Supplemental Table 1. Patient Characteristics (N=101), related to Fig. 1, Fig. 3, Fig. 4

	N (%)	Median (IQR[a])
Institution		
LBJ[b]	24 (23.8)	
MDACC[c]	77 (76.2)	
Age (years)		45 (38 – 52)
Race		
Asian/Black/Other	13 (12.9)	
Hispanic	45 (44.5)	
White	43 (42.6)	
BMI[d] (kg/m^2)		28.8 (25 – 33.4)
Smoking Status		
Never	62 (61.4)	
Former	29 (28.7)	
Current	10 (9.9)	
Histology		
Non-squamous[e]	21 (20.8)	
Squamous	80 (79.2)	
LVSI		
No	22 (21.8)	
Yes	7 (6.9)	
Unknown	72 (71.3)	
FIGO 2009 Stage[f]		
II-II	54 (53.5)	
III-IV	47 (46.5)	
Grade		
Other/Unknown	18 (17.8)	
1	7 (6.9)	
2	41 (40.6)	
3	35 (34.7)	
HPV Type		
HPV 16/18	63 (62.4)	
Negative/Other	33 (32.7)	
Unknown	5 (4.9)	
Cisplatin Cycles		5 (5 – 6)
Radiation Dose (Gy)		8834 (8169 – 9299)
Antibiotic Use[g]		
No	62 (61.4)	
Yes	38 (37.6)	
Unknown	1 (1.0)	
Nodal Status		
Negative/Unknown	39 (38.6)	
Positive	62 (61.4)	
Tumor Dimension (cm)		5.3 (4 – 6.5)

[a] Interquartile range. [b] Lyndon B. Johnson Hospital, Harris Health System, Houston TX. [c] The University of Texas M.D. Anderson Cancer Center, Houston TX. [d] Body mass index. [e] Adenocarcinoma and adenosquamous carcinoma. [f] The International Federation of Gynecology and Obstetrics. [g] Antibiotic use within 30 days of baseline swab collection extracted from inpatient and outpatient pharmacy and electronic medical record data, antifungals not included.

Supplemental Table 2. Availability of tumor swab samples for 16S sequencing at all timepoints, related to all Figures.

Patient	Baseline	Week 1	Week 3	Week 5	Follow-up
1	✓	✓	✓	X	✓
2	✓	✓	✓	✓	X
3	✓	✓	✓	✓	X
4	✓	✓	✓	✓	X
5	✓	✓	✓	✓	X
6	✓	X	X	X	X
7	✓	✓	✓	✓	X
8	✓	✓	✓	✓	X
9	✓	✓	X	✓	X
10	✓	X	X	✓	X
11	✓	X	X	X	X
12	✓	✓	✓	✓	X
13	✓	✓	✓	✓	X
14	✓	✓	✓	✓	X
15	✓	✓	✓	✓	X
16	✓	✓	✓	✓	X
17	✓	✓	✓	✓	X
18	✓	✓	✓	✓	X
19	✓	✓	X	X	X
20	✓	✓	✓	✓	X
21	✓	X	X	X	X
22	✓	✓	✓	✓	X
23	✓	✓	X	✓	X
24	✓	✓	✓	✓	X
25	✓	X	✓	✓	X
26	✓	X	✓	✓	X
27	✓	X	X	✓	X
28	✓	✓	✓	✓	X
29	✓	✓	✓	✓	X
30	✓	X	✓	✓	X
31	✓	✓	✓	X	✓
32	✓	✓	✓	✓	✓
33	✓	✓	X	✓	✓
34	✓	✓	✓	✓	✓
35	✓	✓	✓	✓	✓
36	✓	✓	X	X	✓
37	✓	✓	✓	✓	✓
38	✓	X	X	✓	X
39	X	✓	✓	✓	X

40	✓	✓	✓	X	X
41	X	✓	X	✓	X
42	✓	✓	✓	✓	✓
43	✓	✓	✓	✓	✓
44	✓	X	✓	✓	X
45	✓	✓	✓	✓	✓
46	✓	✓	✓	✓	✓
47	✓	✓	✓	✓	✓
48	✓	X	X	X	✓
49	✓	X	X	✓	X
50	X	✓	✓	✓	✓
51	✓	X	X	✓	✓
52	✓	✓	✓	✓	X
53	✓	✓	✓	✓	X
54	✓	✓	✓	✓	X
55	✓	X	X	X	X
56	✓	✓	✓	✓	X
57	X	✓	✓	✓	X
58	✓	✓	✓	✓	✓
59	✓	✓	✓	✓	✓
60	✓	✓	✓	✓	✓
61	✓	✓	✓	X	✓
62	✓	X	X	✓	✓
63	✓	✓	X	X	✓
64	✓	✓	X	X	X
65	✓	X	✓	✓	X
66	✓	X	X	✓	X
67	✓	✓	X	✓	X
68	✓	✓	✓	✓	X
69	✓	✓	X	X	X
70	✓	X	X	X	X
71	✓	✓	✓	X	X
72	✓	✓	✓	✓	X
73	✓	X	X	✓	X
74	✓	X	X	X	X
75	✓	X	X	X	X
76	✓	X	X	X	X
77	✓	X	✓	✓	X
78	✓	X	✓	✓	X
79	✓	X	X	X	X
80	✓	X	✓	✓	X
81	✓	X	✓	X	✓

82	✓	✓	✓	✓	✓
83	✓	✓	✓	✓	✓
84	✓	✓	✓	✓	X
85	✓	✓	✓	✓	✓
86	✓	X	X	✓	X
87	✓	✓	✓	X	✓
88	✓	X	✓	✓	X
89	✓	X	X	✓	X
90	✓	X	X	✓	X
91	✓	✓	X	✓	✓
92	✓	✓	✓	✓	✓
93	✓	X	✓	✓	X
94	✓	✓	X	✓	X
95	✓	✓	✓	✓	X
96	✓	X	X	✓	X
97	X	✓	✓	✓	X
98	✓	✓	✓	✓	X
99	✓	✓	✓	✓	✓
100	✓	✓	✓	✓	X
101	✓	✓	✓	✓	X

Supplemental Table 3. Univariate Cox proportional hazard survival analysis for other baseline tumor and gut microbiome metrics in all patients with baseline samples available (N=96), related to Figures 1 and 2.

		Recurrence-Free Survival		Overall Survival	
	Type	**HR (95%CI)**	**pval**	**HR (95%CI)**	**pval**
Faith's PD[a]	Tumor	0.97 (0.77-1.22)	0.80	0.97 (0.70-0.36)	0.88
Fisher's Alpha	Tumor	1.00 (0.92-1.09)	0.99	1.00 (1.00-1.00)	1
Observed Features	Tumor	1.00 (0.98-1.01)	0.73	1.00 (0.98-1.02)	0.90
Pielou's Evenness	Tumor	0.80 (0.13-4.96)	0.81	0.77 (0.06-10.54)	0.85
Shannon Diversity	Tumor	0.98 (0.76-1.28)	0.91	0.99 (0.68-1.46)	0.98
Simpson's Evenness	Tumor	0.69 (0.04-13.46)	0.81	1.88 (0.04-85.00)	0.75
Simpson Diversity	Tumor	1.00 (0.22-4.50)	1.00	1.03 (0.12-9.11)	0.98
Faith's PD	Gut	1.01 (0.89-1.15)	0.88	0.89 (0.72-1.09)	0.26
Fisher's Alpha	Gut	1.00 (0.96-1.04)	0.95	0.98 (0.91-1.05)	0.57
Observed Features	Gut	1.00 (0.99-1.01)	0.72	1.00 (0.98-1.01)	0.47
Pielou's Evenness	Gut	0.04 (0.0004-4.21)	0.18	0.001 (1.83E-06 -0.61)	**0.03[c]**
Shannon Diversity	Gut	0.80 (0.52-1.24)	0.32	0.57 (0.29-1.10)	0.09
Simpson's Evenness	Gut	0.02 (2.81E-06 -161.93)	0.40	2.3E-07 (7.5E-14 -0.73)	**0.04**
Simpson Diversity	Gut	0.003 (1.01E-05 -0.99)	**0.049**	6.5E-05 (2.87E-08 -0.15)	**0.01**
Prevotella	Tumor	1.04 (0.11-9.89)	0.97	1.43 (0.06-36.54)	0.83
Porphyromonas	Tumor	1.06 (0.04-29.93)	0.97	0.33 (0.001-95.83)	0.70
Gammaproteobacteria	Tumor	2.24E-05 (5.4E-12-92.32)	0.17	0.80 (0.001-949.69)	0.95
Actinobacteria	Tumor	0.03 (0.00-1.82)	0.09	1.47 (0.05-39.84)	0.82
Proteobacteria	Tumor	0.003 (1.6E-06 -6.94)	0.14	0.15 (0.0001-196.16)	0.61
Gardnerella vaginalis	Tumor	0.19 (0.01-5.68)	0.34	1.42 (0.05-40.17)	0.84
Prevotella bivia	Tumor	0.76 (0.04-16.09)	0.86	0.01 (5.87E-07 -110.07)	0.32
Atopobium vaginae	Tumor	0.01 (1.65E-08 -59968.67)	0.49	308.96 (0.002-5.68E07)	0.35
Escherichia shigella	Gut	23.06 (0.12-4272.69)	0.24	10.24 (0.01-12209.87)	0.52

[a]Phylogenetic diversity [b]bold text denotes p value < 0.05.

Supplemental Figure 1. Other tumor microbiome features in pilot cohort are not associated with response or survival, related to Figure 1.

A. Kaplan-Meier curves for recurrence free survival stratified by baseline presence (N=38) or absence (N=3) of tumoral Proteobacteria in the initial cohort. Log-rank p-value reported.

B. Kaplan-Meier curves for recurrence free survival stratified by baseline presence (N=23) or absence (N=18) of tumoral Gammaproteobacteria in the initial cohort. Log-rank p-value reported.

C. Kaplan-Meier curves for recurrence free survival stratified by baseline presence (N=36) or absence (N=5) of tumoral Actinobacteria in the initial cohort. Log-rank p-value reported.

D. 16S Baseline tumor Simpson Diversity Index by response (Non-responders [N=12] vs. Responders [N=31]) in the initial cohort. Comparison was made using a Wilcoxon Rank Sum test.

E. 16S Baseline tumor Pielou's Evenness Index by response (Non-responders [N=12] vs. Responders [N=31]) in the initial cohort. Comparison was made using a Wilcoxon Rank Sum test.

F. 16S Baseline tumor Observed Features by response (Non-responders [N=12] vs. Responders [N=31]) in the initial cohort. Comparison was made using a Wilcoxon Rank Sum test.

G. 16S Baseline tumor Faith's Phylogenetic Diversity (PD) by response (Non-responders [N=12] vs. Responders [N=31]) in the initial cohort. Comparison was made using a Wilcoxon Rank Sum test.

H. 16S Baseline tumor Fisher's Alpha by response (Non-responders [N=12] vs. Responders [N=31]) in the initial cohort. Comparison was made using a Wilcoxon Rank Sum test.

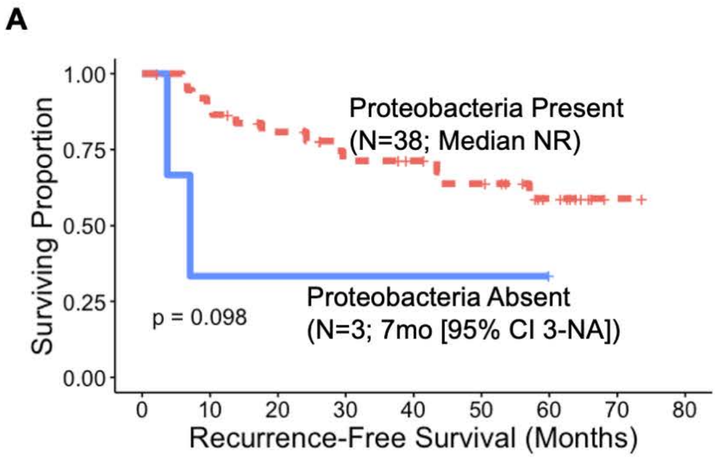
I. Forest plot of a univariate cox proportional hazard model for recurrence-free survival with 16S baseline tumor Simpson Diversity Index (N=41) in the initial cohort.

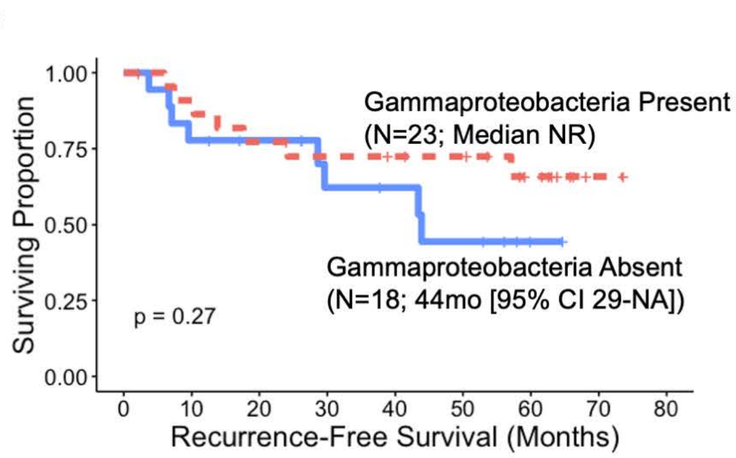
J. Forest plot of a univariate cox proportional hazard model for recurrence-free survival with 16S baseline tumor Pielou's Evenness Index (N=41) in the initial cohort.

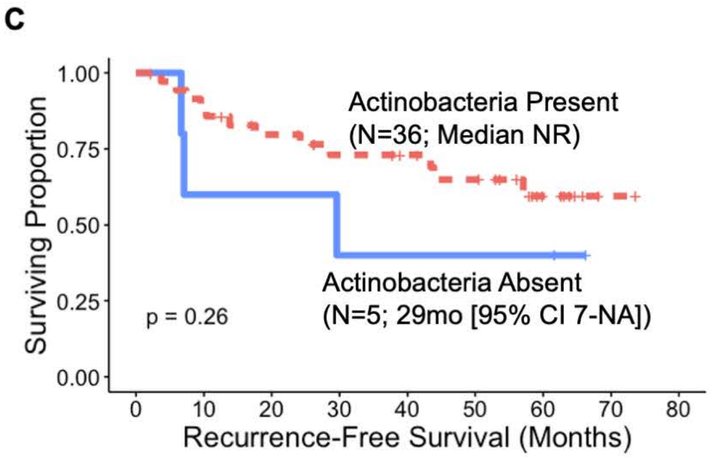
K. Forest plot of a univariate cox proportional hazard model for recurrence-free survival with 16S baseline tumor Observed Features (N=41) in the initial cohort.

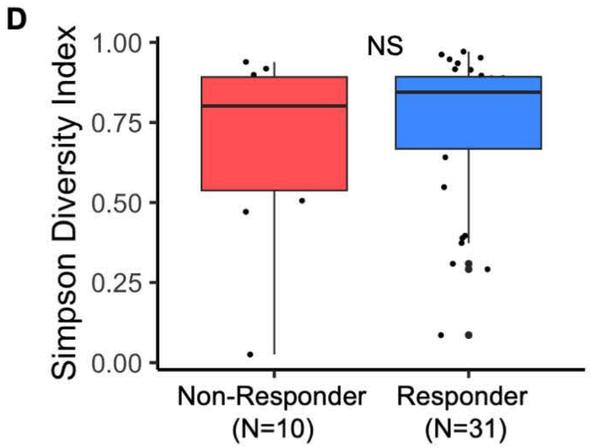
L. Forest plot of a univariate cox proportional hazard model for recurrence-free survival with 16S baseline tumor Faith's Phylogenetic Diversity (PD) (N=41) in the initial cohort.

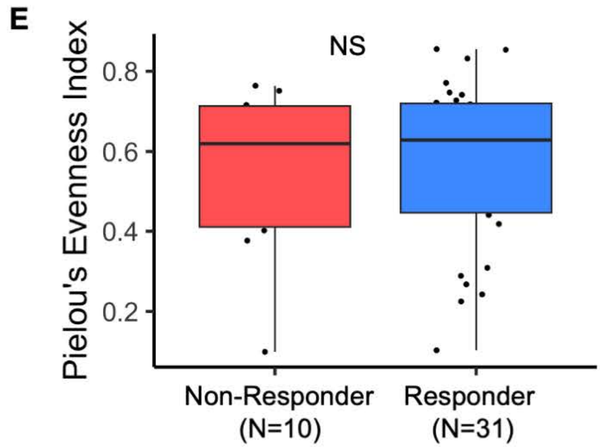
M. Forest plot of a univariate cox proportional hazard model for recurrence-free survival with 16S baseline Fisher's Alpha (N=41) in the initial cohort.

