Supplemental Material

DNA extraction for tissue samples

All the tissue samples were homogenized using a Fast Prep instrument with lysing matrix Y (MP Biomedicals, CA, USA) after addition of 180µl of ATL buffer (QIAGEN, CA, USA). Bead-beating was performed for one minute at 6.0 m sec-1. The supernatant was then recovered and 200µl of lysozyme (20mg/ml) buffer was added. The samples were then incubated at 37ºC for 30 min. Subsequently, 20-µl of proteinase K (20 mg/ml) was added and samples were further incubated at 56ºC for 30 min. Afterwards, 200-µl lysis buffer AL (QIAGEN) was added and samples were incubated at 56ºC for 30 min. Subsequently, 900-µl of 4M guanidine thiocyanate buffer was added, samples were mixed by inversion. Subsequently, 700-µl cold ethanol was added and the DNA was purified using the DNeasy Blood and Tissue kit (69506, QIAGEN) as per the manufacturer's tissue protocol (DNeasy Blood & Tissue Handbook, version 07/2006). DNA concentration was fluorometrically measured using the QuantiT PicoGreen dsDNA High-Sensitivity Assay (Q-33120, Life Technologies) with a BioTek fluorescence plate reader instrument (Ex.λ/Em.λ of 485/548 nm) using the BioTek Gen5 software package.

Bacterial amplification

Bacterial amplification of all the DNA extracted from samples was validated using primers targeting the V3-V4 hypervariable region of the 16S ribosomal RNA gene with identical sequences designed for Illumina sequencing (Primers: 341F 5'-CCTACGGGAGGCAGCAG-3' and 806R 5'GGACTACHVGGGTWTCTAAT-3') without the addition of Illumina adapters and sample barcode sequencing.

Bacterial mock community

Genomic DNA from ten bacterial strains were used to build a bacterial mock community that was sequenced as a positive control in every MiSeq run performed throughout this research. The ten bacterial strains that comprised this bacterial mock community were as follows: *Cryptobacterium curtum* Oral Taxon 579, Bacteroidales [G-2] sp. Oral Taxon 274, *Capnocytophaga sp.* Oral Taxon 338, *Streptococcus anginosus* Oral Taxon 543, *Peptoniphilus sp.* Oral Taxon 386, *Selenomonas noxia* Oral Taxon 130, *Fusobacterium nucleatum ss polymorphum* Oral Taxon 202, *Aggregatibacter aphrophilus* Oral Taxon 545, and *Pyramidobacter piscolens* Oral Taxon 357. Results for relative abundance of these control samples were consistent, and as expected, across each MiSeq run.

PCR

PCR mixtures of 50-µl contained 10-µl of diluted DNA template, 20-µl of HotMasterMix, 1-µl of each primer (10µM). The cycling conditions consisted of an initial template denaturation of 94ºC for 3 min, followed by 30-cycles of denaturation at 94ºC for 45 sec, annealing at 50ºC for 60 sec, extension at 72ºC for 1.5 min, and a final extension at 72ºC for 10 min. Five-microliters of each PCR product loaded with gel loading dye were run on a 1% agarose gel in 1X Tris-acetate-EDTA (TAE) buffer stained with Sybr Safe DNA and visualized using an Alpha-Innotech instrument equipped with the FluorChem Q imaging software (Ex. λ/Em. λ of 475/537nm).

16S rRNA gene Amplicon Illumina Sequencing

10-50 ng of each metagenomic DNA template was first amplified using the sequencing primers designed to incorporate Illumina adapters and a sample barcode sequence, allowing directional sequencing covering the hypervariable region V3-V4. Primers used were as follows: 341F (AATGATACGGCGACCACCGAGATCTACACTATGGTAATTGT*CCTACGGGAGGCAGCAG*) and 806R (CAAGCAGAAGACGGCATACGAGATN NNNNNNNNNNAGTCAGTCAGCC*GGACTACHVGGGTWTCTAAT*) (sequences of the primers are in italics, and N sequences corresponding to the barcodes). PCR mixtures contained 10-µl of diluted DNA template, 10-µl of HotMaster Taq DNA Polymerase Mix (5 Prime), and 1µl of each primer mix (10 µM). The cycling conditions consisted of an initial denaturation of 94°C for 3 min, followed by 30 cycles of denaturation at 94°C for 45 sec, annealing at 50 °C for 60 sec, extension at 72°C for 1.5 min, and a final extension at 72°C for 10 min.

