

Cystic Fibrosis Research News

Title:

A disruption of innervation around CF tissues results in low amount of VIP before CF disease has produced damage to the lungs and small intestine.

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What was your research question?

Why is the tiny, but important, protein named VIP, missing in several organs of people with CF ?

Why is this important?

The VIP peptide is a tiny protein secreted by nerve cells in the lungs, gut and sweat glands. It controls the proper function of these tissues by maintaining a good flow of fluids that help to clear infections and reduce inflammation. We already knew that VIP is missing or only low levels are present in people with CF, but we did not know why.

What did you do?

We studied the amount of VIP in the lung, small intestine and sweat glands of mice genetically modified to have CF at either a young age, with very minimal sign of disease, and at an old age, with severe CF symptoms. We measured the amount of VIP that we extracted from those tissues. We also examined VIP in the tissues using a microscope. As the VIP is released by specific nerve cells, we wanted to know if these nerve cells were different in young mice with minimal disease compared to old mice with severe disease and also how they compare with mice that do not have CF.

What did you find?

We found that low levels of VIP were present in all of the CF tissues we studied, even in young mice with almost no sign of disease.



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We also found that the network of nerves and nerve cells surrounding these tissues was severely disrupted and did not properly supply VIP and other important neurotransmitters. Importantly, that was true even in the young mice with no damage yet visible in the lungs and small intestine.

What does this mean and reasons for caution?

This is an important finding as it shows that nerve cells supplying tissues with VIP and other neurotransmitters are sparse before CF disease causes inflammation and damage. Because VIP is so important for the function of these tissues, we expect the lack of VIP to further worsen the progression of CF and reduce immune defences.

These results were obtained from mice with two copies of the F508del mutation that is found in most patients with CF. We still don't know how other CF-causing mutations impact nerve cells supplying VIP and other neurotransmitters.

What's next?

Our next steps are to: 1. study the pancreas and measure the impact of the reduction in VIP on CF-related diabetes; 2. study the variability in levels of VIP in samples from CF patients; 3. study the efficacy of a pharmaceutical formulation of VIP, which can be safely used in humans, to treat CF.

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