BREATH® BIOPSY

BREATH-BASED MONITORING OF MICROBIOME METABOLIC RESPONSES BEFORE AND AFTER INGESTION OF NUTRIENTS

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Key Findings

- Several metabolites released by the gut microbiome have been associated with disease, and can be measured in the breath after administration of food substrates.
- Breath collection is easy and convenient, and so can be applied on large cohorts to better establish the effect of these metabolites on diseases.

1. Background and Objectives

- Excessive production of metabolites produced by the microbiome of the digestive system may exacerbate certain diseases, for example gut ethanol production has been associated with metabolic dysfunction associated steatohepatitis (MASH).
- Many of these metabolites can be measured non-invasively on breath.
- We investigated the feasibility of quantifiying these metabolites in breath with and without substrate intervention.

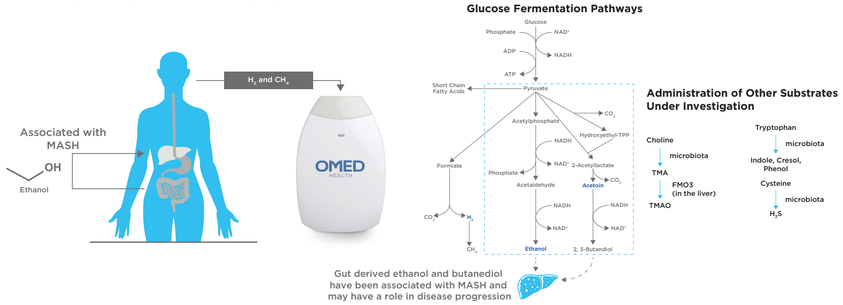

Fig 1. Disease-associated metabolites generated by the microbiome in the digestive system are detectable in breath allowing non-invasive at-home self testing. For example, the OMED Health Breath Analyzer is under development for at-home testing of hydrogen and methane to measure these clinically-validated biomarkers of gut microbiome activity longitudinally, anytime, anywhere.

2. Methods

- For each intervention healthy subjects were enrolled after overnight fasting. Breath was analyzed before and after substrate administration.
- Breath analysis was performed using selected ion flow tube mass spectrometry (SIFT-MS) with direct sampling.

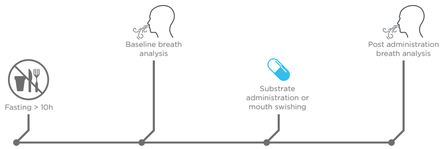

Figure 2. Substrate intervention process.

Table 1. Subject characteristics for glucose (75g) intervention.

Total Number	10
Sex (female/male) n	7/3
Age, median [IQR] (years)	29[28-37]
Weight, median [IQR] (Kg)	62[54-70]
BMI, median [IQR] (Kg/m²)	23[22-25]

3. Results

- Fermentation products associated with metabolic dysfunction-associated fatty liver disease (MAFLD) and gut discomfort showed a spike on breath after substrate administration.
- Some subjects had a different profile when the substrate was ingested, compared to when the substrate was swished around the mouth without ingestion.
- Additonal metabolites associated with neurodegenerative diseases were detected.

