Integrated multi-omics analysis reveals Lactobacillus anti-inflammatory process in vaginal tissue

A demonstration of Rmarkdown using Herman Bumpus' data

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1 Abstract

Abstract test test test

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[3]University of Lalaland

2 Introduction

Introduction ([1]), Introduction **Introduction Introduction** *Introduction* Introduction ([2,3]) .

Problem / question to answer

3 Results

Joint analysis of vaginal microbiome reveals distinct patient subgroups

To understand the longitudinal and tissue-specific microbiome profile in vaginal samples, 111 adult female sex workers were enrolled in [. . .]. Among those, 14 were previously tested positive for HIV during the cohort's sampling procedure. [Describe here what was done and when, which samples, which tissues].

To be able to better undertand the differences in microbiome profile across all datasets collected, we performed a joint graph-based clustering analysis in order to identify co-regulated bacterial communities (see "Methods" section for details). A total of 15 bacterial communities were identified.

Noticebly, bacterial community NA consisted only of Lactobacillus species (**).

Patients were thus subdivided into 8 groups,

Results Results

Results Results

Indentification of bacterial communities metabolic processes linked to Lactobacilli

Results Results

Indentification of bacterial communities metabolic processes linked to Lactobacilli

Results Results

4 Discussion

I have analysed data collected by Herman Bumpus[3] on the relationship between sparrow (*Passer domesticus*) total length and surival following an unusually severe storm. I found that sparrows that died in the storm were longer than sparrows that survived, which suggests that higher sparrow body length decreased survival. Of course, it is not possible to definitively conclude a causal relationship between any aspect of body size and sparrow survival, and even the available data collected by Bumpus would permit a more thoughtful analysis than that conducted in this study (see Appendix Table 1).

Overall, this document demonstrates how high quality, professional looking documents can be written using Rmarkdown. The underlying code for this manuscript is publicly available, along with accompanying notes to understand how it was written. By using Rmarkdown to write manuscripts, authors can more easily use version control (e.g., git) throughout the writing process. The ability to easily integrate citations though BibTeX, LaTeX tools, and dynamic R code can also make writing much more efficient and more enjoyable. Further, obtaining the benefits of using Rmarkdown does not need to come with the cost of isolating colleagues who prefer to work with Word or LaTeX because Rmarkdown can easily be converted to these formats (in the case of Word, with the push of a button). By learning all of the tools used in this manuscript, readers should have all of the necessary knowledge to get started writing and collaborating in Rmarkdown.

5 Methods

6 References

1. Johnston, R. F., Niles, D. M. & Rohwer, S. A. Hermon bumpus and natural selection in the house sparrow *Passer domesticus*. *Evolution* **26**, 20–31 (1972).

2. Darwin, C. *The origin of species*. 495 (Penguin, 1859).

3. Bumpus, H. C. Eleventh lecture. The elimination of the unfit as illustrated by the introduced sparrow, *Passer domesticus*. (A fourth contribution to the study of variation.). *Biological Lectures: Woods Hole Marine Biological Laboratory* 209–225 (1898).

7 Appendix Table 1

An example table is shown below, which includes all of the variables collected by 3 for the first 10 measured sparrows. The full data set can be found online in GitHub.

