Metabolomics Research

Curated Compilation of Articles

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The Pegasus® series of mass spectrometers is doing real work to make real differences in laboratories around the world. This is a curated compilation of articles and papers illustrating how Time-of-Flight Mass Spectrometry is advancing metabolomics research. With the Pegasus supporting them, these labs are doing so much more than running with their samples—*They can fly.*

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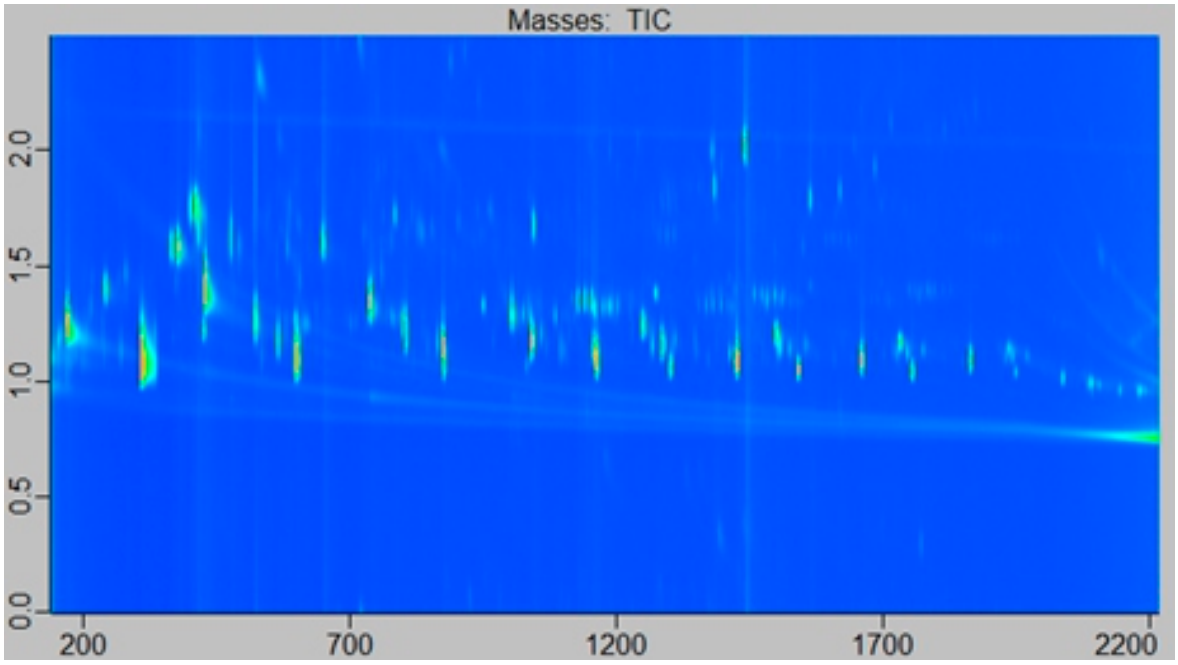


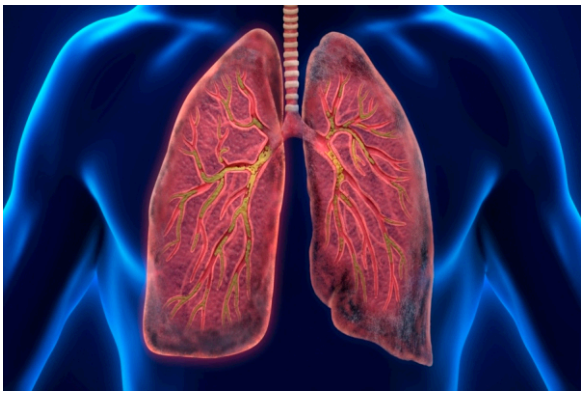
Summary: *Multimodal Combination of GCxGC-HRTOFMS and SIFT-MS for Asthma Phenotyping Using Exhaled Breath*

