Decoding the taxonomic and functional characteristics of the gut mycobiome linked with the development and progression of Non-alcoholic fatty liver disease

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1 Introduction

➤ Non-alcoholic fatty liver disease (NAFLD) is a multifactorial metabolic disorder having attained epidemic proportions, lacking an established intervention.

➤ As the condition advances, it transitions to non-alcoholic steatohepatitis (NASH), which can further progress to cirrhosis associated with hepatocellular carcinoma (HCC).

➤ Recent research has pointed to the substantial impact of specific gut microbial taxa on the development of liver disease.
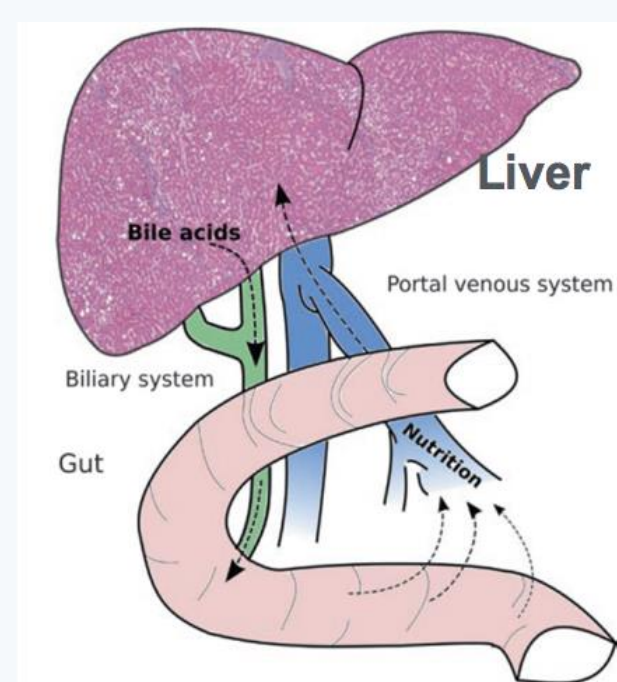
2 Lacunae in current research

➤ Currently, liver biopsy is the only gold standard method to detect the stages and progression of NASH.

➤ The gut mycobiome dysbiosis and progression of NASH in Obese and Lean patients have not been adequately addressed.

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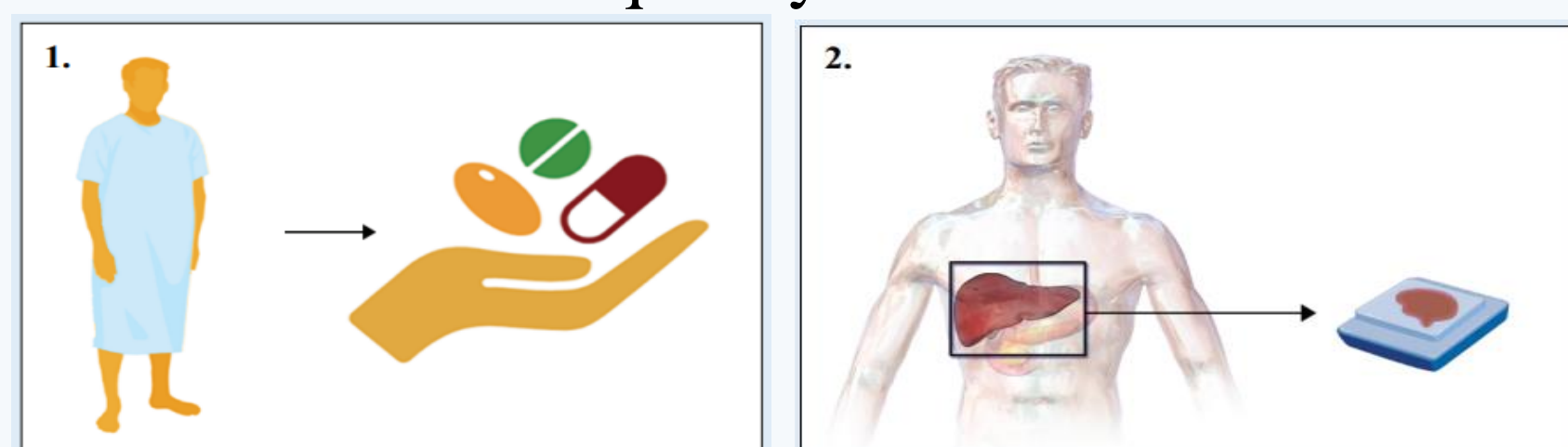
3 Objectives

➤ Explore the microbial balance, functionality, and composition in biopsy-confirmed NAFLD patients, focusing on fungal and bacterial taxa dynamics.

➤ Isolate bacterial and fungal species linked to NASH from fecal samples in lean and obese patients.

➤ In-vitro and in vivo characterization of pro-inflammatory and metabolic functions of bacterial and fungal taxa associated with NASH.

➤ To invent mycobiome signature based non invasive diagnostic test that detect progression of NASH.

