In vitro characterization of lung inflammation mechanisms

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Abstract

Exhaled breath analysis has a high potential for early non-invasive diagnosis of lung conditions. Most of lung diseases involve a certain level of inflammation. The characterization of the ongoing inflammation processes is crucial to define proper medication. The inflammation processes are associated with oxidative stress, which yields to the conversion of chemical from the membranes (as polyunsaturated fatty acids) into volatile compounds secreted by the lungs¹. The understanding of the metabolic pathways involved in volatile markers production could open new therapeutic routes for inflammatory diseases.

In this study, the lung inflammation was simulated in vitro. A549 epithelial cells, originally isolated from human alveoli, were cultured with and without oxidative agents (from chemical or biological origins) as part of a discovery study for lung inflammation mechanisms characterization. The cell culture volatile organic compounds (VOCs) were extracted by solid phase micro-extraction (SPME) and analyzed by comprehensive two-dimensional gas chromatography hyphenated to time-of-flight mass spectrometers (GC×GC-TOFMS). The complete analytical workflow was optimized using central composite design model. Univariate and multivariate feature selection approaches, i.e. Fisher Ratio and Random Forest, were then used to compare the volatile profile of the epithelial cells in different inflammatory conditions and to identify specific inflammatory markers.

According to the type of inflammation induced, significantly different VOCs were produced by the epithelial cells. For both chemical and biological stresses, an increased production of hydrocarbons, aromatics and alcohols was observed. However, more than 50 % of the specific VOCs were produced only after a biological stress. Based on this output, cross-comparison with metabolic pathways databases (e.g. KEGG) was performed. This work is setting up the basis of a multimodal and biomedical project on lung inflammation characterization. The future implementation of multi-omics screening could reveal new information on the complete molecular mechanisms involved in lung inflammation episodes.

References