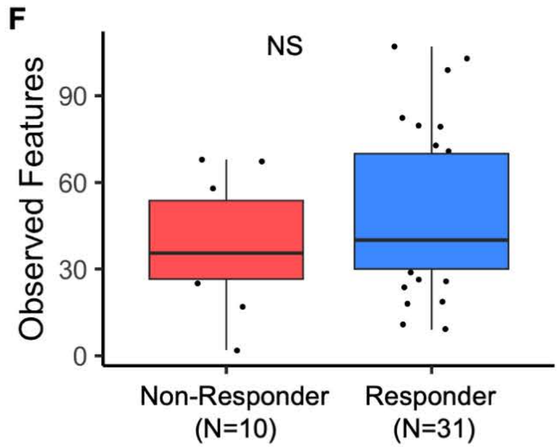

A
Surviving Proportion
1.00
0.75
0.50
0.25
0.00
Proteobacteria Present
(N=38; Median NR)
p = 0.098
Proteobacteria Absent
(N=3; 7mo [95% CI 3-NA])
0 10 20 30 40 50 60 70 80
Recurrence-Free Survival (Months)

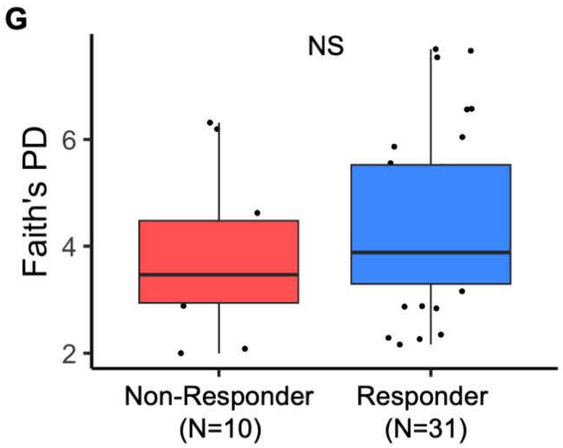

B
Surviving Proportion
1.00
0.75
0.50
0.25
0.00
Gammaproteobacteria Present
(N=23; Median NR)
p = 0.27
Gammaproteobacteria Absent
(N=18; 44mo [95% CI 29-NA])
0 10 20 30 40 50 60 70 80
Recurrence-Free Survival (Months)

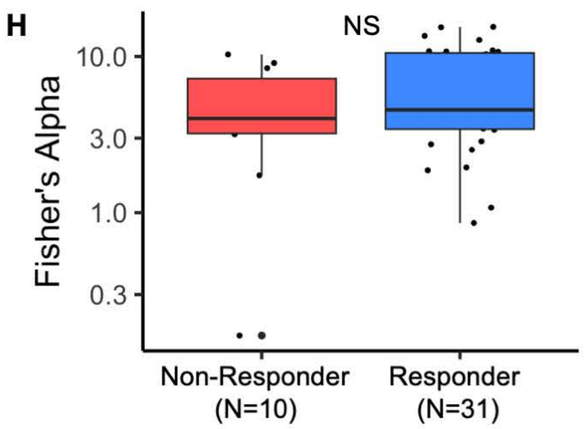

C
Surviving Proportion
1.00
0.75
0.50
0.25
0.00
Actinobacteria Present
(N=36; Median NR)
p = 0.26
Actinobacteria Absent
(N=5; 29mo [95% CI 7-NA])
0 10 20 30 40 50 60 70 80
Recurrence-Free Survival (Months)

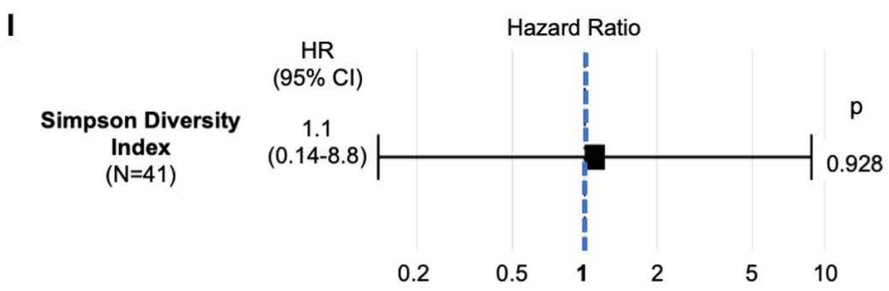

D
Simpson Diversity Index
1.00
0.75
0.50
0.25
0.00
NS
Non-Responder
(N=10)
Responder
(N=31)

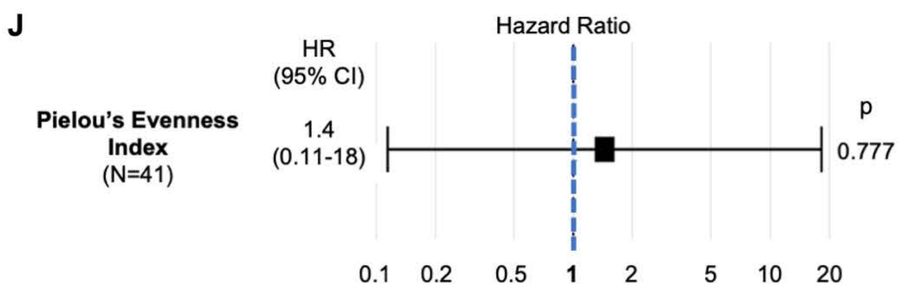

E
Pielou's Evenness Index
0.8
0.6
0.4
0.2
NS
Non-Responder
(N=10)
Responder
(N=31)

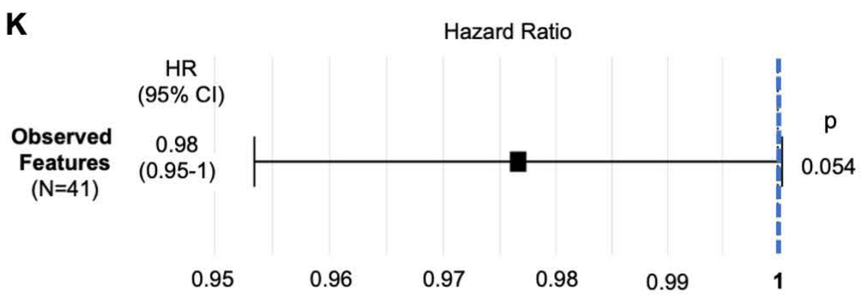

F
Observed Features
90
60
30
0
NS
Non-Responder
(N=10)
Responder
(N=31)

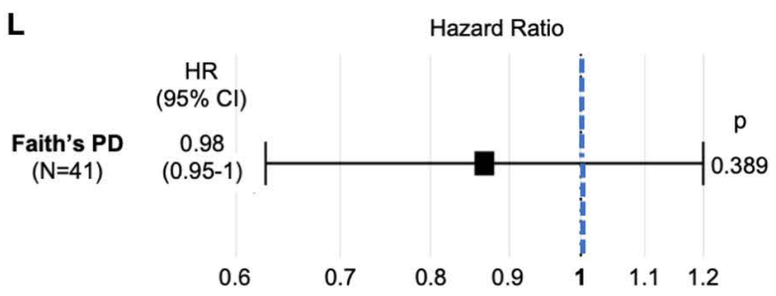

G
Faith's PD
6
4
2
NS
Non-Responder
(N=10)
Responder
(N=31)

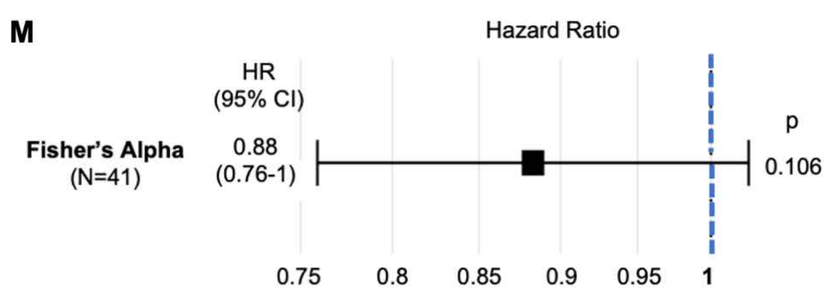

H
Fisher's Alpha
10.0
3.0
1.0
0.3
NS
Non-Responder
(N=10)
Responder
(N=31)


I
Hazard Ratio
HR
(95% CI)
Simpson Diversity Index
(N=41)
1.1
(0.14-8.8)
p
0.928
0.2 0.5 1 2 5 10


J
Hazard Ratio
HR
(95% CI)
Pielou's Evenness Index
(N=41)
1.4
(0.11-18)
p
0.777
0.1 0.2 0.5 1 2 5 10 20


K
Hazard Ratio
HR
(95% CI)
Observed Features
(N=41)
0.98
(0.95-1)
p
0.054
0.95 0.96 0.97 0.98 0.99 1


L
Hazard Ratio
HR
(95% CI)
Faith's PD
(N=41)
0.98
(0.95-1)
p
0.389
0.6 0.7 0.8 0.9 1 1.1 1.2


M
Hazard Ratio
HR
(95% CI)
Fisher's Alpha
(N=41)
0.88
(0.76-1)
p
0.106
0.75 0.8 0.85 0.9 0.95 1

Supplemental Figure 2. Tumor microbiome metrics do not change significantly over time and there is no bacterial, fungal or viral surrogate for *L. iners,* related to Figure 1.

A. Box plot of Simpson's Diversity Index during CRT in tumor samples. Comparisons were made using a paired t-test to compare week 1 (N=68), week 3 (N=66), week 5 (N=78), and follow-up (N=30) timepoints to baseline (N=96). Asterisks denote a significant p-value (<0.05).

B. Box plot of Pielou's Evenness Index during CRT in tumor samples. Comparisons were made using a paired t-test to compare week 1 (N=68), week 3 (N=66), week 5 (N=78), and follow-up (N=30) timepoints to baseline (N=96). Asterisks denote a significant p-value (<0.05).

C. Box plot of Observed Features during CRT in tumor samples. Comparisons were made using a paired t-test to compare week 1 (N=68), week 3 (N=66), week 5 (N=78), and follow-up (N=30) timepoints to baseline (N=96). Asterisks denote a significant p-value (<0.05).

D. Box plot of Faith's Phylogenetic Diversity (PD) during CRT in tumor samples. Comparisons were made using a paired t-test to compare week 1 (N=68), week 3 (N=66), week 5 (N=78), and follow-up (N=30) timepoints to baseline (N=96). Asterisks denote a significant p-value (<0.05).

E. Box plot of Firsher's Alpha during CRT in tumor samples. Comparisons were made using a paired t-test to compare week 1 (N=68), week 3 (N=66), week 5 (N=78), and follow-up (N=30) timepoints to baseline (N=96). Asterisks denote a significant p-value (<0.05).

F. Heatmap of unsupervised hierarchical clustering of the top 25 species in baseline samples. Blue color represents low relative counts of a species while red indicates a high relative count.

G. Box plot of relative counts of *Gardnerella vaginalis* during CRT in tumor samples. Comparisons were made using a paired t-test to compare week 1 (N=68), week 3 (N=66), week 5 (N=78), and follow-up (N=30) timepoints to baseline (N=96).

H. Box plot of relative counts of *Prevotella bivia* during CRT in tumor samples. Comparisons were made using a paired t-test to compare week 1 (N=68), week 3 (N=66), week 5 (N=78), and follow-up (N=30) timepoints to baseline (N=96).

I. Box plot of relative counts of *Atopobium vaginae* during CRT in tumor samples. Comparisons were made using a paired t-test to compare week 1 (N=68), week 3 (N=66), week 5 (N=78), and follow-up (N=30) timepoints to baseline (N=96).

J. Kaplan-Meier analysis for recurrence free survival stratified by baseline presence (N=55) or absence (N=41) of tumoral *Gardnerella vaginalis*. Log-rank p-value reported.

K. Kaplan-Meier analysis for recurrence free survival stratified by baseline presence (N=45) or absence (N=50) of tumoral *Prevotella bivia*. Log-rank p-value reported.

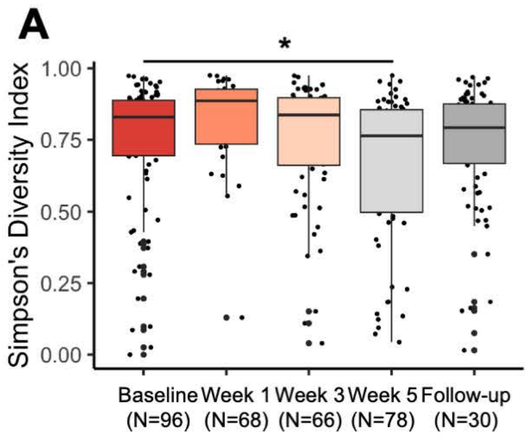
L. Kaplan-Meier analysis for recurrence free survival stratified by baseline presence (N=34) or absence (N=62) of tumoral *Atopobium vaginae*. Log-rank p-value reported.

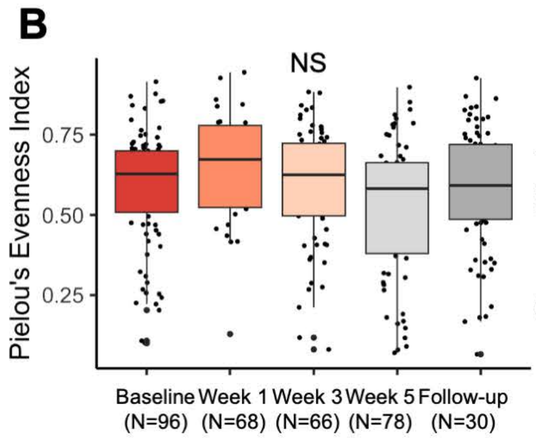
M. Bar plot of baseline fungi reads per million (log normalized) by baseline *L. iners* status (Absent [N=69] vs. Present [N=64]). Comparison was made using an independent t-test.

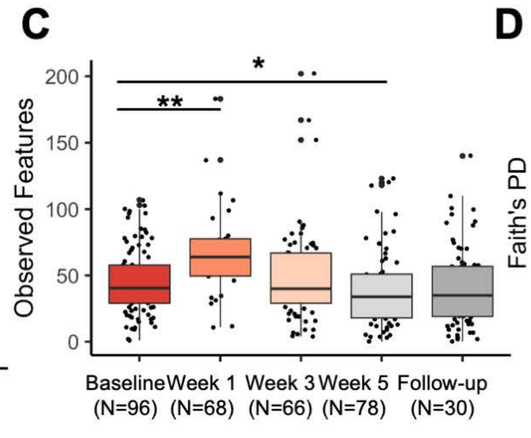
N. Bar plot of baseline fungi reads per million (log normalized) by response (Responders [N=73] vs. Non-responders [N=23]). Comparison was made using an independent t-test.

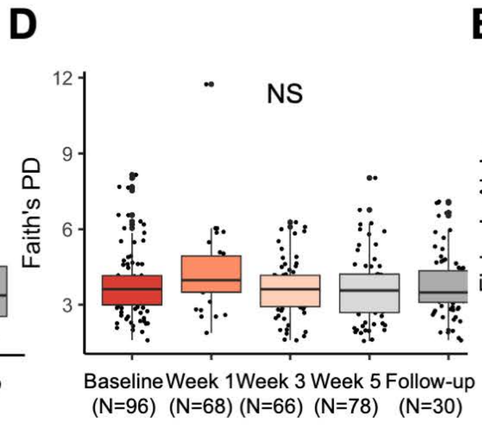
O. Bar plot of baseline total viral reads per million (log normalized) by baseline *L. iners* status (Absent [N=49] vs. Present [N=4]). Comparison was made using an independent t-test.

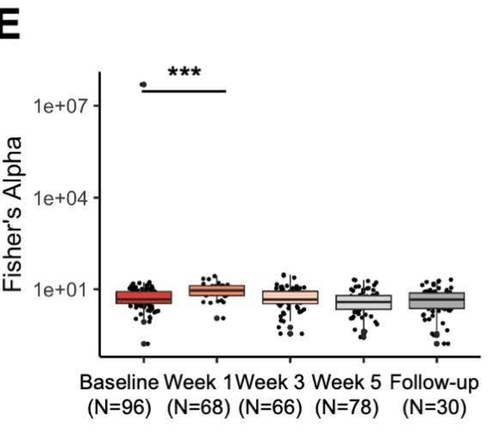
P. Bar plot of baseline total viral reads per million (log normalized) by response (Responders [N=73] vs. Non-responders [N=23]). Comparison was made using an independent t-test.

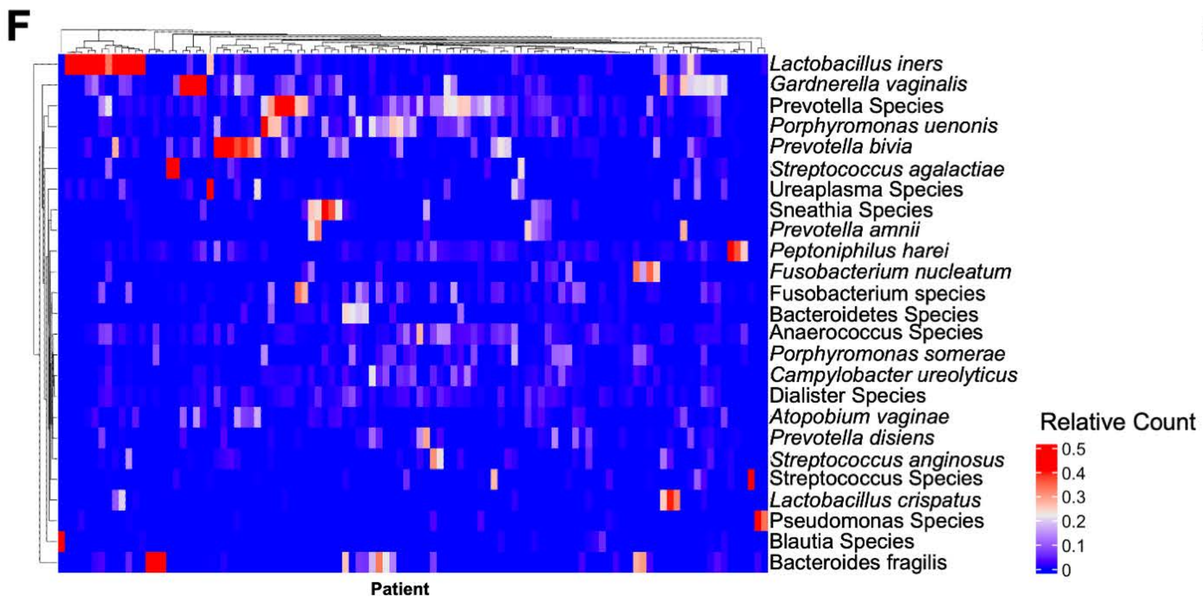

A
Simpson's Diversity Index
1.00
0.75
0.50
0.25
0.00
*
Baseline (N=96)
Week 1 (N=68)
Week 3 (N=66)
Week 5 (N=78)
Follow-up (N=30)

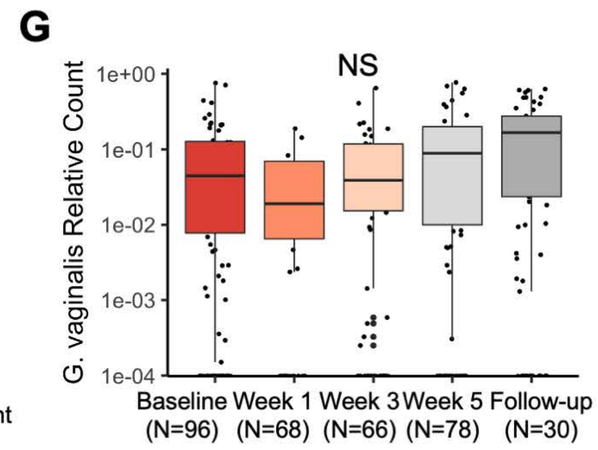

B
Pielou's Evenness Index
0.75
0.50
0.25
NS
Baseline (N=96)
Week 1 (N=68)
Week 3 (N=66)
Week 5 (N=78)
Follow-up (N=30)