8 FIGURES (MAIN)

8.1 Figure 1

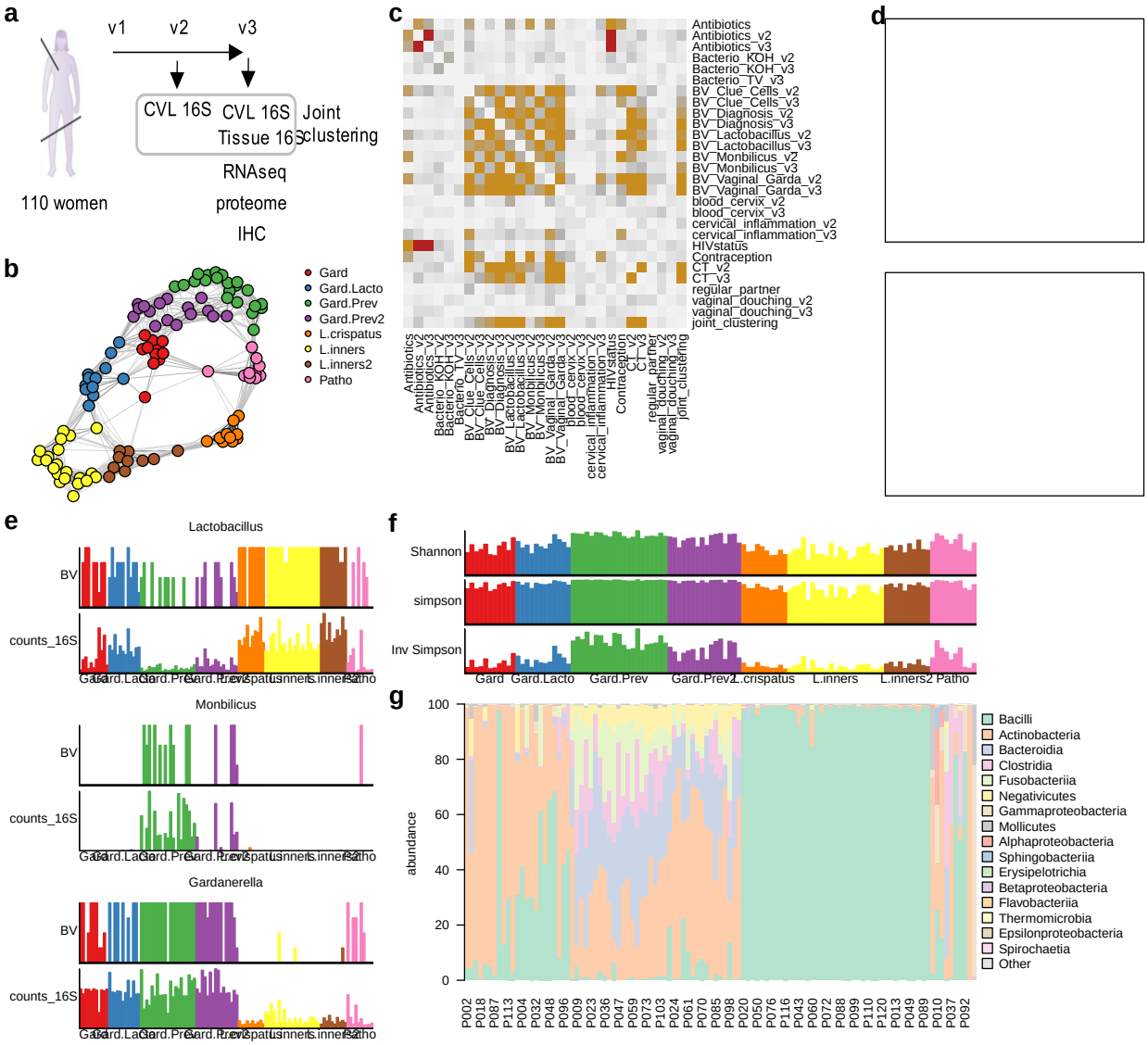
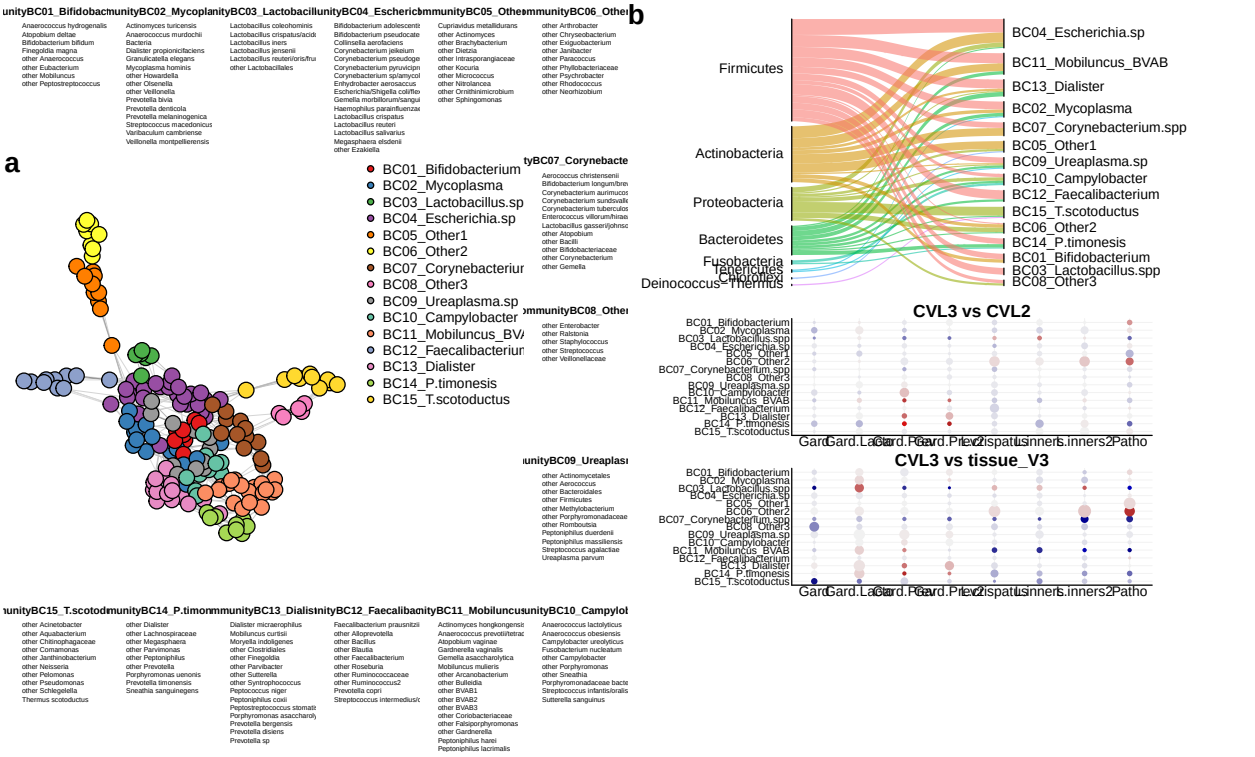
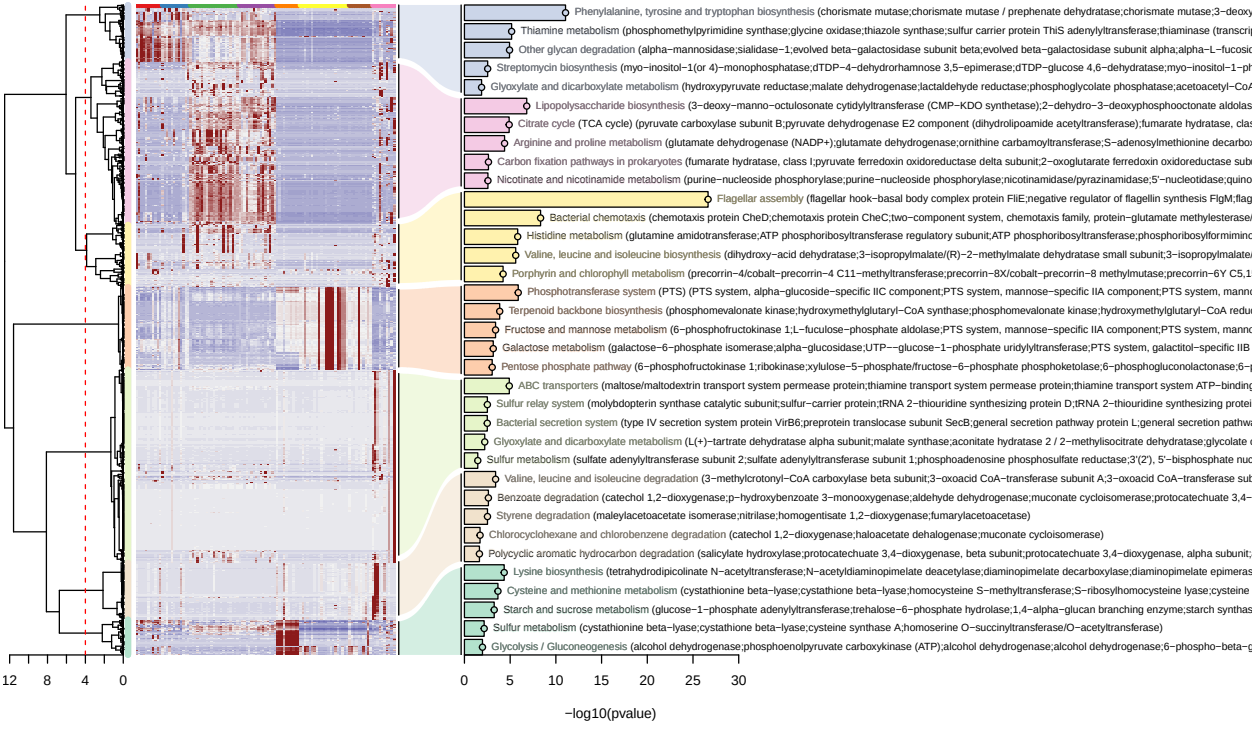
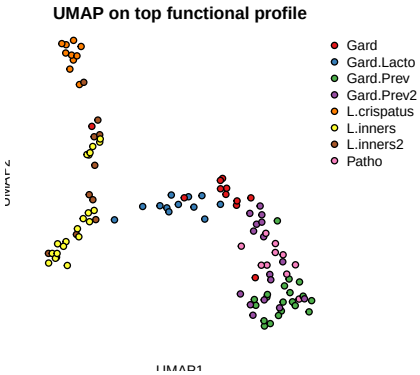


