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# Cystic Fibrosis Research News

**Title:**
Mucus and mucus flake composition and abundance reflect inflammatory and infection status in cystic fibrosis

**Lay Title:**
Inflammation and infection change what mucus is made of, how much gets made, and how much it can dissolve

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## What was your research question?
What are the “snow” flakes that come from bronchoalveolar lavage (where fluid samples are taken from the lungs) in people with CF made of, and are they related to known aspects of CF lung disease?

## Why is this important?
Mucus is kind of like a spaghetti dish. There are long proteins in mucus called mucins that are like the spaghetti noodles, which you can stir and move around in a well-hydrated vessel like the normal lung. In dehydrated CF airways the noodles get stuck together (think a packet of instant ramen), and inflammation and infection can cause the release of other molecules, including proteins and DNA that act like a thick sauce that could further bind up the mucins,

preventing them from being stirred at all in some cases. This inflammation and infection could be a part of CF lung disease.

## What did you do?

We used several techniques to take pictures of and measure the least "stir-able" parts of airway mucus, which we call "flakes". While we can get most types of mucus to dissolve in a lot of water, these flakes need chemical treatments to dissolve them. Some of the techniques tell us what the flakes are made of, and some of them tell us how much of each component of mucus is in them. We also watched how microscopic beads bounced around inside the network of mucins, which told us how resilient these flakes were to breaking apart.

## What did you find?

The main mucin in healthy airway mucus is called MUC5B, but other studies have shown a similar mucin called MUC5AC is produced at nearly the same levels in inflammatory lung diseases like CF. We found that mucus flakes in CF have raised levels of MUC5AC, and over 50% of all mucins in CF are found in insoluble mucus flakes compared to less than 10% of mucins in normal lungs. In addition to mucins, DNA concentration was higher in CF mucus, and we also found DNA inside CF flakes. There were also more mucus flakes in people with CF who had an ongoing infection, and the flakes were thicker and stiffer.

## What does this mean and reasons for caution?

We also found a few mucus flakes in normal lungs, so they might have some role in maintaining airway health. However, the amount and make-up of flakes in CF are clearly different and point toward inflammation and infection having a role in making CF mucus more abundant and less soluble than normal. Even without the added effects of inflammation and infection, though, airway mucus is very complex. It is not yet even clear exactly how flakes form and clear from the lung, or what they are for in normal lungs. Flakes are likely to be a topic of increasing interest in lung diseases.

## What's next?

It remains to be seen what kind of effects modulator therapies like ivacaftor and/or elexacaftor/tezacaftor/ivacaftor will have on the production of mucus flakes and what they are made up of, but our results show that studying treatments that dissolve mucus may limit the possible burden that flakes could pose to airway health in CF.

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