Bacterial food web may be key to cystic fibrosis

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(Medical Xpress)—Cystic fibrosis patients suffer from chronic bacterial infections and thick mucous in their lungs, due largely to a combination of microbial infections and resulting inflammation. A common pathogen, Pseudomonas aeruginosa, which can lay dormant in healthy individuals, becomes virulent in the lungs of cystic fibrosis patients, and Cornell biological engineers think they might know why.

They have shown that P. aeruginosa virulence is "turned on" when it feeds on a particular fermentation product called 2,3 butanediol, demonstrating a direct metabolic relationship between fermenting bacteria and P. aeruginosa. This understanding could lead to more effective treatments for cystic fibrosis patients; rather than the use of antibiotics, disrupting P. aeruginosa's flow of preferred food could be key to preventing cystic fibrosis-related infections in the lungs.

The research was led by Lars Angenent, associate professor of biological and environmental engineering. A paper, along with a related one by San Diego State University researchers, was published online Jan. 9 in the *International Society for Microbial Ecology Journal*.

Angenent et al. had previously used bioreactors to show that the presence of 2,3 butanediol promotes cross-feeding between P. aeruginosa and fermenting bacteria, including Enterobacter aerogenes, which makes 2,3 butanediol as a fermentation byproduct.

They are now applying their knowledge of this mutually beneficial microbial relationship to shed light on the microbial environment of lungs affected by cystic fibrosis. In this work, they again used bioreactors to observe the virulence of P. aeruginosa as it fed on both 2,3 butanediol and glucose; the glucose did not cause virulence, while with the 2,3 butanediol, the bacteria became significantly more virulent.

Scientists already knew that P. aeruginosa plays a key role in sickening patients, but the exact microbial interactions and subsequent inflammatory responses that lead to the symptoms have not been well understood.

Because 2,3 butanediol is the substrate, or food, for P. aeruginosa, 2,3 butanediol is the key in the metabolic relationship between different bacteria.

Their relationship results in higher concentrations of phenazines, which are chemicals produced by P. aeruginosa that interact with the fermenter, and are part of the cascade of events that leads to the pathogen's increased virulence, such as the formation of biofilms that increase lung symptoms in patients. The phenazines combine with oxygen to create free radical compounds, which kill other microbes and cause stress for host cells.

"The signaling is switched on because of the 2,3 butanediol," Angenent explained. "However, the exact mechanism is still unknown."

Understanding why P. aeruginosa does well in the lungs of cystic fibrosis patients, and looking at ways to cut off its preferred food supply within that system, could lead to ways to treat the disease, the scientists say.

More information: "Metabolite transfer with the fermentation product 2,3-butanediol enhances virulence by Pseudomonas aeruginosa." Arvind Venkataraman, Miriam A Rosenbaum, Jeffrey J Werner, Stephen C Winans, Largus T Angenent. *The ISME Journal* advance online publication, 9 January 2014; DOI: 10.1038/ismej.2013.232

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