Figure 1. Identification of patient groups. (**a**) Schematic representation of ########## . (**b**) Schematic representation of ########## . (**c**) Schematic representation of ########## . (**d**) Schematic representation of ########## .

8.2 Figure 2


a
b
BC01_Bifidobacterium
BC02_Mycoplasma
BC03_Lactobacillus.sp
BC04_Escherichia.sp
BC05_Other1
BC06_Other2
BC07_Corynebacterium
BC08_Other3
BC09_Ureaplasma.sp
BC10_Campylobacter
BC11_Mobiluncus_BVA
BC12_Faecalibacterium
BC13_Dialister
BC14_P.timonesis
BC15_T.scotoductus
Firmicutes
Actinobacteria
Proteobacteria
Bacteroidetes
Fusobacteria
Tenericutes
Chloroflexi
Deinococcus−Thermus
CVL3 vs CVL2
CVL3 vs tissue_V3

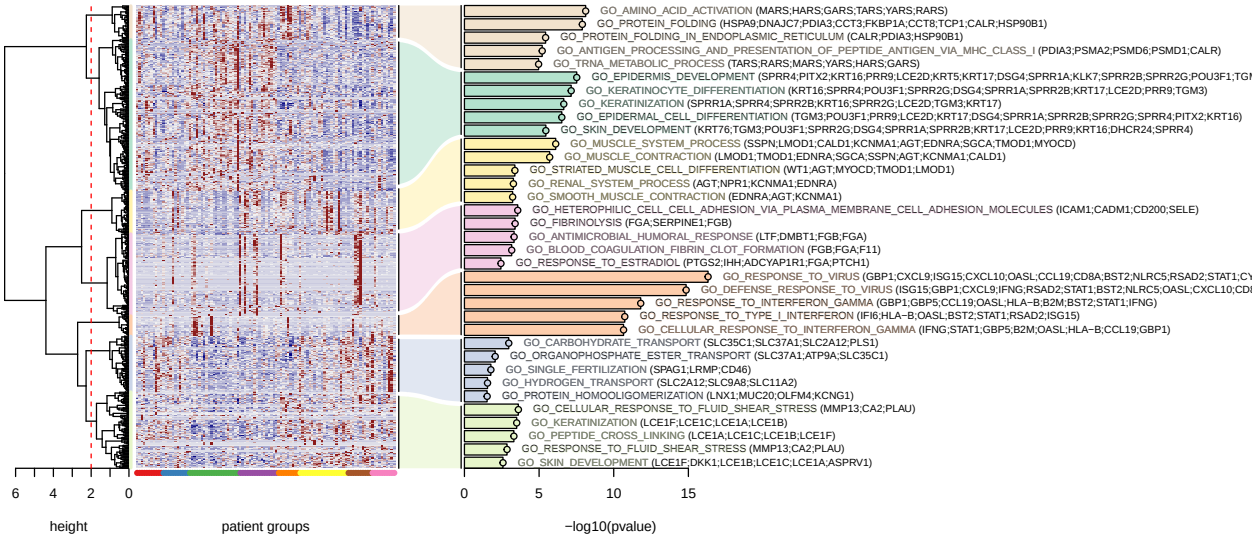

Phenylalanine, tyrosine and tryptophan biosynthesis
Thiamine metabolism
Other glycan degradation
Streptomycin biosynthesis
Glyoxylate and dicarboxylate metabolism
Lipopolysaccharide biosynthesis
Citrate cycle (TCA cycle)
Arginine and proline metabolism
Carbon fixation pathways in prokaryotes
Nicotinate and nicotinamide metabolism
Flagellar assembly
Bacterial chemotaxis
Histidine metabolism
Valine, leucine and isoleucine biosynthesis
Porphyrin and chlorophyll metabolism
Phosphotransferase system (PTS)
Terpenoid backbone biosynthesis
Fructose and mannose metabolism
Galactose metabolism
Pentose phosphate pathway
ABC transporters
Sulfur relay system
Bacterial secretion system
Glyoxylate and dicarboxylate metabolism
Sulfur metabolism
Valine, leucine and isoleucine degradation
Benzoate degradation
Styrene degradation
Chlorocyclohexane and chlorobenzene degradation
Polycyclic aromatic hydrocarbon degradation
Lysine biosynthesis
Cysteine and methionine metabolism
Starch and sucrose metabolism
Sulfur metabolism
Glycolysis / Gluconeogenesis
12 8 4 0
0 5 10 15 20 25 30
−log10(pvalue)



165

166 **Figure 2. Identification and characterization of vaginal bacterial communities.** (**a**) Schematic
167 representation of ########## . (**b**) Schematic representation of ########## . (**c**) Schematic
168 representation of ########## . (**d**) Schematic representation of ########## .

