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Title:

UTILIZING CENTRALIZED BIOREPOSITORY SAMPLES FOR BIOMARKERS OF CYSTIC FIBROSIS LUNG DISEASE SEVERITY

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What was your research question?

To learn whether blood samples stored in a biobank can be used to reliably measure inflammation, which is a predictor of CF disease severity, as high levels are known to lead to structural damage of the CF airways and impaired lung function. And to find out whether

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proteins, lipids (fats), and metabolites (products of biological processes) in these blood samples vary between CF children with different lung function.

Why is this important?
Being able to measure substances in blood that indicate lung disease severity and routinely monitor their levels have the potential to improve patient care and support drug development in CF. That is because it is easier and more feasible to collect blood and do these measurements in blood samples than in sputum and in bronchoalveolar lavage (lung wash) samples.

What did you do?
We selected banked serum samples from children who were categorized into two groups: one with preserved or normal lung function ('mild' group) and one with lower lung function ('severe' group). The children in these two groups were similar in age, gender, *CFTR* genotype (CF mutation), and *P. aeruginosa* (bacterial) infection status. We measured inflammatory proteins, lipids, and metabolites in these serum samples and compared their levels between the two groups.

What did you find?
The group with lower lung function ('severe') had higher blood levels of four inflammatory proteins and lower levels of one lipid compared to the mild cohort. Only one metabolite differed between the two groups. Another statistical test that takes into account the bias in sample selection was used to confirm the differences in inflammatory protein findings between the two groups.

What does this mean and reasons for caution?
These findings demonstrate the value of storing high quality patient derived samples in a biobank and using these samples to identify and measure substances that indicate the presence or severity of a disease state (e.g. lung disease in persons with CF). We did not show that these substances reflect disease activity, only that they were different in CF children who were grouped by their lung function. Also, not knowing the timing of collection of the blood samples relative to meals may have influenced our results as blood levels of lipids and metabolites may vary depending on the timing of food intake.

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What's next?
Our data could serve as a point of reference comparing other substances that indicate CF lung disease. Also, the inflammatory proteins will have more value if they can be shown to vary among persons with the same lung function or predict who is at higher risk of facing lung function decline.

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