4 Methodology
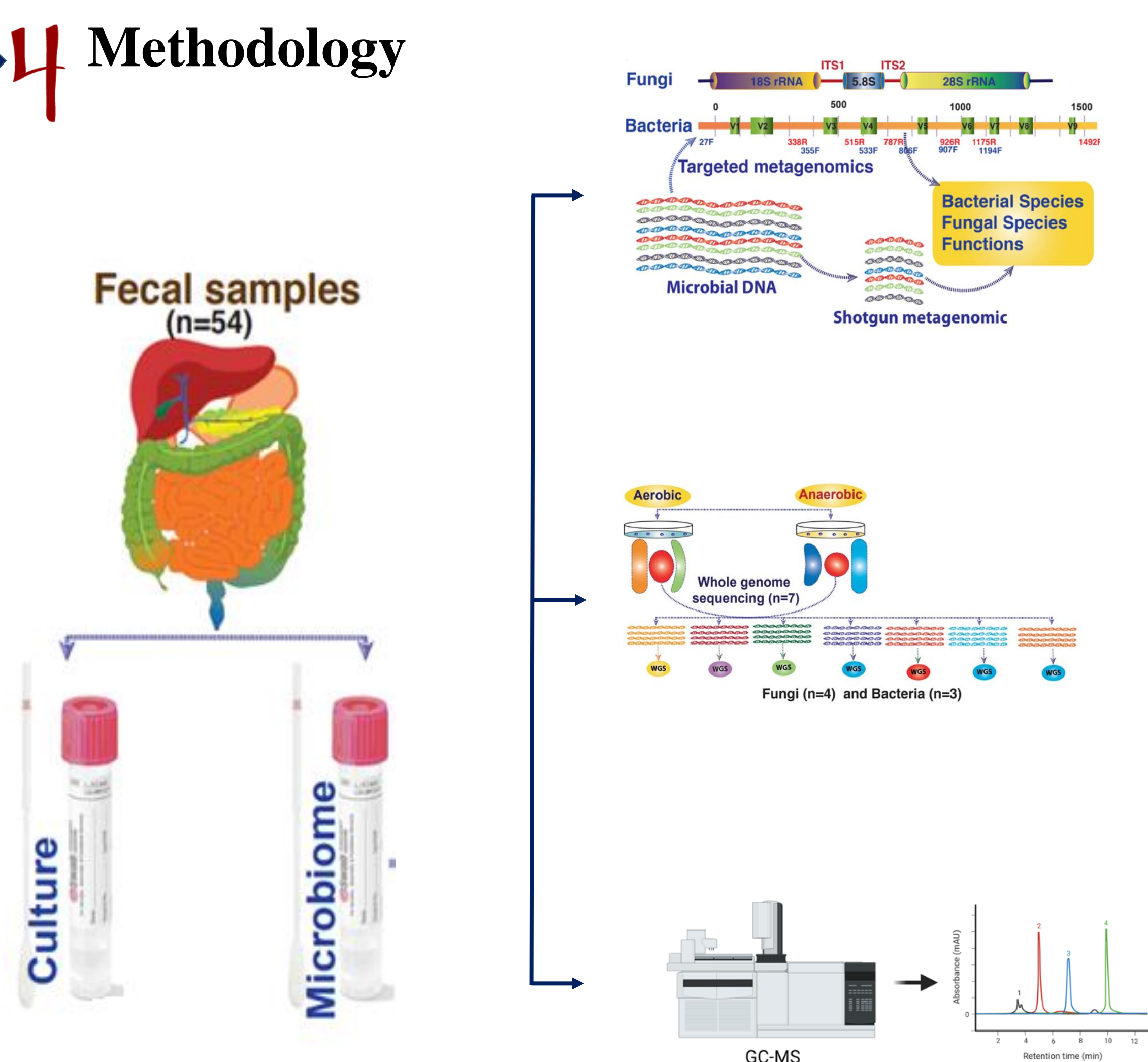
5 Discussion

➤ In the gut fungal community of individuals with NASH, *Candida* and *Diaporthe* emerge as notably abundant genera.

➤ The effectiveness of fungal taxa will be assessed in the Caco-2 and HCT-116 cell lines to gauge their impact.

➤ The Concentration of SCFA were found less in NASH as compare to NAFLD Patients.

➤ We have isolated **Parabacteroides distasonis** from the fecal sample of *NAFLD patients.*

6 Conclusion & Future Perspective

➤ The metagenomic finding of NASH patients is correlated with metabolic signatures of NASH patients.

➤ We have first time isolated & sequenced fungal taxa from NASH patients in Indian population.

➤ This study will help us to create a non-invasive diagnostic test that will predict early progression of NASH, thus decrease the dependency of Liver biopsy
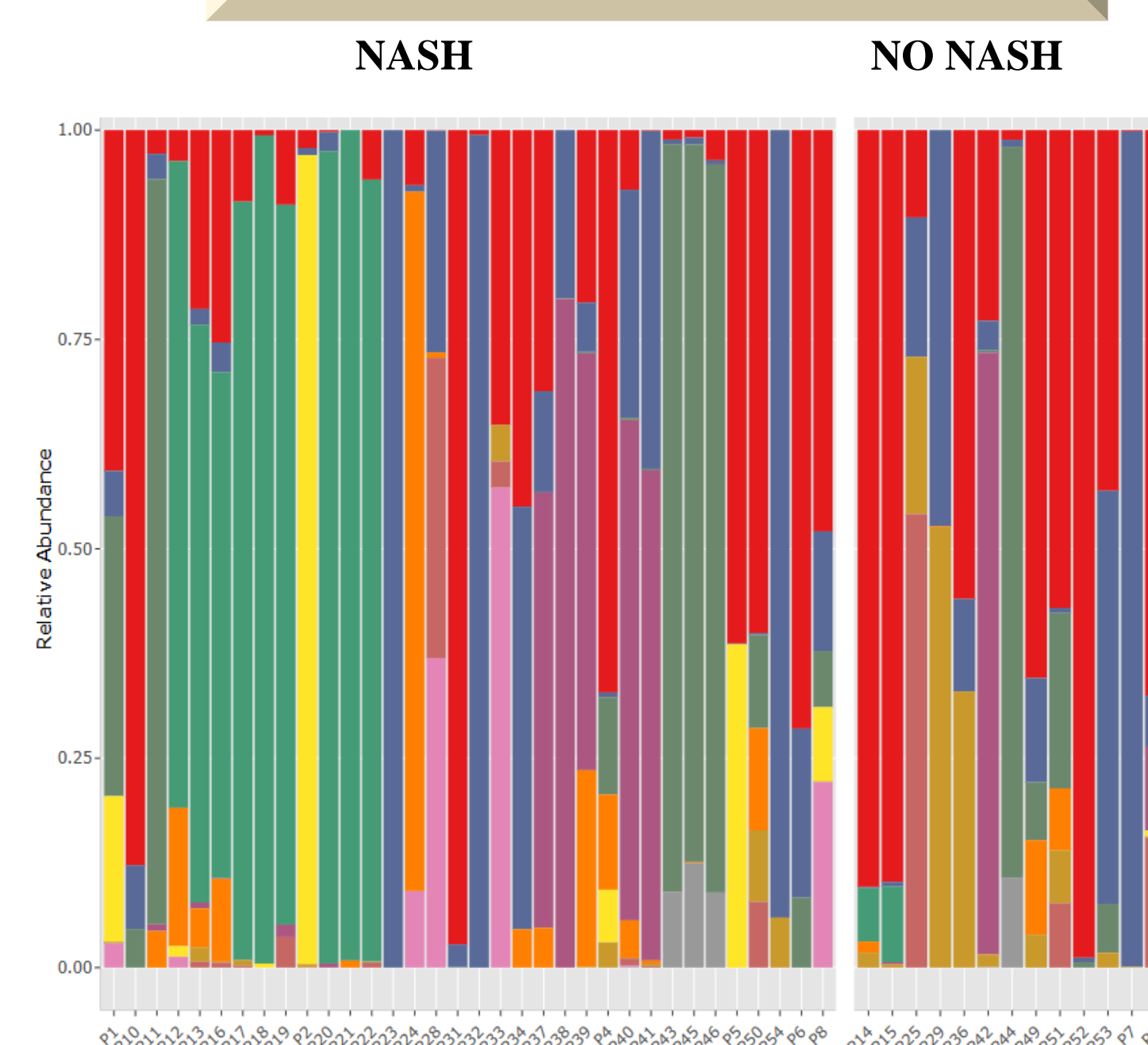
The Gut Mycobiome