8.3 Figure 3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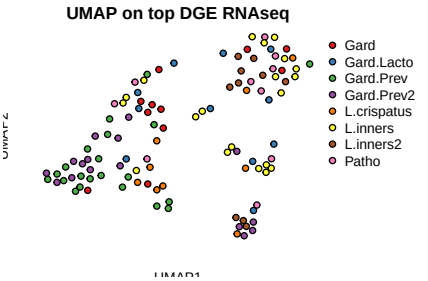
GO_PROTEIN_FOLDING_IN_ENDOPLASMIC_RETICULUM (CALR;PDIA3;HSP90B1)
GO_ANTIGEN_PROCESSING_AND_PRESENTATION_OF_PEPTIDE_ANTIGEN_VIA_MHC_CLASS_I (PDIA3;PSMA2;PSMD6;PSMD1;CALR)
GO_TRNA_METABOLIC_PROCESS (TARS;RARS;MARS;YARS;HARS;GARS)
GO_EPIDERMIS_DEVELOPMENT (SPRR4;PITX2;KRT16;PRR9;LCE2D;KRT5;KRT17;DSG4;SPRR1A;KLK7;SPRR2B;SPRR2G;POU3F1;TG
GO_KERATINOCYTE_DIFFERENTIATION (KRT16;SPRR4;POU3F1;SPRR2G;DSG4;SPRR1A;SPRR2B;KRT17;LCE2D;PRR9;TGM3)
GO_KERATINIZATION (SPRR1A;SPRR4;SPRR2B;KRT16;SPRR2G;LCE2D;TGM3;KRT17)
GO_EPIDERMAL_CELL_DIFFERENTIATION (TGM3;POU3F1;PRR9;LCE2D;KRT17;DSG4;SPRR1A;SPRR2B;SPRR2G;SPRR4;PITX2;KRT16)
GO_SKIN_DEVELOPMENT (KRT76;TGM3;POU3F1;SPRR2G;DSG4;SPRR1A;SPRR2B;KRT17;LCE2D;PRR9;KRT16;DHCR24;SPRR4)
GO_MUSCLE_SYSTEM_PROCESS (SSPN;LMOD1;CALD1;KCNMA1;AGT;EDNRA;SGCA;TMOD1;MYOCD)
GO_MUSCLE_CONTRACTION (LMOD1;TMOD1;EDNRA;SGCA;SSPN;AGT;KCNMA1;CALD1)
GO_STRIATED_MUSCLE_CELL_DIFFERENTIATION (WT1;AGT;MYOCD;TMOD1;LMOD1)
GO_RENAL_SYSTEM_PROCESS (AGT;NPR1;KCNMA1;EDNRA)
GO_SMOOTH_MUSCLE_CONTRACTION (EDNRA;AGT;KCNMA1)
GO_HETEROPHILIC_CELL_CELL_ADHESION_VIA_PLASMA_MEMBRANE_CELL_ADHESION_MOLECULES (ICAM1;CADM1;CD200;SELE)
GO_FIBRINOLYSIS (FGA;SERPINE1;FGB)
GO_ANTIMICROBIAL_HUMORAL_RESPONSE (LTF;DMBT1;FGB;FGA)
GO_BLOOD_COAGULATION_FIBRIN_CLOT_FORMATION (FGB;FGA;F11)
GO_RESPONSE_TO_ESTRADIOL (PTGS2;IHH;ADCYAP1R1;FGA;PTCH1)
GO_RESPONSE_TO_VIRUS (GBP1;CXCL9;ISG15;CXCL10;OASL;CCL19;CD8A;BST2;NLRC5;RSAD2;STAT1;C
GO_DEFENSE_RESPONSE_TO_VIRUS (ISG15;GBP1;CXCL9;IFNG;RSAD2;STAT1;BST2;NLRC5;OASL;CXCL10;CD
GO_RESPONSE_TO_INTERFERON_GAMMA (GBP1;GBP5;CCL19;OASL;HLA−B;B2M;BST2;STAT1;IFNG)
GO_RESPONSE_TO_TYPE_I_INTERFERON (IFI6;HLA−B;OASL;BST2;STAT1;RSAD2;ISG15)
GO_CELLULAR_RESPONSE_TO_INTERFERON_GAMMA (IFNG;STAT1;GBP5;B2M;OASL;HLA−B;CCL19;GBP1)
GO_CARBOHYDRATE_TRANSPORT (SLC35C1;SLC37A1;SLC2A12;PLS1)
GO_ORGANOPHOSPHATE_ESTER_TRANSPORT (SLC37A1;ATP9A;SLC35C1)
GO_SINGLE_FERTILIZATION (SPAG1;LRMP;CD46)
GO_HYDROGEN_TRANSPORT (SLC2A12;SLC9A8;SLC11A2)
GO_PROTEIN_HOMOOLIGOMERIZATION (LNX1;MUC20;OLFM4;KCNG1)
GO_CELLULAR_RESPONSE_TO_FLUID_SHEAR_STRESS (MMP13;CA2;PLAU)
GO_KERATINIZATION (LCE1F;LCE1C;LCE1A;LCE1B)
GO_PEPTIDE_CROSS_LINKING (LCE1A;LCE1C;LCE1B;LCE1F)
GO_RESPONSE_TO_FLUID_SHEAR_STRESS (MMP13;CA2;PLAU)
GO_SKIN_DEVELOPMENT (LCE1F;DKK1;LCE1B;LCE1C;LCE1A;ASPRV1)
6
4
2
0
height
patient groups
0
5
10
15
−log10(pvalue)


UMAP on top DGE RNAseq
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L.inners
L.inners2
Patho
UMAP2
UMAP1