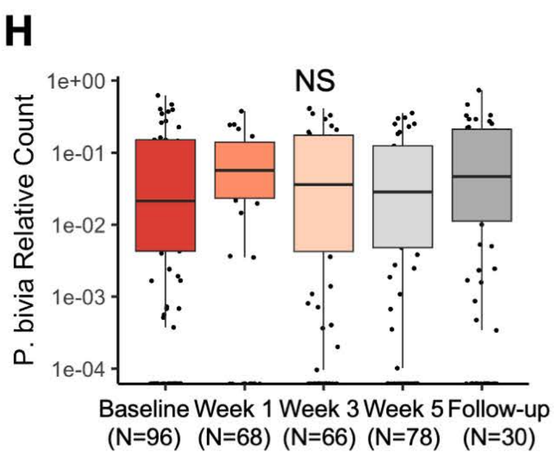

C
Observed Features
200
150
100
50
0
*
**
Baseline (N=96)
Week 1 (N=68)
Week 3 (N=66)
Week 5 (N=78)
Follow-up (N=30)

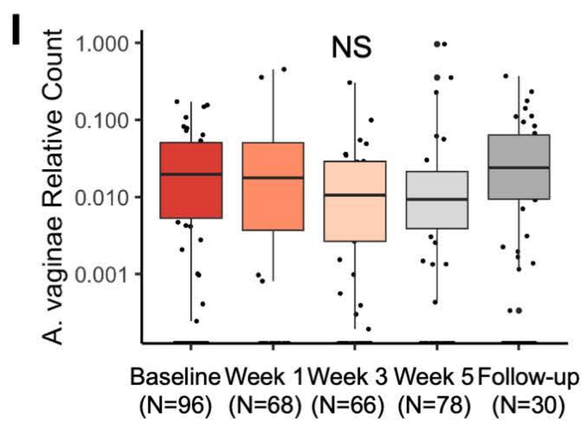

D
Faith's PD
12
9
6
3
NS
Baseline (N=96)
Week 1 (N=68)
Week 3 (N=66)
Week 5 (N=78)
Follow-up (N=30)

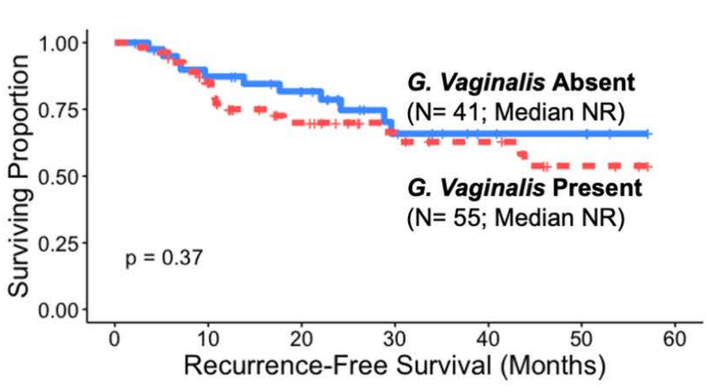

E
Fisher's Alpha
1e+07
1e+04
1e+01
***
Baseline (N=96)
Week 1 (N=68)
Week 3 (N=66)
Week 5 (N=78)
Follow-up (N=30)

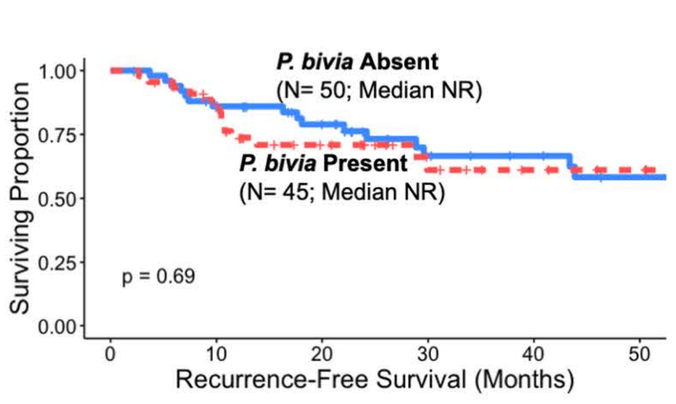

F
Lactobacillus iners
Gardnerella vaginalis
Prevotella Species
Porphyromonas uenonis
Prevotella bivia
Streptococcus agalactiae
Ureaplasma Species
Sneathia Species
Prevotella amnii
Peptoniphilus harei
Fusobacterium nucleatum
Fusobacterium species
Bacteroidetes Species
Anaerococcus Species
Porphyromonas somerae
Campylobacter ureolyticus
Dialister Species
Atopobium vaginae
Prevotella disiens
Streptococcus anginosus
Streptococcus Species
Lactobacillus crispatus
Pseudomonas Species
Blautia Species
Bacteroides fragilis
Patient
Relative Count
0.5
0.4
0.3
0.2
0.1
0

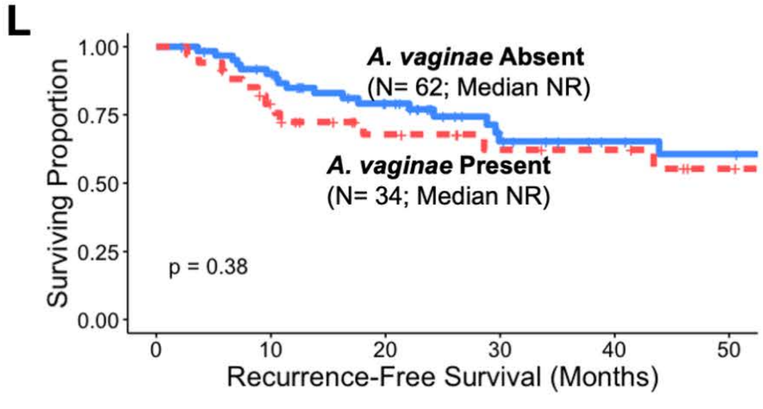

G
G. vaginalis Relative Count
1e+00
1e-01
1e-02
1e-03
1e-04
NS
Baseline (N=96)
Week 1 (N=68)
Week 3 (N=66)
Week 5 (N=78)
Follow-up (N=30)

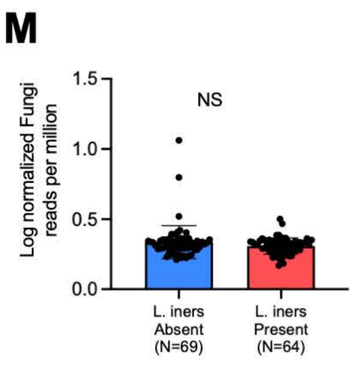

H
P. bivia Relative Count
1e+00
1e-01
1e-02
1e-03
1e-04
NS
Baseline (N=96)
Week 1 (N=68)
Week 3 (N=66)
Week 5 (N=78)
Follow-up (N=30)

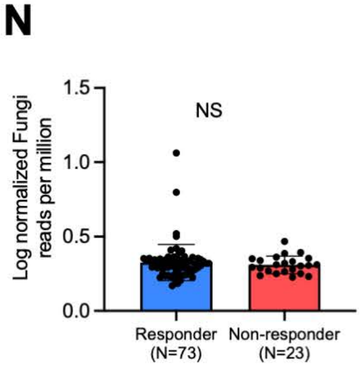

I
A. vaginae Relative Count
1.000
0.100
0.010
0.001
NS
Baseline (N=96)
Week 1 (N=68)
Week 3 (N=66)
Week 5 (N=78)
Follow-up (N=30)

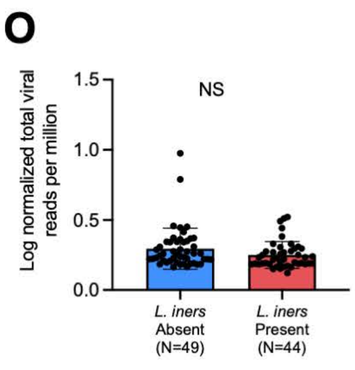

J
Surviving Proportion
1.00
0.75
0.50
0.25
0.00
G. Vaginalis Absent
(N= 41; Median NR)
G. Vaginalis Present
(N= 55; Median NR)
p = 0.37
0
10
20
30
40
50
60
Recurrence-Free Survival (Months)

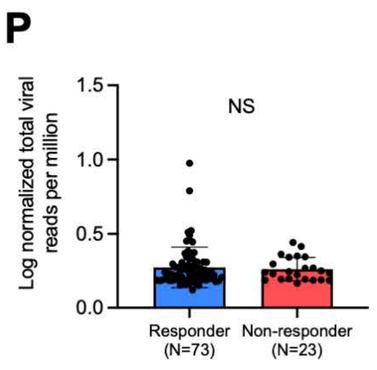

K
Surviving Proportion
1.00
0.75
0.50
0.25
0.00
P. bivia Absent
(N= 50; Median NR)
P. bivia Present
(N= 45; Median NR)
p = 0.69
0
10
20
30
40
50
Recurrence-Free Survival (Months)


L
Surviving Proportion
1.00
0.75
0.50
0.25
0.00
A. vaginae Absent
(N= 62; Median NR)
A. vaginae Present
(N= 34; Median NR)
p = 0.38
0
10
20
30
40
50
Recurrence-Free Survival (Months)


M
Log normalized Fungi reads per million
1.5
1.0
0.5
0.0
NS
L. iners Absent (N=69)
L. iners Present (N=64)


N
Log normalized Fungi reads per million
1.5
1.0
0.5
0.0
NS
Responder (N=73)
Non-responder (N=23)


O
Log normalized total viral reads per million
1.5
1.0
0.5
0.0
NS
L. iners Absent (N=49)
L. iners Present (N=44)


P
Log normalized total viral reads per million
1.5
1.0
0.5
0.0
NS
Responder (N=73)
Non-responder (N=23)

Supplemental Figure 3. Gut microbiome features are significant in univariate, but not multivariate analysis, and patients with gut *L. iners* have tumor *L. iners,* related to Figure 1.

A. Multivariate cox proportional hazard analysis of overall survival including Pielou Evenness in the gut microbiome (N=90) and relative counts of baseline tumoral *L. iners* (N=90).

B. Linear discriminant analysis effect size (LEfSe) was performed using 16S data for baseline gut bacteria associated with response (Non-responders [N=22] vs. Responders [N=70] to CRT. Default parameters were used for LEfSe analysis with an LDA threshold of 3.0.

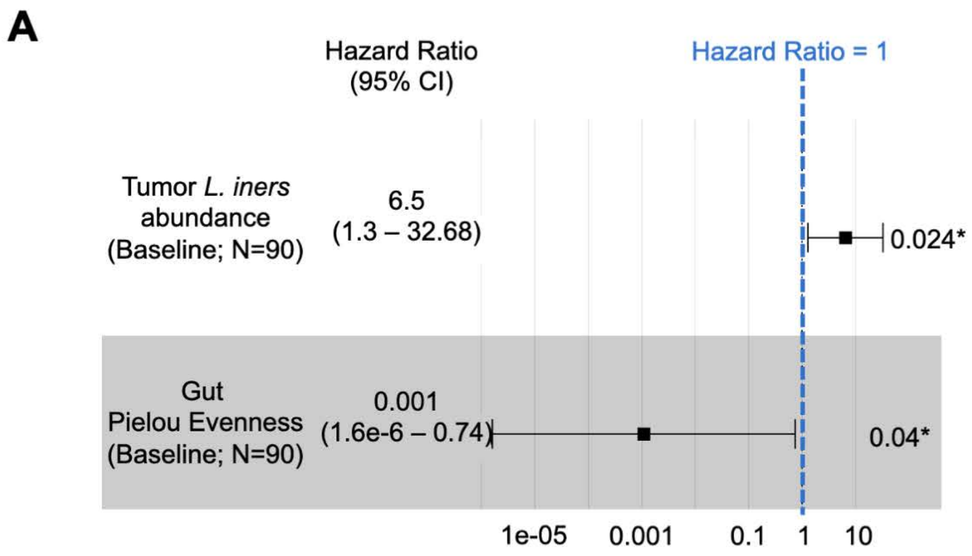
C. Multivariate cox proportional hazard analysis of recurrence-free survival including 16S relative counts of baseline *E. shigella* in the gut microbiome (N=89) and relative counts of baseline tumoral *L. iners* (N=89).

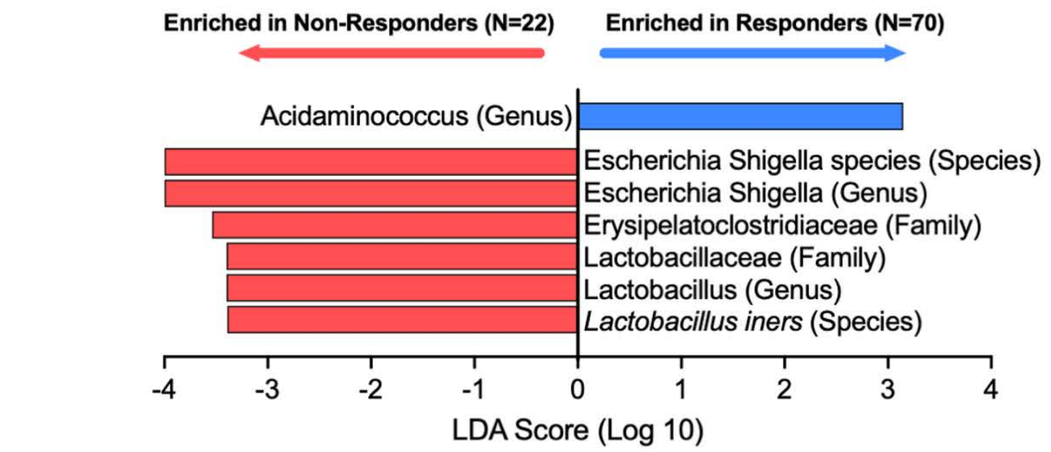
D. Kaplan-Meier curves for recurrence-free survival stratified by baseline presence (N=71) or absence (N=21) of gut *Escherichia Shigella* on 16S. Log-rank p-value reported.

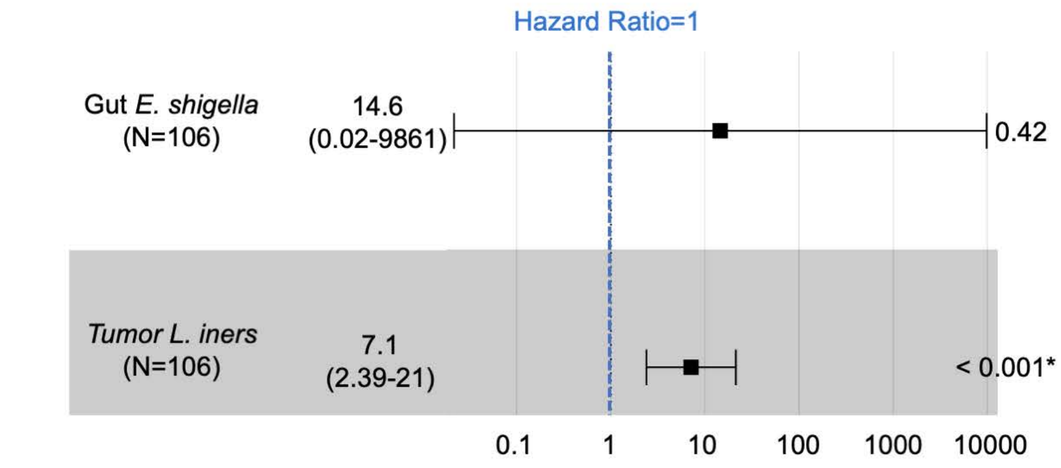
E. Linear discriminant analysis effect size (LEfSe) was performed using 16S ribosomal RNA sequencing data for baseline gut bacteria associated with tumor *L. iners* status (Absent [N=48] vs. Present [N=42] to CRT. Default parameters were used for LEfSe analysis with an LDA threshold of 3.5.

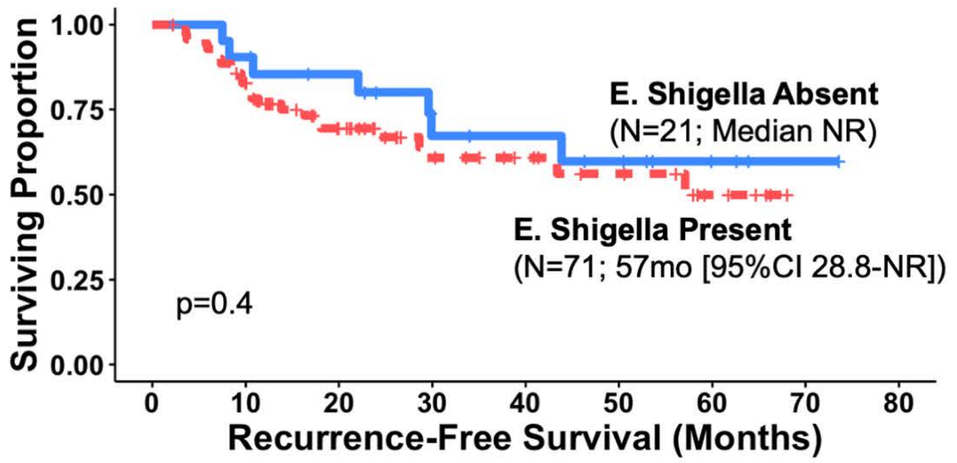
F. Absolute number of patients with tumoral *L. iners* alone (N=17) vs. gut microbiome *L. iners* alone (N=5) vs. both (N=25). 43 patients did not have *L. iners* present in their gut or tumor microbiome.