PCR products were then purified using a magnetic bead capture kit Agencourt Ampure XP purification beads (Beckman Coulter, Brea, CA, USA). Amplicons from each library were quantified and pooled in equimolar concentrations. Pooled libraries were electrophoresed in a 2% agarose gel with gel loading dye and Sybr Safe DNA gel stain. Bands were visualized under under UV transillumination, the band at ~590 bp was excised and DNA was purified using the Minelute Gel Extraction kit (Qiagen). The purified DNA libraries pool was quantitated on an Agilent bioanalyzer DNA 1000 chips (Agilent, Santa Clara, CA, USA) using a Bioanalyzer to verify the DNA size fragment. The final concentration of the library was determined using a SYBR green quantitative PCR (qPCR) assay with primers specific to the Illumina adapters (Kapa Biosystems, Woburn, MA, USA) using a LightCycler 96 Real-Time PCR System Roche Diagnostics GmbH, Mannheim, Germany). The final amplicon pool was denatured at 4 nM before diluting to a final concentration of 12 pM. The libraries pool was then mixed with >5% PhiX Illumina control and were sequenced by 2 x 250 bp paired-end sequencing on the Miseq

platform using MiSeq V2 reagent kit (Illumina, CA, USA), according to the manufacturer's specifications and generating paired-end reads of 250b in length in each direction.

Statistical analysis

In addition, PERMANOVA tests were conducted to compare beta-diversity measures (i.e., Bray-Curtis) between sites (i.e., pancreatic duct, pancreatic tail, pancreatic head, etc.), and sample groups (i.e., disease versus non-diseased, etc.). Briefly, PERMANOVA is an extension of the traditional analysis of variance (ANOVA) to a square matrix of pairwise distances with significance testing performed by permutation [1].

Zero-inflated beta regression models represent a general class of mixture models where the response variable is assumed to have mixed continuous-discrete distribution with probability mass at zero. For our application, a logistic regression component to model OTU presence/absence (p0) and a beta regression component was used to model non-zero microbial abundance (μ). The rationale for selecting this model stems from two distinct characteristics of microbiome data: the preponderance of zero OTU counts across samples [2], commonly referred to as zero-inflation, and the fact that OTU relative abundance measurements are continuous and bounded between 0 and 1, and as a result, are reasonably well approximated with a beta distribution. Zero-inflated beta regression models were fit using the function "BEINF0", as implemented in the R package "gamlss".

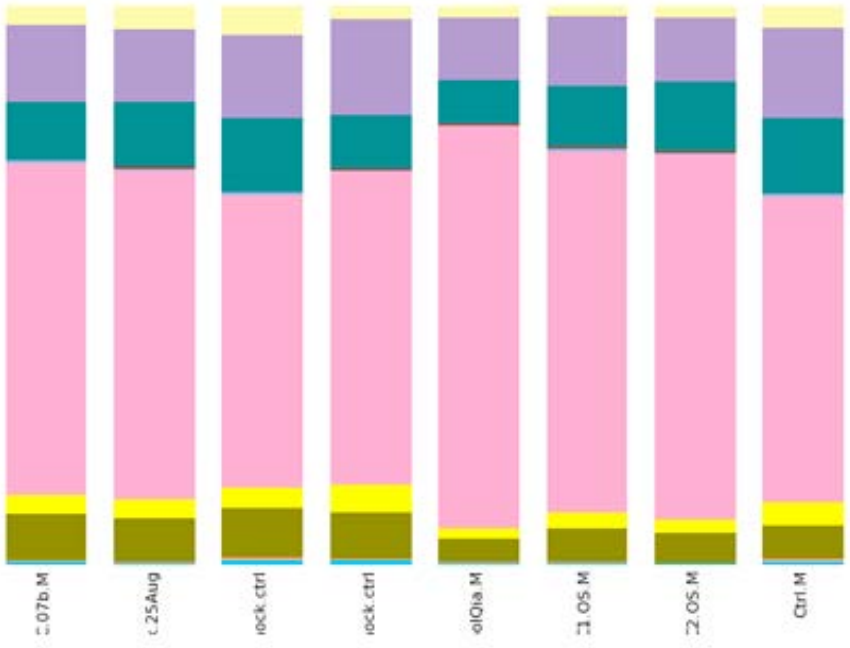
Due to sample size limitations, associations between genus-level relative abundances and demographic/clinical variables were identified marginally by fitting zero-inflated beta regression models regressing on a single predictor. Models were fit only to genera with less than 90% of the counts being 0. As such, the total number of genera that were tested thus varied across the considered model. Models failing to converge due to data sparseness were considered not significant and were not carried forward for subsequent analyses. Associations were identified by conducting likelihood-ratio tests (LRT) and considered potentially meaningful when either the LRT p-value was less than 0.05 or the Akaike Information Criterion (AIC) of the alternative model was smaller when compared to the null model.