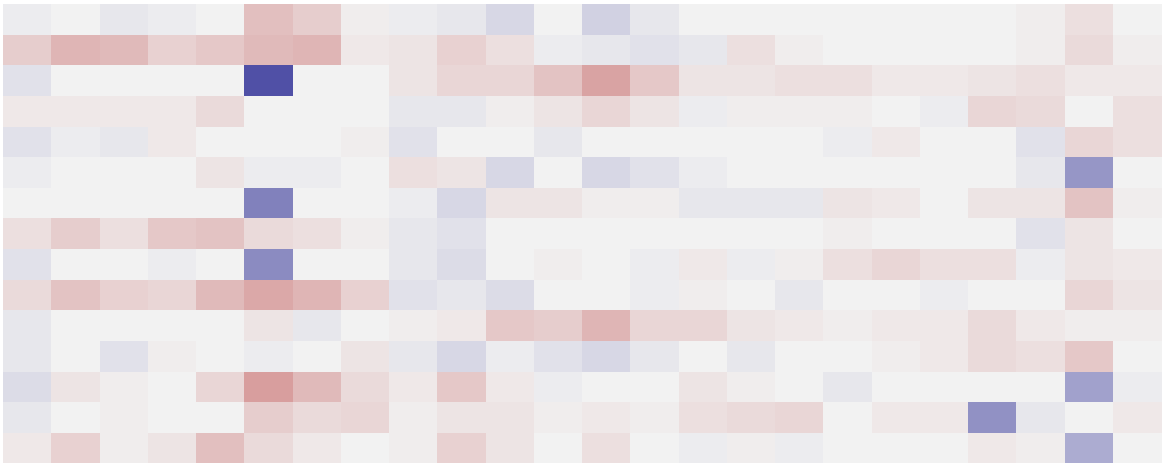
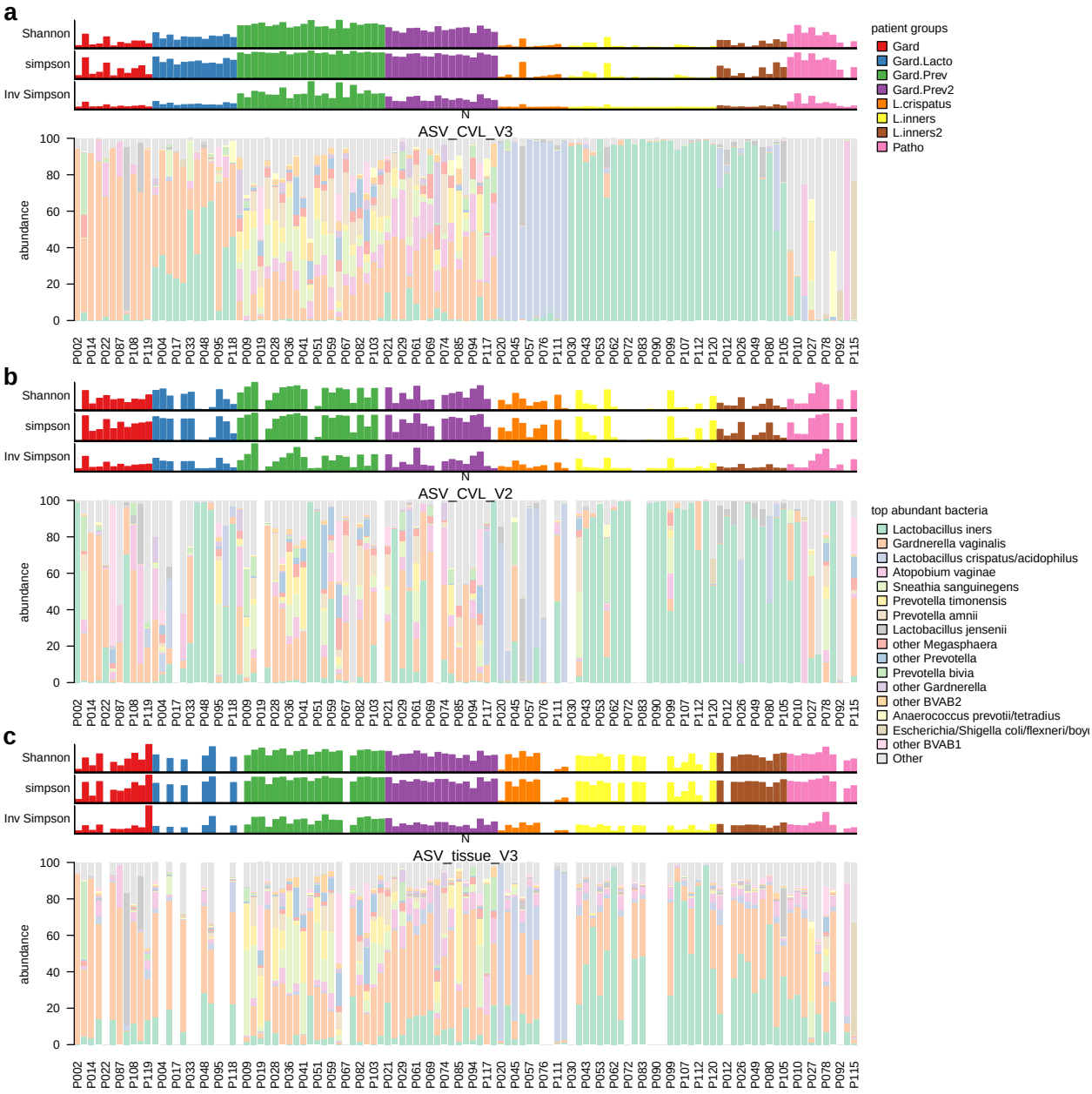


