Supporting information

Circulating Microbiota-Based Metagenomic Signature for Detection of Hepatocellular Carcinoma

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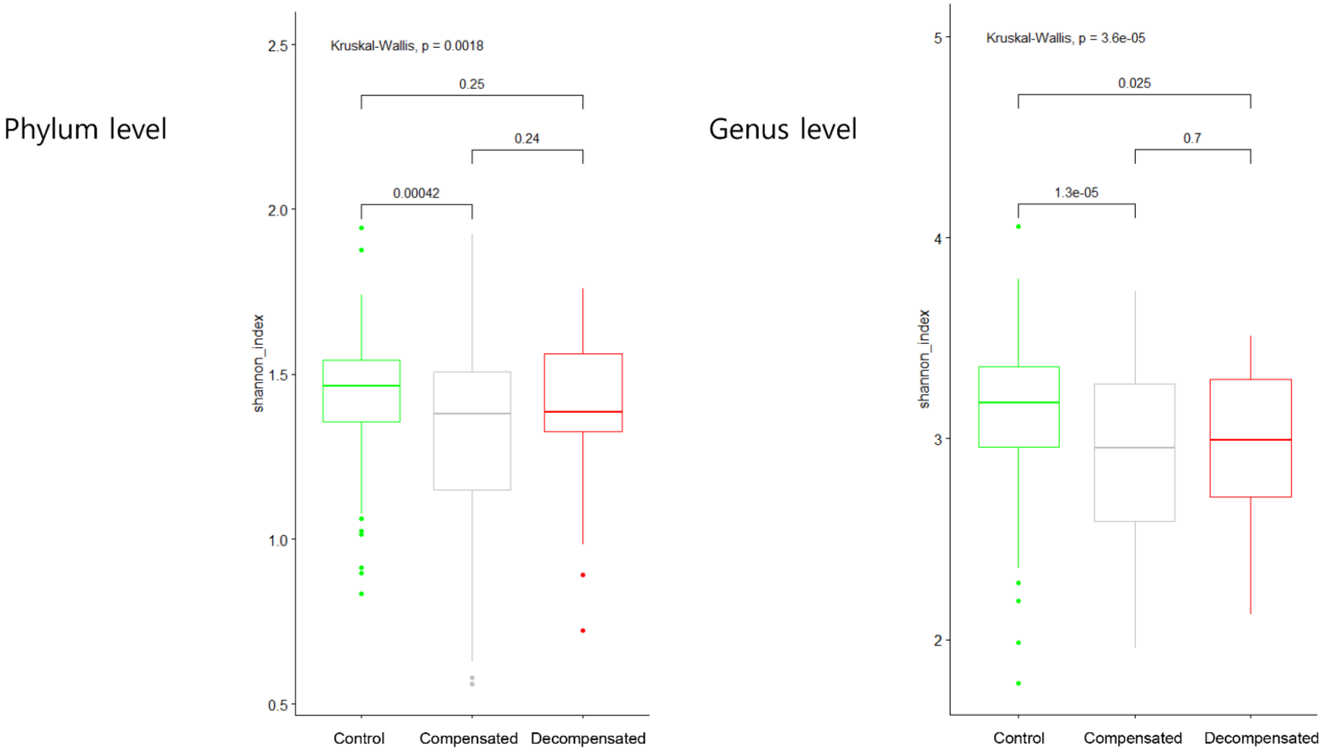
Supplementary Table 1. Taxonomic composition used in the diagnostic models of table 2

