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Cystic Fibrosis Research News

Title:

Beyond insulin: Unraveling the complex interplay of ER stress, oxidative damage, and CFTR modulation in CFRD

Lay Title:

Beyond Insulin: Unraveling the Complex Interplay of Cell Stress and Cell Communication in CFRD

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What was your research question?

Despite much research, the exact process by which diabetes occurs in cystic fibrosis (CF) is still not fully understood, with conflicting scientific results published. Our paper aims to review these varied findings and introduces a new perspective for consideration.

Why is this important?

Insulin injections are currently the primary treatment for managing cystic fibrosis related diabetes (CFRD). The effectiveness can vary widely among individuals, suggesting that more

tailored approaches are needed. A greater understanding of the complex processes that underlie CFRD could lead to new forms of treatment, that aim to manage symptoms and target its causes, ultimately improving life for those with CF.

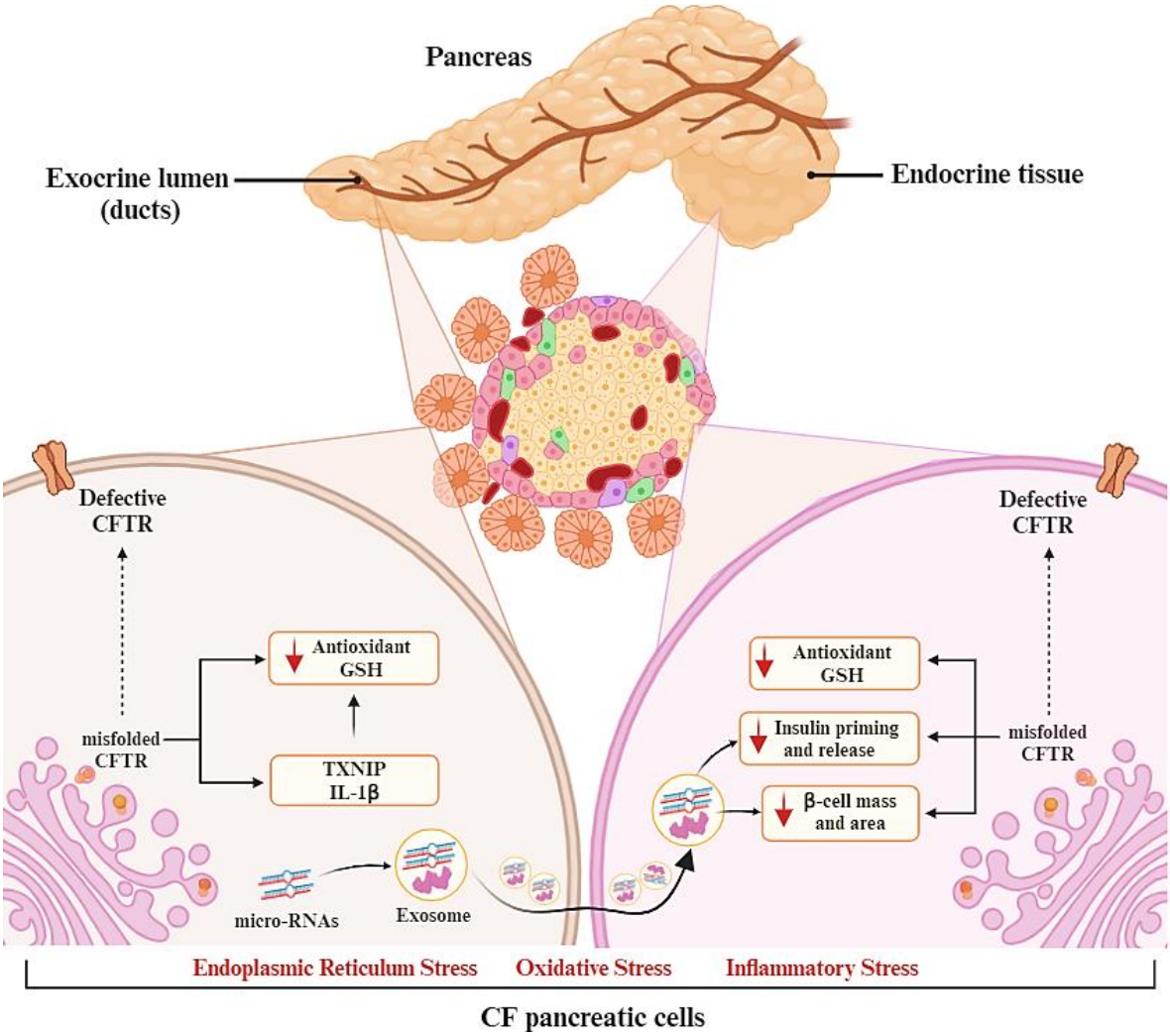
What did you do?

We conducted a review of the current literature that examined the mechanism of CFRD and identified the gaps in knowledge. CF harms organs that have lumens – tube-like structures essential for transporting and exchanging substances in the body, similar to water pipes. In CF organs, there is a gene which contains a spelling mistake (mutation) and codes (when spelt properly) for a protein called CFTR. This protein regulates the flow of salt and water across the surfaces of the tubes in the lungs, pancreas and intestines. This flow is vital to keep the surface of the tubes lubricated and free from blockages.

What did you find?

The pancreas has two main jobs: 1) producing digestive enzymes through its 'exocrine' system to break down food and 2) releasing hormones like insulin through its 'endocrine' system to regulate blood sugar levels. In people with CF, defective CFTR in the tubes of the exocrine pancreas leads to a dry and blocked lumen, causing a build-up of enzymes and damaging surrounding tissues. One common theory in CFRD is that the problems seen in the insulin

producing part of the pancreas are a direct result of damage in the enzyme-producing part due to their proximity (see Figure).



What does this mean and reasons for caution?

There is also evidence suggesting that the insulin-producing part can be disrupted without damage found in the enzyme-producing part of the pancreas. Therefore, we explored the potential impact of stress caused by the faulty CFTR protein on both the enzyme- and insulin-producing parts of the pancreas. Emerging research suggests that exosomes, tiny carriers that transport molecules between cells (see Figure), might have a role. These molecules are

important for cell communication and may influence gene activity. Exosomes are also known to play a part in type 1 and type 2 diabetes and might transmit stress signals within the pancreas in CF, exacerbating damage and contributing to CFRD.

What's next?

Future research should conduct studies to test the novel hypotheses presented in this manuscript.

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