CYSTIC FIBROSIS AND VOLATILE BIOMARKERS FROM BREATH ANALYSIS

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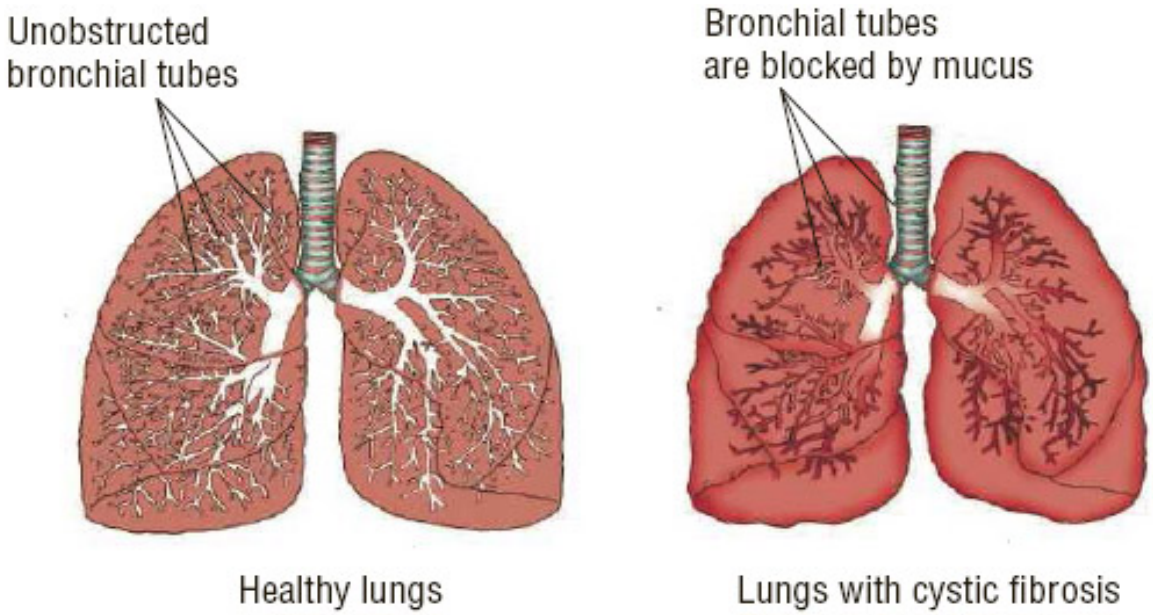
INTRODUCTION

Volatile biomarkers (VOC) are the fundamental component used for the non-invasive diagnosis of various diseases and many researchers are developing sensors that can detect volatiles from various human and animal excretions such as breath, sweat, urine, etc. Any biological activity causes volatile release from organisms. The volatile released may be a new volatile created by the biological activity or a change in the amount of the volatile produced that is already released by the organism. Therefore, the role of VOCs in clinical diagnosis and therapeutic monitoring is expected to become increasingly significant due to recent advances in the field of health and science. The evaluation of airway inflammation in lung diseases is typically carried out by employing bronchoscopy. Since it is an invasive technique, non-invasive volatile detection is considered for the diagnosis of that particular disease.

WHAT IS THE CYSTIC FIBROSIS DISEASE?

Cystic fibrosis (CF), an inherited life-threatening disease that damages the human body, especially the lungs. Cystic fibrosis restricts the airways of the lungs by producing thick mucus

inside the lungs and leads to difficulty in breathing. The lungs then become a rich nutrient medium for opportunistic pathogens that are normally harmless for healthy people but cannot be removed fast enough in CF thus encouraging chronic respiratory infections such as Pseudomonas aeruginosa (PA), Staphylococcus aureus and Burkholderia cepacia, and the fungus Aspergillus fumigatus (AF). Currently, these pathogens are identified by culturing sputum samples, but CF children have difficulty in expectorating sputum, hence volatile detection is an effective and less time-consuming method of detecting such pathogens.



BREATH ANALYSIS

Researchers are still looking for different biomarkers and their corresponding concentrations that have been released that are associated with CF in order to improve detection efficiency. Various technologies are employed to find these biomarkers in the smallest concentrations possible since only trace amounts of such VOCs are released through breath. Breath analysis is the most

prominent method employed for biomarker detection for most lung diseases. Technologies like gas chromatography-mass spectrometry (GC-MS), SPME, Selected ion flow tube mass spectrometry, (SIFT-MS), etc are employed for volatile biomarker detection. Using SIFT-MS, breath analysis has been accomplished of significantly large cohorts of healthy individuals and thus the establishment of common volatiles or metabolites that are released is achieved. From having a database of the common metabolites and their concentration ranges that are released by an organism, the change in the metabolites or metabolite concentrations released can be monitored effectively.

EXHALED BREATH AND VOLATILES

The collection of exhaled breath provides a noninvasive method to assess lower airway surface liquid biomarkers. Non-volatile compounds can be assessed through the collection and analysis of exhaled breath condensate while volatile compounds need to be assessed in real-time or immediately after the collection of exhaled breath. Numerous biomarkers have been shown to be elevated in exhaled breath condensate in patients with CF and current research significant volatiles are hydrogen cyanide (HCN) and acetic acid. HCN is a major biomarker that is detected in CF patients by SIFT-MS who have PA in their lungs. Children and adults with PA have a

significant concentration of HCN from the exhaled breaths compared to healthy controls and CF patients without PA. Thus HCN can be considered a potential biomarker for the detection of CF patients with PA. Since HCN only detects patients with PA, it is necessary to find CF patients without PA.

Acetic acid was detected in four groups of individuals (Individuals with CF with PA, without PA, patients with GERD(Gastroesophageal reflux disease), and healthy controls) and no significant difference was observed between PA-infected and PA-negative groups. Therefore, the conclusion states that the acid is not produced by the PA bacteria. So what is its origin?
This could be due to a decrease in the pH of the mucus lining the CF airways. As a result, scientists speculate that non-invasive measurement of breath acetic acid concentration could serve as an indicator of the acidity of the CF airway mucosa as well as a potential biomarker of Cystic fibrosis.

CONCLUSION AND FUTURE RESEARCH POTENTIAL

The paper focuses on the importance and presents research methods for non-invasive diagnosis of Cystic fibrosis and improving the efficacy of CF therapy. The results obtained from the literature clearly indicate the potential of volatile biomarkers and they can be used as a fingerprint for the detection of CF. Clearly, further work is needed to substantiate these findings using greater cohorts of healthy volunteers and CF patients and large databases of volatile releases. Sensitive biomarkers of early CF lung disease that are non-invasive and can provide clinicians with useful clinical information quickly are being developed, with exhaled breath analysis holding great promise.

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