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Cystic Fibrosis Research News

Title:
Investigating serum extracellular vesicles in Cystic Fibrosis

Lay Title:
Investigating the diagnostic potential of small cell particles in the blood of people with CF

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What was your research question?
In this small study, we researched different methods to isolate small particles (vesicles) in the blood of people with CF (PWCF) to determine if these vesicles have any diagnostic potential in CF as the disease progresses or with Trikafta (Kaftrio) treatment.

Why is this important?
Extracellular (outside the cell) vesicles are small particles released from every cell and they can communicate with other cells around them. In CF, this means they can be released into the lung or blood and communicate with nearby white blood cells. This potentially means an increase in the inflammatory response and compromised anti-bacterial response seen in PWCF. Additionally, a larger number of vesicles tend to be released in different disease states and we previously found this in the lung of PWCF indicating the diagnostic potential of these vesicles. In this study, we looked at vesicles in the blood as this is a better sample than from the lungs and a less invasive procedure than bronchoscopy.

What did you do?
We compared two different methods using small volumes of blood to see which method is better to find the most vesicles. This is particularly important for children with CF where we don't want to cause distress drawing large volumes of blood. These vesicles contain RNA, protein, and lipids. We have a lot of experience in protein analysis so we examined the protein content of the vesicles from PWCF at different ages and with Trikafta treatment.

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What did you find?

The vesicles were successfully isolated in greater numbers with a separation method called size exclusion chromatography compared to another method called ultracentrifugation from PWCF using low blood volumes (250 ul). We saw a twofold change in the number of vesicles with age. We identified different proteins to be present in the vesicles between CF and control persons and between children and adults with CF. Changes were also observed in proteins in blood vesicles in PWCF before and after Trikafta treatment.

What does this mean and reasons for caution?

This is the first study of the vesicles in serum from PWCF and without CF (> 30 donors) to our knowledge hopefully leading to future studies in the area. The study revealed differences in the levels of inflammatory/pathogen binding proteins in these vesicles during disease progression and Trikafta treatment. There is a clinical potential for PWCF to use vesicles as an additional diagnostic marker in CF with exacerbated disease and with drug treatment. Larger donor numbers and testing the same subjects over time would be needed to further establish the potential of vesicles in CF.

What's next?

We will continue to study vesicles in PWCF - both in the lung and serum - using larger donor numbers, with a focus on how Trikafta treatment influences their release and content. Another focus will be to investigate how the presence of bacteria such as *Pseudomonas aeruginosa* effects the release of these vesicles.

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