TARGETED ANALYSIS OF VOLATILE METABOLITES FROM THE GUT MICROBIOME IN EXHALED BREATH

Martina Iacubino[1], Lorenzo Rocco[2], Marco Vicenzi[2], Chiara Bellocchi[2], Marta Mozzo[3], Adriana Severino[3], Monica Caronni[3], Alessandro Santaniello[3], Gaia Montanelli[3], Barbara Vigone[3], Liam Grimmett[4], Matt Kerr[4], Ben Constant[4], Huw Davies[4], Lorenzo Beretta[5]

[1]UNIMI, Milan, Italy, [2]University of Milan, Milan, Italy, [3]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico di Milano, Milan, Italy, [4]Owlstone Medical, Cambridge, United Kingdom, [5]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico di MIlano, Milan, Italy

At a Glance

- Breathomics provides a non-invasive, real-time window into microbial metabolism, capturing gut-derived metabolites that interact directly with the host.
- Case study in SLE: Breath VOCs revealed microbial signatures consistent with dysbiosis and potential markers of gut barrier function.
- The Breath Biopsy® Microbiome Panel offers a curated set of 36 biologically relevant microbial metabolites, enabling systematic and standardised investigation across health and disease.
- Integrated with the Breath Biopsy VOC Atlas®, the panel provides chemical, biological, and clinical context to accelerate discovery and translation.

1. Introduction

Exhaled breath contains a wide range of volatile organic compounds (VOCs) that reflect fundamental metabolic processes[1]. Many VOCs found in breath, including short-chain fatty acids, indoles, sulphur compounds, and alcohols, are microbial in origin[2]. Breath offers a number of advantages over more traditional methods, such as metabolomic analysis of stool. These include avoiding the collection and handling of faecal material, the ability to assess real-time dynamics, rather than needing to wait for metabolites to pass the gastrointestinal transit window, and the ability to assess gut microbiome derived metabolites which have passed through the GI barrier, and so are interacting with the host, rather than those which are excreted[3]. The bioactive metabolites reported on by breath can modulate immunity, influence gut barrier function, and contribute to systemic inflammation. Breathomics therefore provides a unique opportunity to assess microbial activity dynamically, with strong potential for clinical translation.

Systemic lupus erythematosus (SLE) provides a clear example of the importance of microbiome activity in disease[4]. Germ-free murine studies show that specific microbial communities can induce or worsen SLE-like symptoms, while patient studies consistently demonstrate gut dysbiosis, including changes in both microbial diversity and composition[5,6]. Together, these findings highlight the need for non-invasive tools to study host–microbiome interactions.

To support this, we have developed the Breath Biopsy Microbiome Panel, a targeted solution for quantifying microbiome-derived metabolites previously reported in the literature. This panel can be used alongside the Breath Biopsy VOC Atlas, which provides clinical, chemical, and biological context for VOCs across populations and disease states.

2. Methods

SLE Study

Cohort: 30 patients with well-controlled systemic lupus erythematosus (SLE) and 30 age- and sex-matched healthy controls.

Breath collection: Samples collected using the ReCIVA® Breath Sampler with CASPER™ Portable Air Supply. End-tidal exhaled breath was adsorbed on Breath Biopsy® Cartridges containing Tenax TA/Carbograph 5TD sorbent tubes, excluding dead space.

Analysis: Two tubes per sample analysed on the Breath Biopsy OMNI® v1 Platform (TD-GC-MS/Orbitrap HRAM). Quality control included blanks, spiked QC tubes (every six samples), and column resolution checks.

Statistical analyses:
Linear regression was used to test the effect of disease status on VOC concentrations, adjusting for demographic covariates. T-tests were applied for group comparisons of individual VOCs.

Breath Biopsy® Microbiome Panel

Panel design: 36 microbiome-derived VOCs curated from published literature, prioritised for biological relevance and translational potential.

Technology: Use of the Breath Biopsy® Collection Station followed by TD-GC-MS analysis using high-resolution accurate mass (HRAM) Q Extractive Orbitrap systems.

Supporting resources: Compounds mapped to the Breath Biopsy VOC Atlas, allowing comparison across healthy populations and disease states.

For more information about the Microbiome Panel, head over to our dedicated page via the QR code, or email us for more information:

breathbiopsy@owlstone.co.uk

Conflict of Interest: Authors are affiliated with Owlstone Medical.

3. Results

Case Study: Systemic Lupus Erythematosus (SLE)

1-Propanol and 2-butanol were significantly reduced in SLE patients compared to controls (Figure 1). These alcohols lack known mammalian production pathways but can be generated via microbial pyruvate fermentation, predominantly by Firmicutes rather than Bacteroidetes[7]. Their reduction is therefore consistent with a lower Firmicutes/Bacteroidetes ratio, a hallmark of SLE gut dysbiosis reported across multiple studies and observed irrespective of disease activity[8,9].

