DEVELOPMENT AND VALIDATION OF A NON-TARGETED SCREENING APPROACH FOR THE CHARACTERIZATION OF LUNG FLUIDS

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Abstract

The constant improvement of analytical instrumentation generates more and more insights for non-targeted metabolomics. In this context of untargeted screening of complex biological mixtures, comprehensive two-dimensional gas chromatography (GC×GC) coupled to time-of-flight mass spectrometry (TOFMS) offers a powerful solution to obtain a detailed overview of sample compositions. However, this increase of analytical resolution comes with an increase of system and data complexity [1,2]. This generated a critical need for clearly defined adequate method optimization and quality control (QC) protocols to insure the proper use of the analytical instrument, and robust data processing flow for interpretation. Unfortunately, few untargeted GC×GC studies display these important aspects and a general misuse of the terms validation and semi-quantification are flourishing in the related literature. These bias are contributing to the general problem of lack of study reproducibility in some aspects of scientific research, as pointed out in recent Nature publications [3,4]. To overcome this problem, several initiatives, like the metabolomics standard initiative (MSI), set up some general guidelines to reduce such lack of analytical robustness [5,6].

This study presents the application and adaptation of MSI guidelines for volatile mixture analysis using GC×GC-TOFMS. To illustrate this approach, bronchoalveolar lavage fluid (BALF) volatile profiles were analyzed. BALF is a widely performed medical procedure that provides important information about immunologic, inflammatory, and infectious processes in the airways. First, a QC solution was developed by pooling BALF samples from different patients. This solution was subsequently used for method development, i.e. sampling and chromatographic conditions. Based on these optimal conditions, a method validation was conducted. The QC solution was also used as a reference for the implementation of a QC protocol for non-targeted analysis of volatile mixtures on biological matrices. This study aims to provide guidance for the establishment of robust GC×GC-TOFMS strategies for non-targeted analysis.

References

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