Fig- 1. Illustrating the relative abundance of top 10 fungal Taxa at genus level.

Highly Abundant fungal taxa in Obese & Lean NASH

Control	Lean NASH	Obese NASH	
47.15	17.44	25.43	g__Candida
19.82	22.68	14.27	g__Aspergillus
1.53	30.10	19.54	g__Diaporthe
9.11	7.85	15.23	g__Alternaria
5.94	8.03	7.47	g__Acremonium
1.49	8.42	3.74	g__Issatchenkia
0.20	3.32	6.12	g__Sarocladium
4.79	0.14	1.97	g__Cladosporium
3.90	0.00	0.00	g__Curvularia
0.83	1.05	0.81	g__Torula

Fig- 2. Presenting the prevalence of the **Diaporthe** genus at 30.10% abundance in lean NASH. Notably, **Candida, Diaporthe**, and **Sarocladium** genera exhibit distinct abundance levels across Control, Lean, and Obese subjects.
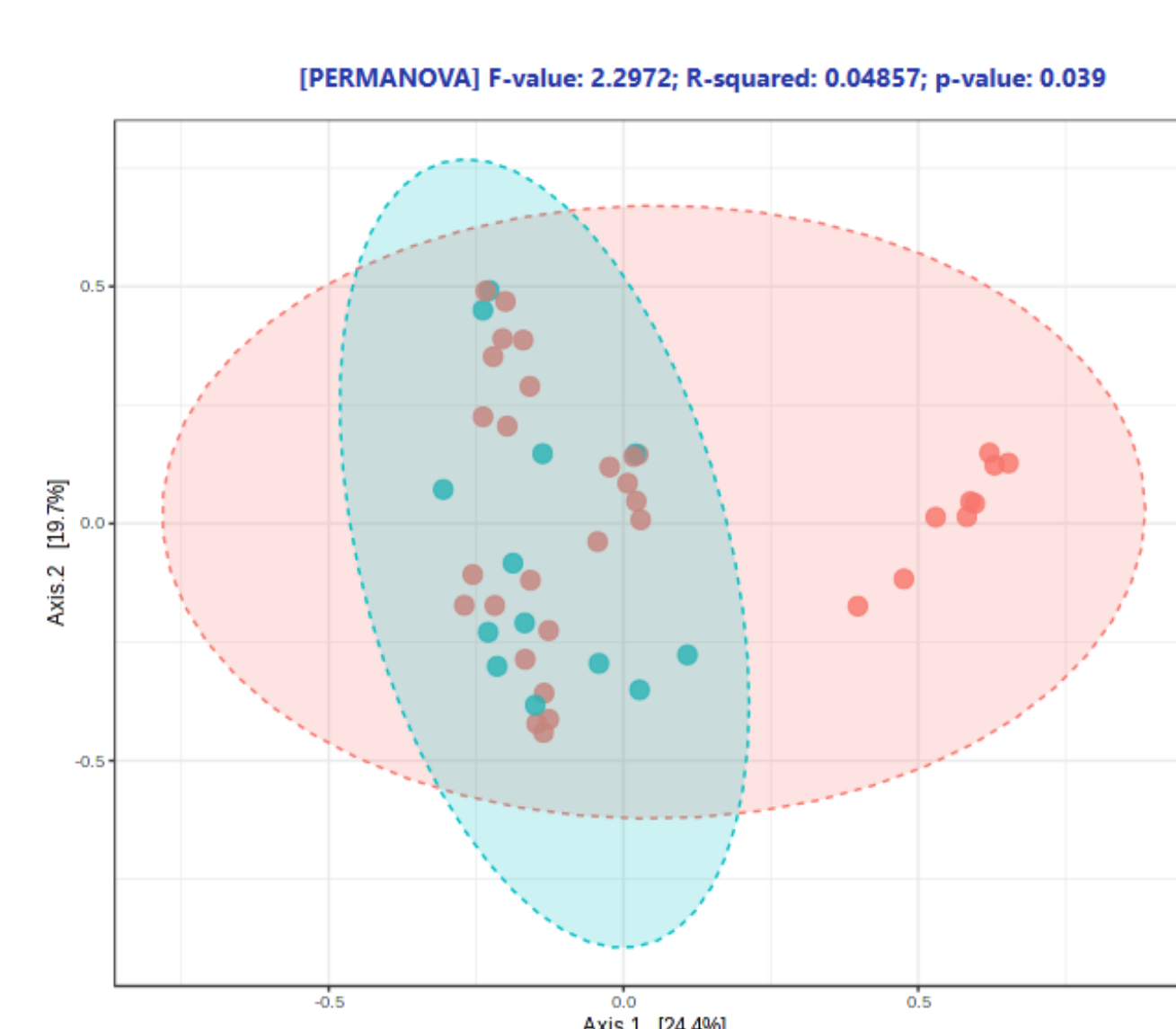
The Beta Diversity