OTU symbol	Genus	Control	Cirrhosis	HCC	*p* value
g778	Pseudomonas	10.12% (7.22%)	9.59% (6.17%)	7.03% (4.14%)	0.0097
g362	Streptococcus	5.80% (5.40%)	1.37% (1.73%)	1.93% (3.76%)	1.7e-06
g319	Staphylococcus	1.99% (2.46%)	5.04% (7.18%)	8.64% (8.98%)	4.0e-08
g769	Acinetobacter	2.17% (2.83%)	3.93% (4.38%)	6.90% (8.10%)	5.7e-06
g147	Bifidobacterium	4.03% (3.68%)	2.52% (2.78%)	2.07% (2.68%)	0.0016
g725	Klebsiella	2.02% (2.97%)	2.11% (4.23%)	4.83% (5.91%)	0.0020
g348	Enterococcus	2.21% (2.49%)	2.10% (2.40%)	1.51% (2.31%)	0.5927
g837	Akkermansia	1.85% (2.33%)	1.11% (1.65%)	1.03% (1.89%)	0.2725
g732	Trabulsiella	0.56% (0.95%)	1.43% (2.18%)	3.85% (4.46%)	2.0e-07
g179	Prevotella	1.13% (1.44%)	0.65% (1.34%)	0.69% (1.57%)	0.6813

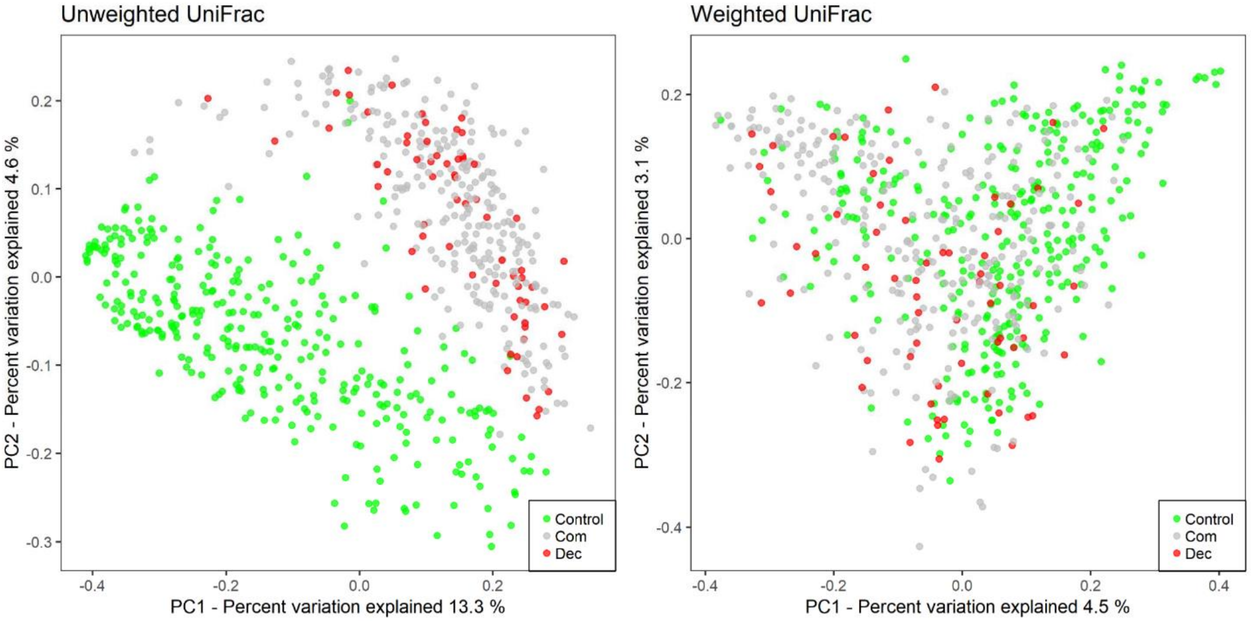
Median and SDs of relative abundances of 10 genus used in the diagnostic models. *Significant *p* value (HCC vs healthy control with adjustment of age and sex covariates) after multiple test correction. All *p*-values of OTUs before multiple test corrections are lower than 0.05.

Supplementary Figure 1. (a) α-diversity (Shannon index) of taxa according to liver function at the phylum and genus levels. *p* values from the Kruskal–Wallis tests are shown. (b) The PCoA plot based on the unweighted and weighted UniFrac distances. The control samples are colored as green, compensated group as gray, and decompensated group as red.