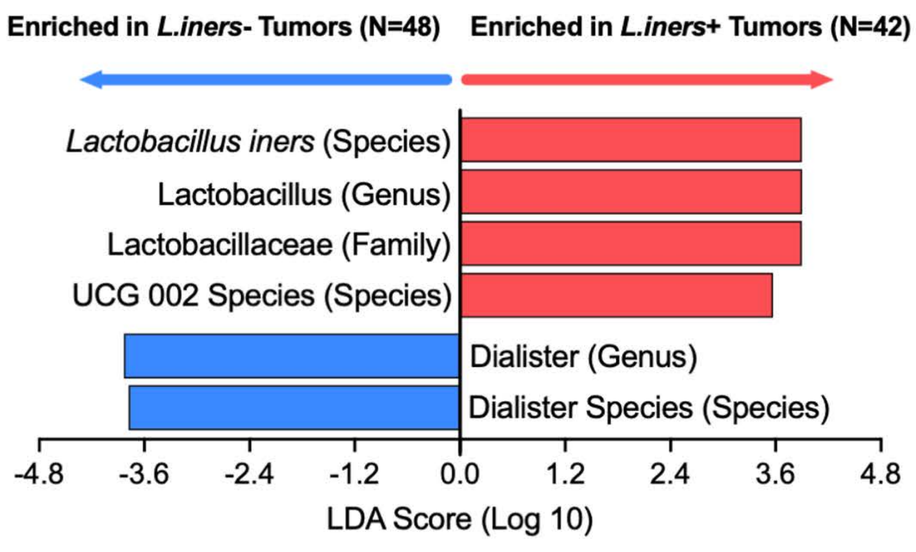
G. Kendall Rank correlation between baseline gut and tumor *L. iners.*

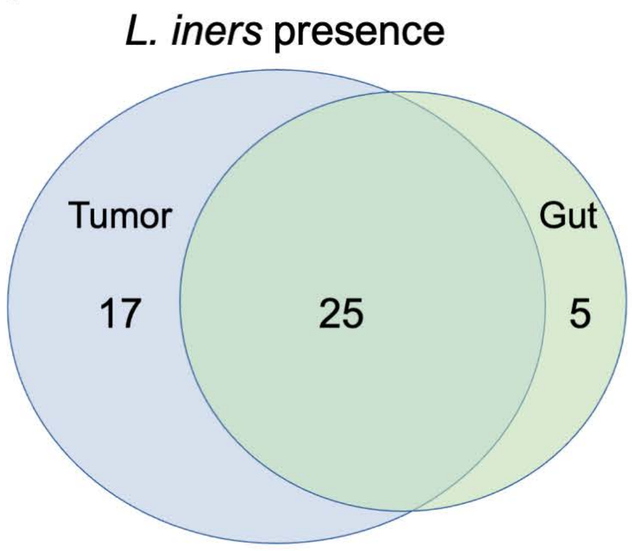




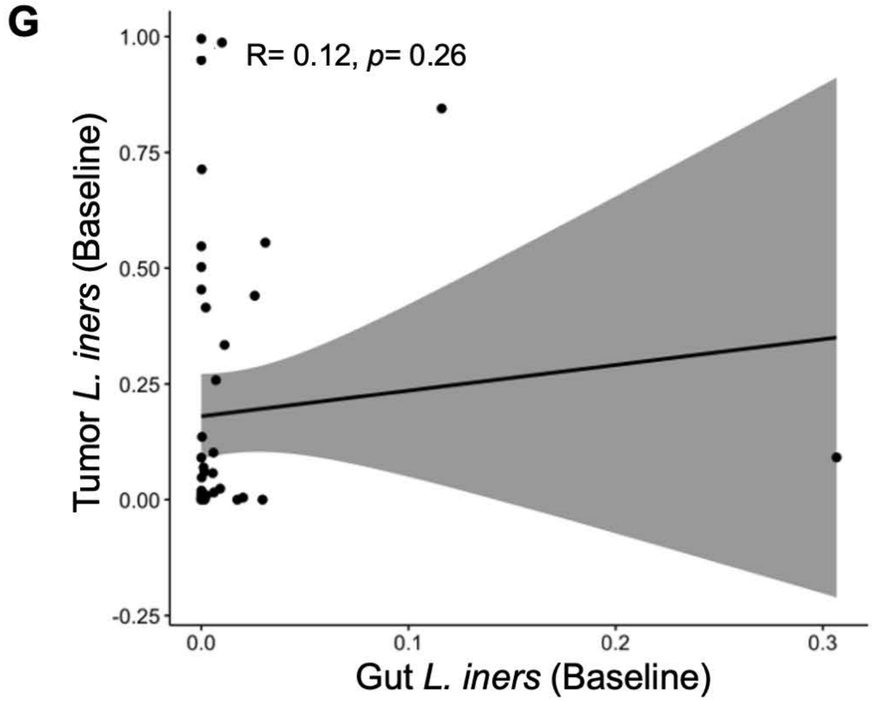








*43 patients did not have L. iners present in the gut or tumor microbiome



Supplemental Figure 4. *L. iners*- have increased T-cell infiltration and T-cells are more resilient to CRT, related to Figure 1.

A. Overall productive templates in tumor samples from T-cell receptor sequencing. N=59. unpaired t-test for comparison. * $p<0.05$, <0.01.

B. Overall tumor CD3+ cells (% lymphocytes) on flow cytometry. N=70. unpaired t-test for comparison. * $p<0.05$, <0.01.

C. Overall tumor CD4+ cells (% lymphocytes) on flow cytometry. N=70. unpaired t-test for comparison. * $p<0.05$, <0.01. ** $p>0.01$, <0.001

D. Overall tumor CD8+ cells (% lymphocytes) on flow cytometry. N=70. unpaired t-test for comparison. * $p<0.05$, <0.01.

E. Total templates over time in tumor samples from T-cell receptor sequencing in *L. iners* + patients. N=30. paired t-test for comparison.

F. Total templates over time in tumor samples from T-cell receptor sequencing in *L. iners* - patients. N=26. paired t-test for comparison.

G. Productive clonality over time in tumor samples from T-cell receptor sequencing in *L. iners* + patients. N=30. paired t-test for comparison.

H. Productive clonality over time in tumor samples from T-cell receptor sequencing in *L. iners* - patients. N=26. paired t-test for comparison.

I. Productive templates over time in tumor samples from T-cell receptor sequencing in *L. iners* + patients. N=30. paired t-test for comparison.

J. Productive templates over time in tumor samples from T-cell receptor sequencing in *L. iners* - patients. N=26. paired t-test for comparison.

K. Maximum productive frequency over time in tumor samples from T-cell receptor sequencing in *L. iners* + patients. N=30. paired t-test for comparison.

L. Maximum productive frequency over time in tumor samples from T-cell receptor sequencing in *L. iners* - patients. N=26. paired t-test for comparison.

M. Maximum frequency over time in tumor samples from T-cell receptor sequencing in *L. iners* + patients. N=30. paired t-test for comparison.

N. Maximum frequency over time in tumor samples from T-cell receptor sequencing in *L. iners* - patients. N=26. paired t-test for comparison.

O. Productive rearrangements over time in tumor samples from T-cell receptor sequencing in *L. iners* + patients. N=30. paired t-test for comparison.

P. Productive rearrangements over time in tumor samples from T-cell receptor sequencing in *L. iners* - patients. N=26. paired t-test for comparison.

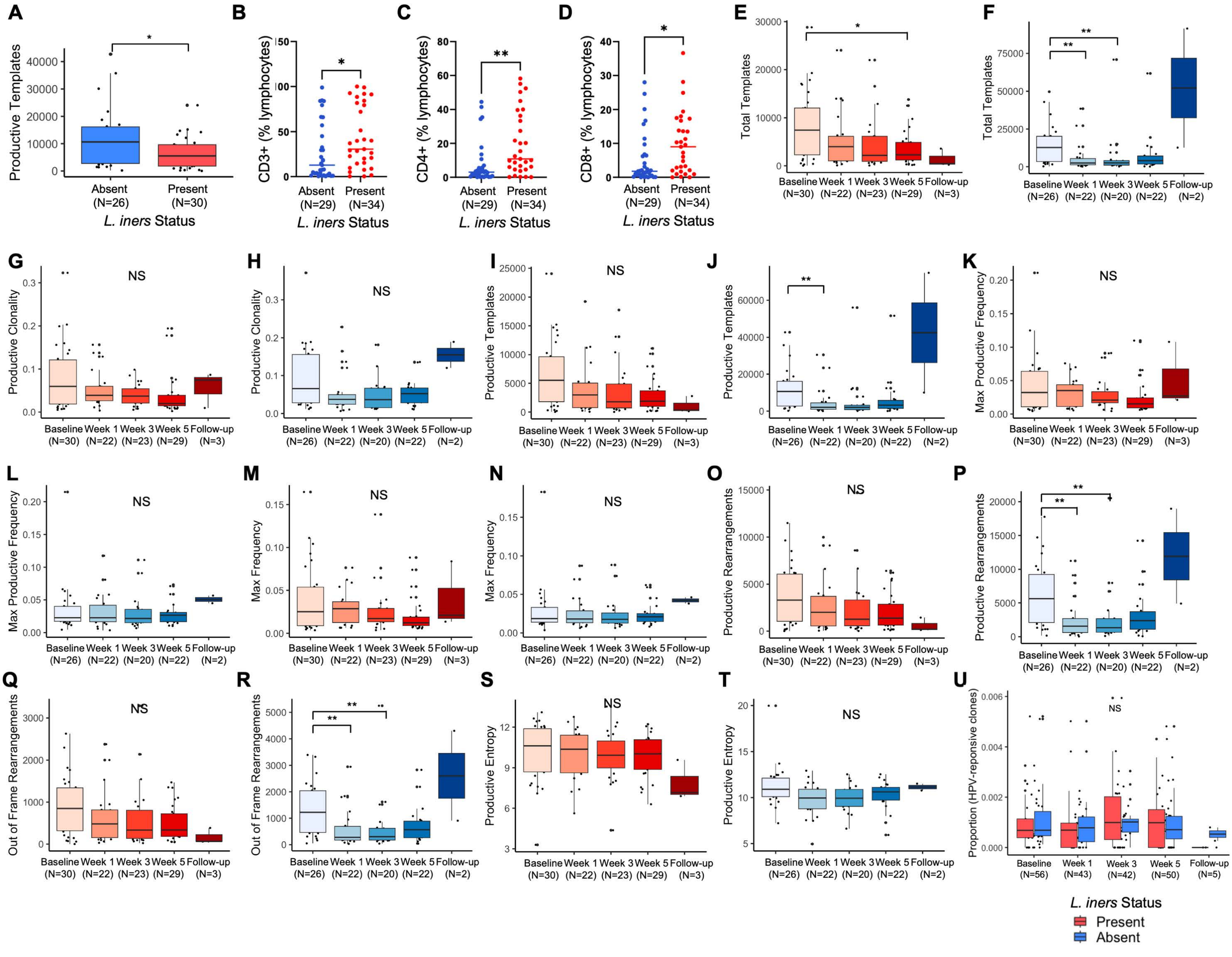
Q. Out of frame rearrangements over time in tumor samples from T-cell receptor sequencing in *L. iners* + patients. N=30. paired t-test for comparison.

R. Out of frame rearrangements over time in tumor samples from T-cell receptor sequencing in *L. iners* - patients. N=26. paired t-test for comparison.

S. Productive entropy over time in tumor samples from T-cell receptor sequencing in *L. iners* + patients. N=30. paired t-test for comparison.

T. Productive entropy over time in tumor samples from T-cell receptor sequencing in *L. iners* - patients. N=26. paired t-test for comparison.

U. HPV-specific TCR sequences as a proportion of total TCR sequences at each time point for *L. iners*+ vs. *L.iners*- patients. HPV-specific T-cells were identified from previously published datasets. 3-way ANOVA for comparison.


A
Productive Templates
Absent (N=26)
Present (N=30)
L. iners Status
B
CD3+ (% lymphocytes)
Absent (N=29)
Present (N=34)
L. iners Status
C
CD4+ (% lymphocytes)
Absent (N=29)
Present (N=34)
L. iners Status
D
CD8+ (% lymphocytes)
Absent (N=29)
Present (N=34)
L. iners Status
E
Total Templates
Baseline (N=30)
Week 1 (N=22)
Week 3 (N=23)
Week 5 (N=29)
Follow-up (N=3)
F
Total Templates
Baseline (N=26)
Week 1 (N=22)
Week 3 (N=20)
Week 5 (N=22)
Follow-up (N=2)
G
Productive Clonality
NS
Baseline (N=30)
Week 1 (N=22)
Week 3 (N=23)
Week 5 (N=29)
Follow-up (N=3)
H
Productive Clonality
NS
Baseline (N=26)
Week 1 (N=22)
Week 3 (N=20)
Week 5 (N=22)
Follow-up (N=2)
I
Productive Templates
NS
Baseline (N=30)
Week 1 (N=22)
Week 3 (N=23)
Week 5 (N=29)
Follow-up (N=3)
J
Productive Templates
Baseline (N=26)
Week 1 (N=22)
Week 3 (N=20)
Week 5 (N=22)
Follow-up (N=2)
K
Max Productive Frequency
NS
Baseline (N=30)
Week 1 (N=22)
Week 3 (N=23)
Week 5 (N=29)
Follow-up (N=3)
L
Max Productive Frequency
NS
Baseline (N=26)
Week 1 (N=22)
Week 3 (N=20)
Week 5 (N=22)
Follow-up (N=2)
M
Max Frequency
NS
Baseline (N=30)
Week 1 (N=22)
Week 3 (N=23)
Week 5 (N=29)
Follow-up (N=3)
N
Max Frequency
NS
Baseline (N=26)
Week 1 (N=22)
Week 3 (N=20)
Week 5 (N=22)
Follow-up (N=2)
O
Productive Rearrangements
NS
Baseline (N=30)
Week 1 (N=22)
Week 3 (N=23)
Week 5 (N=29)
Follow-up (N=3)
P
Productive Rearrangements
Baseline (N=26)
Week 1 (N=22)
Week 3 (N=20)
Week 5 (N=22)
Follow-up (N=2)
Q
Out of Frame Rearrangements
NS
Baseline (N=30)
Week 1 (N=22)
Week 3 (N=23)
Week 5 (N=29)
Follow-up (N=3)
R
Out of Frame Rearrangements
Baseline (N=26)
Week 1 (N=22)
Week 3 (N=20)
Week 5 (N=22)
Follow-up (N=2)
S
Productive Entropy
NS
Baseline (N=30)
Week 1 (N=22)
Week 3 (N=23)
Week 5 (N=29)
Follow-up (N=3)
T
Productive Entropy
NS
Baseline (N=26)
Week 1 (N=22)
Week 3 (N=20)
Week 5 (N=22)
Follow-up (N=2)
U
Proportion (HPV-reponsive clones)
NS
Baseline (N=56)
Week 1 (N=43)
Week 3 (N=42)
Week 5 (N=50)
Follow-up (N=5)
L. iners Status
Present
Absent

Supplemental Figure 5. Experimental data for CFS in other cell lines, related to Figure 2.

A. CaSki and B1188 cells treated with increasing concentrations of CFS. No statistical comparison. 20% CFS was chosen

B. Cell viability of B1188 alone after cisplatin treatment.

C. Cell viability of B1188 alone after irradiation (2Gy)

D. Histogram of organoid size and count (percentage of total counted) for PDO B1188 pretreated with CC-L. iners 366 CFS (red), CC-L. iners 370 CFS (dark red) vs. non-cancer derived L. iners (NC-L. iners; pink) vs. control (NYC Broth; grey) followed by 4Gy irradiation.

E. Histogram of organoid size and count (percentage of total counted) for PDO B1188 pretreated with CC-*L. iners 366* CFS (red), CC-*L. iners 370* CFS (dark red) vs. non-cancer derived *L. iners* (NC-*L. iners*; pink) vs. control (NYC Broth; grey) followed by 8Gy irradiation..

F. Cell viability (measured by CellTiter Glo) of Ca Ski cells pretreated with CC-*L. iners* cell-free supernatant (CFS) vs. NC-*L. iners* CFS vs. control (NYC Broth) followed by cisplatin. 3 experiments, 3 replicates, 2 patient-derived CC-*L. Iners* strains pooled. Mean and SEM are presented. One way ANOVA between each CFS and control shown.

G. Cell viability (measured by CellTiter Glo) of Ca Ski cells pretreated with CC-*L. iners* cell-free supernatant (CFS) vs. NC-*L. iners* CFS vs. control (NYC Broth) followed by gemcitabine. 3 experiments, 3 replicates, 2 patient-derived CC-*L. Iners* strains pooled. Mean and SEM are presented. One way ANOVA between each CFS and control shown.

H. Cell viability (measured by CellTiter Glo) of Ca Ski cells pretreated with CC-*L. iners* cell-free supernatant (CFS) vs. NC-*L. iners* CFS vs. control (NYC Broth) followed by 5-Fluorouracil. 4 experiments, 3 replicates, 2 patient-derived CC-*L. Iners* strains pooled. Mean and SEM are presented. One way ANOVA between each CFS and control shown.

I. Cell viability (measured by CellTiter Glo) of SiHa cells pretreated with CC-*L. iners* cell-free supernatant (CFS) vs. NC-*L. iners* CFS vs. control (NYC Broth) followed by cisplatin. 3 experiments, 3 replicates, 2 patient-derived CC-*L. Iners* strains pooled. Mean and SEM are presented. One way ANOVA between each CFS and control shown.

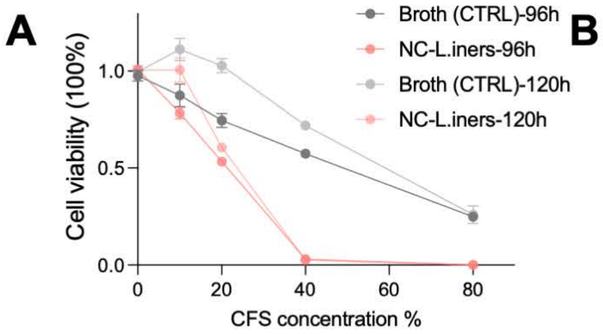
J. Cell viability (measured by CellTiter Glo) of SiHa cells pretreated with CC-*L. iners* cell-free supernatant (CFS) vs. NC-*L. iners* CFS vs. control (NYC Broth) followed by gemcitabine. 3 experiments, 3 replicates, 2 patient-derived CC-*L. Iners* strains pooled. Mean and SEM are presented. One way ANOVA between each CFS and control shown.

