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# Cystic Fibrosis Research News

## Title:
VIP reduction in the pancreas of F508del homozygous CF mice and early signs of Cystic Fibrosis Related Diabetes (CFRD)

## Lay Title:
Early signs of Cystic Fibrosis Related Diabetes (CFRD) and low amount of the neuropeptide VIP in ΔF508-CF mice.

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## What was your research question?
How does the amount of VIP, a tiny but important protein, impact the release of insulin and glucagon from the pancreas of CF mice?

## Why is this important?
The VIP peptide is a tiny protein secreted by nerve cells in the lungs, gut, sweat glands and pancreas. VIP controls proper function of these tissues by maintaining a good flow of fluids that help to clear infections and reduce inflammation. In the pancreas, VIP enhances the release of insulin and glucagon to regulate blood glucose after a meal. It is already known that VIP is missing or only present in very low amount in some tissues in people with CF. But it was unknown if that is also the case for the pancreas and/or if it has any link with CF Related Diabetes.

## What did you do?
We wanted to know if we could detect early signs of diabetes in mice, genetically modified to have CF, at either a young age with minimal CF disease, and at an old age with severe CF symptoms. Therefore, we measured the amount of VIP, insulin and glucagon from their pancreas. We also wanted to know if the nerves producing VIP in the pancreas were different in young mice with minimal CF disease and in old mice with severe CF disease, compared to

mice that do not have CF. Therefore, we examined the mice nerves that produce VIP, using a microscope.

## What did you find?

We found low amounts of VIP even in the pancreas of young age CF mice that had minimal CF disease. We also found that the network of nerves surrounding the pancreas was severely disrupted and did not properly supply VIP and other important neuropeptides. Importantly, we found that the reduced amount of VIP in mice with CF, is causing reduced insulin secretion, increased glucagon production and high blood glucose levels, which are all associated with the onset of CF Related Diabetes.

## What does this mean and reasons for caution?

Because VIP is important for the control of insulin and glucagon secretion by the pancreas, its absence leads to a bad regulation of blood glucose. This is an important finding as lower amounts of VIP are seen before CF has caused any damage to the tissues, and before CF Related Diabetes starts. This provides a window of opportunity for treatment.

These results were obtained in male mice with two copies of the F508del mutation that is found in most people with CF. We still don't know how other CF-causing mutations impact nerve cells supplying VIP in the pancreas and if females are different. Our study was conducted in mice.

## What's next?

The next steps will be to: 1. Study the impact of low amounts of VIP on other hormones that regulate blood glucose; 2. Study the variation in VIP amounts between people with CF; 3. Use VIP in pre-clinical tests to treat CF disease.

## Original manuscript citation in PubMed

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