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Asthma phenotyping using exhaled breath analysis and full-scan SIFT-MS data

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Background: The ballistic rise of analytical technologies has opened a large playground for all type of untargeted “omics” screening. In that trend, there is a rising interest for the characterization of the human volatilome. Indeed, the characterization and the understanding of the volatile organic compounds (VOCs) production in different ex vivo matrices could open the route for improved diagnosis approaches and more individualized treatments. For large-scale screening, direct introduction instruments, such as selected ion flow tube mass spectrometry (SIFT-MS) offer the capacity to perform both targeted and untargeted analyses within a few minutes. SIFT-MS can generate compositional patterns from direct sample introduction at the same time than other routine medical actions. However, the use of SIFT-MS for untargeted screening requires the acquisition of full-scan mass spectra for every precursor of interest. To investigate this type of data, multiple factors such as the different chemistries of each precursor and structure of the data set, have to be considered to extract useful information.

Objectives: We compared full scan SIFT-MS with another exhaled breath analysis method, namely comprehensive gas chromatography coupled to high resolution mass spectrometry (GC×GC-HRTOFMS) and fractional exhaled nitric oxide (FeNO), for asthma phenotyping using exhaled breath. The comparison was addressing the classification accuracy and the easiness of implementation into the clinic.

Methods: We analyzed the exhaled breath of 50 well characterized patients suffering from different type of asthma. Breath samples were collected in duplicate using 5 L Tedlar bags; one bag for the SIFT-MS and one for the GC×GC-HRTOFMS. For the GC×GC-HRTOFMS, a previously validated protocol was employed. For the SIFT-MS, the VOC profile was analyzed using three chemical precursors (i.e., H_3O^+, NO^+, and O_2^+), using the quadrupole analyzer in full scan mode. From there, different data processing approaches were compared to identify specific asthma inflammatory phenotypes in a mixed asthma population. Targeted and untargeted approaches have been applied and compared to evaluate their potential to translate into the clinic.

Results: We had to develop a dedicated data processing workflow for the full scan SIFT-MS data. We evaluate the impact of normalization and scaling for the pre-processing. Then, we used machine learning algorithms (e.g., random forest and PLS-DA) to build a classification model. A similar workflow was used for GC×GC-HRTOFMS data. SIFT-MS and GC×GC-HRTOFMS techniques provided good classification accuracy (around 75%), similar to the efficiency of other clinical tools routinely used for asthma phenotyping. Different data fusion methods were also applied to the full scan SIFT-MS data to combine the information from the different precursors. This approach allows identifying the most informative ion channels in the data matrix and improved the classification accuracy to 80%.

Conclusion: SIFT-MS used in targeted or untargeted mode clearly meet the criteria to make routine clinical breath analysis a reality.