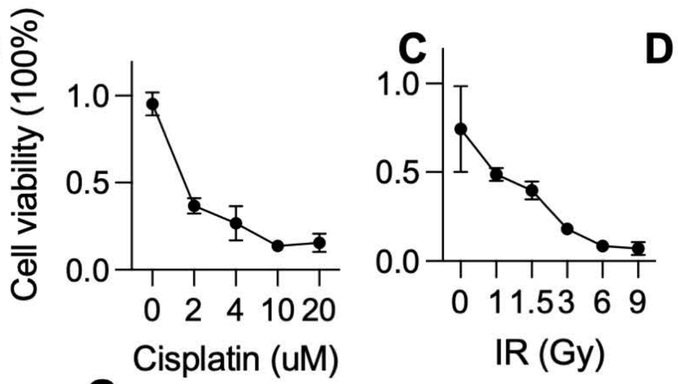
K. Cell viability (measured by CellTiter Glo) of SiHa cells pretreated with CC-*L. iners* cell-free supernatant (CFS) vs. NC-*L. iners* CFS vs. control (NYC Broth) followed by 5-Fluorouracil. 2 experiments, 3 replicates, 2 patient-derived CC-*L. Iners* strains pooled. Mean and SEM are presented. One way ANOVA between each CFS and control shown.

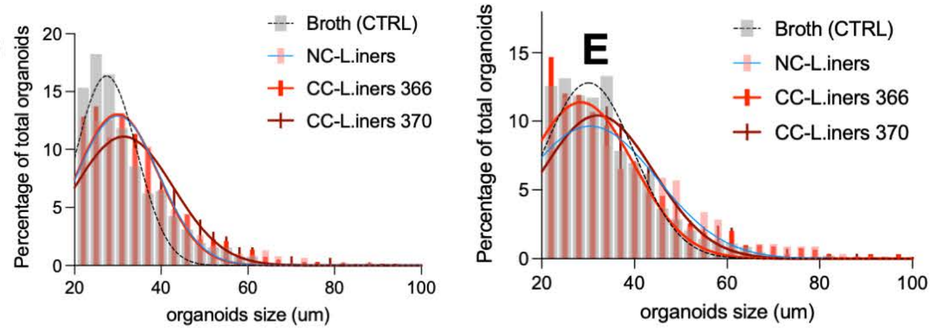
L. Cell viability (measured by CellTiter Glo) of HeLa cells pretreated with CC-*L. iners* cell-free supernatant (CFS) vs. NC-*L. iners* CFS vs. control (NYC Broth) followed by gemcitaine. 3 experiments, 3 replicates, 2 patient-derived CC-*L. Iners* strains pooled. Mean and SEM are presented. One way ANOVA between each CFS and control shown.

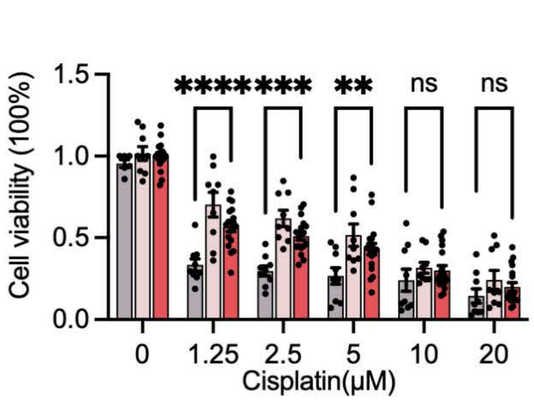
M. Cell viability (measured by CellTiter Glo) of HeLa cells pretreated with CC-*L. iners* cell-free supernatant (CFS) vs. NC-*L. iners* CFS vs. control (NYC Broth) followed by 5-Fluorouracil. 3 experiments, 3 replicates, 2 patient-derived CC-*L. Iners* strains pooled. Mean and SEM are presented. One way ANOVA between each CFS and control shown.

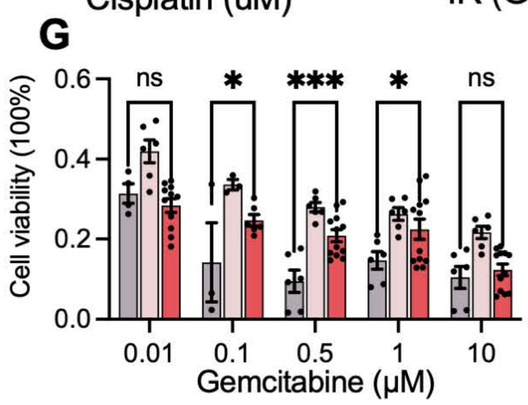
N. HeLa cells treated with cancer-derived *L. crispatus* CFS, non-cancer derived *L. crispatus* CFS, or NYC broth control at increasing doses of irradiation. 1 experiment, 3 replicates. No statistical comparison made.

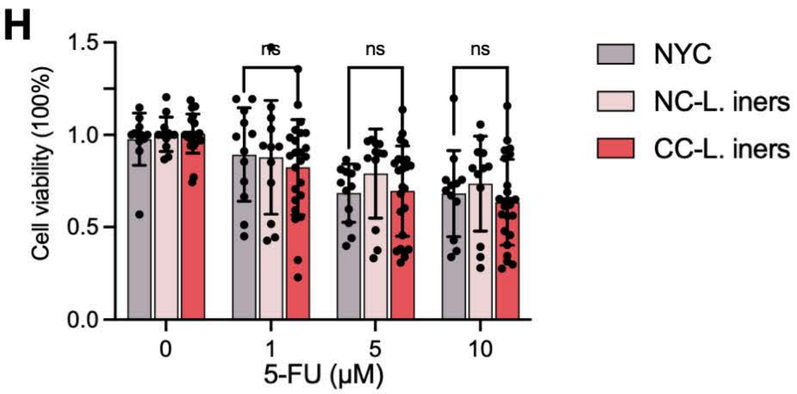

A
Broth (CTRL)-96h
NC-L.iners-96h
Broth (CTRL)-120h
NC-L.iners-120h
Cell viability (100%)
CFS concentration %

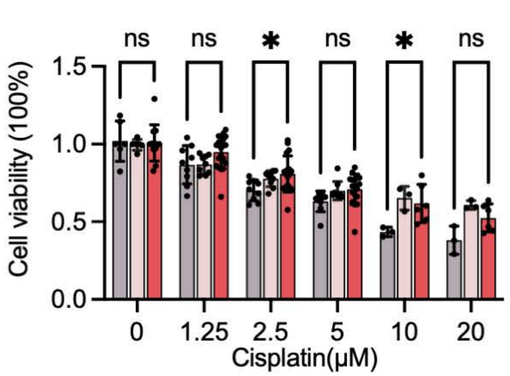

B
Cell viability (100%)
Cisplatin (uM)
C
IR (Gy)

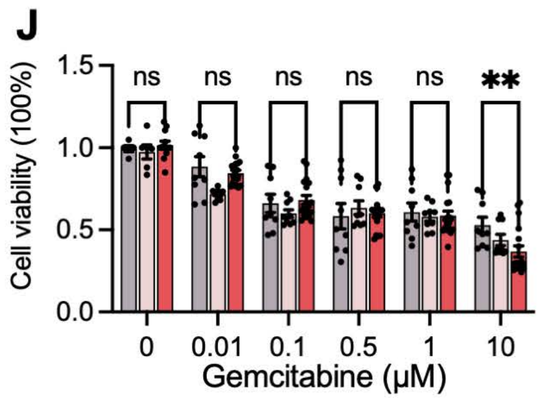

D
Broth (CTRL)
NC-L.iners
CC-L.iners 366
CC-L.iners 370
Percentage of total organoids
organoids size (um)
E

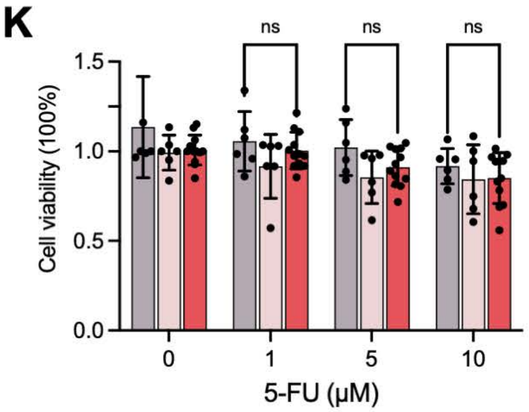

F
Cell viability (100%)
Cisplatin(μM)

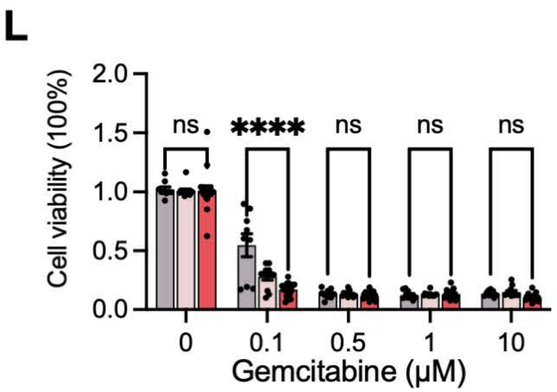

G
Cell viability (100%)
Gemcitabine (μM)

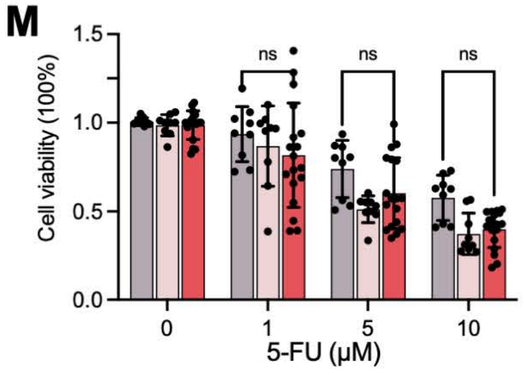

H
Cell viability (100%)
5-FU (μM)
NYC
NC-L. iners
CC-L. iners

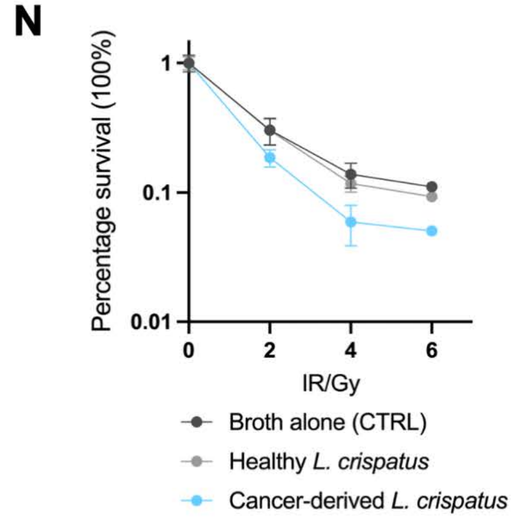

I
Cell viability (100%)
Cisplatin(μM)


J
Cell viability (100%)
Gemcitabine (μM)


K
Cell viability (100%)
5-FU (μM)


L
Cell viability (100%)
Gemcitabine (μM)


M
Cell viability (100%)
5-FU (μM)


N
Percentage survival (100%)
IR/Gy
Broth alone (CTRL)
Healthy L. crispatus
Cancer-derived L. crispatus

Supplemental Figure 6. L-lactate causes treatment resistance and lactate signaling pathways are upregulated, related to Figures 3 and 4.

A. Hallmark pathways for primary cells B1188 were pre-treated with *L. iners* (1 NC-*L. iners* strain, 2 CC-*L. iners* strains) CFS vs. control (NYC broth) prior to RNA sequencing. Fold change in gene expression from control (right) to L. iners (left) is shown. Log2 (Fold Change) threshold of -1, 1. – Log10 (FDR- adjusted p-value) threshold is 1.2. 1 experiment, 3 replicates for each group.

B. Cell viability (measured by CellTiter Glo) of CaSki cells pretreated with lactate isoforms (20mM) prior to being treated with Gem 0.5 μM (1 experiment, 3 replicates) Unpaired t-test for comparison L-lactate to CTRL.

C. Cell viability (measured by CellTiter Glo) of CaSki cells pretreated with lactate isoforms (20mM) prior to being treated with 5-FU 1μM (1 experiment, 3 replicates) Unpaired t-test for comparison L-lactate to CTRL.

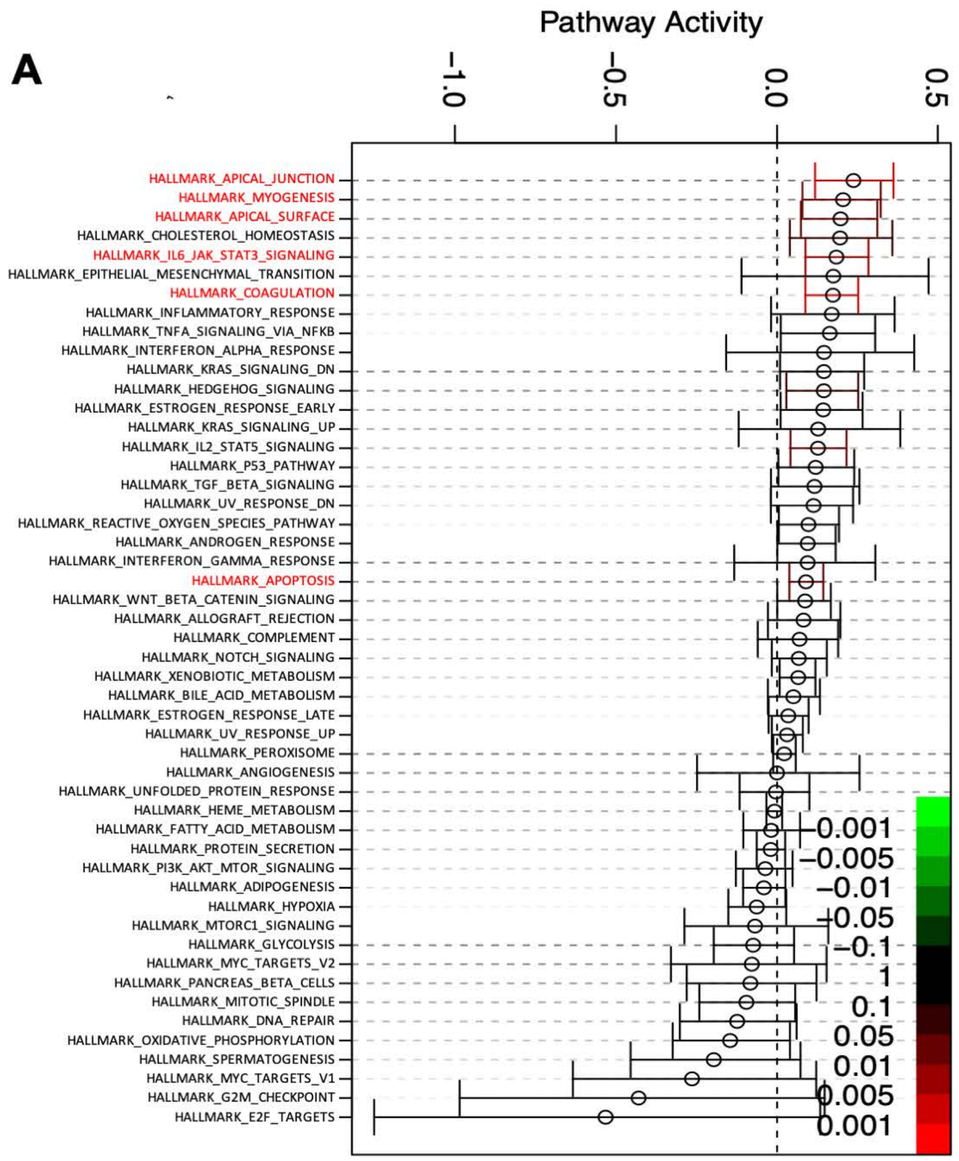
D. Cell viability (measured by CellTiter Glo) of CaSki cells pretreated with lactate isoforms (20mM) prior to being treated with IR 3.0 gy (1 experiment, 3 replicates) Unpaired t- for comparison L-lactate to CTRL.

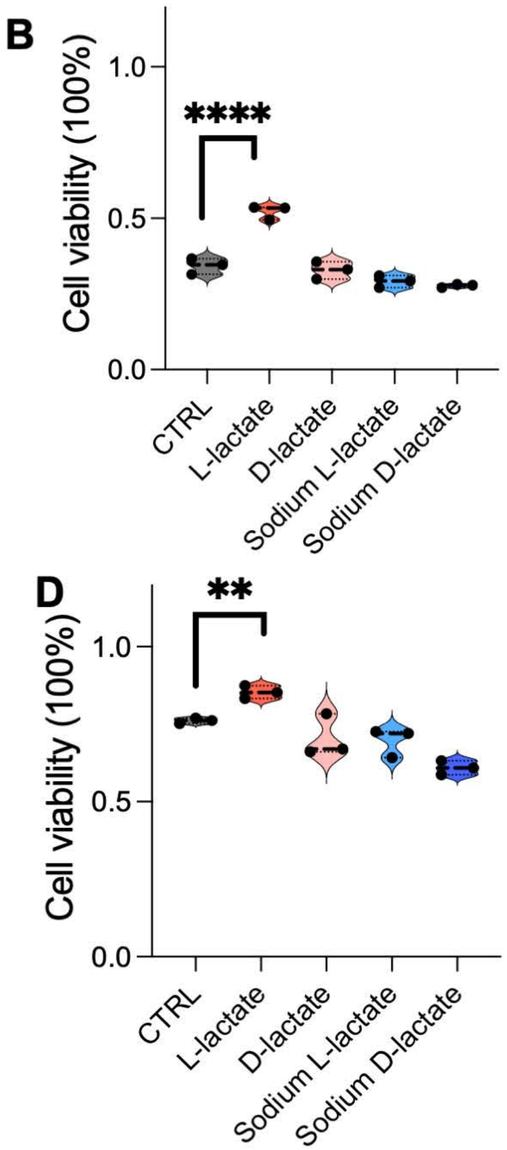
E. Cell viability (measured by CellTiter Glo) of primary cells B1188 pretreated with lactate isoforms (20mM) prior to being treated with 8 uM Cisplatin (3 experiment, 3 replicates) unpaired t-test for comparison L-lactate to CTRL.