We conducted statistical analyses focused on identifying genera for which relative abundance differed significantly between RIH cancer patients and NDRI non-cancer patients across the set of pancreatic sites. Models were fit to the OTU data from the following tissue samples: pancreatic duct, pancreatic head, pancreatic tail, pancreatic tumor, pancreatic normal and duodenum. In order to account for within-subject correlation, a random intercept term for

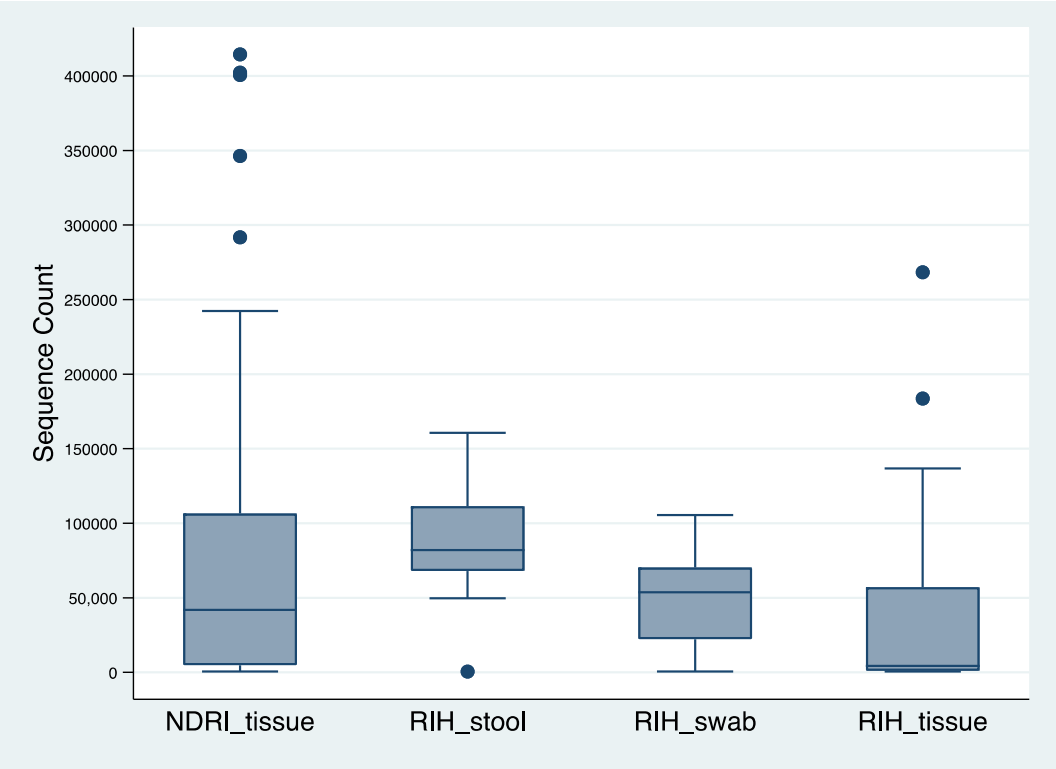
subject IDs was incorporated into the zero-inflated beta regression models. The utilized models also adjusted for age, sex, and log library size as fixed effects. Other multi-level categorical predictors such as sequencing run or body site were not included into the models in order to reduce sparseness and improve convergence behavior. Unfortunately, testing fixed effects in generalized linear mixed models via simple LRTs is known to be inefficient and unreliable for small to moderate sample sizes [3]. To address this issue, permutation based tests were utilized. First, the observed likelihood ratio statistic (LRS) comparing the full against the null model, excluding study ID as covariate, was calculated. The null distribution of the LRS was then estimated by permuting study ID labels across patients. P-values were derived from 500 permutations per genus and adjusting for multiple testing was achieved via the false discovery rate method.

We also considered zero-inflated beta regression to compare relative abundance of bacteria by ICD code to evaluate whether profiles differed across the different types of RIH patients. For the purpose of this analysis, ICD10 codes were grouped into three categories: pancreatic cancer (ICD10 codes C25.0-C25.9), periampullary cancer (ICD10 codes C24.0-C24.1), and other pancreatic conditions (ICD10 codes K86.0-K86.3)(Table 1). We hereafter refer to these categories as C25, C24, and K86, respectively. Two strategies were considered: First, 30 NDRI pancreatic-head samples were compared with 30 RIH tumor-samples and adjusted for age, BMI, sex and sequencing run. The same strategy was also applied to compare the effects of ICD codes in RIH samples from NDRI samples using data from duodenum and pancreatic duct tissue. In the second approach, we restricted the analysis to RIH patients to account for other clinical variables (e.g. prior chemotherapy or use of antibiotics in prior 6 months); covariates that were adjusted for were selected empirically by identifying variables that exhibited an association with at least 30% of the OTUs that were formally tested. Bonferroni corrections were made to adjust for multiple comparisons when interpreting relative mean abundances of genera across the ICD codes; p-values from the Wald-tests for the mean value comparisons for the ICD codes were considered meaningful if they were less than 0.00057 (0.05/88; given that a maximum of 88 genera were tested).

Supplemental Figure 1. Bacterial taxonomy (genera level) for the control samples of bacterial mock communities included in each of the MiSeq runs for this project.



Supplemental Figure 2. Range of sequence counts in all the samples (after rarefaction at 500 counts).



Sample source (n)	**Sequence count: median (Interquartile range)**
NDRI tissue samples (113)	41,930 (4781 - 106,585)
RIH swab samples (57)	53,670 (22,231 - 70,376)
RIH tissue samples (76)	4342 (1025 – 57,130)
RIH stool samples (12)	82,018 (67,934 - 111,447

Supplemental Table 1. Number of samples per anatomical site from the Rhode Island Hospital [RIH] and the National Disease Research Interchange [NDRI].

