**Title:**

Dysmotility in the ileum of CFTR null swine

**Lay Title:**

CF pigs have an intestinal motility deficiency

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**What was your research question?**

We investigated if cystic fibrosis (CF) pigs have impaired motility in their intestines (intestinal dysmotility).

**Why is this important?**

Gastrointestinal (GI) complications are common in people with CF (pwCF) and have a negative impact on quality of life. Among these, constipation and abdominal pain are prevalent, and in some cases, complications can become severe and even life-threatening. A potential underlying factor is intestinal dysmotility, a condition in which the movement of the intestines is slower than normal due to nerves or muscles not working as they should. This disrupts the normal movement of food and waste through the digestive tract. Despite the clinical importance of GI complications, CF-related intestinal dysmotility remains poorly understood.

**What did you do?**

We investigated intestinal motility in CF pigs. We focused on the small intestine (the ileum) of both wild-type (WT or non-CF) and CFTR-deficient (CF) pigs. We assessed the ability of the ileum to move its contents through the digestive tract using a measurement called the intestinal contractile force.

We assessed two responses:

* *Spontaneous responses:* How much (amplitude or strength) and how often (frequency or timing) the intestinal muscle spontaneously contracted and relaxed, generating a wave-like movement called *peristalsis*.
* *Induced responses*: The amplitude and frequency of intestinal muscle contractions after giving different doses of acetylcholine (ACh)- a signal naturally released to stimulate muscle contraction.

**What did you find?**

Our findings revealed that both WT and CF ileum had spontaneous responses (peristalsis); however, in the CF ileum, the amplitude of the movement was reduced compared to the WT ileum. Moreover, when stimulated with ACh, the WT ileum responded with stronger contractions as the dose of ACh increased, whereas the CF ileum had a blunted response. Interestingly, the frequency of the contractions was similar between the WT and CF ileum.

**What does this mean and reasons for caution?**

Overall, the results suggest an issue with the strength —not the timing— of intestinal contractions in CF pigs. Similar intestinal dysmotility may occur in pwCF, which could contribute to the GI complications commonly associated with CF. However, it is important to note that the CF pig used in this study was CFTR-null (meaning that it completely lacks the CFTR protein) rather than carrying the most prevalent CF-causing mutation, F508del. Therefore, further research is necessary to determine the relevance of these findings to pwCF.

**What’s next?**

We plan to extend this study by investigating whether intestinal dysmotility contributes to GI dysfunction in another animal model (humanized mice carrying the F508del mutation of the human CFTR gene). Additionally, we will assess the efficacy of CFTR-targeting drugs (modulators) in alleviating GI abnormalities in these mice.

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