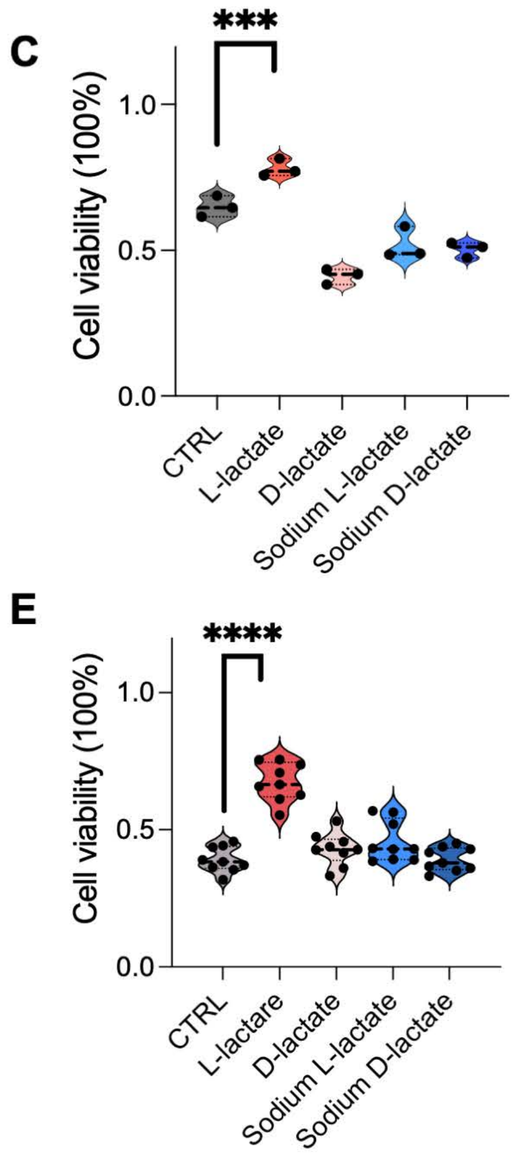
F. Principle coordinate analysis (PCA) of non-targeted metabolomics for validation cohort. DSC p-value shown.

G. Supervised clustering of metabolites for L. iners+ and L. iners- tumors in validation cohort, with assigned pathways. N=29. No statistical comparison.

H. Unsupervised clustering of metabolites for CFS alone in validation cohort, with assigned lactate regulated pathways. NS $P > 0.05$, *$P \leq 0.05$, ** $P \leq 0.01$, *** $P \leq 0.001$, **** $P \leq 0.0001$.

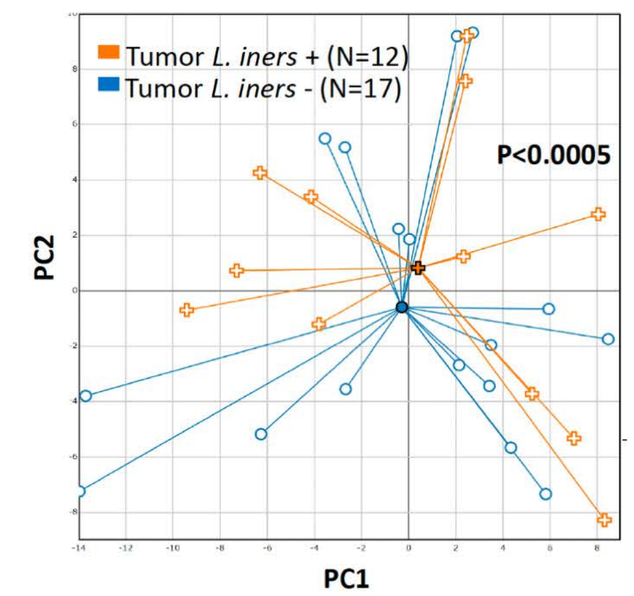

A
Pathway Activity
−1.0
−0.5
0.0
0.5
HALLMARK_APICAL_JUNCTION
HALLMARK_MYOGENESIS
HALLMARK_APICAL_SURFACE
HALLMARK_CHOLESTEROL_HOMEOSTASIS
HALLMARK_IL6_JAK_STAT3_SIGNALING
HALLMARK_EPITHELIAL_MESENCHYMAL_TRANSITION
HALLMARK_COAGULATION
HALLMARK_INFLAMMATORY_RESPONSE
HALLMARK_TNFA_SIGNALING_VIA_NFKB
HALLMARK_INTERFERON_ALPHA_RESPONSE
HALLMARK_KRAS_SIGNALING_DN
HALLMARK_HEDGEHOG_SIGNALING
HALLMARK_ESTROGEN_RESPONSE_EARLY
HALLMARK_KRAS_SIGNALING_UP
HALLMARK_IL2_STAT5_SIGNALING
HALLMARK_P53_PATHWAY
HALLMARK_TGF_BETA_SIGNALING
HALLMARK_UV_RESPONSE_DN
HALLMARK_REACTIVE_OXYGEN_SPECIES_PATHWAY
HALLMARK_ANDROGEN_RESPONSE
HALLMARK_INTERFERON_GAMMA_RESPONSE
HALLMARK_APOPTOSIS
HALLMARK_WNT_BETA_CATENIN_SIGNALING
HALLMARK_ALLOGRAFT_REJECTION
HALLMARK_COMPLEMENT
HALLMARK_NOTCH_SIGNALING
HALLMARK_XENOBIOTIC_METABOLISM
HALLMARK_BILE_ACID_METABOLISM
HALLMARK_ESTROGEN_RESPONSE_LATE
HALLMARK_UV_RESPONSE_UP
HALLMARK_PEROXISOME
HALLMARK_ANGIOGENESIS
HALLMARK_UNFOLDED_PROTEIN_RESPONSE
HALLMARK_HEME_METABOLISM
HALLMARK_FATTY_ACID_METABOLISM
HALLMARK_PROTEIN_SECRETION
HALLMARK_PI3K_AKT_MTOR_SIGNALING
HALLMARK_ADIPOGENESIS
HALLMARK_HYPOXIA
HALLMARK_MTORC1_SIGNALING
HALLMARK_GLYCOLYSIS
HALLMARK_MYC_TARGETS_V2
HALLMARK_PANCREAS_BETA_CELLS
HALLMARK_MITOTIC_SPINDLE
HALLMARK_DNA_REPAIR
HALLMARK_OXIDATIVE_PHOSPHORYLATION
HALLMARK_SPERMATOGENESIS
HALLMARK_MYC_TARGETS_V1
HALLMARK_G2M_CHECKPOINT
HALLMARK_E2F_TARGETS
0.001
0.005
0.01
0.05
0.1
1
0.1
0.05
0.01
0.005
0.001

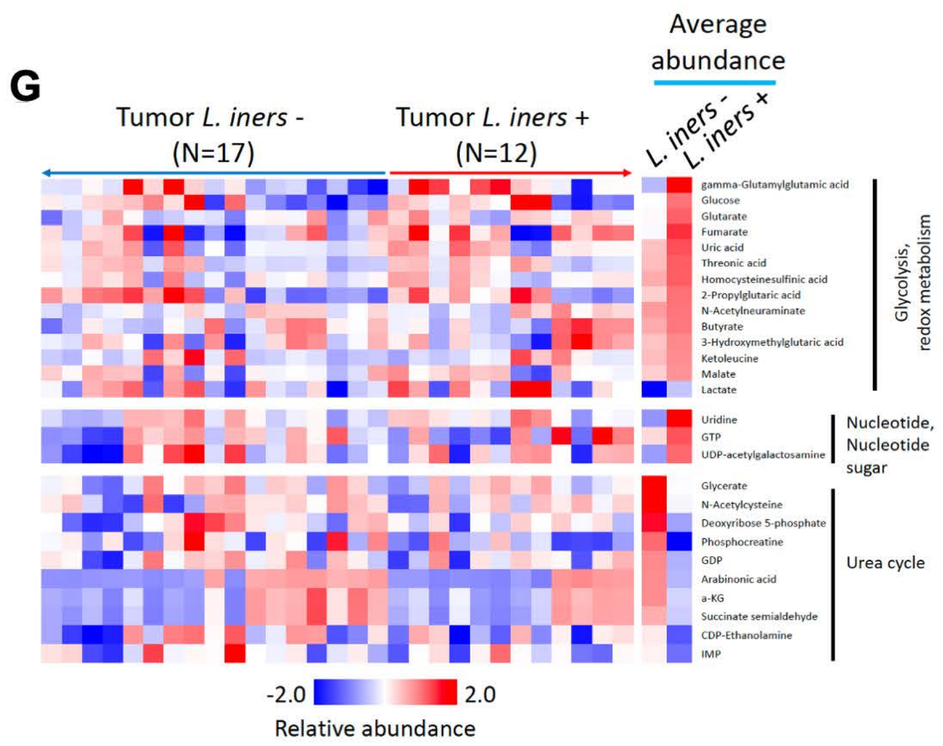

B
Cell viability (100%)
1.0
0.5
0.0
****
CTRL
L-lactate
D-lactate
Sodium L-lactate
Sodium D-lactate

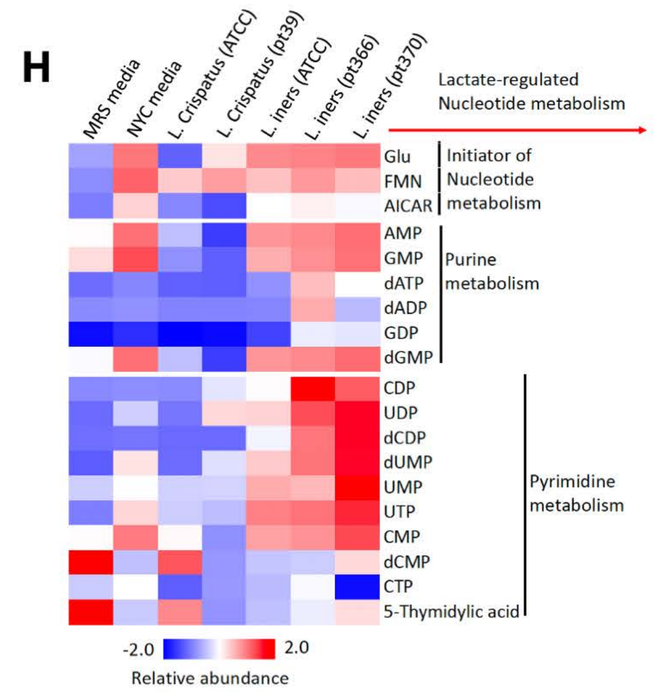

C
Cell viability (100%)
1.0
0.5
0.0
***
CTRL
L-lactate
D-lactate
Sodium L-lactate
Sodium D-lactate

D
Cell viability (100%)
1.0
0.5
0.0
**
CTRL
L-lactate
D-lactate
Sodium L-lactate
Sodium D-lactate

E
Cell viability (100%)
1.0
0.5
0.0
****
CTRL
L-lactare
D-lactate
Sodium L-lactate
Sodium D-lactate


F
Tumor L. iners + (N=12)
Tumor L. iners - (N=17)
P<0.0005
PC2
PC1


G
Tumor L. iners -
(N=17)
Tumor L. iners +
(N=12)
Average abundance
L. iners -
L. iners +
gamma-Glutamylglutamic acid
Glucose
Glutarate
Fumarate
Uric acid
Threonic acid
Homocysteinesulfinic acid
2-Propylglutaric acid
N-Acetylneuraminate
Butyrate
3-Hydroxymethylglutaric acid
Ketoleucine
Malate
Lactate
Glycolysis, redox metabolism
Uridine
GTP
UDP-acetylgalactosamine
Nucleotide, Nucleotide sugar
Glycerate
N-Acetylcysteine
Deoxyribose 5-phosphate
Phosphocreatine
GDP
Arabinonic acid
a-KG
Succinate semialdehyde
CDP-Ethanolamine
IMP
Urea cycle
-2.0
2.0
Relative abundance


H
MRS media
NYC media
L. Crispatus (ATCC)
L. Crispatus (pt39)
L. iners (ATCC)
L. iners (pt366)
L. iners (pt370)
Lactate-regulated Nucleotide metabolism
Glu
FMN
AICAR
Initiator of Nucleotide metabolism
AMP
GMP
dATP
dADP
GDP
dGMP
Purine metabolism
CDP
UDP
dCDP
dUMP
UMP
UTP
CMP
dCMP
CTP
5-Thymidylic acid
Pyrimidine metabolism
-2.0
2.0
Relative abundance

Supplementary Figure 7. Unique genomic features of CC-L. iners vs. NC-L. iners may be responsible for differing effects on cancer gene expression, related to Figure 6.

A. Number of genes in Lactobacillus pangenome from Shotgun metagenome sequencing of tumor swabs, with those assigned to *L. iners* (blue) vs. other Lactobacilli (orange).

B. KEGG orthology molecular functions specific for cervical cancer *L. iners* not identified in healthy *L. iners* are common across different patients and associated with bacterial immunity and pathogenic phenotypes, R-M: Restriction-modification system; PTS: PhosphoTransferase System; TA: Toxin-antitoxin system.

C. KEGG orthology pathways for cancer-derived *L. iners* are differentially identified vs. healthy *L. iners.*

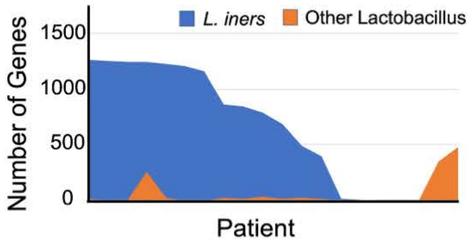
D. Fully assembled genome for one CC-*L. iners* isolate.

E. Primary cells B1188 were pre-treated with NC-*L. iners* CFS (1 NC-*L. iners* strain) vs. CC-*L. iners* CFS (2 strains) prior to RNA sequencing. Fold change in gene expression from NC-*L.iners* CFS (right) to CC-L. iners CFS (left) is shown. Log2 (Fold Change) threshold of -1, 1. –Log10 (FDR-adjusted p-value) threshold is 1.2. 1 experiment, 3 replicates for each group.

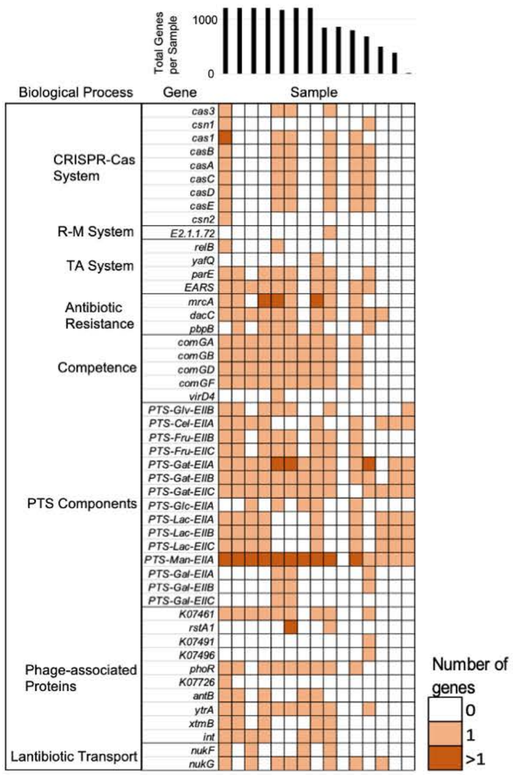
F. Hallmark pathways for unirradiated primary cells B1188 pre-treated with NC-*L. iners* (1 NC-*L. iners* strain) CFS vs. CC-*L. iners* (2 strains) CFS prior to RNA sequencing. Fold change in gene expression from NC-*L.iners* (right) CFS to CC-*L. iners* (left) CFS is shown. Log2 (Fold Change) threshold of -1, 1. –Log10 (FDR- adjusted p-value) threshold is 1.2. 1 experiment, 3 replicates for each group.

G. Hallmark pathways for irradiated (8Gy) primary cells B1188 pre-treated with NC-*L. iners* (1 NC-*L. iners* strain) CFS vs. CC-*L. iners* (2 strains) CFS prior to RNA sequencing. Fold change in gene expression from NC-*L. iners* (right) CFS to CC-*L. iners* (left) CFS is shown. Log2 (Fold Change) threshold of -1, 1. –Log10 (FDR- adjusted p-value) threshold is 1.2. 1 experiment, 3 replicates for each group.