Fig- 3. Illustrating the beta-diversity observed in fecal samples between subjects with and without NASH.
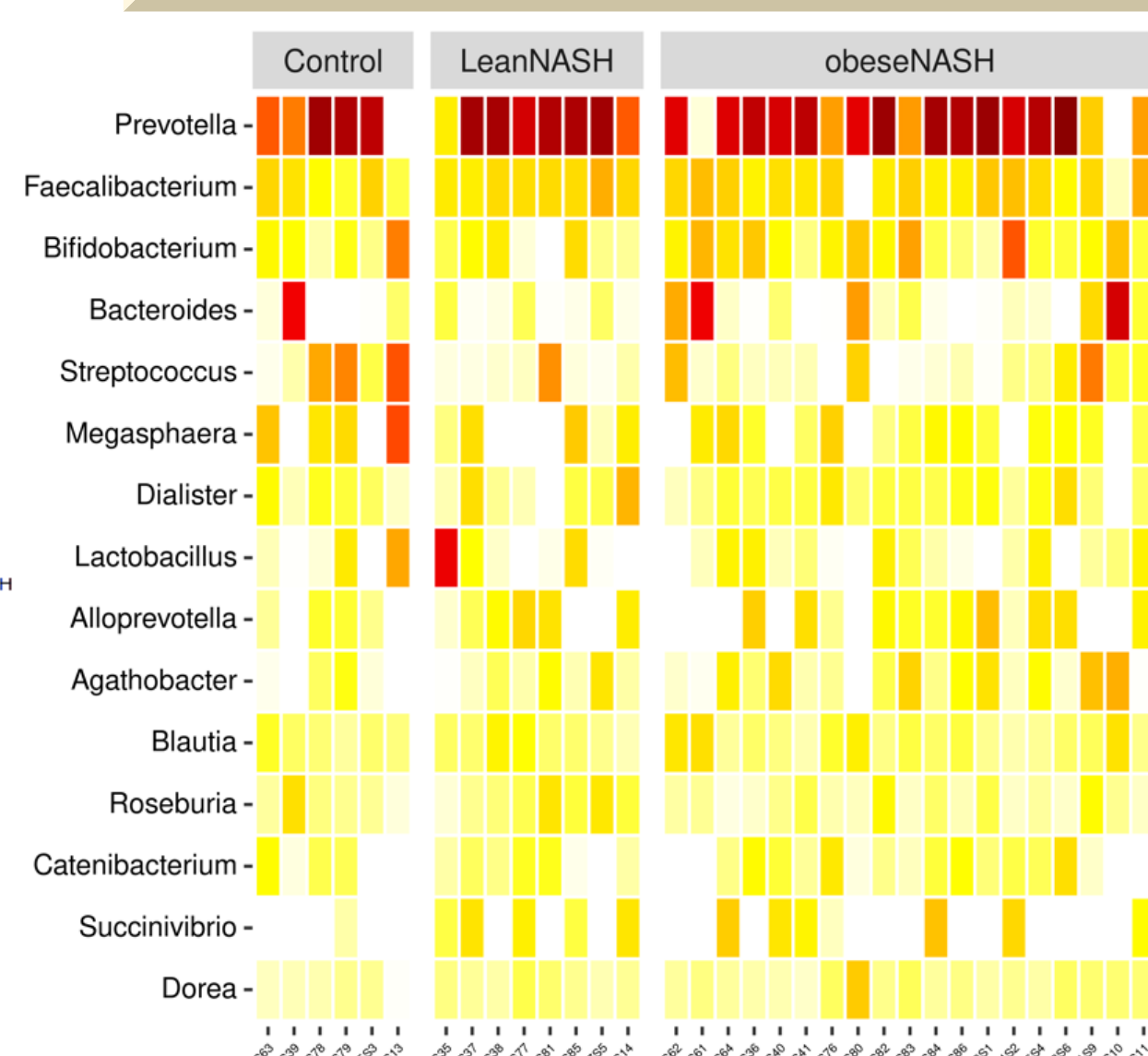
The Gut Microbiome

Fig- 4. Heat map showing the relative abundance of top 15 bacterial taxa at genus level.