Source: https://www.nature.com/articles/s41598-020-73408-2
Nature, Published September 2020

Researchers at the University of Liege used LECO's GCxGC-High Resolution TOFMS system and SIFT-MS with the goal to improve success in phenotyping asthma and chronic obstructive pulmonary diseases (COPD) by analyzing volatiles in human breath. Chronic inflammatory lung diseases affect over 300 million people worldwide and the effectiveness of treatment strategies for these diseases rely heavily on proper inflammation phenotyping. Researchers have stated that due to the wide variety of phenotypes, nearly one third of patients receive ineffective treatment. The authors explain that "better phenotyping is therefore needed to improve the efficacy of prescribed treatments and to preserve patients from suffering unnecessary side effects."

According to the researchers, "current phenotyping of asthma and COPD relies on invasive sputum analysis," but due to its associated difficulties, "this method is not suitable for frequent longitudinal monitoring of disease evolution."

The important research detailed in this article focuses on the use of LECO's GCxGC-High Resolution TOFMS as well as SIFT-MS to validate a set of volatile markers present in the breath of 50 asthmatic patients allowing differentiation of inflammatory phenotypes. The researchers conclude the techniques are complementary: both provided the ability to classify asthma phenotypes while each had their own advantages. "The main advantages of GCxGC-HRTOFMS is its capacity for compound identification." "It can separate and identify hundreds of compounds in a single run." "On the other side, SIFT-MS is a rapid, pattern-based screening technique, which has the potential to fulfill the role of clinical tool for breath-based diagnostics." The authors note that this research "represents an important step forward in the quest for a non-invasive rapid diagnostic method."



Access the Article

Summary: Comparison of the Effect of Chemically and Biologically Induced Inflammation on the Volatile Metabolite Production of Lung Epithelial Cells by GCxGC-TOFMS

Source: https://pubs.rsc.org/en/content/articlelanding/2020/AN/D0AN00720J
Analyst, Issue 15, 2020

Enhancing Insights into Inflammatory Lung Disease

The understanding of the causes of inflammatory lung diseases such as asthma is a challenging yet vital field of research in order to improve diagnostics, and treatment capabilities and their effectiveness. Asthma is a serious public health condition, affecting 235 million people globally. It has a huge impact on quality of life and is a significant contributor to healthcare costs and resources.

In this field, the analysis of exhaled breath is appealing as it is a non-invasive but insightful approach, due to the complexity and variances of VOC production linked to inflammatory metabolomic pathways. However, the origin of VOC biomarkers and correct understanding of metabolomic processes can be influenced by various environmental, dietary, and other factors. Therefore, modelled, in-vitro investigations are vital.

In this literature review, we focus on a study by Delphine Zanella et al. (Analyst, 2020, 145, 5148), where GCxGC-TOFMS was used to characterize and compare VOCs produced in vitro, via biologically and chemically induced stress treatment of sputum obtained from patients with and without asthma.

The study compared VOC production from A549 epithelial cells following both chemically induced oxidative stress in vitro by exposing the cells to H2O2, and biological stress by exposing the cells to an inflammatory pool of sputum supernatants. Special attention was devoted to define proper negative and positive controls (8 different types) for the in-vitro models, including healthy sputum co-culture. Sputum from 25 asthmatic and 8 healthy patients were collected to create each pool of supernatants. Each sample type was analyzed in 4 replicates using solid-phase microextraction (SPME) comprehensive two-dimensional gas chromatography hyphenated to time-of-flight mass spectrometry (GCxGC-TOFMS). This approach offers high resolving power for complex VOC mixtures.

According to the type of inflammation induced, significantly different VOCs were produced by the epithelial cells compared to all controls. For both chemical and biological challenges, an increase of carbonyl compounds (54%) and hydrocarbons (31%) was observed. Interestingly, only the biological inflammation model showed a significant cell proliferation together with an increased VOC production linked to asthma airway inflammation.

