New test for cystic fibrosis may lead to more treatments

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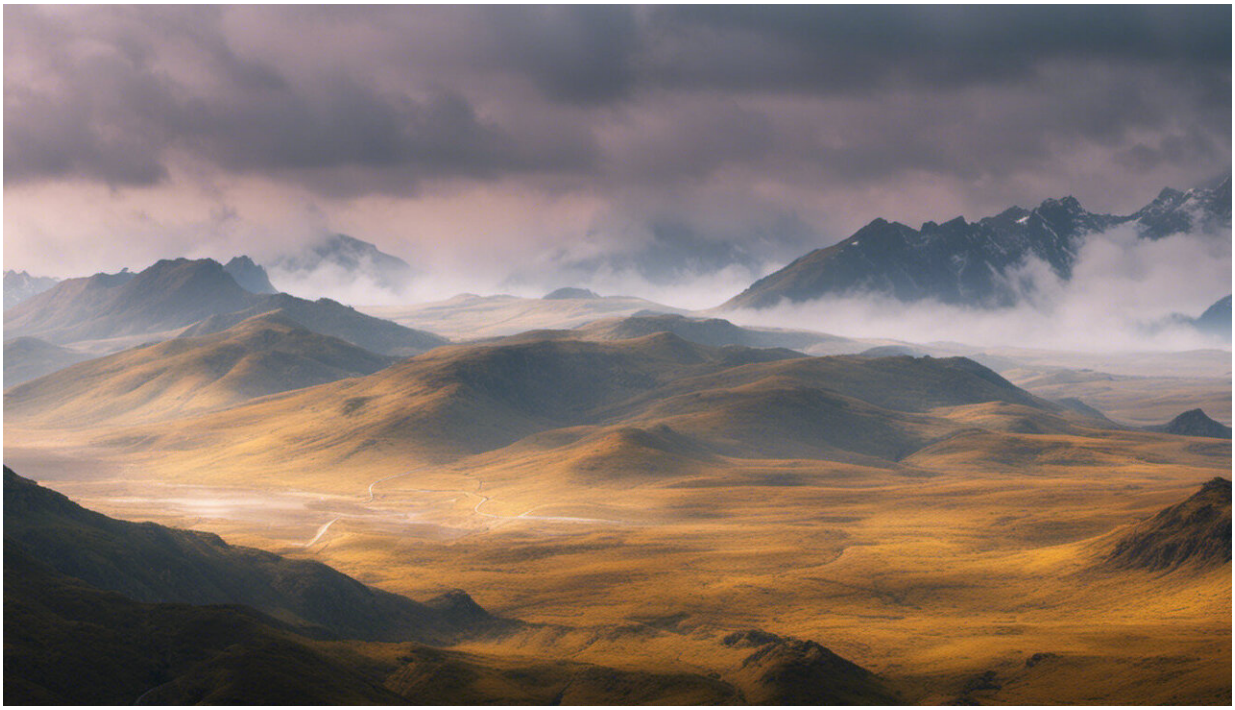

Credit: AI-generated image (disclaimer)

(Medical Xpress)—Treatments for cystic fibrosis may be easier to develop with the use of a new test created by Stanford researchers.

The test – taken by sampling sweat – shows that smaller amounts of a particular protein are necessary to stop cystic fibrosis symptoms than

previously thought, according to Jeffrey Wine, a professor of psychology and biology who is the director of Stanford's Cystic Fibrosis Research Laboratory.

"I was amazed it worked out as well as it did," Wine said. Wine and colleagues in the Stanford School of Medicine described the test in October in the journal *PLoS ONE*. Since then, they have used the test to measure protein levels in patients taking a cystic fibrosis drug. That research has now also been published in *PLoS ONE*.

Cystic fibrosis is a recessive genetic disorder that disables a key protein – known as the cystic fibrosis transmembrane conductance regulator, or CFTR – that is responsible for transferring fluid and minerals in and out of cells.

The effect on the 30,000 Americans diagnosed with the condition is debilitating: they suffer from chronic lung infections, male sterility and a host of other symptoms. In the past, carriers struggled to survive past infancy.

Wine knows the cost of the disease firsthand: his 32-year-old daughter, Nina, has cystic fibrosis. She's been lucky so far and is healthy enough to run marathons and pursue a master's degree in global health, Wine said. But she relies on a cocktail of drugs to maintain her health.

Doctors usually treat cystic fibrosis by tackling symptoms as they appear. Very few drugs target the underlying problem: a patient's CFTR is broken, damaged or missing.

CFTR defects vary greatly: the entire protein might be missing, or it could have just a few flaws. Current tests, which measure the amount of chloride in sweat, can't precisely identify how much functioning CFTR is present.

The new test determines the ratio between two types of sweat in each individual by using dyes to form bubbles on the skin. That ratio accounts for differences in sweat volume – between a conditioned athlete and a sedentary person, for example – and reveals an individual's CFTR levels.

Wine's work showed that even healthy people have varying levels of CFTR and that only a small amount of CFTR is needed to remain disease-free. "The biggest surprise for me was how small the response was. I don't think anybody expected that," Wine said.

Therefore, drug developers have a lower target: they only need to restore 10 percent of CFTR functionality to relieve symptoms. Also, patients can be treated with drugs that supplement their personal CFTR levels to relieve symptoms. That is particularly important because people with the same genetic flaw can have different amounts of CFTR, Wine said.

The researchers, who include lead author Jessica Char, a research assistant in Wine's group, examined the CFTR levels in eight subjects with cystic fibrosis. Six of the patients were taking ivacaftor, a drug currently available to treat some types of cystic fibrosis. Ivacaftor boosted CFTR levels as expected, but it also increased CFTR levels in a type of cystic fibrosis it is not currently designed to treat, Wine said.

Next, Wine said, he plans to examine differences in CFTR in healthy individuals. He hopes eventually to determine the precise amount of CFTR needed to alleviate symptoms.

"(My daughter) would really love to have a drug," Wine said.

More information: Wine JJ, Char JE, Chen J, Cho H-j, Dunn C, et al. (2013) "In Vivo Readout of CFTR Function: Ratiometric Measurement of CFTR-Dependent Secretion by Individual, Identifiable Human Sweat Glands." *PLoS ONE* 8(10): e77114. DOI: 10.1371/journal.pone.0077114

Char JE, Wolfe MH, Cho H-j, Park I-H, Jeong JH, et al. (2014) "A Little CFTR Goes a Long Way: CFTR-Dependent Sweat Secretion from G551D and R117H-5T Cystic Fibrosis Subjects Taking Ivacaftor." *PLoS ONE* 9(2): e88564. DOI: 10.1371/journal.pone.0088564