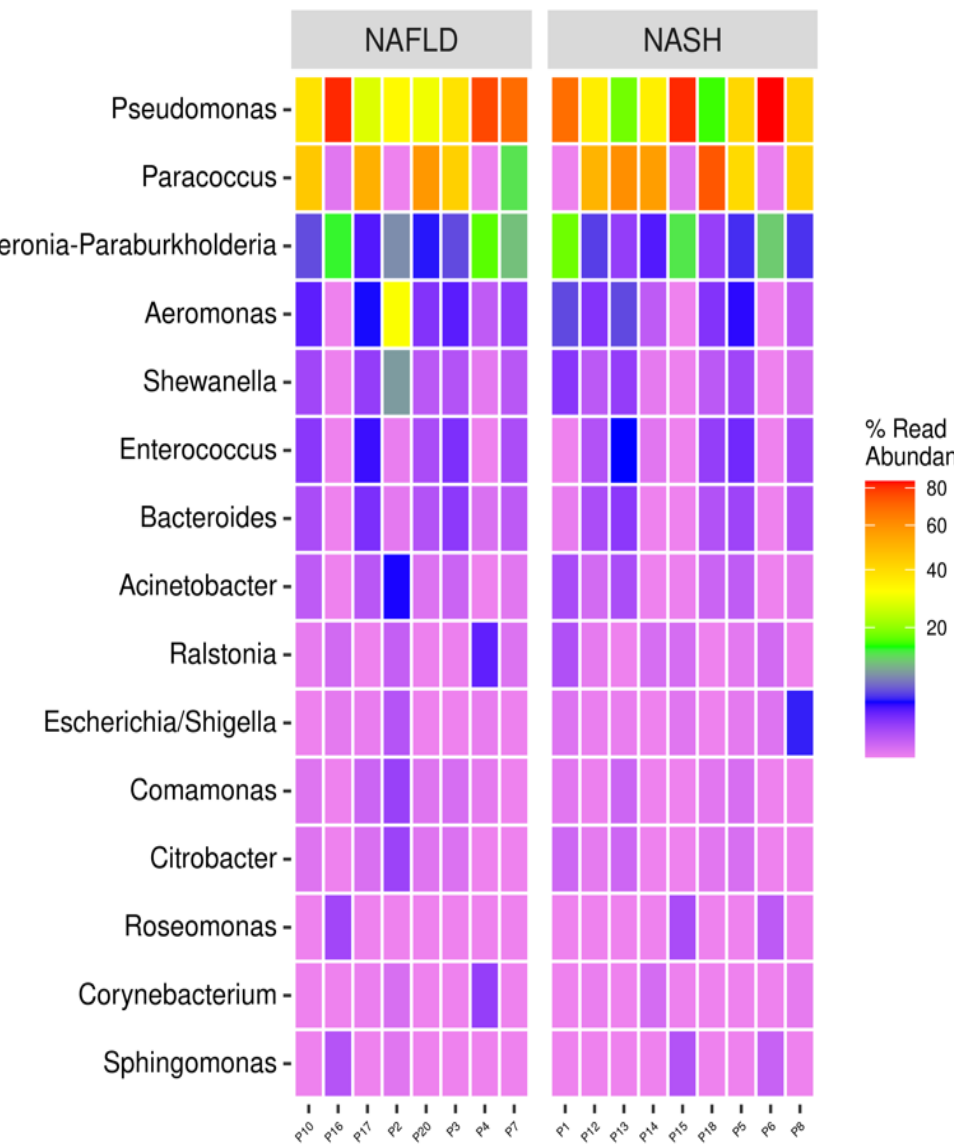### Bacterial signatures in the tissue of NASH patients

Fig- 5. Portray the microbial signatures evident in the hepatic tissue of individuals with NAFLD and NASH.

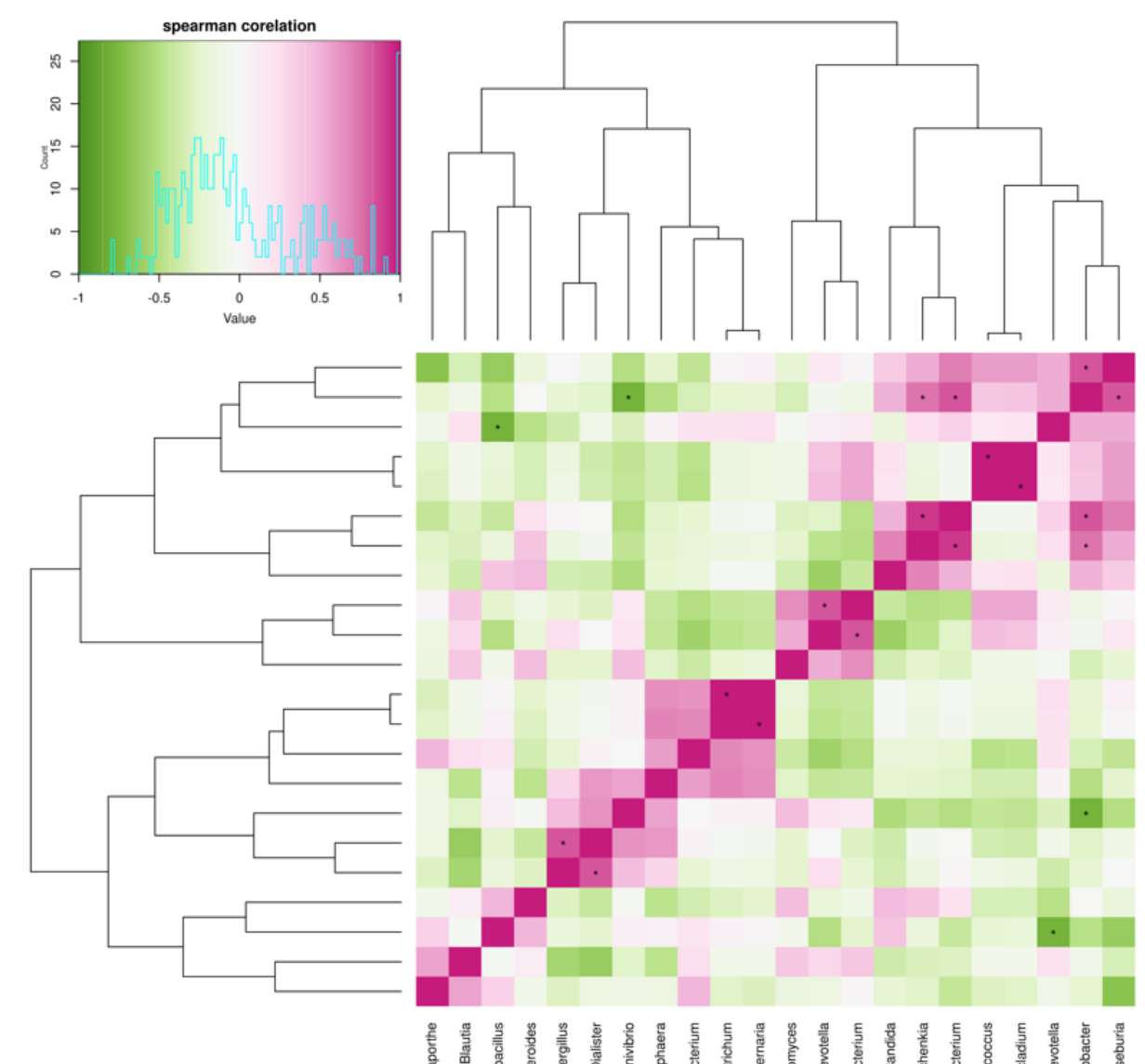### Cross-Kingdom interaction in bacteria and fungi among Lean NASH patients