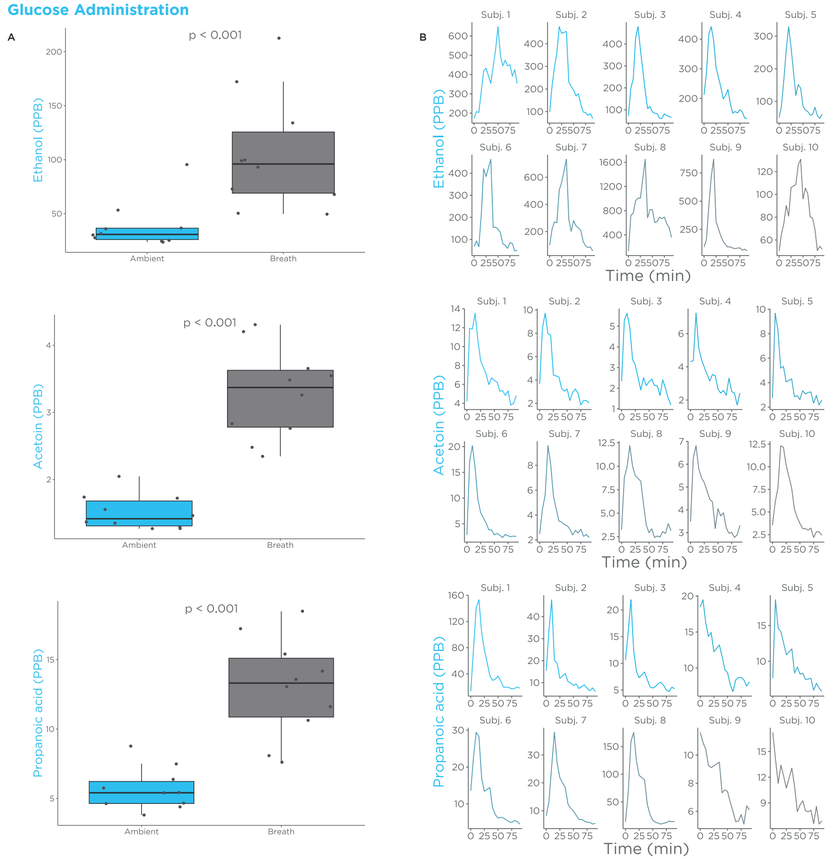

Fig 3. Breath measurments before (A) and after glucose administration (B) for ethanol, acetoin, an intermediate of the 2,3-butanediol fermentation, and propanoic acid. Note that a Tmax at 5-10 minutes may represent an oral signal.

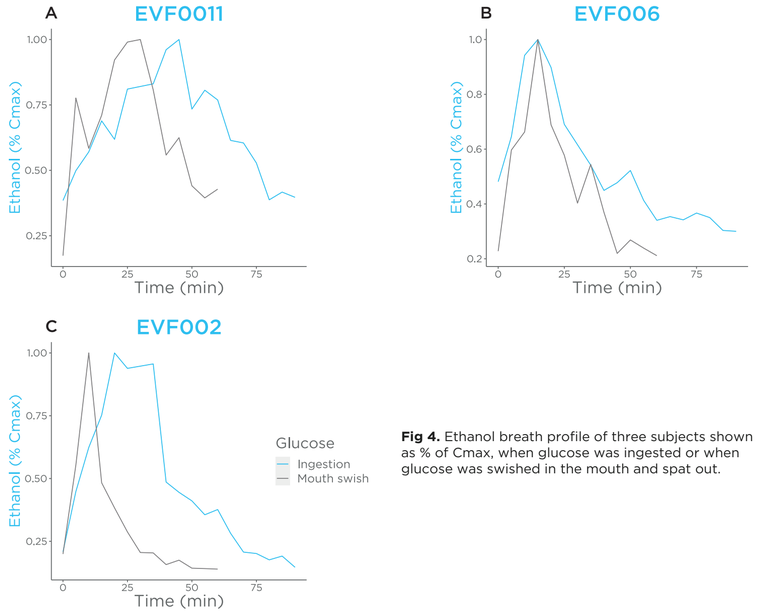

Fig 4. Ethanol breath profile of three subjects shown as % of Cmax, when glucose was ingested or when glucose was swished in the mouth and spat out.

Table 2. Summary of microbiome-derived metabolites measured in the breath.

Phenol	Acetone	Ammonia	Ethanol
p-Cresol	Ethyl phenol	Hydrogen sulfide	Acetoin
Acetaldehyde	Dimethyl sulfide	Propanoic acid	Methyl mercaptan
Indole	2,3 butanediol	Pentane	1,2 Propandiol
Methanol	Propanol	Methane	Trimethylamine
Propanol	Acetic acid		

4. Conclusions

- Many metabolites generated by the microbiome of the digestive system that are associated with different diseases are detectable in breath.
- This non-invasive method can replace the current need for blood collection allowing scaling to large cohort populations.