(a)



(b)

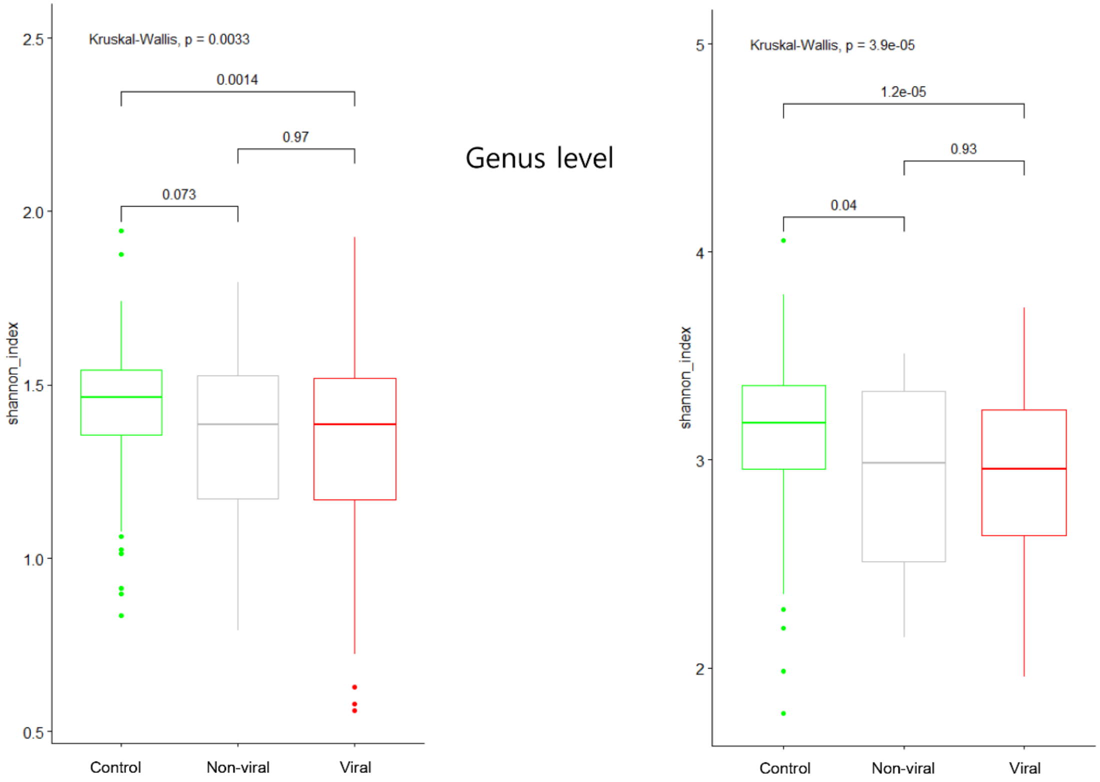


Unweighted UniFrac

Weighted UniFrac

Supplementary Figure 2. (a) α-diversity (Shannon index) of taxa according to etiology of liver disease at the phylum and genus levels. *p* values from the Kruskal–Wallis tests are shown. (b) The PCoA plot based on the unweighted and weighted UniFrac distances. The control samples are colored as green, non-viral group as gray, and hepatitis virus-related group as red.