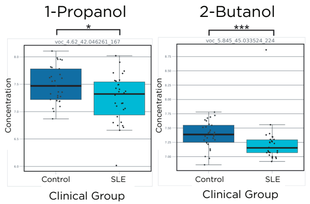

Figure 1. Concentrations of 1-propanol (left) and 2-butanol (right) in healthy controls versus SLE patients. Both were significantly reduced in SLE, consistent with impaired microbial alcohol production and a decreased Firmicutes/ Bacteroidetes ratio. *p < 0.05; ***p < 0.001.

The complement system plays a central role in SLE, both as a biomarker of disease activity and as a driver of tissue injury[10]. Emerging evidence also highlights bidirectional links between the complement system and the gut microbiome[11]. Given the evidence for microbiome perturbation in SLE, we next examined VOC differences between patients with low vs. normal complement. Of 21 VOCs associated with complement status, 13 mapped to the gut microbiome (Figure 2). Most were increased (e.g. dimethyl sulfide, p-cresol, 3-pentanol), while some decreased (2,3-butanedione, 2-butanol). These associations may reflect microbiome alterations driving complement activation (reported in murine depression models[12]) or complement defects promoting dysbiosis (seen in C3-knockout mice[13]).

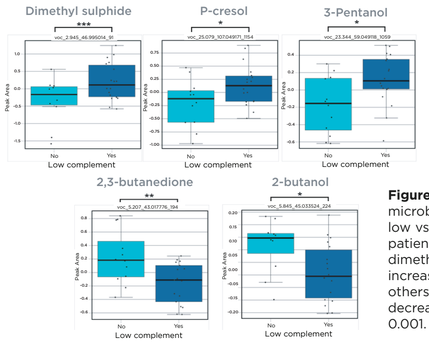

Figure 2. Boxplots of representative microbiome-linked VOCs associated with low vs. normal complement levels in SLE patients. Several compounds (e.g. dimethyl sulphide, p-cresol, 3-pentanol) increased with low complement, while others (2,3-butanedione, 2-butanol) decreased. *p < 0.05; **p < 0.01; ***p < 0.001.

4. Conclusions

Breath VOC analysis in SLE revealed clear microbiome-linked alterations, including reduced fermentation products (suggesting Firmicutes/Bacteroidetes imbalance) and complement-associated differences. These findings demonstrate the value of breathomics as a non-invasive, dynamic readout of microbial metabolism and its interaction with the host. The Breath Biopsy Microbiome Panel provides a targeted, standardised framework for quantifying microbiome-derived metabolites, supporting translational research across autoimmune, metabolic, and gastrointestinal disease.

Together, these results highlight the potential of breath to uncover microbiome signatures of disease and accelerate the development of non-invasive biomarkers.

Using the VOC Atlas Alongside the Breath Biopsy Microbiome Panel

The Breath Biopsy Microbiome Panel is a precise quantification of 36 microbiome-related volatile metabolites, previously reported in the literature to have a range of associations with health and disease. A subset of these is illustrated in figure 3. It enables real-time, longitudinal insights into microbial activity and host interaction, independent of gut transit time.

Due to the quantitative and reproducible methods of Breath Biopsy VOC collection and analysis, panel compounds can be compared to reference levels found in both healthy and diseased populations. This is facilitated by using the Breath Biopsy VOC Atlas, a catalog of breath VOCs that have been distinguished from background contaminants, and includes the chemical, clinical, and biological context of each compound.

Together, the Microbiome Panel and VOC Atlas support the systematic study of microbiome-derived metabolites in breath and their role in health and disease including GI disease, cardiometabolic health, immune modulation and cancer.

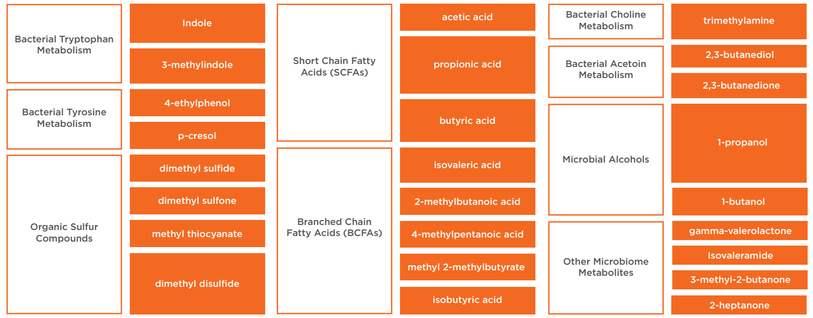

Figure 3. A subset of the Breath Biopsy Microbiome Panel. The panel comprises 36 microbiome-related volatile metabolites grouped here by metabolic class and pathway, including indoles, phenols, short- and branched-chain fatty acids (SCFAs/BCFAs), sulphur compounds, microbial alcohols, and amines. These metabolites represent diverse microbial processes such as tryptophan, tyrosine, choline, and acetoin metabolism, and have been linked to gut barrier integrity, immune modulation, and systemic disease.

5. References

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