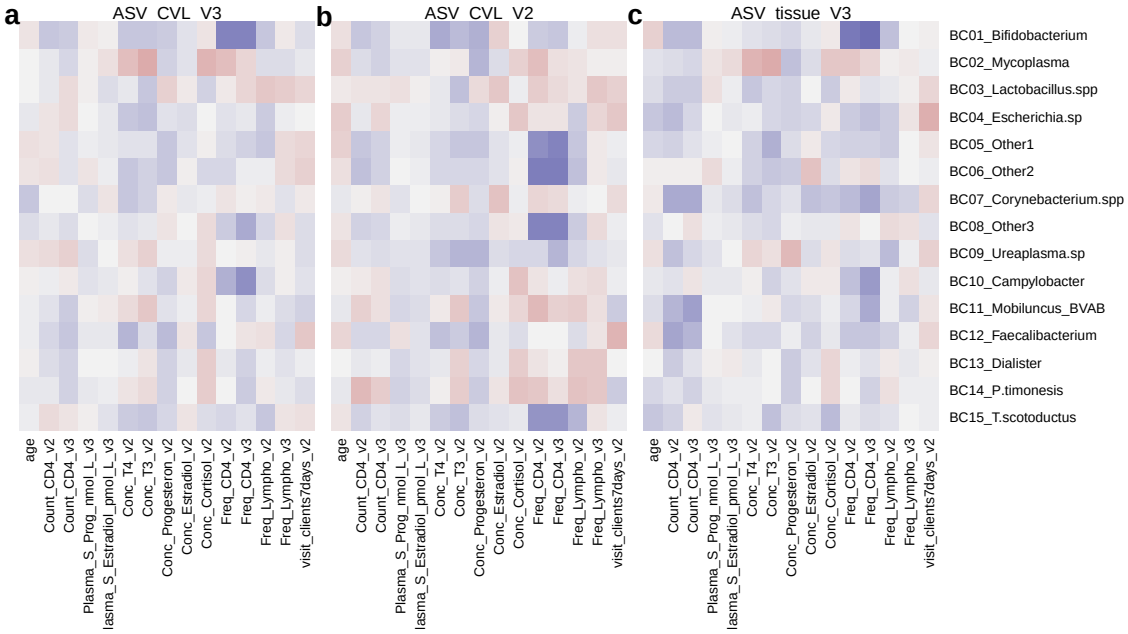
Figure 1. Identification of patient groups. (**a**) Schematic representation of ########## . (**b**) Schematic representation of ########## . (**c**) Schematic representation of ########## . (**d**) Schematic representation of ########## .

9 FIGURES (SUPPL)

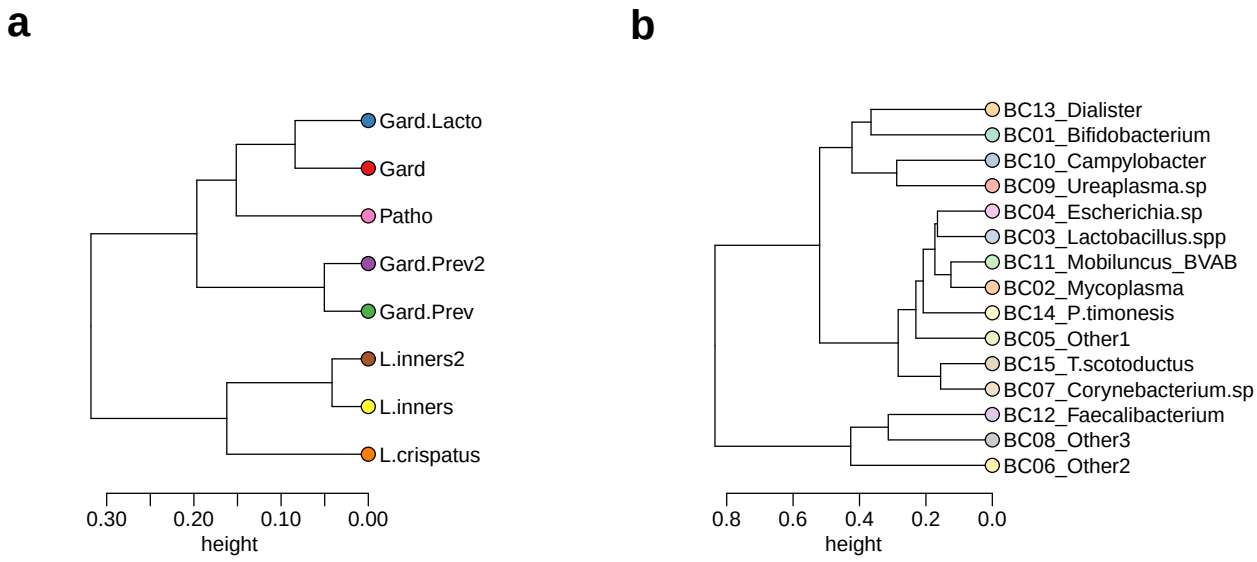
9.1 Figure S1



9.2 Figure S2


a
ASV CVL V3
b
ASV CVL V2
c
ASV tissue V3
BC01_Bifidobacterium
BC02_Mycoplasma
BC03_Lactobacillus.spp
BC04_Escherichia.sp
BC05_Other1
BC06_Other2
BC07_Corynebacterium.spp
BC08_Other3
BC09_Ureaplasma.sp
BC10_Campylobacter
BC11_Mobiluncus_BVAB
BC12_Faecalibacterium
BC13_Dialister
BC14_P.timonesis
BC15_T.scotoductus
age
Count_CD4_v2
Count_CD4_v3
Plasma_S_Prog_nmol_L_v3
lasma_S_Estradiol_pmol_L_v3
Conc_T4_v2
Conc_T3_v2
Conc_Progesteron_v2
Conc_Estradiol_v2
Conc_Cortisol_v2
Freq_CD4_v2
Freq_CD4_v3
Freq_Lympho_v2
Freq_Lympho_v3
visit_clients7days_v2