Source	Anatomical Site	N
RIH	Bile Duct Swab	20
RIH	Duodenum	17
RIH	Jejunum Swab	31
RIH	Normal Pancreas	6
RIH	Pancreas Tumor	31
RIH	Pancreatic Duct	22
RIH	Stomach Swab	6
RIH	Stool	12
NDRI	Duodenum	32
NDRI	Pancreas Head	30
NDRI	Pancreas Tail	19
NDRI	Pancreatic Duct	32
Total		258

Supplemental Table 2. Results (at the species level) from multivariable zero-inflated beta regression models comparing bacteria presence/absence and relative abundance in tissue and swab samples from NDRI and RIH subjects*

Species	Total Read Counts	Non-zero Samples	Estimated Mean Relative Abundance (μ)**			Estimated Proportion of Presence (P1)			Global Perm Test*		
			RIH	NDRI	Wald p-value	RIH	NDRI	Wald p-value	p-value	p-adjusted^	AIC difference
G.multispecies_spp670_3	6160	27	0.0004	< 0.0001	< 0.0001	0.1238	0.0050	0.0001	< 0.0001	< 0.0001	5.32
L. gasseri	526388	120	0.0090	0.0144	0.0328	0.2598	0.8260	< 0.0001	< 0.0001	< 0.0001	21.78
L. salivarius	354859	111	0.0068	0.0202	0.0000	0.2767	0.6752	< 0.0001	< 0.0001	< 0.0001	13.92
S. intermedius	1295	52	0.0003	0.0003	0.2429	0.4586	0.1190	0.0003	< 0.0001	< 0.0001	1.55
S. multispecies_spp573_2	16829	44	0.0021	0.0007	0.0170	0.1662	0.0110	0.0000	< 0.0001	< 0.0001	7.52
L. saburreum	327	25	0.0004	0.0012	0.0026	0.0725	0.0019	0.0001	< 0.0001	< 0.0001	6.24
A. vaginalis	47175	26	0.0009	0.0045	0.0154	0.0107	0.1349	0.0008	< 0.0001	< 0.0001	9.13
P. micra	35977	60	0.0087	0.0047	0.0532	0.4428	0.1040	< 0.0001	< 0.0001	< 0.0001	8.04
F. nucleatum_subsp._vincentii	4538	29	0.0041	0.0048	0.7534	0.1173	0.0150	0.0012	< 0.0001	< 0.0001	2.11
B. wadsworthia	102226	60	0.0070	0.0013	0.0000	0.2000	0.0197	0.0001	< 0.0001	< 0.0001	2.95
A .junii	2735	51	0.0007	0.0002	0.0000	0.3859	0.1411	0.0010	< 0.0001	< 0.0001	8.51
A. rimae	1160	27	0.0012	0.0028	0.0824	0.0525	0.0049	0.0038	0.0020	0.0197	0.06
G. multispecies_spp669_2	43586	95	0.0143	0.0039	0.0000	0.6426	0.3961	0.0035	0.0020	0.0197	5.90
S. gordonii	1470	42	0.0004	0.0004	0.9423	0.4310	0.0884	0.0001	0.0020	0.0197	2.61
S. lactarius	1482	54	0.0004	0.0003	0.0383	0.5216	0.1164	0.0000	0.0020	0.0197	1.40
C. disporicum	261404	88	0.0074	0.0082	0.6160	0.5326	0.2768	0.0055	0.0020	0.0197	4.93
D. pneumosintes	11534	38	0.0012	0.0012	0.9904	0.1523	0.0061	0.0000	0.0020	0.0197	1.71
F. multispecies_spp923_6	1886	24	0.0001	< 0.0001	0.0027	0.0024	0.0001	0.0000	0.0020	0.0197	1.43
F. multispecies_spp930_3	3878	29	0.0003	0.0001	0.0083	0.0934	0.0058	0.0002	0.0020	0.0197	2.37
F. multispecies_spp933_3	75928	63	0.0079	0.0045	0.0532	0.5203	0.1627	0.0001	0.0020	0.0197	2.87
F .multispecies_spp935_4	1898	26	0.0006	0.0001	0.0018	0.0179	0.0003	0.0002	0.0020	0.0197	2.75
K. ascorbata_nov_87.30%	1277	25	0.0020	0.0010	0.1912	0.0851	0.0101	0.0055	0.0020	0.0197	3.87
G. parahaemolysans	10971	33	0.0050	0.0059	0.5264	0.2940	0.0456	0.0006	0.0040	0.0310	0.51
L. fermentum	39573	59	0.0035	0.0070	0.0377	0.0169	0.2266	0.0000	0.0040	0.0310	6.34
S .multispecies_spp386_18	184	38	0.0001	0.0001	0.0023	0.3784	0.0716	0.0007	0.0040	0.0310	1.16
S. multispecies_spp597_2	357	37	0.0001	0.0002	0.3053	0.3223	0.0029	0.0000	0.0040	0.0310	3.30
B. gnavus	112467	62	0.0019	0.0024	0.3974	0.1019	0.3278	0.0018	0.0040	0.0310	1.43
A. variabilis	970	50	0.0008	0.0004	0.0016	0.3482	0.1502	0.0042	0.0040	0.0310	6.60
L. multispecies_spp767_2	73192	57	0.0063	0.0062	0.9679	0.0401	0.2282	0.0001	0.0060	0.0434	5.44

