* and the fungus *Aspergillus fumigatus* are both opportunistic pathogens often found together in the lung microbiota. When the two pathogens come into direct contact, previous research has shown that the bacteria produces compounds that inhibit fungal growth. Because microbes often produce volatile compounds that can travel through the air, Jean-Paul Latgé Christoph, Heddergott and Benoit Briard, members of the *Aspergillus* unit at the Pasteur Institute in Paris, wondered if these two pathogens could also communicate via volatile signals.

"To our big surprise, volatiles produced by *Pseudomonas aeruginosa* were promoting the growth of the *Aspergillus fumigatus* fungus," says Latgé. "Even more surprising, we found that these volatiles were actually taken up by the fungus to support growth."

To test how volatile compound signals might travel between and influence the microbes, Heddergott and Briard placed a small Petri dish of *Aspergillus* to one side inside a larger Petri dish of a *Pseudomonas*

culture. Physically separated by the plastic dishes, the microbes shared common airspace above the dishes' surfaces.

"We simply put these two organisms together and in a couple of days, we were surprised to see the fungus growing faster and growing towards the bacteria," says Heddergott. "This really indicated something stimulatory [coming from the bacteria]."

To find out what it might be, he used special fibers to absorb the volatile compounds released from each pathogen and then identified them. Heddergott then tested each of the volatiles produced by *Pseudomonas* individually on the fungus alone.

"The most stinky ones containing sulfur stimulated the fungus to grow at the same concentration as co-growing with the bacteria," says Heddergott. He narrowed it down to just one airborne compound mainly responsible for the growth—dimethyl sulfide.

Because sulfur is an essential component that *Aspergillus* needs for growth, the team tested whether dimethyl sulfide was actually being taken up and used as food by the fungus. Heddergott and Briard placed the fungus on a plate of food lacking sulfur, then pumped dimethyl sulfide into the airspace. They showed that the fungus grew better with dimethyl sulfide present and sucked the dimethyl sulfide directly out of the air as fuel.

"Before now, no one thought that a fungus could grow on volatile compounds bringing sulfur," says Latgé. In the context of CF lung infections, Latgé says, this might explain why the bacteria usually colonize lungs first and the fungus colonizes later: "When the fungus reaches the patient's lung, having bacteria that are releasing this volatile will help the fungus establish itself."

Understanding the relationships between these microorganisms and how they colonize lungs could lead to better ways to prevent these bacterial-fungal co-infections, which are responsible for acute worsening of symptoms and declining lung function in CF patients.

"This opens our eyes to look not at just a single organism in human infections, but rather a series of microorganisms," says Latgé. "They can be far away from each other, communicating over a distance, and even using volatile compounds produced by another microbe to grow."

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