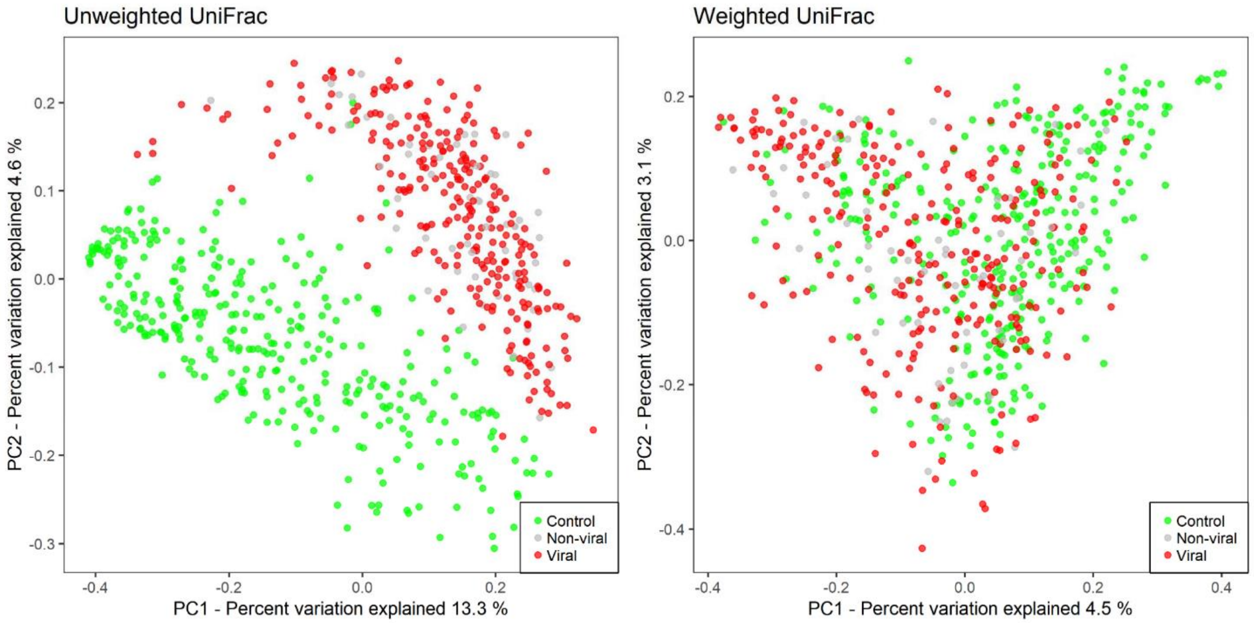
(a)



Phylum level

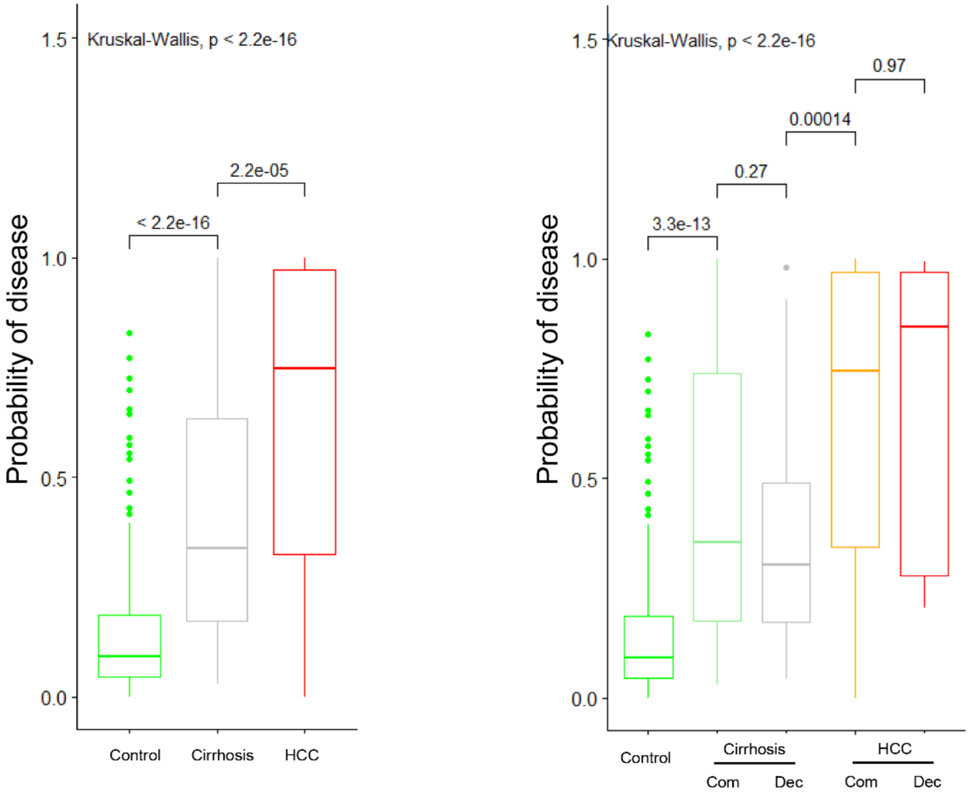
Genus level

(b)

