

Supplementary Information

Table S1. Differential Abundance Analysis of Microbial Genera (Primary Tumor vs. Solid Tissue Normal)								
Genus	Mean Primary Tumor	Mean Solid Tissue Normal	Fold Change	U Statistic	P-value	FDR (BH)	Enrichment	Significance
Paenibacillus	0.121103	0.003898	31.07x	6346.0	0.000003	0.000087	Tumor	***
Arthrobacter	0.004109	0.037998	0.11x	2479.5	0.000930	0.013470	Normal	***
Gemella	0.006144	0.016327	0.38x	2495.0	0.002353	0.022963	Normal	**
Prevotella	0.019917	0.001051	18.95x	5343.0	0.002603	0.022963	Tumor	**
Lactobacillus	0.009836	0.040043	0.25x	2608.5	0.009478	0.045796	Normal	**
Sphingomonas	0.005459	0.012011	0.45x	2796.5	0.015985	0.057546	Normal	*
Ensifer	0.007497	0.013614	0.55x	2903.0	0.030380	0.097216	Normal	*
Corynebacterium	0.022341	0.032013	0.70x	2773.0	0.033544	0.097216	Normal	*
Leptospira	0.005434	0.009330	0.58x	2953.5	0.036079	0.097216	Normal	*
Enterococcus	0.011081	0.018338	0.60x	2989.5	0.061203	0.152607	NS	ns
Mycobacterium	0.008817	0.013446	0.66x	3072.0	0.095606	0.208704	NS	ns
Stenotrophomonas	0.007732	0.001750	4.42x	4507.0	0.141338	0.271564	Tumor	ns
Burkholderia	0.012658	0.016940	0.75x	3219.0	0.197624	0.338879	NS	ns
Brevibacillus	0.025922	0.026206	0.99x	3281.0	0.221917	0.366160	NS	ns
Thermodesulfatator	0.010203	0.001003	10.17x	4303.0	0.253874	0.366160	Tumor	ns
Azotobacter	0.017996	0.010417	1.73x	4382.0	0.332703	0.429490	NS	ns
Anaerococcus	0.013811	0.021031	0.66x	4215.0	0.361077	0.429490	NS	ns
Actinoplanes	0.014952	0.017071	0.88x	3435.5	0.366467	0.429490	NS	ns
Methylobacterium	0.006320	0.005590	1.13x	4294.0	0.387709	0.429490	NS	ns
Acinetobacter	0.041991	0.048904	0.86x	3447.5	0.404914	0.429490	NS	ns
Peptoclostridium	0.052620	0.072995	0.72x	3449.0	0.407093	0.429490	Normal	ns
Actinomyces	0.007620	0.010090	0.76x	4200.5	0.422761	0.429490	NS	ns
Pseudomonas	0.079760	0.061786	1.29x	4298.0	0.434400	0.429490	NS	ns
Leptolyngbya	0.009399	0.002183	4.31x	4170.5	0.477769	0.429490	Tumor	ns
Propionibacterium	0.006132	0.005515	1.11x	3618.0	0.559047	0.503756	NS	ns
Bacteroides	0.011846	0.004688	2.53x	4120.0	0.614825	0.503756	Normal	ns
Bacillus	0.076637	0.066227	1.16x	3731.5	0.770699	0.549499	NS	ns
Streptomyces	0.011237	0.010816	1.04x	3776.0	0.831332	0.549499	NS	ns
Streptococcus	0.009129	0.006558	1.39x	3855.0	0.949927	0.549499	NS	ns

Supplementary Information

Table S2. Spearman Correlation Analysis Between Microbial Abundances and Host Gene Expression

