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# Cystic Fibrosis Research News

**Title:**
Emerging preclinical modulators developed for F508del-CFTR have the potential to be effective for ORKAMBI resistant processing mutants

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## What was your research question?
Are new CFTR modulators in development for F508del-CFTR effective in other CFTR mutations that are similar to F508del-CFTR but that have previously been shown to respond poorly to the drug combination ORKAMBI (lumacaftor/ivacaftor)? Do we observe positive effects of these new CFTR modulators in model cell systems, and nasal cells carrying these other CFTR mutations obtained from CF patients?

## Why is this important?
There are many different CF causing CFTR mutations and it is unlikely that a drug combination will be developed for each one. It is important to know if CFTR modulators in development are potentially effective for less common mutations, so that people with these other CFTR mutations can be included in clinical trials. Many more individuals with CF may be helped if these drugs are shown to be effective for more mutations in clinical trials.

## What did you do?
We tested drugs of similar classes to those being tested in clinical trials by the pharmaceutical company Abbvie, in model cell systems with the mutations M1101K, G85E and N1303K. We then tested the compounds in nasal cell samples from patients with two copies of each of these CFTR mutations.

## What did you find?
We found that certain combinations of these compounds were effective in model cell systems and patient nasal tissues with the M1101K and G85E mutations; but were less effective in the cells with the N1303K mutation. We also learned more about how these compounds work to improve CFTR protein function.

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### What does this mean and reasons for caution?

Some CFTR mutations that we thought couldn't be treated with CFTR modulators, may respond to new drugs in development. Patient nasal cells seem like a good way to test if these drugs might help. However, testing in nasal cells alone isn't sufficient and a clinical trial would be needed to understand if the compounds could really help CF patients with these mutations.

### What's next?

Further studies should test the nasal cells of CF patients with more CF modulator drugs in development to see if they will potentially work for additional mutations, and if so, consider people with these mutations for clinical trials.

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