Fig- 6. Represent the inter-kingdom interaction of bacterial and fungal taxa in lean NASH patients. **Aspergillus, Sarocladium, Issatchenkia** have strong positive correlation with **Dialister, Streptococcus & Agathobacter.**

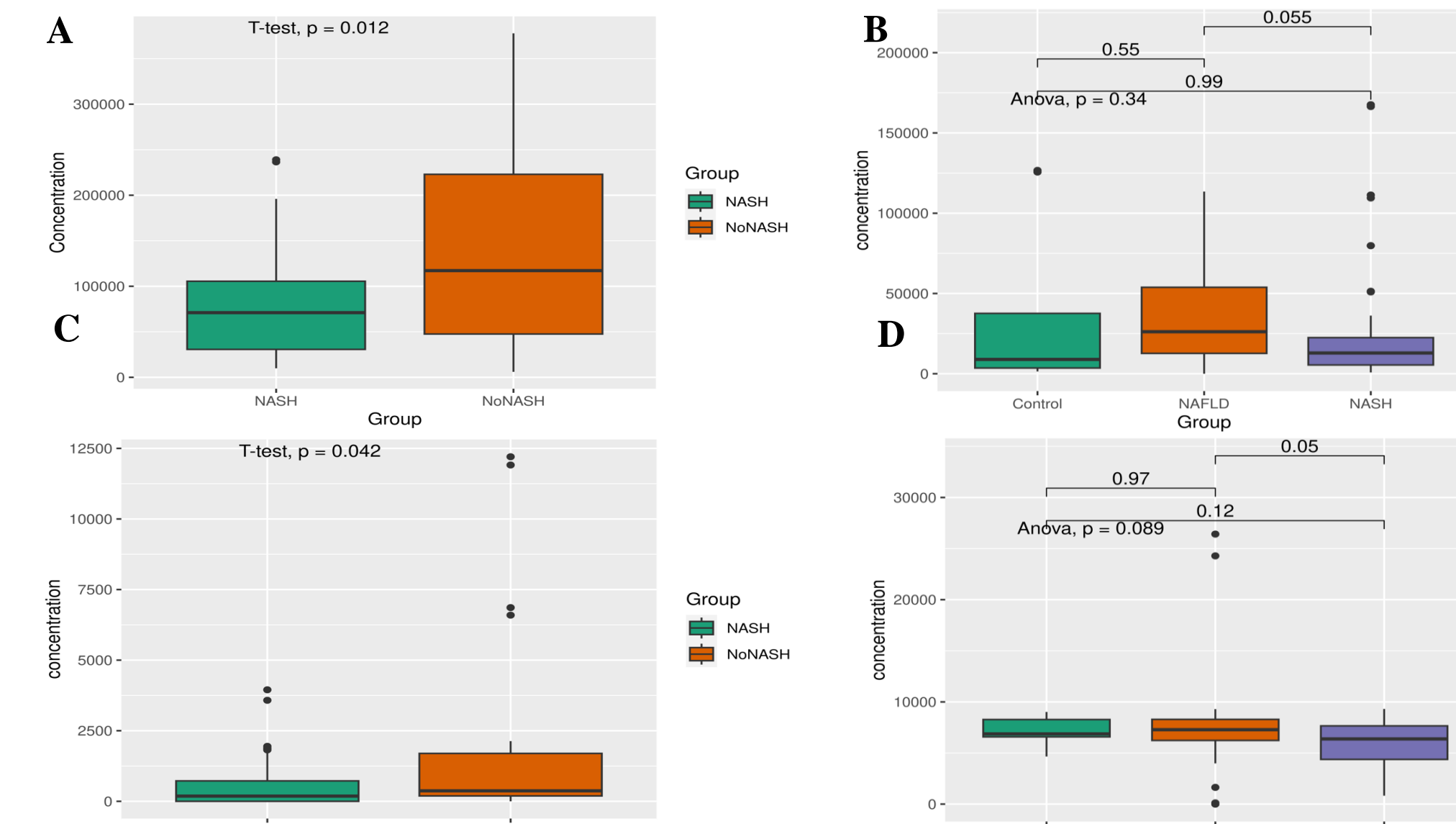### Elevated short-chain fatty acids in fecal samples from NAFLD patients

Fig- 7. Showing Short-chain fatty acids profile of NAFLD Patients. The Concentration of SFCA were found more in NAFLD as compared to the NASH group. **A**– Acetic acids, **B**– Propionic acid, **C**– Iso-butyric acid, **D**– Formic acid.

Culturomics / Fungal

Fig- 8 Fungal species isolated in fecal samples from individuals diagnosed with NASH.

Bacterial

Fig- 10. Bacterial species isolated form fecal sample of NASH patients.