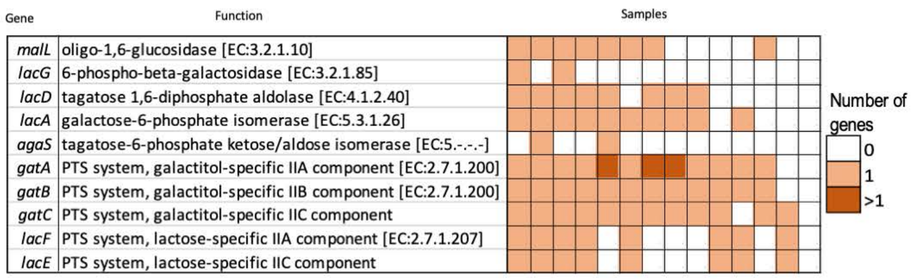
A


L. iners
Other Lactobacillus
Number of Genes
1500
1000
500
0
Patient

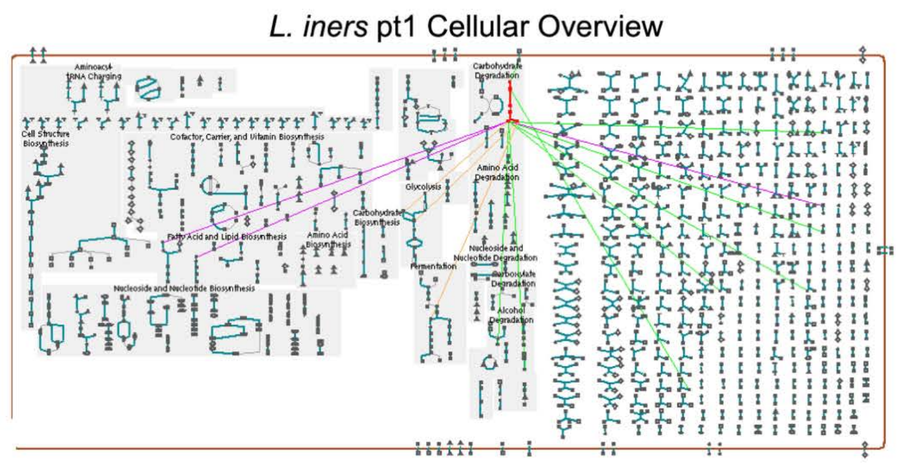
B


Total Genes per Sample
1000
0
Biological Process
Gene
Sample
CRISPR-Cas System
cas3
csn1
cas1
casB
casA
casC
casD
casE
csn2
R-M System
E2.1.1.72
TA System
relB
yafQ
parE
EARS
Antibiotic Resistance
mrcA
dacC
pbpB
Competence
comGA
comGB
comGD
comGF
virD4
PTS Components
PTS-Glv-EIIB
PTS-Cel-EIIA
PTS-Fru-EIIB
PTS-Fru-EIIC
PTS-Gat-EIIA
PTS-Gat-EIIB
PTS-Gat-EIIC
PTS-Glc-EIIA
PTS-Lac-EIIA
PTS-Lac-EIIB
PTS-Lac-EIIC
PTS-Man-EIIA
PTS-Gal-EIIA
PTS-Gal-EIIB
PTS-Gal-EIIC
Phage-associated Proteins
K07461
rstA1
K07491
K07496
phoR
K07726
antB
ytrA
xtmB
int
Lantibiotic Transport
nukF
nukG
Number of genes
0
1
>1

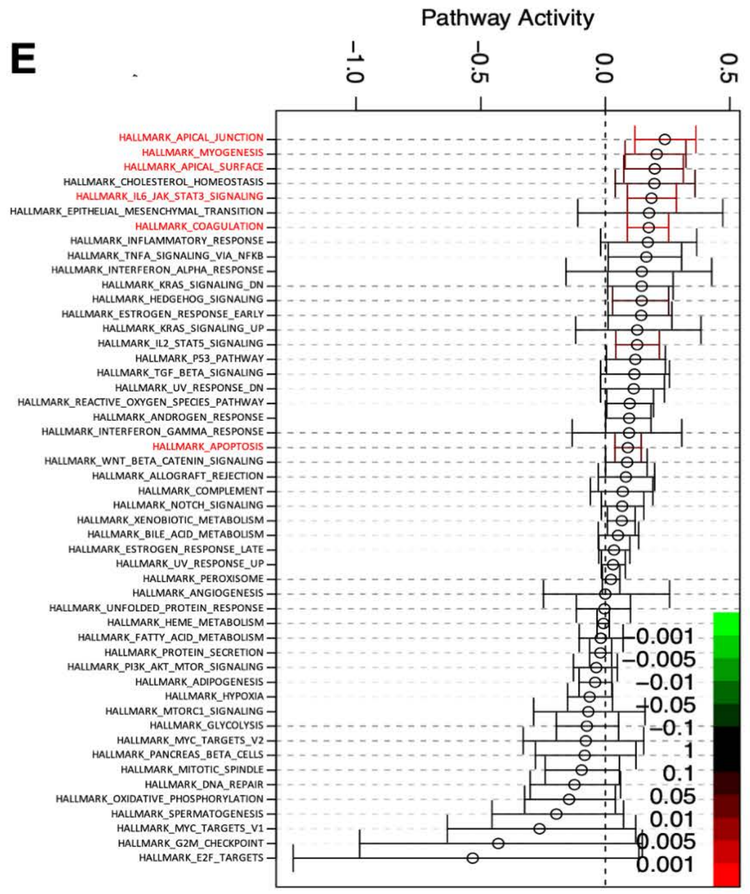
C


Gene
Function
Samples
malL oligo-1,6-glucosidase [EC:3.2.1.10]
lacG 6-phospho-beta-galactosidase [EC:3.2.1.85]
lacD tagatose 1,6-diphosphate aldolase [EC:4.1.2.40]
lacA galactose-6-phosphate isomerase [EC:5.3.1.26]
agaS tagatose-6-phosphate ketose/aldose isomerase [EC:5.-.-.-]
gatA PTS system, galactitol-specific IIA component [EC:2.7.1.200]
gatB PTS system, galactitol-specific IIB component [EC:2.7.1.200]
gatC PTS system, galactitol-specific IIC component
lacF PTS system, lactose-specific IIA component [EC:2.7.1.207]
lacE PTS system, lactose-specific IIC component
Number of genes
0
1
>1

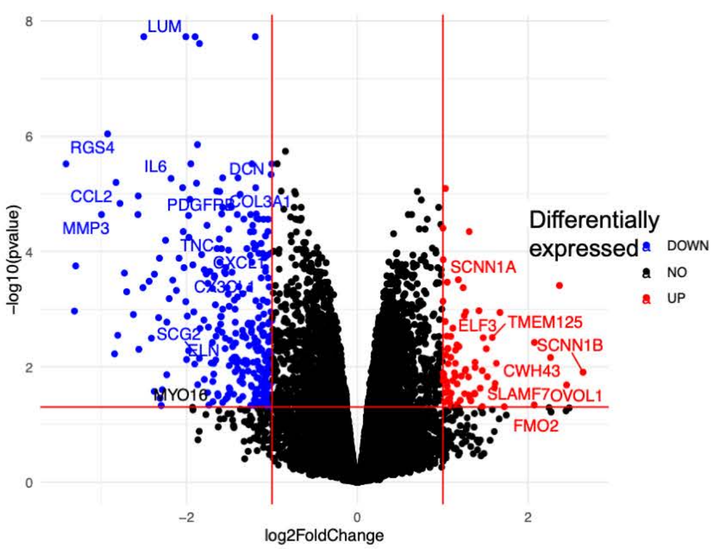
D


L. iners pt1 Cellular Overview
Aminoacyl-tRNA Charging
Cell Structure Biosynthesis
Cofactor, Carrier, and Vitamin Biosynthesis
Carbohydrate Degradation
Amino Acid Degradation
Glycolysis
Carbohydrate Biosynthesis
Fatty Acid and Lipid Biosynthesis
Amino Acid Biosynthesis
Fermentation
Nucleoside and Nucleotide Degradation
Carboxylate Degradation
Alcohol Degradation
Nucleoside and Nucleotide Biosynthesis

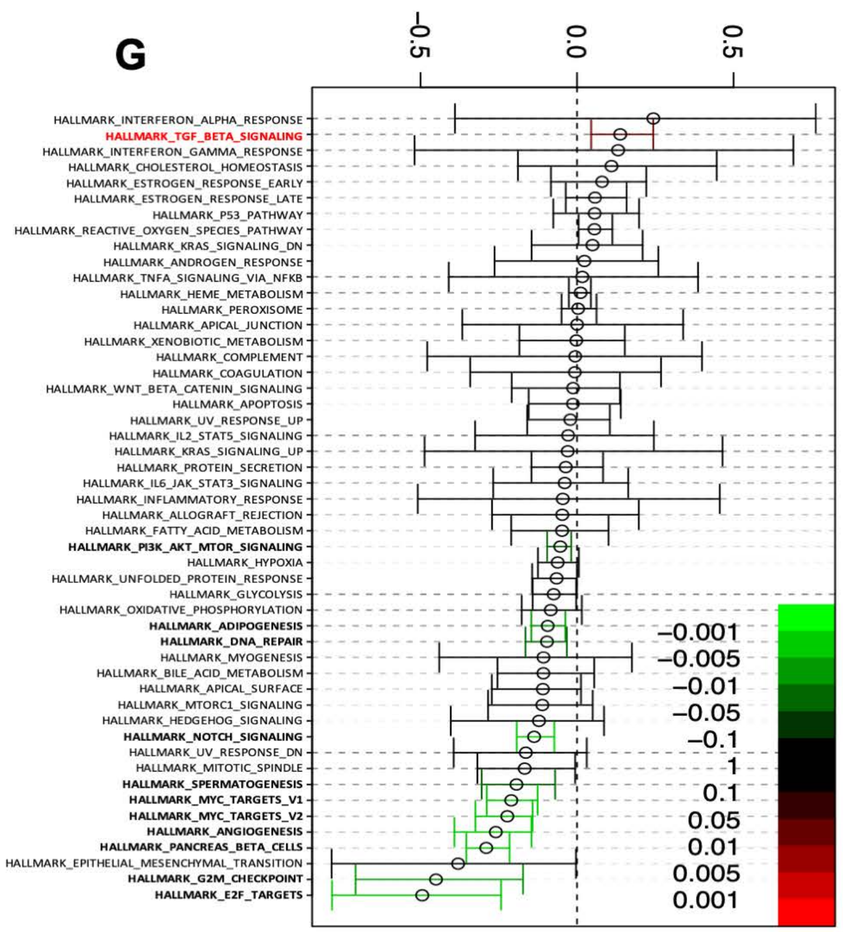
E


Pathway Activity
−1.0
−0.5
0.0
0.5
HALLMARK_APICAL_JUNCTION
HALLMARK_MYOGENESIS
HALLMARK_APICAL_SURFACE
HALLMARK_CHOLESTEROL_HOMEOSTASIS
HALLMARK_IL6_JAK_STAT3_SIGNALING
HALLMARK_EPITHELIAL_MESENCHYMAL_TRANSITION
HALLMARK_COAGULATION
HALLMARK_INFLAMMATORY_RESPONSE
HALLMARK_TNFA_SIGNALING_VIA_NFKB
HALLMARK_INTERFERON_ALPHA_RESPONSE
HALLMARK_KRAS_SIGNALING_DN
HALLMARK_HEDGEHOG_SIGNALING
HALLMARK_ESTROGEN_RESPONSE_EARLY
HALLMARK_KRAS_SIGNALING_UP
HALLMARK_IL2_STAT5_SIGNALING
HALLMARK_P53_PATHWAY
HALLMARK_TGF_BETA_SIGNALING
HALLMARK_UV_RESPONSE_DN
HALLMARK_REACTIVE_OXYGEN_SPECIES_PATHWAY
HALLMARK_ANDROGEN_RESPONSE
HALLMARK_INTERFERON_GAMMA_RESPONSE
HALLMARK_APOPTOSIS
HALLMARK_WNT_BETA_CATENIN_SIGNALING
HALLMARK_ALLOGRAFT_REJECTION
HALLMARK_COMPLEMENT
HALLMARK_NOTCH_SIGNALING
HALLMARK_XENOBIOTIC_METABOLISM
HALLMARK_BILE_ACID_METABOLISM
HALLMARK_ESTROGEN_RESPONSE_LATE
HALLMARK_UV_RESPONSE_UP
HALLMARK_PEROXISOME
HALLMARK_ANGIOGENESIS
HALLMARK_UNFOLDED_PROTEIN_RESPONSE
HALLMARK_HEME_METABOLISM
HALLMARK_FATTY_ACID_METABOLISM
HALLMARK_PROTEIN_SECRETION
HALLMARK_PI3K_AKT_MTOR_SIGNALING
HALLMARK_ADIPOGENESIS
HALLMARK_HYPOXIA
HALLMARK_MTORC1_SIGNALING
HALLMARK_GLYCOLYSIS
HALLMARK_MYC_TARGETS_V2
HALLMARK_PANCREAS_BETA_CELLS
HALLMARK_MITOTIC_SPINDLE
HALLMARK_DNA_REPAIR
HALLMARK_OXIDATIVE_PHOSPHORYLATION
HALLMARK_SPERMATOGENESIS
HALLMARK_MYC_TARGETS_V1
HALLMARK_G2M_CHECKPOINT
HALLMARK_E2F_TARGETS
−0.001
−0.005
−0.01
−0.05
−0.1
1
0.1
0.05
0.01
0.005
0.001

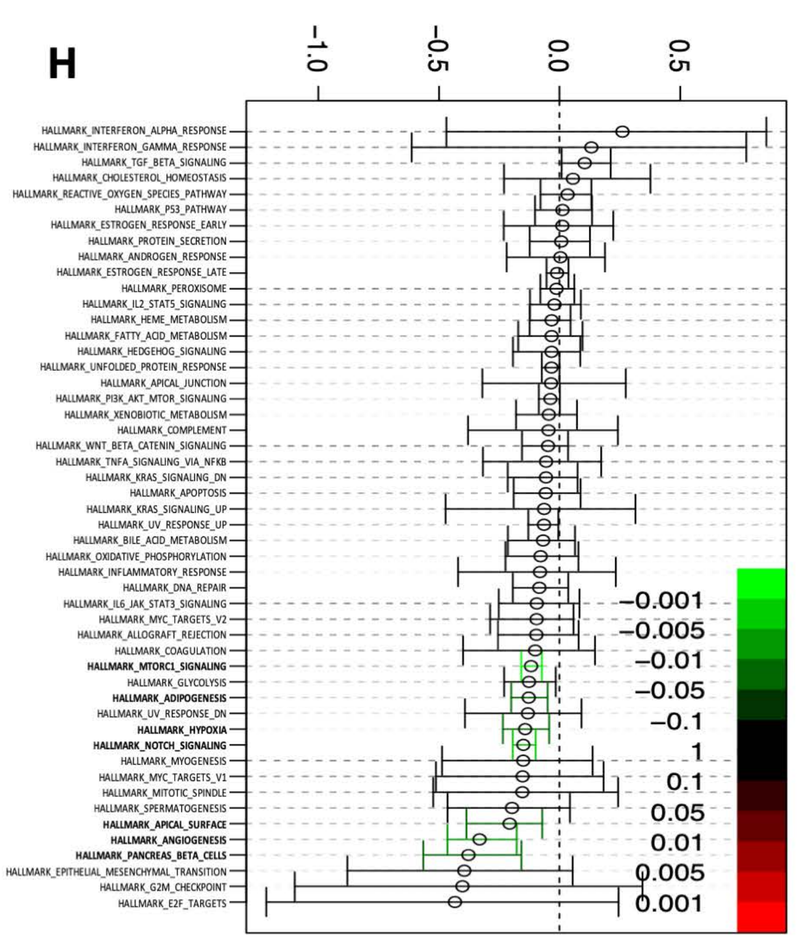
F


−log10(pvalue)
log2FoldChange
LUM
RGS4
IL6
DCN
CCL2
PDGFRB
COL3A1
MMP3
TNC
CXCL1
C3
SCG2
FLNC
MYO16
SCNN1A
ELF3
TMEM125
SCNN1B
CWH43
SLAMF7
OVOL1
FMO2
Differentially expressed
DOWN
NO
UP

G

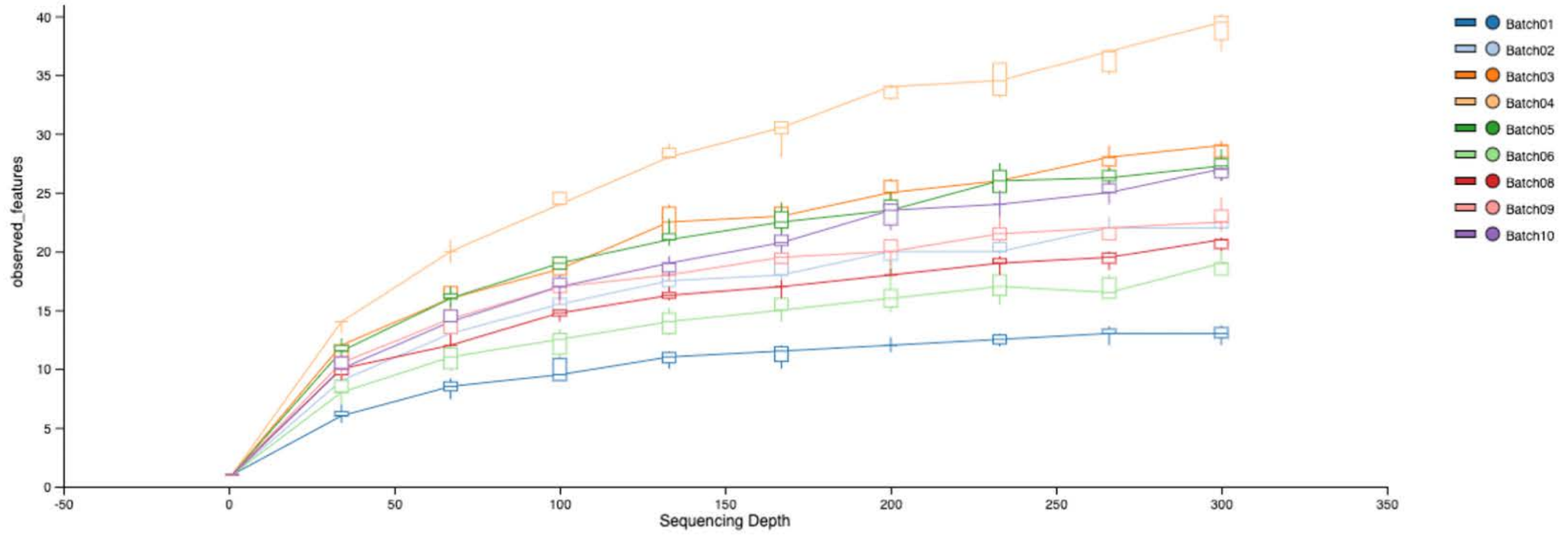

−0.5
0.0
0.5
HALLMARK_INTERFERON_ALPHA_RESPONSE
HALLMARK_TGF_BETA_SIGNALING
HALLMARK_INTERFERON_GAMMA_RESPONSE
HALLMARK_CHOLESTEROL_HOMEOSTASIS
HALLMARK_ESTROGEN_RESPONSE_EARLY
HALLMARK_ESTROGEN_RESPONSE_LATE
HALLMARK_P53_PATHWAY
HALLMARK_REACTIVE_OXYGEN_SPECIES_PATHWAY
HALLMARK_KRAS_SIGNALING_DN
HALLMARK_ANDROGEN_RESPONSE
HALLMARK_TNFA_SIGNALING_VIA_NFKB
HALLMARK_HEME_METABOLISM
HALLMARK_PEROXISOME
HALLMARK_APICAL_JUNCTION
HALLMARK_XENOBIOTIC_METABOLISM
HALLMARK_COMPLEMENT
HALLMARK_COAGULATION
HALLMARK_WNT_BETA_CATENIN_SIGNALING
HALLMARK_APOPTOSIS
HALLMARK_UV_RESPONSE_UP
HALLMARK_IL2_STAT5_SIGNALING
HALLMARK_KRAS_SIGNALING_UP
HALLMARK_PROTEIN_SECRETION
HALLMARK_IL6_JAK_STAT3_SIGNALING
HALLMARK_INFLAMMATORY_RESPONSE
HALLMARK_ALLOGRAFT_REJECTION
HALLMARK_FATTY_ACID_METABOLISM
HALLMARK_PI3K_AKT_MTOR_SIGNALING
HALLMARK_HYPOXIA
HALLMARK_UNFOLDED_PROTEIN_RESPONSE
HALLMARK_GLYCOLYSIS
HALLMARK_OXIDATIVE_PHOSPHORYLATION
HALLMARK_ADIPOGENESIS
HALLMARK_DNA_REPAIR
HALLMARK_MYOGENESIS
HALLMARK_BILE_ACID_METABOLISM
HALLMARK_APICAL_SURFACE
HALLMARK_MTORC1_SIGNALING
HALLMARK_HEDGEHOG_SIGNALING
HALLMARK_NOTCH_SIGNALING
HALLMARK_UV_RESPONSE_DN
HALLMARK_MITOTIC_SPINDLE
HALLMARK_SPERMATOGENESIS
HALLMARK_MYC_TARGETS_V1
HALLMARK_MYC_TARGETS_V2
HALLMARK_ANGIOGENESIS
HALLMARK_PANCREAS_BETA_CELLS
HALLMARK_EPITHELIAL_MESENCHYMAL_TRANSITION
HALLMARK_G2M_CHECKPOINT
HALLMARK_E2F_TARGETS
−0.001
−0.005
−0.01
−0.05
−0.1
1
0.1
0.05
0.01
0.005
0.001

