



Cystic Fibrosis Mechanism and Treatment

[music plays]

[NARRATOR:] A patient with cystic fibrosis is susceptible to infections of the lungs.

This is due to a mutation that affects a protein on the surface of lung cells.

Many different mutations can cause cystic fibrosis, but all of them involve a transmembrane protein called CFTR that functions as a channel for chloride to move in and out of cells.

In this case, CFTR is less able to transfer chloride ions out of the cell, compared to the functioning protein in people without cystic fibrosis. The channel is, in effect, locked shut.

This inability to transfer chloride ions has an effect on the outside of the cell.

In people without cystic fibrosis, there is a balance of chloride ions inside and outside lung cells, which maintains the right amount of water and salt ions in the mucus lining the airways.

Cilia normally sweep the watery mucus from the lung lining, keeping the surface clean.

In patients with cystic fibrosis, chloride ions concentrate inside cells and draw in water by osmosis. With less water, the mucus becomes thicker and cilia can't move. Flow is reduced, providing an environment for bacterial infection.

But there are now drugs that can help patients.

To find a drug, researchers tested over 200,000 small molecules to see if any would bind to the CFTR protein. Then, for each small molecule that had some binding ability, researchers chemically synthesized different variations of that molecule and tested them for the ability to improve the function of some types of mutant CFTR channels.

They identified a drug that, when taken by patients with a certain type of CFTR mutation, binds to the CFTR protein, opening the channel and allowing improved ion transfer. This increases chloride ion flow and maintains a watery, clear mucus, which helps the cilia move more freely and reduces the risk of bacterial infection.