Microbiome-driven metabotypes influence response to the low FODMAP diet in IBS and implicate short chain fatty acids

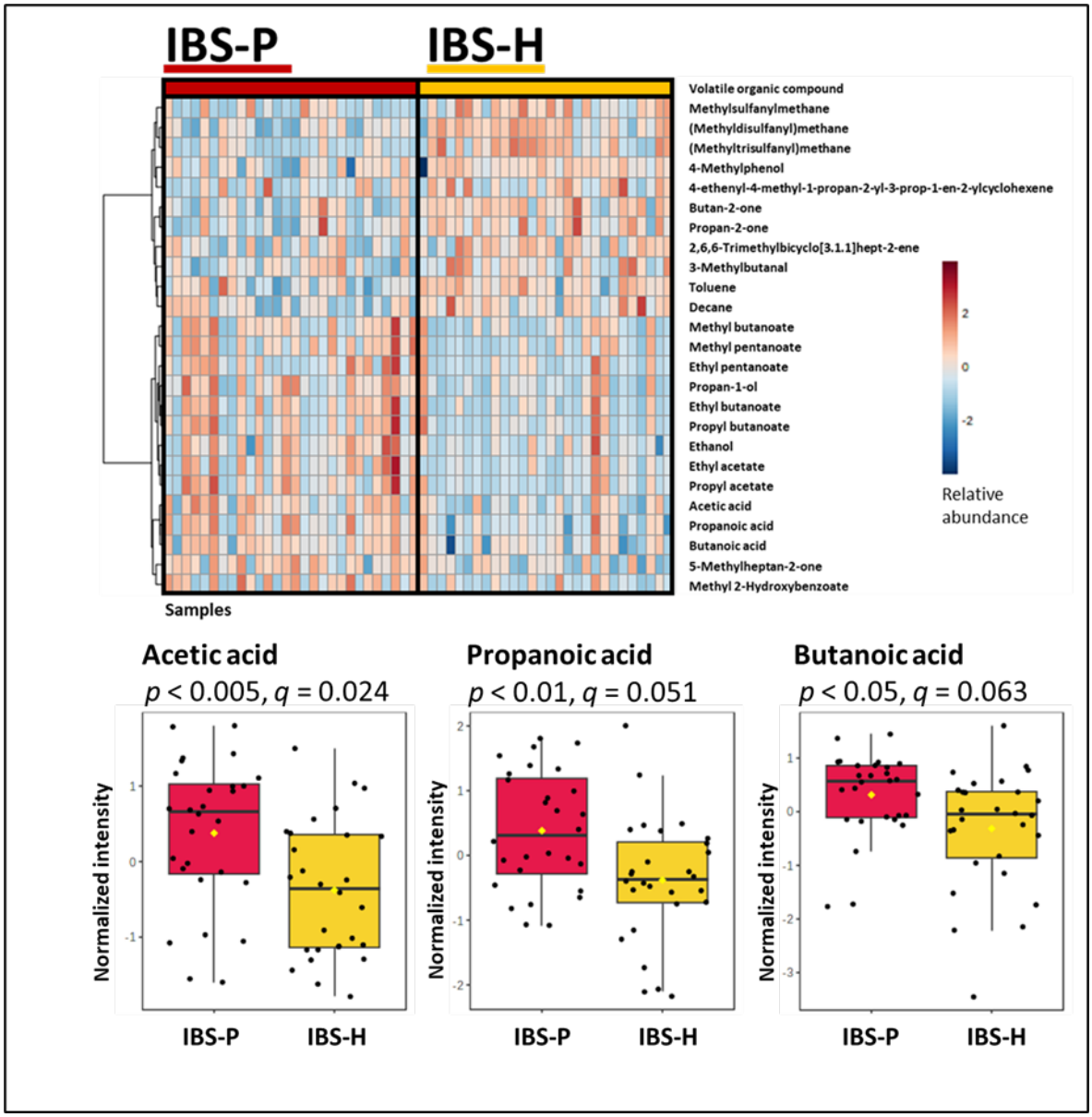
INTRODUCTION In irritable bowel syndrome (IBS), a greater response to the restriction of FODMAPs (fermentable oligosaccharides, disaccharides, monosaccharides and polyols) has been reported in those with a distinct 'pathogenic-like' microbiome (IBS-P) (1). We investigated whether the enhanced symptom response was associated with specific microbiome-driven changes in the metabolome.

METHODS Solid phase microextraction gas chromatography-mass spectrometry was used to examine the faecal headspace of 56 IBS cases (each paired with a non-IBS household control) at baseline, and after 4-weeks of a low FODMAP diet (39 pairs). 50% cases had IBS-P microbial subtype, the others had a microbiome that resembled healthy controls (IBS-H). Clinical response was measured with the IBS-symptom severity scale from which a pain sub-score was calculated.

RESULTS Two distinct metabotypes were identified and mapped onto the two microbial subtypes. IBS-P was characterised by a hyper-fermentative metabolic profile rich in short chain fatty acids (SCFAs) – Figure 1. More individuals with IBS-P had severe IBS symptoms at baseline, and after FODMAP restriction more individuals in the IBS-P subgroup achieved symptom remission compared with IBS-H (43.8% vs 25.0%; OR 2.30, 95% CI [1.26, 4.21], $p<0.005$). After FODMAP restriction significant reductions in SCFA abundance were observed in IBS-P, but not the IBS-H group. The relative abundance of SCFAs observed in IBS-P following FODMAP restriction aligned with the baseline levels observed in healthy controls, suggesting that levels are normalised rather than depleted by FODMAP restriction. In the IBS-P group the magnitude of pain and overall symptom improvement was significantly greater ($p=0.016$ and $p=0.026$, respectively).

CONCLUSIONS The magnitude of clinical response to the low FODMAP diet varies according to metabotype. A metabotype high in baseline SCFAs can be manipulated by restricting FODMAPs and associates with an enhanced clinical response. This further suggests the pro-nociceptive potential of SCFAs when produced in a specific IBS niche. The identification of this metabotype at baseline could lead to personalized and pragmatic therapy in IBS.

1. Vervier K, Moss S, Kumar N, et al. Two microbiota subtypes identified in irritable bowel syndrome with distinct responses to the low FODMAP diet. Gut. 2022;71(9):1821-30.


IBS-P
IBS-H
Volatile organic compound
Methylsulfanylmethane
(Methyldisulfanyl)methane
(Methyltrisulfanyl)methane
4-Methylphenol
4-ethenyl-4-methyl-1-propan-2-yl-3-prop-1-en-2-ylcyclohexene
Butan-2-one
Propan-2-one
2,6,6-Trimethylbicyclo[3.1.1]hept-2-ene
3-Methylbutanal
Toluene
Decane
Methyl butanoate
Methyl pentanoate
Ethyl pentanoate
Propan-1-ol
Ethyl butanoate
Propyl butanoate
Ethanol
Ethyl acetate
Propyl acetate
Acetic acid
Propanoic acid
Butanoic acid
5-Methylheptan-2-one
Methyl 2-Hydroxybenzoate
2
0
-2
Relative abundance
Samples
Acetic acid
p < 0.005, q = 0.024
Propanoic acid
p < 0.01, q = 0.051
Butanoic acid
p < 0.05, q = 0.063
Normalized intensity
IBS-P
IBS-H