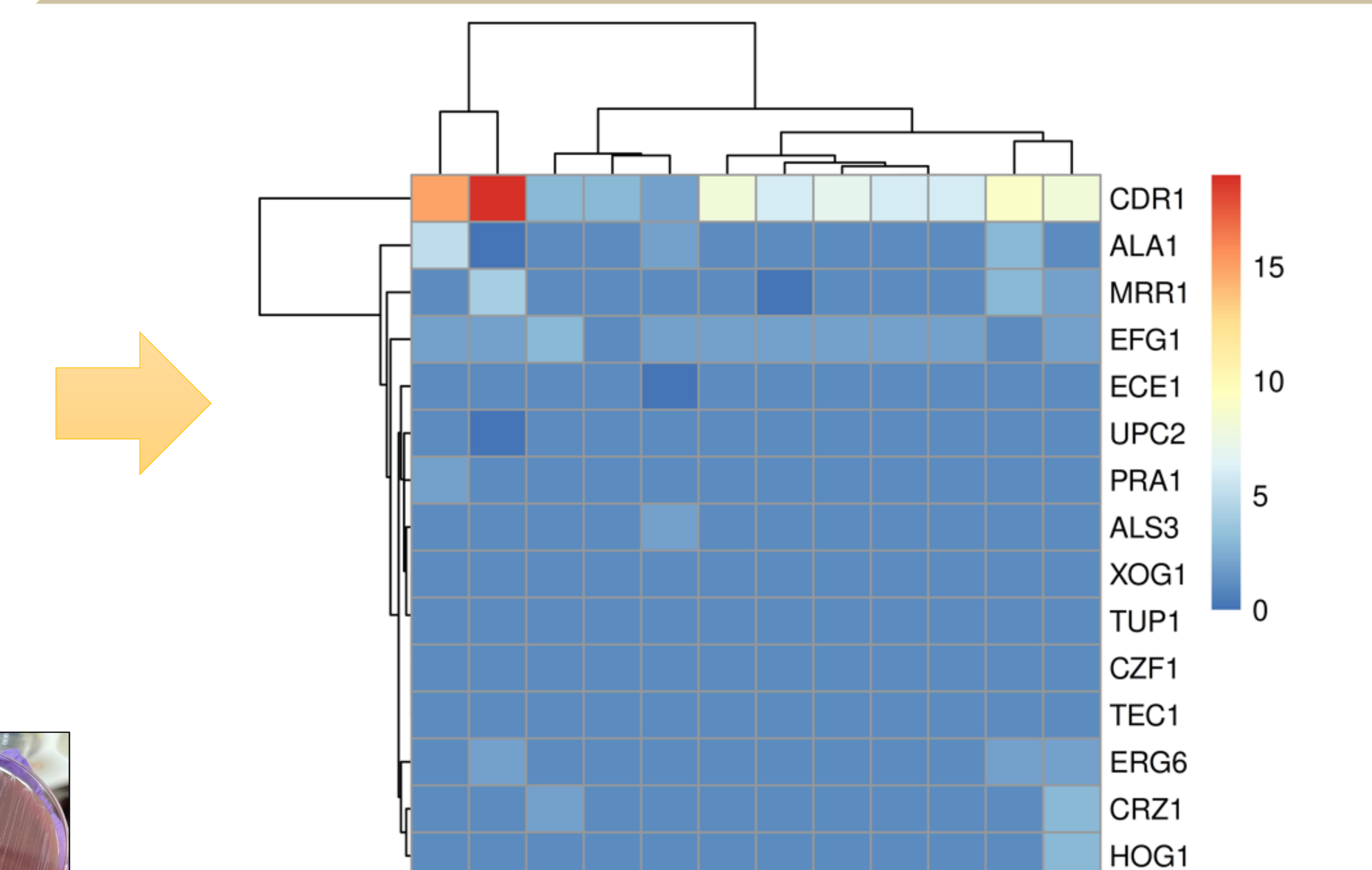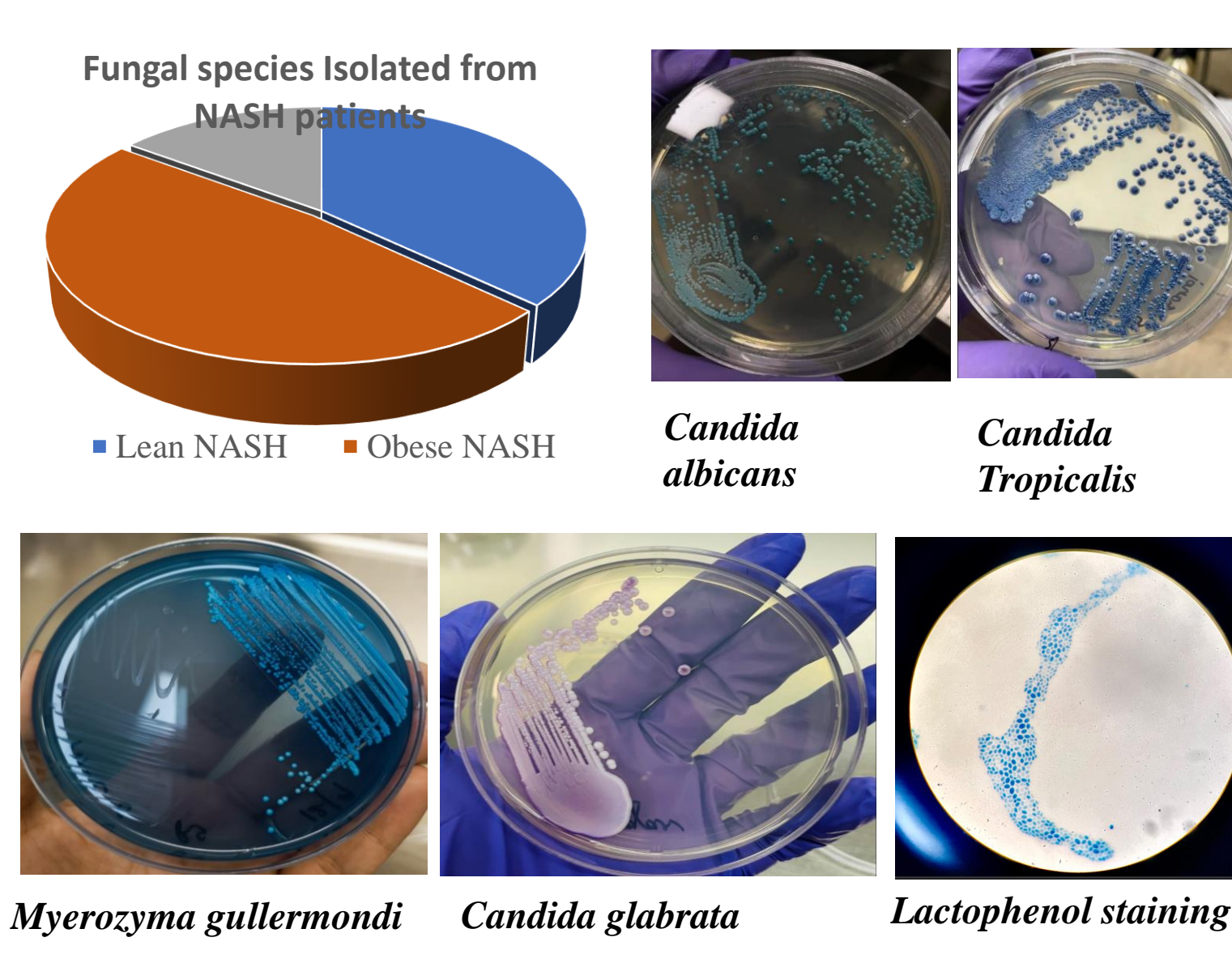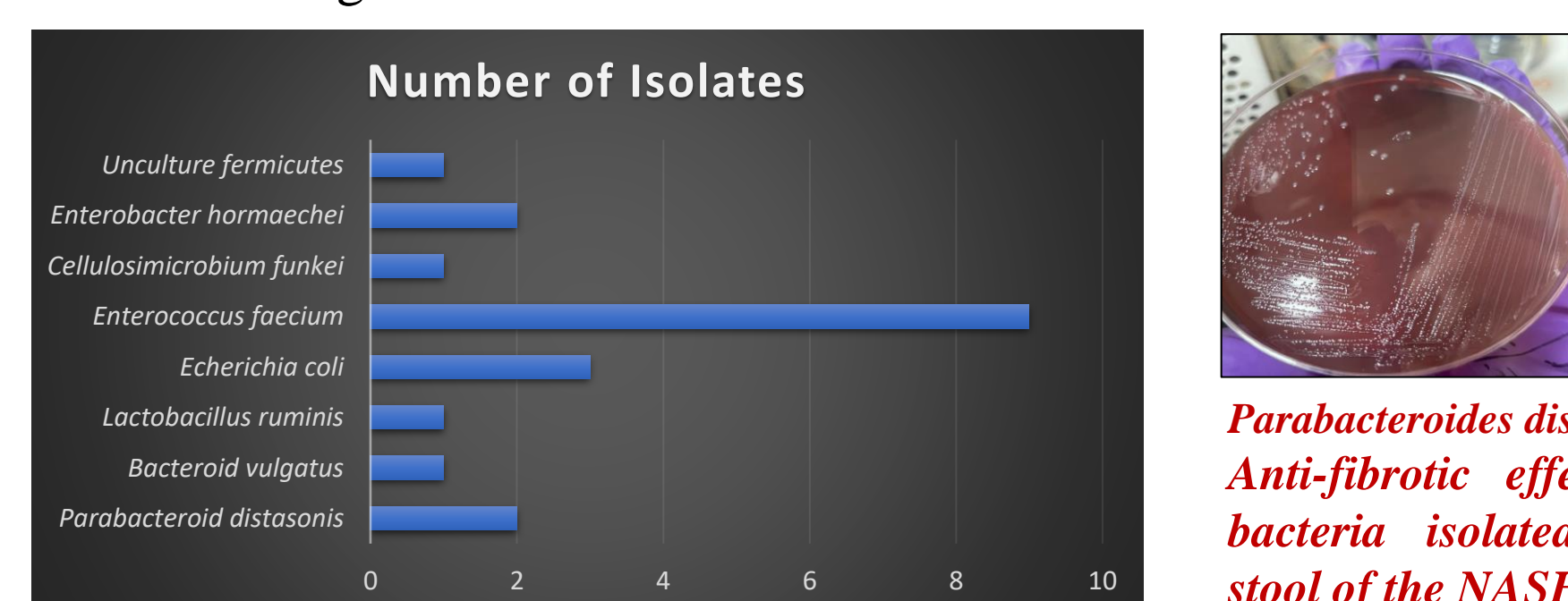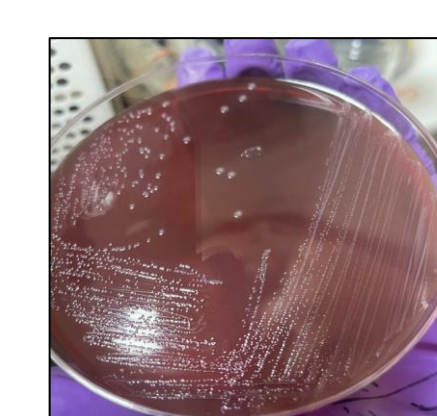### Virulent genes encoded by the fungal species

Fig- 9 Genomic analysis of the fungal genome sequence reveals the presence of virulent genes in **Candida albicans** species isolated from patients with NASH.