S .multispecies_spp756_2	1332	29	0.0005	0.0009	0.0155	0.2675	0.0595	0.0015	0.0060	0.0434	1.92

**All models are adjusted for age, sex, BMI and log library size. Only bacteria (at species-level) associated with source of samples at p≤0.05 after correcting for multiple comparisons are shown. Permutation testing accounts for within subject correlation via random intercept.*

***Among non-zero samples.*

^Adjusted for multiple testing

Supplemental Table 2 Full OTU

k__Bacteria;p__Firmicutes;c__Bacilli;o__Bacillales;f__NA;g__Gemella;s__multispecies_spp670_3
k__Bacteria;p__Firmicutes;c__Bacilli;o__Lactobacillales;f__Lactobacillaceae;g__Lactobacillus;s__gasseri
k__Bacteria;p__Firmicutes;c__Bacilli;o__Lactobacillales;f__Lactobacillaceae;g__Lactobacillus;s__salivarius
k__Bacteria;p__Firmicutes;c__Bacilli;o__Lactobacillales;f__Streptococcaceae;g__Streptococcus;s__intermedius
k__Bacteria;p__Firmicutes;c__Bacilli;o__Lactobacillales;f__Streptococcaceae;g__Streptococcus;s__multispecies_spp573_2
k__Bacteria;p__Firmicutes;c__Clostridia;o__Clostridiales;f__Lachnospiraceae_[XIV];g__Lachnoanaerobaculum;s__saburreum
k__Bacteria;p__Firmicutes;c__Tissierellia;o__Tissierellales;f__Peptoniphilaceae;g__Anaerococcus;s__vaginalis
k__Bacteria;p__Firmicutes;c__Tissierellia;o__Tissierellales;f__Peptoniphilaceae;g__Parvimonas;s__micra
k__Bacteria;p__Fusobacteria;c__Fusobacteriia;o__Fusobacteriales;f__Fusobacteriaceae;g__Fusobacterium;s__nucleatum_subsp._vincentii
k__Bacteria;p__Proteobacteria;c__Deltaproteobacteria;o__Desulfovibrionales;f__Desulfovibrionaceae;g__Bilophila;s__wadsworthia
k__Bacteria;p__Proteobacteria;c__Gammaproteobacteria;o__Pseudomonadales;f__Moraxellaceae;g__Acinetobacter;s__junii
k__Bacteria;p__Actinobacteria;c__Coriobacteriia;o__Coriobacteriales;f__Coriobacteriaceae;g__Atopobium;s__rimae
k__Bacteria;p__Firmicutes;c__Bacilli;o__Bacillales;f__NA;g__Gemella;s__multispecies_spp669_2
k__Bacteria;p__Firmicutes;c__Bacilli;o__Lactobacillales;f__Streptococcaceae;g__Streptococcus;s__gordonii
k__Bacteria;p__Firmicutes;c__Bacilli;o__Lactobacillales;f__Streptococcaceae;g__Streptococcus;s__lactarius
k__Bacteria;p__Firmicutes;c__Clostridia;o__Clostridiales;f__Clostridiaceae;g__Clostridium;s__disporicum
k__Bacteria;p__Firmicutes;c__Clostridia;o__Clostridiales;f__Veillonellaceae;g__Dialister;s__pneumosintes
k__Bacteria;p__Fusobacteria;c__Fusobacteriia;o__Fusobacteriales;f__Fusobacteriaceae;g__Fusobacterium;s__multispecies_spp923_6
k__Bacteria;p__Fusobacteria;c__Fusobacteriia;o__Fusobacteriales;f__Fusobacteriaceae;g__Fusobacterium;s__multispecies_spp930_3
k__Bacteria;p__Fusobacteria;c__Fusobacteriia;o__Fusobacteriales;f__Fusobacteriaceae;g__Fusobacterium;s__multispecies_spp933_3
k__Bacteria;p__Fusobacteria;c__Fusobacteriia;o__Fusobacteriales;f__Fusobacteriaceae;g__Fusobacterium;s__multispecies_spp935_4
k__Bacteria;p__Proteobacteria;c__Gammaproteobacteria;o__Enterobacteriales;f__Enterobacteriaceae;g__Kluyvera;s__ascorbata_nov_87.30%
k__Bacteria;p__Firmicutes;c__Bacilli;o__Bacillales;f__NA;g__Gemella;s__parahaemolysans
k__Bacteria;p__Firmicutes;c__Bacilli;o__Lactobacillales;f__Lactobacillaceae;g__Lactobacillus;s__fermentum
k__Bacteria;p__Firmicutes;c__Bacilli;o__Lactobacillales;f__Streptococcaceae;g__Streptococcus;s__multispecies_spp386_18
k__Bacteria;p__Firmicutes;c__Bacilli;o__Lactobacillales;f__Streptococcaceae;g__Streptococcus;s__multispecies_spp597_2
k__Bacteria;p__Firmicutes;c__Clostridia;o__Clostridiales;f__Lachnospiraceae;g__Blautia;s__gnavus
k__Bacteria;p__Proteobacteria;c__Gammaproteobacteria;o__Pseudomonadales;f__Moraxellaceae;g__Acinetobacter;s__variabilis
k__Bacteria;p__Firmicutes;c__Bacilli;o__Lactobacillales;f__Lactobacillaceae;g__Lactobacillus;s__multispecies_spp767_2