This study presents a complete GCxGC-TOFMS workflow for in-vitro VOC analysis, and its potential to characterize complex lung inflammatory mechanisms.

Access the Article

Summary: *Breathomics to Diagnose Systemic Sclerosis Using Thermal Desorption and Comprehensive Two-Dimensional Gas Chromatography High-Resolution Time-of-Flight Mass Spectrometry*

Source: https://link.springer.com/article/10.1007/s00216-021-03333-4
Analytical and Bioanalytical Chemistry 413, 3813-3822 (2021)

LECO's GCxGC-TOFMS HRT 4D played an important role in recent research aimed at determining biomarkers for systematic sclerosis, an autoimmune disease that causes degeneration and scarring throughout the body, including in internal organs like the lungs. Determining routine biomarkers for systematic sclerosis could help with early diagnoses and prognoses, for the prediction of disease progression, and with determining targeted therapies. A biomarker's utility would be even greater if it could be routinely screened with fast and minimally invasive sampling procedures: for example, from exhaled breath.

Zanella et al. describe their recent work towards this goal in *Analytical and Bioanalytical Chemistry*. In their work, exhaled breath from 62 subjects (32 patients with systematic sclerosis and 30 healthy controls) was analyzed with GCxGC-HR-TOFMS. Exhaled breath is a fairly complex sample that has analytes from the breath itself as well as various sampling artifacts (from the system, Tedlar bag, etc.). GCxGC is well-suited for separating the individual analytes in these complex samples, though, and the authors note that "the separation power of GCxGC enabled the separation of on average 500 peaks, which would possibly co-elute in the first dimension using classical GC." The separation helped uncover more individual analytes in these complex samples, and thorough statistical work helped focus in on which of these were best able to distinguish the patients with systematic sclerosis from the healthy controls. Sixteen candidate biomarkers were determined that successfully discriminated the samples. (Receiver operator curves provided 90% accuracy, 92% sensitivity, and 89% specificity.) Analyte identifications were supported with mass spectral matching and accurate mass information, with the authors noting that "HRTOF MS was particularly valuable to further increase the confidence in the identification of these compounds." While research is ongoing, these results demonstrate the potential of using the *Pegasus* HRT 4D and data analysis techniques to uncover differentiating biomarkers in exhaled breath.

Access the Article

Summary: *The Ultimate Untargeted Technique*

Source: https://theanalyticalscientist.com/techniques-tools/the-ultimate-untargeted-technique
The Analytical Scientist, 2020

Pierre-Hugues Stefanuto, Delphine Zanella, and Jean-François Focant are researchers at the University of Liège in Belgium trying to find a solution to best enhancing metabolomics analysis. With such high sample complexity, there is no one-size-fits-all approach. Multimodality is the only way to make sense of the sheer volume of information in a metabolomics sample.

The authors find comprehensive two-dimensional GC (GCxGC) combined with high-resolution MS (HRMS) as a compelling option, as this approach combines multiple techniques with several levels of orthogonality to improve the versatility and robustness of untargeted identification.

A large part of the problem with –omics such as volatilomics is the difficulty performing interlaboratory testing. This team of researchers has been focusing on developing a complete analytical workflow for exhaled breath characterization. In order to make a process replicable, especially with such volatile samples, all steps must be carefully controlled. At the same time, the strategies must be adaptable to various contextual needs. GCxGC-HRTOFMS has proved to be the most reliable instrumentation for this type of research as the authors continue to improve on quality control procedures and help develop software solutions to minimize the variance introduced by humans in every step from injection to processing output. Despite all the challenges, the authors are excited about the future of untargeted metabolomics research.

Access the Article

To learn more about LECO's Metabolomics Research, visit our metabolomics page

Featured Collaborator: OBiAChem Lab

The OBiAChem team's main objective is to remain at the forefront of analytical technology. This is why they dedicate many of their resources to the most promising areas of their field: the "data" aspects. The next analytical revolutions will be built on the use of artificial intelligence and big data to optimize methods and exploit analytical results. The OBiAChem team is ready for these new challenges!