H

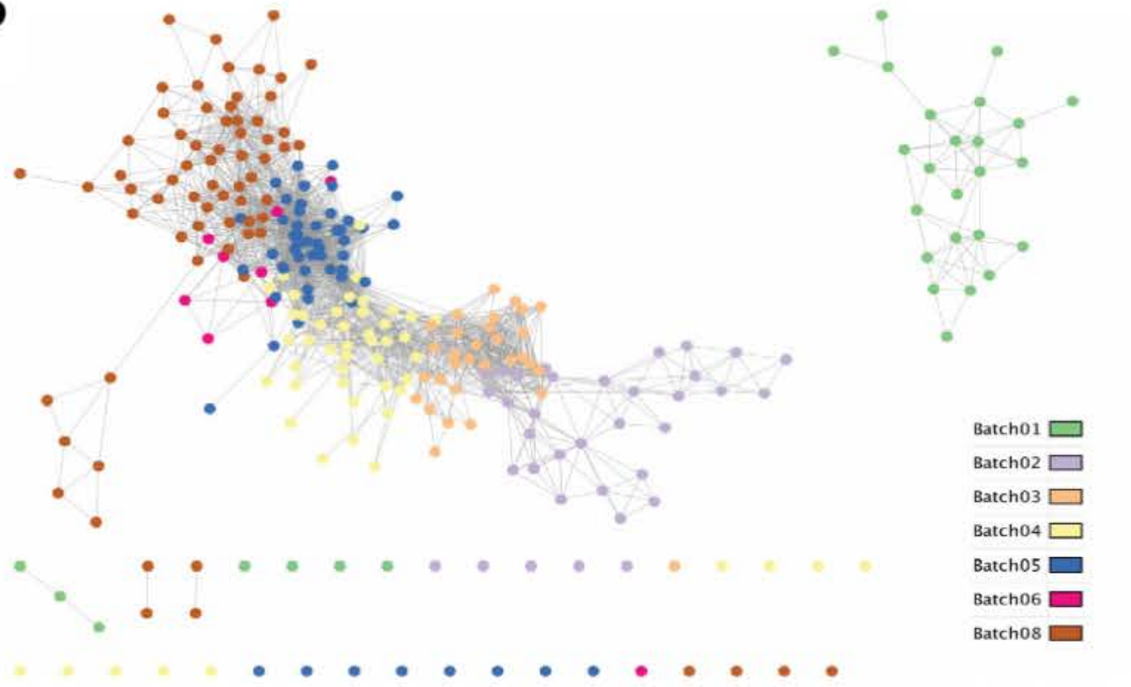

−1.0
−0.5
0.0
0.5
HALLMARK_INTERFERON_ALPHA_RESPONSE
HALLMARK_INTERFERON_GAMMA_RESPONSE
HALLMARK_TGF_BETA_SIGNALING
HALLMARK_CHOLESTEROL_HOMEOSTASIS
HALLMARK_REACTIVE_OXYGEN_SPECIES_PATHWAY
HALLMARK_P53_PATHWAY
HALLMARK_ESTROGEN_RESPONSE_EARLY
HALLMARK_PROTEIN_SECRETION
HALLMARK_ANDROGEN_RESPONSE
HALLMARK_ESTROGEN_RESPONSE_LATE
HALLMARK_PEROXISOME
HALLMARK_IL2_STAT5_SIGNALING
HALLMARK_HEME_METABOLISM
HALLMARK_FATTY_ACID_METABOLISM
HALLMARK_HEDGEHOG_SIGNALING
HALLMARK_UNFOLDED_PROTEIN_RESPONSE
HALLMARK_APICAL_JUNCTION
HALLMARK_PI3K_AKT_MTOR_SIGNALING
HALLMARK_XENOBIOTIC_METABOLISM
HALLMARK_COMPLEMENT
HALLMARK_WNT_BETA_CATENIN_SIGNALING
HALLMARK_TNFA_SIGNALING_VIA_NFKB
HALLMARK_KRAS_SIGNALING_DN
HALLMARK_APOPTOSIS
HALLMARK_KRAS_SIGNALING_UP
HALLMARK_UV_RESPONSE_UP
HALLMARK_BILE_ACID_METABOLISM
HALLMARK_OXIDATIVE_PHOSPHORYLATION
HALLMARK_INFLAMMATORY_RESPONSE
HALLMARK_DNA_REPAIR
HALLMARK_IL6_JAK_STAT3_SIGNALING
HALLMARK_MYC_TARGETS_V2
HALLMARK_ALLOGRAFT_REJECTION
HALLMARK_COAGULATION
HALLMARK_MTORC1_SIGNALING
HALLMARK_GLYCOLYSIS
HALLMARK_ADIPOGENESIS
HALLMARK_UV_RESPONSE_DN
HALLMARK_HYPOXIA
HALLMARK_NOTCH_SIGNALING
HALLMARK_MYOGENESIS
HALLMARK_MYC_TARGETS_V1
HALLMARK_MITOTIC_SPINDLE
HALLMARK_SPERMATOGENESIS
HALLMARK_APICAL_SURFACE
HALLMARK_ANGIOGENESIS
HALLMARK_PANCREAS_BETA_CELLS
HALLMARK_EPITHELIAL_MESENCHYMAL_TRANSITION
HALLMARK_G2M_CHECKPOINT
HALLMARK_E2F_TARGETS
−0.001
−0.005
−0.01
−0.05
−0.1
1
0.1
0.05
0.01
0.005
0.001

Supplementary Figure 8. Batch effect control for 16S, related to Figure 1.
A. Alpha rarefaction curves for baseline, samples colored by batch.
B. Association networks of all samples included in the study colored by batch.
C. Association networks of all samples included in the study colored by institution.
D. Association networks of all samples included in the study colored by clinical response.
E. Association networks of all samples included in the study colored by sample ID.
F. Association networks of all baseline samples included in the study colored by batch.
G. Association networks of all baseline samples included in the study colored by clinical response.

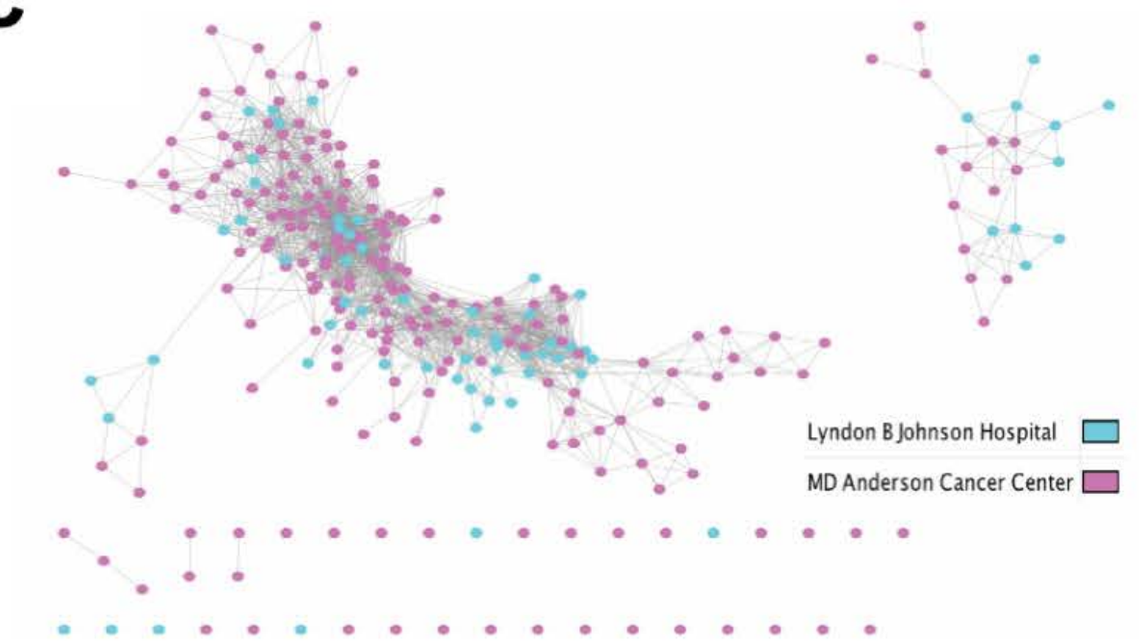
A


observed_features
Sequencing Depth
0
5
10
15
20
25
30
35
40
-50
0
50
100
150
200
250
300
350
Batch01
Batch02
Batch03
Batch04
Batch05
Batch06
Batch08
Batch09
Batch10

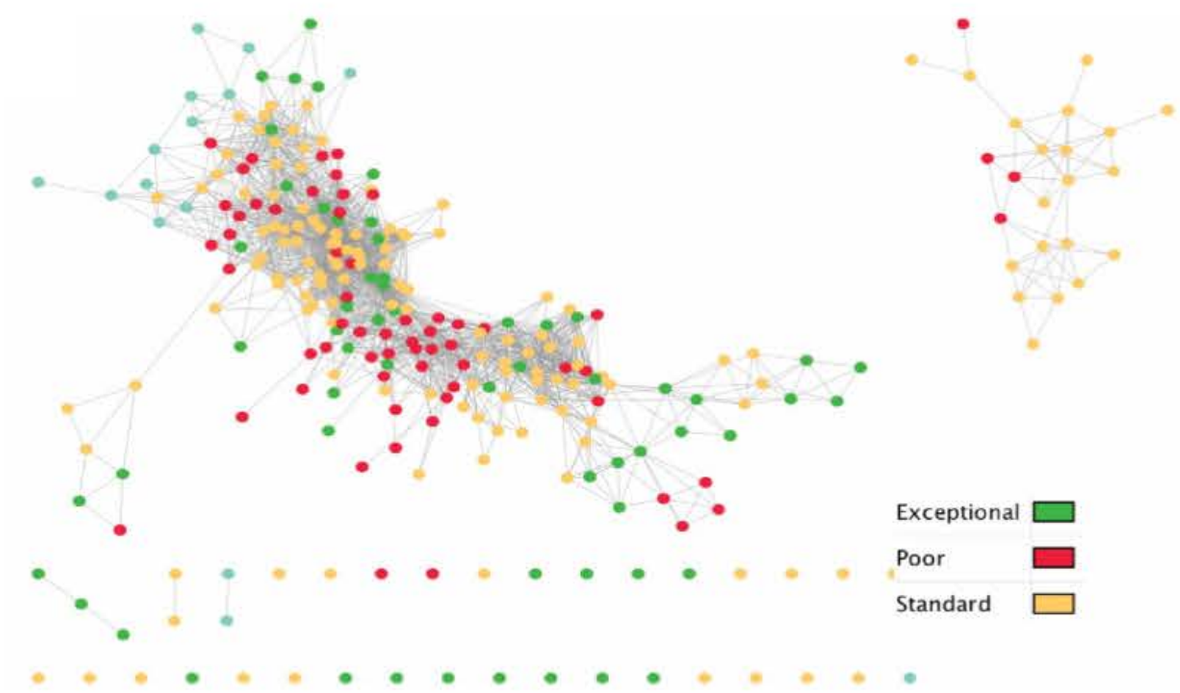
B


Batch01
Batch02
Batch03
Batch04
Batch05
Batch06
Batch08

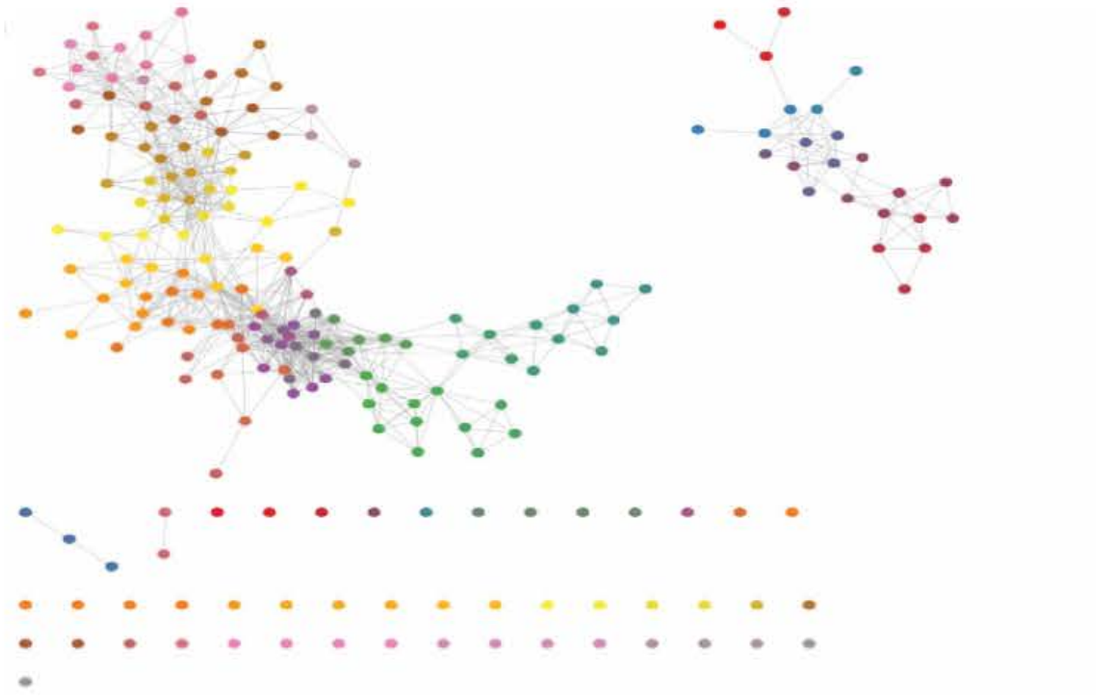
C


Lyndon B Johnson Hospital
MD Anderson Cancer Center

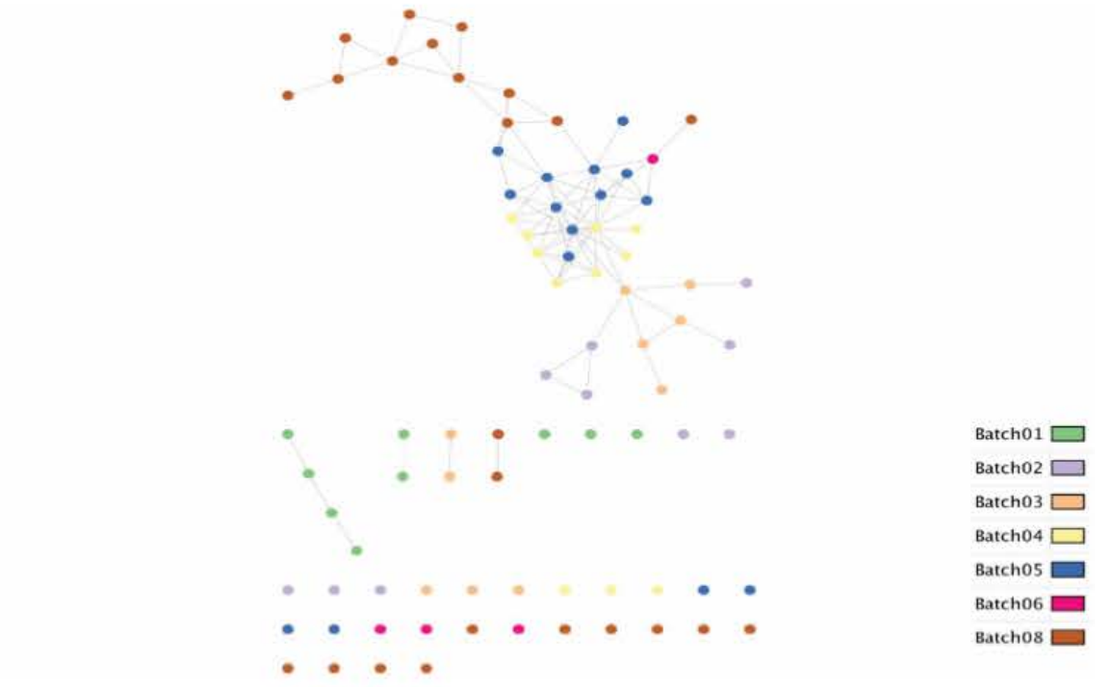
D


Exceptional
Poor
Standard

E



F


Batch01
Batch02
Batch03
Batch04
Batch05
Batch06
Batch08

G


Exceptional
Poor
Standard