Supplemental Table 3. Results from zero-inflated beta regression models comparing bacteria presence/absence and relative abundance across subject disease ICD codes*

Genus	Total read counts	Non-zero samples	Estimated Mean Relative Abundance (μ)**				Estimated Proportion of Presence (P1)				p-value	AIC difference	p-adjusted^
			Control (N=29)	C24 (N=7)	C25 (N=16)	K86.2 (N=6)	Control (N=29)	C24 (N=7)	C25 (N=16)	K86.2 (N=6)			
Porphyromonas	7008	15	0.0006	0.0903	0.0006	0.0062	0.3333	0.1429	0.0588	0.5000	0.0000	28.03	0.0000
Peptoclostridium	4137	14	0.0022	0.0010	0.0927	0.0025	0.3667	0.0000	0.0588	0.3333	0.0004	12.40	0.0273
Acinetobacter	7916	43	0.0238	0.0386	0.0733	0.0583	0.5333	1.0000	0.8824	0.8333	0.0007	11.20	0.0454
Kluyvera	2000	15	0.0015	0.0061	0.0087	0.0082	0.0667	0.2857	0.4706	0.5000	0.0030	7.83	0.1841
Lactobacillus	251585	40	0.1540	0.0801	0.1371	0.1007	0.8667	0.5714	0.2941	0.8333	0.0033	7.54	0.2072
Aggregatibacter	591	18	0.0001	0.0002	0.0007	0.0049	0.3333	0.5714	0.1765	0.1667	0.0034	7.48	0.2120
Ralstonia	153	15	0.0024	0.0012	0.0280	0.0047	0.2667	0.0000	0.2353	0.5000	0.0038	7.23	0.2349
Capnocytophaga	316	12	0.0001	0.0002	0.0010	0.0018	0.1667	0.2857	0.1176	0.5000	0.0061	6.06	0.3768
Enterococcus	28254	29	0.0385	0.0429	0.0508	0.0316	0.5333	1.0000	0.1765	0.5000	0.0065	5.91	0.4004
Clostridium	100517	29	0.0659	0.0519	0.0475	0.0521	0.5667	0.8571	0.1176	0.6667	0.0099	4.85	0.6112
Gemella	7769	24	0.0042	0.0107	0.0146	0.0077	0.2667	0.2857	0.5294	0.8333	0.0127	4.21	0.7852
Prevotella	53918	36	0.0241	0.0334	0.0972	0.0453	0.7000	0.7143	0.3529	0.6667	0.0225	2.72	1.0000
Pseudomonas	64128	31	0.0526	0.0684	0.1324	0.2021	0.3667	0.8571	0.6471	0.5000	0.0248	2.47	1.0000
Raoultella	31688	9	0.0212	0.0449	0.0400	0.0028	0.0333	0.5714	0.2353	0.0000	0.0255	2.40	1.0000
Slackia	14667	36	0.1066	0.0491	0.0858	0.1034	0.8000	0.4286	0.4706	0.1667	0.0259	2.36	1.0000
Selenomonas	438	13	0.0002	0.0003	0.0035	0.0005	0.2000	0.4286	0.1176	0.3333	0.0298	1.98	1.0000
Haemophilus	41752	34	0.0469	0.0496	0.0570	0.0745	0.6667	0.7143	0.2353	0.8333	0.0521	0.48	1.0000
Atopobium	5767	15	0.0015	0.0017	0.0068	0.0097	0.3667	0.2857	0.0588	0.1667	0.0602	0.08	1.0000
Neisseria	2253	11	0.0102	0.0066	0.0010	0.0158	0.2000	0.2857	0.0000	0.5000	0.0760	-0.57	1.0000
Bilophila	10685	13	0.0131	0.1220	0.0316	0.0121	0.2000	0.4286	0.1765	0.1667	0.0807	-0.74	1.0000
Streptococcus	354060	59	0.1089	0.2092	0.2472	0.1273	0.9667	1.0000	1.0000	1.0000	0.0837	-0.85	1.0000
Leptotrichia	15419	21	0.0036	0.0058	0.0133	0.0140	0.3667	0.5714	0.1765	0.5000	0.0854	-0.90	1.0000