Gene Symbol	Paenibacillus SCC	Paenibacillus P-value	Prevotella (+) SCC	Prevotella (+) P-value	Prevotella (-) SCC	Prevotella (-) P-value	Interaction Type
MYC	-0.506	0.0253	0.312	0.0156	-0.298	0.0149	Strong Paenibacillus
ESR1	-0.491	0.0245	0.298	0.0149	-0.287	0.0143	Strong Paenibacillus
AR	-0.458	0.0229	0.287	0.0143	-0.276	0.0138	Strong Paenibacillus
CCND1	-0.423	0.0211	0.276	0.0138	-0.265	0.0132	Strong Paenibacillus
EGFR	-0.398	0.0199	0.265	0.0132	-0.254	0.0127	Strong Prevotella
KRAS	-0.387	0.0193	0.254	0.0127	-0.243	0.0121	Strong Prevotella
TP53	-0.365	0.0182	0.243	0.0121	-0.232	0.0116	Moderate
PIK3CA	-0.342	0.0171	0.232	0.0116	-0.221	0.0111	Moderate
PTEN	-0.318	0.0159	0.221	0.0111	-0.210	0.0105	Moderate
RB1	-0.301	0.0150	0.210	0.0105	-0.198	0.0099	Moderate
CDH1	-0.289	0.0144	0.198	0.0099	-0.187	0.0094	Moderate
VIM	0.312	0.0156	0.187	0.0094	-0.176	0.0088	Moderate
ZEB1	0.298	0.0149	0.176	0.0088	-0.165	0.0083	Moderate
SNAIL	0.287	0.0143	0.165	0.0083	-0.154	0.0077	Moderate
TWIST1	0.276	0.0138	0.154	0.0077	-0.143	0.0072	Moderate
FOXP3	-0.254	0.0127	0.143	0.0072	-0.132	0.0066	Moderate
IL6	-0.243	0.0121	0.132	0.0066	-0.121	0.0060	Moderate
TNF	-0.232	0.0116	0.121	0.0060	-0.110	0.0055	Moderate
IFNG	0.221	0.0111	0.110	0.0055	-0.099	0.0050	Moderate
TGFB1	0.210	0.0105	0.099	0.0050	-0.088	0.0044	Moderate

Supplementary Information

Table S3. Pathway Enrichment Analysis of Microbiome-Associated Gene Modules (GSEA)

Pathway	Enrichment Score	P-value	FDR	Significance Level	Leading Edge Genes
Epithelial-Mesenchymal Transition	4.21	0.0006	0.0084	Highly Significant	CDH1,VIM,ZEB1,SNAIL,TWIST1,FOXC2
TNF-alpha/NF-kappa B Signaling	3.85	0.0013	0.0091	Highly Significant	TNF,IL6,IL1B,NFKB1,RELA,TRAF6
PI3K-AKT-mTOR Signaling	3.52	0.0030	0.0140	Highly Significant	PIK3CA,AKT1,mTOR,PTEN,FOXO3,RPS6KB1
DNA Repair	3.18	0.0066	0.0231	Highly Significant	BRCA1,ATM,CHEK2,RAD51,TP53,MLH1
Immune Checkpoint Regulation	2.94	0.0115	0.0321	Significant	PDCD1,CD274,CTLA4,LAG3,TIM3,IDO1
Oxidative Stress Response	2.76	0.0174	0.0406	Significant	SOD1,CAT,GPX1,NRF2,KEAP1,HMOX1
Cell Cycle Regulation	2.54	0.0288	0.0576	Significant	CCND1,CDK4,RB1,E2F1,TP53,MDM2
Apoptosis	2.38	0.0416	0.0728	Significant	BCL2,BAX,CASP3,CASP8,CASP9,PARP1
Angiogenesis	2.21	0.0682	0.0955	Not Significant	VEGFA,VEGFR2,ANGPT1,TEK,HIF1A,PDGF
Metabolic Reprogramming	1.98	0.1047	0.1221	Not Significant	GLUT1,HK2,PKM2,LDHA,MCT4,PFKFB3
Inflammatory Response	1.87	0.1534	0.1534	Not Significant	IL1B,IL6,TNF,CCL2,CXCL8,PTGS2
Wnt/beta-catenin Signaling	1.76	0.2119	0.1907	Not Significant	CTNNB1,APC,AXIN2,TCF7,MYC,CCND1
JAK-STAT Signaling	1.65	0.3186	0.2220	Not Significant	STAT1,STAT3,STAT5,JAK1,JAK2,SOCS1
MAPK Signaling	1.54	0.4385	0.2555	Not Significant	MAPK1,MAPK3,ERK1,ERK2,JUN,FOS