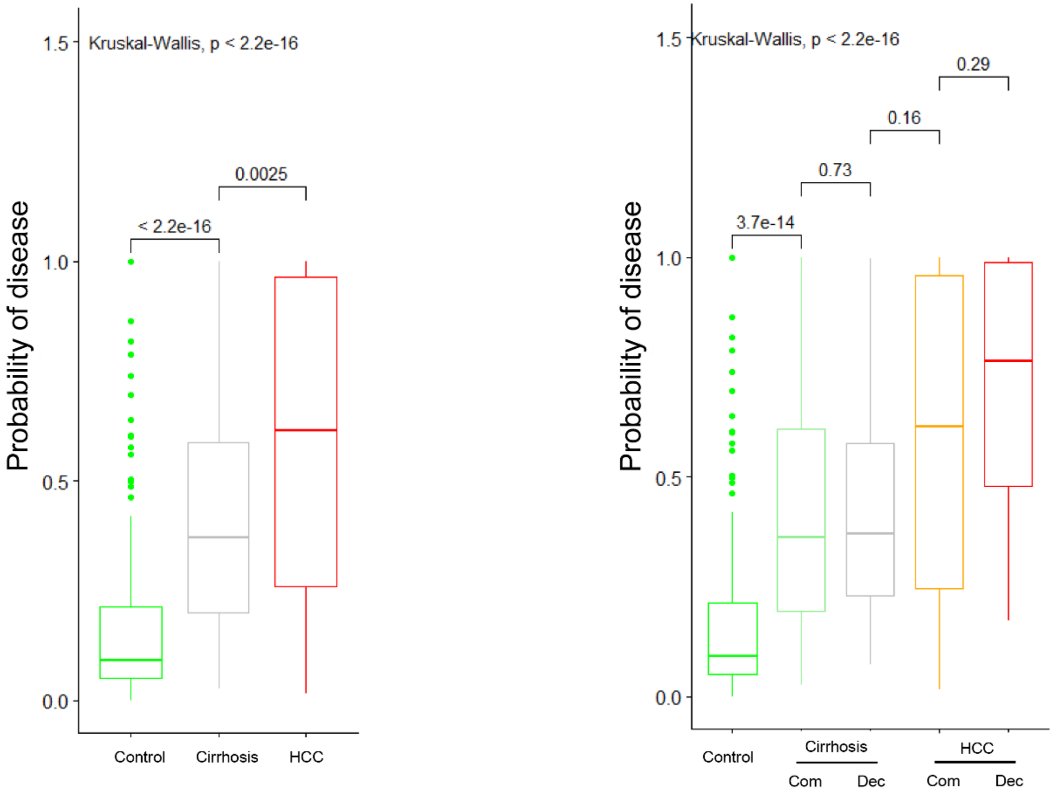

Unweighted UniFrac
PC2 - Percent variation explained 4.6 %
0.2
0.1
0.0
-0.1
-0.2
-0.3
-0.4
-0.2
0.0
0.2
PC1 - Percent variation explained 13.3 %
Control
Non-viral
Viral
Weighted UniFrac
PC2 - Percent variation explained 3.1 %
0.2
0.0
-0.2
-0.4
-0.4
-0.2
0.0
0.2
0.4
PC1 - Percent variation explained 4.5 %
Control
Non-viral
Viral

Supplementary Figure 3. The predicted probability of HCC in the three groups in the (a) model development set and (b) test set. *p* values from the Kruskal–Wallis tests or the Wilcoxon rank-sum test are shown. Com, compensated liver function, Dec, decompensated liver function, HCC, hepatocellular carcinoma

(a)



(b)


Probability of disease
Kruskal-Wallis, p < 2.2e-16
1.5
1.0
0.5
0.0
< 2.2e-16
0.0025
Control
Cirrhosis
HCC
Probability of disease
Kruskal-Wallis, p < 2.2e-16
1.5
1.0
0.5
0.0
3.7e-14
0.73
0.16
0.29
Control
Cirrhosis
Com
Dec
HCC
Com
Dec