***** *Only bacteria (at genus-level) associated with ICD code (overall) at p≤0.10 prior to correcting for multiple comparisons are shown. Due to missing BMI on two individuals, numbers are based on 58 tissue samples (for comparability to Table 2 these samples were left out).*

***Among non-zero samples.*
^Adjusted for multiple testing.

Supplementary Table 2. Full OTU

k__Bacteria;p__Bacteroidetes;c__Bacteroides;o__Bacteroidales;f__Porphyromonadaceae;g__Porphyromonas
k__Bacteria;p__Firmicutes;c__Clostridia;o__Clostridiales;f__Peptostreptococcaceae;g__Peptoclostridium
k__Bacteria;p__Proteobacteria;c__Gammaproteobacteria;o__Pseudomonadales;f__Moraxellaceae;g__Acinetobacter
k__Bacteria;p__Proteobacteria;c__Gammaproteobacteria;o__Enterobacteriales;f__Enterobacteriaceae;g__Kluyvera
k__Bacteria;p__Firmicutes;c__Bacilli;o__Lactobacillales;f__Lactobacillaceae;g__Lactobacillus
k__Bacteria;p__Proteobacteria;c__Gammaproteobacteria;o__Pasteurellales;f__Pasteurellaceae;g__Aggregatibacter
k__Bacteria;p__Proteobacteria;c__Betaproteobacteria;o__Burkholderiales;f__Burkholderiaceae;g__Ralstonia
k__Bacteria;p__Bacteroidetes;c__Flavobacteria;o__Flavobacteriales;f__Flavobacteriaceae;g__Capnocytophaga
k__Bacteria;p__Firmicutes;c__Bacilli;o__Lactobacillales;f__Enterococcaceae;g__Enterococcus
k__Bacteria;p__Firmicutes;c__Clostridia;o__Clostridiales;f__Clostridiaceae;g__Clostridium
k__Bacteria;p__Firmicutes;c__Bacilli;o__Bacillales;f__Gemellaceae;g__Gemella
k__Bacteria;p__Bacteroidetes;c__Bacteroides;o__Bacteroidales;f__Prevotellaceae;g__Prevotella
k__Bacteria;p__Proteobacteria;c__Gammaproteobacteria;o__Pseudomonadales;f__Pseudomonadaceae;g__Pseudomonas
k__Bacteria;p__Proteobacteria;c__Gammaproteobacteria;o__Enterobacterales;f__Enterobacteriaceae;g__Raoultella
k__Bacteria;p__Actinobacteria;c__Coriobacteriia;o__Eggerthellales;f__Eggerthellaceae;g__Slackia
k__Bacteria;p__Firmicutes;c__Clostridia;o__Clostridiales;f__Veillonellaceae;g__Selenomonas
k__Bacteria;p__Proteobacteria;c__Gammaproteobacteria;o__Pasteurellales;f__Pasteurellaceae;g__Haemophilus
k__Bacteria;p__Actinobacteria;c__Coriobacteriia;o__Coriobacteriales;f__Atopobiaceae;g__Atopobium
k__Bacteria;p__Proteobacteria;c__Betaproteobacteria;o__Neisseriales;f__Neisseriaceae;g__Neisseria
k__Bacteria;p__Proteobacteria;c__Deltaproteobacteria;o__Desulfovibrionales;f__Desulfovibrionaceae;g__Bilophila
k__Bacteria;p__Firmicutes;c__Bacilli;o__Lactobacillales;f__Streptococcaceae;g__Streptococcus
k__Bacteria;p__Fusobacteria;c__Fusobacteriia;o__Fusobacteriales;f__Leptotrichiaceae;g__Leptotrichia

Supplemental Table 4. Results from multivariable zero-inflated beta regression models comparing bacteria presence/absence and relative abundance across subject disease ICD codes for RIH samples (excluding NDRI samples)*

Genus	Total read counts	Non-zero samples	Estimated Mean Relative Abundance (μ)**			Estimated Proportion of Presence (P1)			p-value	AIC difference	p-adjusted^
			C24 (N=7)	C25 (N=17)	K86.2 (N=6)	C24 (N=7)	C25 (N=17)	K86.2 (N=6)			
Porphyromonas	6553	5	0.0901	0.0004	0.0060	0.1429	0.0588	0.5000	0.0001	16.83	0.0031
Atopobium	984	4	0.0005	0.0052	0.0081	0.2857	0.0588	0.1667	0.0001	15.20	0.0066
Enterococcus	2370	13	0.0247	0.0301	0.0174	1.0000	0.1765	0.5000	0.0016	9.41	0.0916
Dialister	5111	6	0.0702	0.0109	0.0010	0.1429	0.1765	0.3333	0.0044	7.14	0.2523
clostridium	895	12	0.0098	0.0086	0.0099	0.8571	0.1176	0.6667	0.0053	6.72	0.3036
Stomatobaculum	961	8	0.0006	0.0074	0.0045	0.2857	0.1765	0.5000	0.0083	5.71	0.4717
Neisseria	1982	5	0.0025	0.0004	0.0074	0.2857	0.0000	0.5000	0.0186	3.84	1.0000
Lactobacillus	837	14	0.0018	0.0084	0.0031	0.5714	0.2941	0.8333	0.0190	3.79	1.0000
Ralstonia	100	7	0.0022	0.0292	0.0054	0.0000	0.2353	0.5000	0.0204	3.62	1.0000
Aggregatibacter	569	8	0.0003	0.0008	0.0051	0.5714	0.1765	0.1667	0.0260	3.05	1.0000
Mogibacterium	55	4	0.0001	0.0015	0.0003	0.2857	0.0588	0.1667	0.0269	2.97	1.0000
Capnocytophaga	310	7	0.0002	0.0011	0.0019	0.2857	0.1176	0.5000	0.0278	2.89	1.0000
Propionibacterium	5	5	0.0001	0.0004	0.0001	0.2857	0.0588	0.3333	0.0289	2.80	1.0000
Granulicatella	1649	14	0.0014	0.0023	0.0023	0.7143	0.2353	0.8333	0.0414	1.95	1.0000
Megasphaera	1765	6	0.0025	0.0203	0.0035	0.2857	0.0588	0.5000	0.0457	1.70	1.0000

