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Researchers identify potential drug that could help treat cystic fibrosis

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From an early age, the lungs of individuals with cystic fibrosis (CF) are colonised and infected by bacteria, a common example being *S. aureus*. These bacterial infections cause the lungs to become inflamed, infected, and can eventually lead to permanent lung damage. Researchers from the University of Pennsylvania and the Howard Hughes Medical Institute previously showed that an enzyme called Sphingomyelin phosphodiesterase C (SMaseC) produced by the *S. aureus* bacterium may harm the health of CF patients. Now, they have discovered an inhibitor for this pathogenic bacterial enzyme.

In patients suffering from CF, the cystic fibrosis "transmembrane conductance regulator" (CFTR) channels are faulty, causing a thick mucus to build up in their lungs. In these experiments, the authors used oocytes from the Xenopus type of frog—that had been genetically modified to express CFTR channels on their cell surface—to measure the effect that SMaseC has on CFTR channels. They saw that the SMaseC enzyme suppresses CFTR channel activity in these experimentally modified frog oocytes, and also in a human lung cell line.

These results suggest that the SMaseC enzyme, produced by the S. aureas bacterium, may reduce any residual channel activity in CF patients. The problems originating from genetic defects in CFTR channels are likely made greater if the enzyme reduces the function of the CFTR channel even further.

SMaseC also suppresses a type of voltage-gated potassium channel,

known as the Kv1.3 channel, in immune cells. Suppression of these potassium channels is known to weaken host immunity, which would make it more difficult for the CF patients to recover from lung infections.

To try and counteract the effects of the enzyme, the researchers went on to test a collection of approved drugs and natural products in a chemical library. They found that tannic acid—a readily available and inexpensive natural product that has been used to treat disease as far back as 1850—stopped SMaseC from having a negative effect on both the CFTR and the Kv1.3 channels. "We hope to test whether the application of the SMaseC inhibitor tannic acid, in conjunction with effective antibiotic treatment and supportive measures, will provide a significant therapeutic improvement over current treatments for cystic fibrosis," Dr. Zhe Lu, the senior author, says. His team is also working hard to understand the exact mechanism by which tannic acid counters the negative actions of SMaseC.

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