OBIACHEM
Organic and Biological Analytical Chemistry Group

The Organic and Biological Analytical Chemistry Laboratory of the University of Liege, the OBiAChem Lab, was created in 2005 by Prof. JF Focant. During the last 15 years, the lab has become a world leader in the development of multidimensional methods, combining multidimensional gas chromatography and mass spectrometry.

Prof. Focant started his scientific career with a PhD thesis in the field of persistent organic pollutants in the early 2000s. This work was part of the Belgian government's efforts to combat the dioxin crisis. Following his thesis work, he worked at the prestigious CDC (Centers for Disease Control and Prevention, USA). It was during these post-doctoral years that Prof. Focant developed his expertise in multidimensional gas chromatography and mass spectrometry. Upon his return to Belgium, he obtained a professorship position at the University of Liege to develop a research group in this field.

For the last three years, Dr. PH Stefanuto has joined permanently the team to lead the scientific development. Dr. Stefanuto was the first PhD student of the OBiAChem laboratory. After graduating, he moved to the Dartmouth College to develop his expertise in Omics research.

Currently, the OBiAChem research team groups 10-15 international researchers with diverse expertise. The majority of these researchers are analytical chemists; however the team regularly welcomes researchers from Life Sciences who need analytical support to characterize their complex samples.

The development of analytical methods for research in metabolomics and volatilomics.

This research axis represents one of the main pillars of OBiAChem's research themes. As a technology platform, they have specialized over the years in the development of non-targeted analyses of small molecules, in various volatile biological matrices, such as breath, in vitro cultures (cells, bacteria...), and ex vivo samples (plasma, sputum, blood...). For the last 6 years, they have been working with the clinical community who, after having spent years working on large molecules to understand the genome and the proteome, are now interested in the metabolome.

The understanding of the metabolome composition requires a paradigm shift on the analytical side. Indeed, metabolites are usually small molecules which are GC-compatible. This represents a unique opportunity to take advantage of the added value of GC(×GC)-MS for compounds identification in untargeted research.

The OBiAChem team works on different projects as an analytical technology support, in particular breath analysis. On the same principle of the alcohol control with a small device on the side of the road with a green lamp (good) and a red lamp (bad), they want to create the same thing for some diseases such as asthma, COPD, and some cancers.

They are trying to find molecules, markers of these diseases, that could be used with small portable detectors to screen the population.

Let's take the case of lung cancer. In normal circumstances, the patient has to undergo several costly and invasive imaging tests. Ideally instead, there would first be a much cheaper screening with a small device in the clinic before turning to heavier methods in a hospital. For asthma and chronic diseases, these are diseases that are incurable for the moment. Asthma can be treated and the symptoms can be reduced. Adjusting the treatment is difficult, especially if it concerns a child. The idea is to measure pulmonary inflammation with a small device in order to determine the dose of anti-inflammatory drugs to be given to children and adults alike.

Chemistry to serve personalized medicine!

Together with the University Hospital of Liège and the University of Maastricht, OBiAChem has taken part in an international consortium to differentiate inflammatory phenotypes related to asthma. This study, conducted in 2019, is based on breath analysis of more than 500 people. This is the largest published study in the field of non-targeted breath analysis in the American journal of respiratory and critical care medicine (IF 21.4), a leading journal in the field of respiratory medicine.

From this study, sister projects are currently running to extend our understanding of the lung inflammation by including other chronic inflammatory diseases, such as chronic obstructive pulmonary disease (COPD) or fibrosis.

The OBiAChem laboratory is also working on other ex vivo and in vitro matrices to establish a flexible analytical workflow, compatible with any metabolomics matrices.

https://www.obiachem.uliege.be/cms/c_5722253/en/obiachem-obiachem

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