**Only bacteria (at genus-level) associated with ICD code (overall) at p<0.10 before correcting for multiple comparisons are shown; given small numbers, these models are marginal models for the ICD codes without other covariates. Only Porphyromonas remained statistically significant after adjusting for previous chemotherapy and presence of stent.*
***Among non-zero samples.*
^Adjusted for multiple testing.

Supplementary Table 3. Full OTU

k__Bacteria;p__Bacteroidetes;c__Bacteroides;o__Bacteroidales;f__Porphyromonadaceae;g__Porphyromonas
k__Bacteria;p__Actinobacteria;c__Coriobacteriia;o__Coriobacteriales;f__Atopobiaceae;g__Atopobium
k__Bacteria;p__Firmicutes;c__Bacilli;o__Lactobacillales;f__Enterococcaceae;g__Enterococcus
k__Bacteria;p__Firmicutes;c__Clostridia;o__Clostridiales;f__Veillonellaceae;g__Dialister
k__Bacteria;p__Firmicutes;c__Clostridia;o__Clostridiales;f__Clostridiaceae;g__Clostridium
k__Bacteria;p__Firmicutes;c__Clostridia;o__Clostridiales;f__Lachnospiraceae;g__Stomatobaculum
k__Bacteria;p__Proteobacteria;c__Betaproteobacteria;o__Neisseriales;f__Neisseriaceae;g__Neisseria
k__Bacteria;p__Firmicutes;c__Bacilli;o__Lactobacillales;f__Lactobacillaceae;g__Lactobacillus
k__Bacteria;p__Proteobacteria;c__Betaproteobacteria;o__Burkholderiales;f__Burkholderiaceae;g__Ralstonia
k__Bacteria;p__Proteobacteria;c__Gammaproteobacteria;o__Pasteurellales;f__Pasteurellaceae;g__Aggregatibacter
k__Bacteria;p__Firmicutes;c__Clostridia;o__Clostridiales;f__Peptostreptococcaceae_[XI];g__Mogibacterium
k__Bacteria;p__Bacteroidetes;c__Flavobacteria;o__Flavobacteriales;f__Flavobacteriaceae;g__Capnocytophaga
k__Bacteria;p__Actinobacteria;c__Actinobacteria;o__Actinomycetales;f__Propionibacteriaceae;g__Propionibacterium
k__Bacteria;p__Firmicutes;c__Bacilli;o__Lactobacillales;f__Carnobacteriaceae;g__Granulicatella
k__Bacteria;p__Firmicutes;c__Clostridia;o__Clostridiales;f__Veillonellaceae;g__Megasphaera
k__Bacteria;p__Proteobacteria;c__Gammaproteobacteria;o__Pasteurellales;f__Pasteurellaceae;g__Haemophilus
k__Bacteria;p__Firmicutes;c__Clostridia;o__Clostridiales;f__Veillonellaceae;g__Selenomonas
k__Bacteria;p__Actinobacteria;c__Coriobacteriia;o__Eggerthellales;f__Eggerthellaceae;g__Slackia
k__Bacteria;p__Firmicutes;c__Bacilli;o__Bacillales;f__Staphylococcaceae;g__Staphylococcus
k__Bacteria;p__Proteobacteria;c__Gammaproteobacteria;o__Enterobacteriales;f__Enterobacteriaceae;g__Enterobacter

References for supplemental material

1. Anderson MJ. A new method for non-parametric multivariate analysis of variance. Austral Ecology 2001;26(1):32-46.
2. Chen EZ, Li H. A two-part mixed-effects model for analyzing longitudinal microbiome compositional data. Bioinformatics 2016;32(17):2611-7.
3. Bolker BM, Brooks ME, Clark CJ*, et al.* Generalized linear mixed models: a practical guide for ecology and evolution. Trends Ecol Evol 2009;24(3):127-35.