9.3 Figure S3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Gard
Patho
Gard.Prev2
Gard.Prev
L.inners2
L.inners
L.crispatus
0.30
0.20
0.10
0.00
height
b
BC13_Dialister
BC01_Bifidobacterium
BC10_Campylobacter
BC09_Ureaplasma.sp
BC04_Escherichia.sp
BC03_Lactobacillus.spp
BC11_Mobiluncus_BVAB
BC02_Mycoplasma
BC14_P.timonesis
BC05_Other1
BC15_T.scotoductus
BC07_Corynebacterium.sp
BC12_Faecalibacterium
BC08_Other3
BC06_Other2
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0.6
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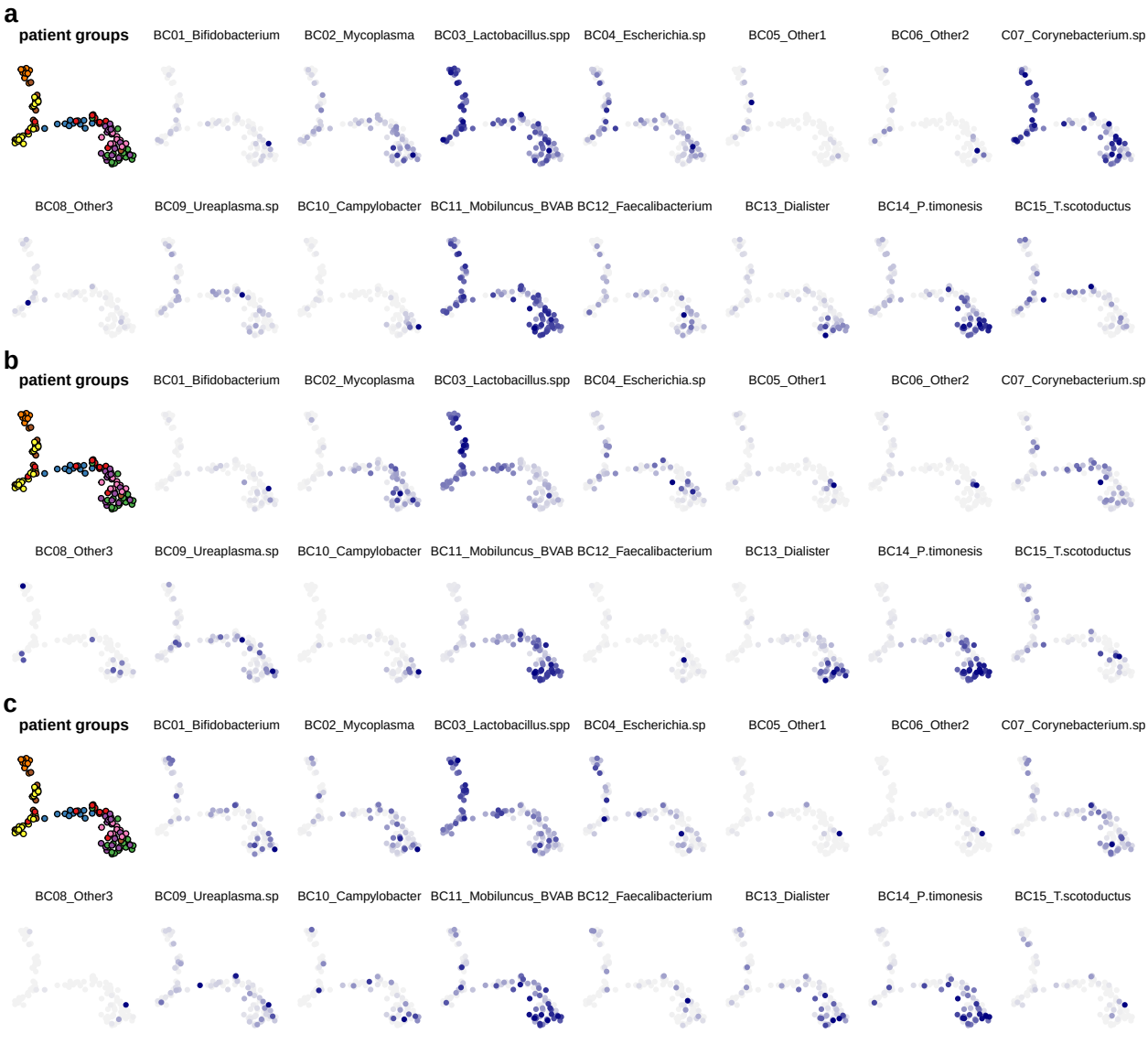
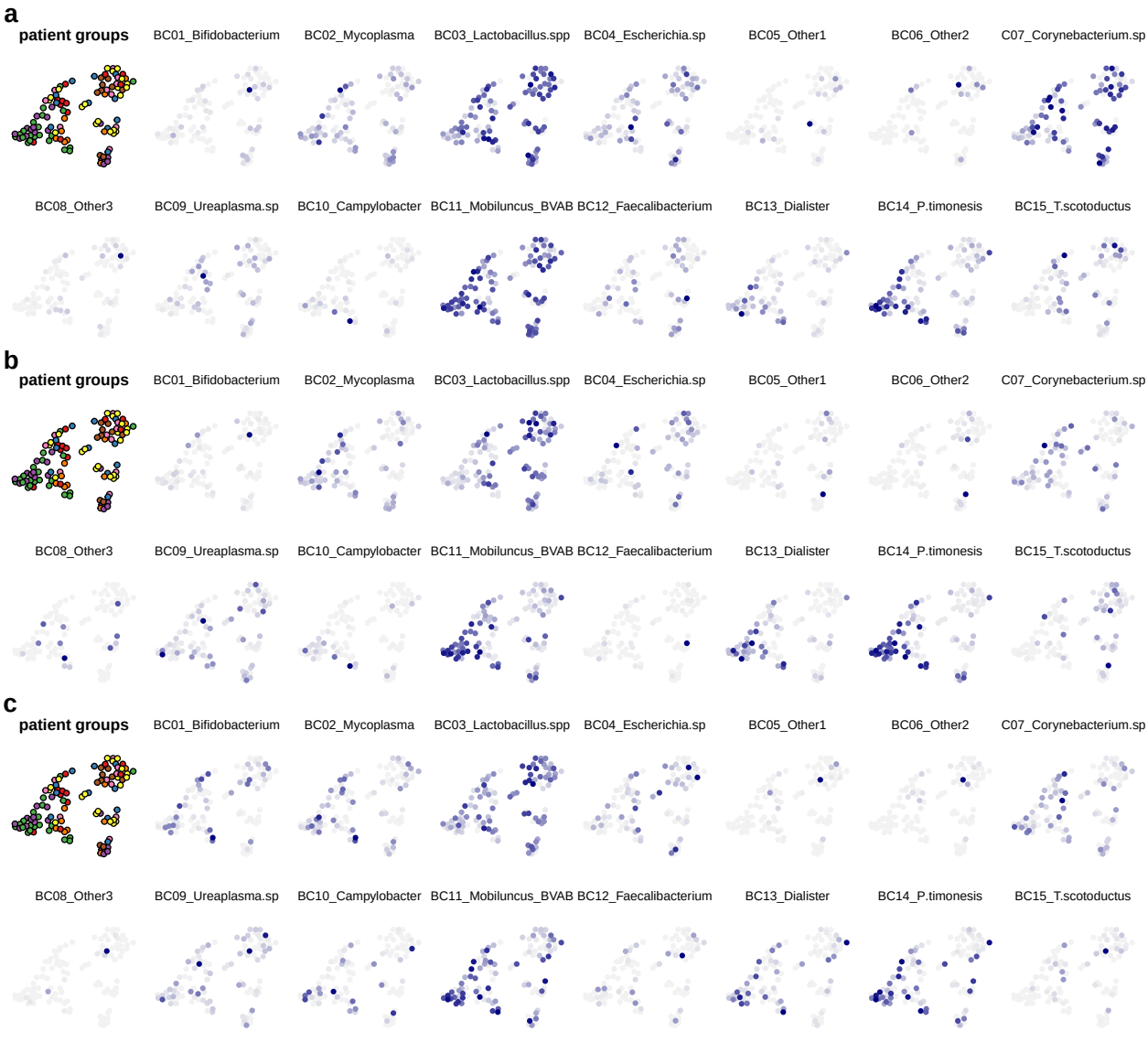
0.2
0.0
height

