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EXPERT INSIGHTS FOR ANALYTICAL SCIENTISTS

SMARTER SCIENCE

Aligning Data, Devices, and Decisions

FIELD INNOVATION

Portable LC Transforms Jet Fuel Testing

On-site MDA detection accelerates analysis and supports new standards.

VACCINE QUALITY

Ensuring Confidence in QC

New analytical methods and technologies address vaccine validation challenges.

FUTURE OUTLOOK

Data, AI, and the Changing Lab

Automation and mindset shifts reshape analytical science for the next decade.

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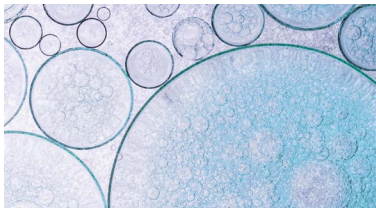



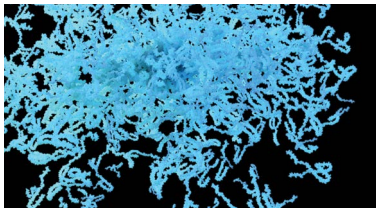

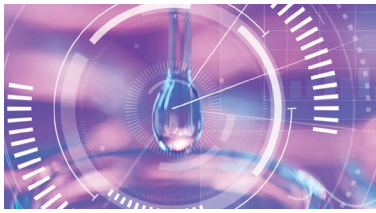

Expert Q&A: Biomarker Analysis in the Modern Lab

Discover how Dr. Jean-François Focant's lab is advancing biomarker analysis through rigorous validation protocols and innovative identification strategies.

by Shiama Thiageswaran and Jean-François Focant

Dr. Jean-François Focant, head of the Organic and Biological Analytical Chemistry (OBiAChem) Laboratory at the University of Liège, leads biomarker discovery research focused on volatile and semi-volatile compounds. His team uses comprehensive two-dimensional gas chromatography coupled with mass spectrometry (GC×GC–MS) to explore biomarker identification and validation. In this expert Q&A, he shares insights on how these efforts are evolving in the modern lab and what's on the horizon for point-of-care diagnostics and forensic science.

How does your current work in biomarker analysis support your broader research objectives?

A significant part of our lab's approach is focused on identifying disease biomarkers, in collaboration with our clinical colleagues at the University Hospital. Around a decade ago, we learned that they had biobanked a variety of biological samples. We proposed investigating the volatile components of those samples—something that could complement the genomics and proteomics work already underway—with a metabolomics-style approach.

The samples included exhaled breath condensate, blood, feces, urine, serum, and plasma. Initial trials confirmed that the volatile fraction was both informative and promising. From there, we began dedicated studies using samples collected specifically for us, under rigorously controlled conditions. That's when our biomarker analysis efforts truly began, with a longer-term goal of integrating these approaches more broadly in hospital workflows.

What are some of the main analytical and sampling challenges when validating biomarkers in complex biological matrices?

Sampling is arguably the most critical step in the biomarker workflow. If the protocol isn't strictly followed, even the best analytical chemistry won't rescue compromised data. For instance, when asthmatic patients visit the hospital, they may be asked to give blood as part of routine testing. We would then also request a breath sample, where the patient exhales into a specialized bag. This procedure must be performed in the same room each time and under tightly controlled conditions. Patients can't smoke, drink alcohol, or engage in activities that might introduce variability.

In our early studies, we found that sample variability was more affected by the day the sample was taken than by whether it came from a patient or a control. That revealed the importance of standardized conditions and timing in achieving meaningful biomarker validation.

This led us to develop detailed QA/QC sampling protocols specifically designed for clinical settings, helping ensure that collected data is reproducible and meaningful. Among the various matrices we work with, blood remains the most accepted and practical, as patients are generally accustomed to blood draws as part of routine care. In contrast, compliance tends to be lower for other non-invasive matrices, such as feces, largely due to discomfort or hesitancy surrounding the collection process.

What makes GC×GC–MS particularly effective for biomarker identification?

GC×GC–MS is a powerful tool for biomarker identification. Compared to standard GC–MS, having two dimensions

of chromatographic separation significantly improves resolution. It's much easier to identify compounds when they are separated up front, even though mass spectrometry can sometimes handle overlapping peaks through deconvolution.

This becomes particularly useful in lipidomics. Most lipids are not naturally GC-amenable—they're often too polar or heavy. We have to derivatize them to make them suitable for GC. While we can't generate a fully comprehensive lipid profile, GC×GC works well for targeted analysis of small lipids and is generally more cost-effective than liquid chromatography (LC).

Once potential biomarkers are identified in low-resolution mode, we transition to high-resolution mass spectrometry to determine exact masses and molecular formulas. When possible, we confirm compound identities by injecting commercial standards. In some cases, absolute identification isn't necessary. What matters is that the same compound consistently appears in relevant sample groups.

When working with trace-level analytes, how do you approach the quantification of biomarkers?

Right now, we don't typically quantify biomarkers in absolute terms. Our focus is on qualification, determining whether a compound is present and whether it appears in statistically higher or lower amounts between sample groups. We use statistical tools to validate these patterns, but we do not express concentrations in parts per billion (ppb) or similar units.

To pursue full quantification, we would need to introduce internal standards, including isotopically labeled compounds. At present, our research objectives haven't required that level of precision.

What emerging technologies or analytical trends are you most excited about in biomarker analysis?

Our current GC×GC–MS systems are large and require significant lab space and infrastructure, making them impractical for routine clinical use. That is why we are excited about miniaturization. New generations of compact detectors and micro-GC systems are emerging, offering promising solutions for smaller laboratory or point-of-care setups.

Once biomarkers are identified and validated, we can envision translating these analytical workflows to more direct-introduction mass spectrometry platforms, such as proton transfer reaction mass spectrometry (PTR-MS) or selected ion flow tube mass spectrometry (SIFT-MS). These technologies are particularly well-suited to real-time, non-invasive applications, such as breath analysis.

We are closely following developments in this space. Imagine a future where patients can blow into a handheld device or even their phone, not to receive a diagnosis, but to trigger a recommendation for further clinical evaluation. That is the direction we are moving toward. Our lab is also contributing to external medicine initiatives that support this transition. Miniaturization and portability will be central to the next generation of biomarker tools.

Are there any broader applications for these analytical technologies outside of medicine?

Although around 80% of our current work focuses on medical applications, we also support industrial partners in the energy transition. One area of focus is characterizing alternative feedstocks, including recycled plastics and biomass waste. For example, converting plastic through pyrolysis produces a dark oil; however, this oil contains oxygenated compounds that are not well understood and may not be compatible with process catalysts or engine operation. We spend considerable time profiling these substances.

In addition, we recently submitted an EU project in forensic science. Our lab is exploring how VOC analysis could help locate mass graves via cadaveric decomposition signatures. We're also looking into chemical fingerprinting that could support legal evidence in cases involving toxic substances. The aim is to develop scientifically sound and court-admissible analytical tools.

Conclusion: The Road Ahead for Biomarker Analysis

As biomarker analysis evolves toward more accessible, real-time diagnostics, Dr. Focant's work illustrates the critical role of rigorous validation, smart identification strategies, and emerging tools for characterization. His lab's focus on translational utility points to a future where precision diagnostics could be just a breath away.

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