9.4 Figure S4


a
patient groups
BC01_Bifidobacterium
BC02_Mycoplasma
BC03_Lactobacillus.spp
BC04_Escherichia.sp
BC05_Other1
BC06_Other2
C07_Corynebacterium.sp
BC08_Other3
BC09_Ureaplasma.sp
BC10_Campylobacter
BC11_Mobiluncus_BVAB
BC12_Faecalibacterium
BC13_Dialister
BC14_P.timonesis
BC15_T.scotoductus
b
patient groups
BC01_Bifidobacterium
BC02_Mycoplasma
BC03_Lactobacillus.spp
BC04_Escherichia.sp
BC05_Other1
BC06_Other2
C07_Corynebacterium.sp
BC08_Other3
BC09_Ureaplasma.sp
BC10_Campylobacter
BC11_Mobiluncus_BVAB
BC12_Faecalibacterium
BC13_Dialister
BC14_P.timonesis
BC15_T.scotoductus
c
patient groups
BC01_Bifidobacterium
BC02_Mycoplasma
BC03_Lactobacillus.spp
BC04_Escherichia.sp
BC05_Other1
BC06_Other2
C07_Corynebacterium.sp
BC08_Other3
BC09_Ureaplasma.sp
BC10_Campylobacter
BC11_Mobiluncus_BVAB
BC12_Faecalibacterium
BC13_Dialister
BC14_P.timonesis
BC15_T.scotoductus

9.5 Figure S5


a
patient groups
BC01_Bifidobacterium
BC02_Mycoplasma
BC03_Lactobacillus.spp
BC04_Escherichia.sp
BC05_Other1
BC06_Other2
C07_Corynebacterium.sp
BC08_Other3
BC09_Ureaplasma.sp
BC10_Campylobacter
BC11_Mobiluncus_BVAB
BC12_Faecalibacterium
BC13_Dialister
BC14_P.timonesis
BC15_T.scotoductus
b
patient groups
BC01_Bifidobacterium
BC02_Mycoplasma
BC03_Lactobacillus.spp
BC04_Escherichia.sp
BC05_Other1
BC06_Other2
C07_Corynebacterium.sp
BC08_Other3
BC09_Ureaplasma.sp
BC10_Campylobacter
BC11_Mobiluncus_BVAB
BC12_Faecalibacterium
BC13_Dialister
BC14_P.timonesis
BC15_T.scotoductus
c
patient groups
BC01_Bifidobacterium
BC02_Mycoplasma
BC03_Lactobacillus.spp
BC04_Escherichia.sp
BC05_Other1
BC06_Other2
C07_Corynebacterium.sp
BC08_Other3
BC09_Ureaplasma.sp
BC10_Campylobacter
BC11_Mobiluncus_BVAB
BC12_Faecalibacterium
BC13_Dialister
BC14_P.timonesis
BC15_T.scotoductus

9.6 Figure S6


bac.com.1
HALLMARK_XENOBIOTIC_METABOLISM
HALLMARK_COAGULATION
HALLMARK_CHOLESTEROL_HOMEOSTASIS
HALLMARK_P53_PATHWAY
HALLMARK_GLYCOLYSIS
HALLMARK_ADIPOGENESIS
0.0 0.2 0.4 0.6
bac.com.10
HALLMARK_TGF_BETA_SIGNALING
HALLMARK_NOTCH_SIGNALING
HALLMARK_GLYCOLYSIS
HALLMARK_UV_RESPONSE_DN
HALLMARK_OXIDATIVE_PHOSPHORYLATION
HALLMARK_ANDROGEN_RESPONSE
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HALLMARK_INFLAMMATORY_RESPONSE
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HALLMARK_IL6_JAK_STAT3_SIGNALING
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HALLMARK_KRAS_SIGNALING_DN
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HALLMARK_KRAS_SIGNALING_DN
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HALLMARK_P53_PATHWAY
HALLMARK_ALLOGRAFT_REJECTION
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HALLMARK_XENOBIOTIC_METABOLISM
HALLMARK_TGF_BETA_SIGNALING
HALLMARK_ADIPOGENESIS
HALLMARK_KRAS_SIGNALING_UP
HALLMARK_KRAS_SIGNALING_DN
HALLMARK_BILE_ACID_METABOLISM
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HALLMARK_CHOLESTEROL_HOMEOSTASIS
HALLMARK_UV_RESPONSE_DN
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HALLMARK_IL2_STAT5_SIGNALING
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10 TABLES (MAIN)

10.1 Table 1

10.2 Table 2

196 ### 10.3 Table 3

11 TABLES (SUPPL)

11.1 Table S1

11.2 Table S2

200 ### 11.3 Table S3