

Table S1A. Identified intratumoral microorganisms and their effects on immune TME compartment in different types of malignancies

Microorganism	Tumor type	Immune TME	Reference
<i>Blautia</i> , <i>Faecalibacterium</i> , <i>Faecalitea</i>	CRC	↑CD3 infiltration	[113]
<i>Sachharopolyspora</i> , <i>Pseudoxanthomonas</i> , <i>Streptomyces</i>	PDAC	↑CD8 infiltration, granzyme B production	[19]
<i>Lachnoclostridium</i>	Melanoma	↑CD8 infiltration, elevated CXCL9, CXCL10 and CCL5	[114]
<i>Fusobacterium nucleatum</i>	OSCC	↓B cells, CD4+ T helper cells & M2 macrophages	[83]
<i>Streptococcus</i>	ESCC	↑ CD8+, Granzyme B+ cells	[115]
<i>Clostridium novyi</i> spores	Refractory solid tumors	↑CD8+, Tregs, MDSCs	[116]
PVSRIO	Melanoma	↑CD4+, CD8+, NK cells, elevated IFN γ and granzyme B	[117]
<i>Neospora caninum</i>	Melanoma	↑ CD8+, CD68+ cells, ↑ Th1 cytokines	[94]
<i>Firmicutes</i> , <i>Proteobacteria</i>	GBM	↑Activation of TIL-derived CD4+ clones, ↑pro- inflammatory cytokines & chemokines	[118]
<i>Lactobacillus reuteri</i> (effect mediated by I3A)	Melanoma	↑Tc1 phenotype, ↑ Ahr signaling in CD8+ cells, ↑ IFN γ	[110]
<i>Bifidobacterium</i>	CRC	↑STING-mediated type I IFN signaling in dendritic cells	[119]
<i>Lactobacillus reuteri</i> (effect mediated by SCFA)	HCC	↓IL17A in hepatic ILC3	[121]
<i>Malassezia</i>	PDAC	↑Mannose-binding lectin/C3 complement cascade	[122]
Engineered <i>Salmonella</i> strain VNP20009	Melanoma	↑Activation of dendritic cells	[123]
Engineered <i>E. coli</i> Nissle 1917 strain	Breast cancer	↑CD4+, ↑ IFN γ , TNF α	[124]
Engineered <i>E. coli</i> strain	Breast cancer	↑MHC-II, CD86 on dendritic cells ↑ CD8+ IFN γ + T cells, ↓ Tregs	[125]
Engineered <i>E. coli</i> strain MG1655	Renal cancer /CRC	↑IFN γ , IL-12	[126]
Engineered <i>E. coli</i> strain Nissle 1917	B-cell lymphoma	↑IFN γ & Granzyme B secretion by CD4+ & CD8+ T cells	[127]
<i>Enterococcus faecalis</i> , <i>Lactobacillus johnsonii</i> , <i>Escherichia coli</i>	Melanoma	↑ MHC-II, CD40, CD80, CD86 on dendritic cells	[128]
Firmicutes, Bacteroidetes	CRC	↓IL-17A, CCL20	[129]
<i>Achromobacter deleyi</i> , <i>Microcella alkaliphila</i>	Ovarian cancer	↑M1 macrophages	[130]
<i>Devosia</i> sp. LEGU1, <i>Ancylobacter pratisalsi</i> , <i>Acinetobacter seifertii</i>	Ovarian cancer	↓M1 macrophages	[130]
<i>Bacillus</i> , <i>Paenibacillus</i> (effect mediated by TMAO)	PDAC	Skewing TAMs, MDSCs, CD4+, CD8+, dendritic cells to immunostimulatory phenotypes	[131]

<i>Alistipes</i>	CRC	↑CD8 naïve & memory T cells ↓ macrophages, NK, MAIT cells	[134]
<i>Parvimonas, Bilophila</i>	CRC	↓NK & MAIT cells	[134]
<i>F. nucleatum</i>	CRC	↓CD3+ infiltration, ↑TAMs, MDSCs, dendritic cells, ↑CD163+ ↓ Foxp3+ T cells	[61,135, 136]
Clostridiales	CRC	↓CD8+ cells	[138]
<i>Porphyromonas gingivalis</i>	CRC	↑CD11b+, macrophages, dendritic cells ↑ TNFα, IL-6 and IL-1β	[139]
<i>Porphyromonas gingivalis</i>	PDAC	↓CD8+ cells ↑ neutrophils ↑ CXCL1, CXCL2, CXCR2, neutrophil-derived elastase	[62]
<i>Acidovorax ebreus</i> TPSY	PDAC	↓CD8+ cells, activated memory T cells, M2 macrophages	[140]
<i>Algibacter, Epilithonimonas</i>	Melanoma	↓CD8+ cells, CXCL9, CXCL10 and CCL5	[114]
<i>Pseudomonas putida</i> strain KT2440	LUSC	↓naïve B cells and activated dendritic cells	[143]
<i>Rothia dentocariosa</i> ATCC 17931	LUSC	↓naïve B cells, resting mast cells, M1 and M2 macrophages	[143]
<i>Thermotaphylospora chromogena</i>	LUSC	↓naïve B cells, resting CD4+, NK, activated mast cells	[143]
<i>Actinobacter</i>	Breast cancer	↑CD8+ T cells	[144]
<i>Methylibium</i>	Breast cancer	↓T cell infiltration	[144]
<i>Stenotrophomonas, Acinetobacter, Gemella, Neisseria, Aquabacterium, Haemophilus, Novosphingobium, Streptococcus, Massilia, Gemmiger, Chryseobacterium, Brevundimonas</i>	Gastric cancer	↑BDCA2+ plasmacytoid dendritic cells	[146]
<i>Streptococcus, Massilia, Fusobacterium, Oribacterium, Campylobacter, Selenomonas, Dialister, Photobacterium</i>	Gastric cancer	↑Foxp3+ Tregs	[146]
<i>Lactobacillus, F. nucleatum</i>	ESCC	↑PD-L1+ TAMs	[147]
<i>Malassezia</i>	PDAC	↑IL-33, ILC2 cells	[150]
<i>Mycoplasma hyopneumoniae, Citrobacter freundii</i>	PDAC	↑Immune suppression pathways, proinflammatory immune cascades	[140]
<i>Candida albicans</i>	CRC	↑IL-7 production in macrophages, ↑ IL-22 in ILC3 cells	[151]
<i>Lactobacillus murinus, Lactobacillus reuteri</i> (mediated by indoles)	PDAC	↓CD8+, ↑ MDSCs, Ahr activity on TAMs	[153]
<i>Methylobacterium</i>	Gastric cancer	↓CD8+, CD103+ TRM cells	[154]

Table S1B. Identified intratumoral microorganisms and their effects on Hypoxic & Acidic TME compartments in different types of malignancies

Microorganism	Tumor type	Hypoxic TME	Acidic TME	Reference
<i>F. nucleatum</i>	OSCC		↑ GLUT1 on cancer cells, glycolysis, lactate production	[159]
<i>Pseudomonas</i>	Oral cavity tumors	↑Hypoxia score		[91]
<i>Actinomyces, Sulfurimonas</i>	Oropharynx tumors	↑Hypoxia score		[91]
<i>Neospora caninum tachyzoites</i>	Melanoma	↑HIF-1α		[94]
<i>Pelomonas</i>	Breast cancer	↑VEGF-A		[144]
<i>Bradyrhizobium</i>	Breast cancer	↓VEGF-A		[144]
<i>Parapoxvirus</i>	TNBC	↑viral homologs of human VEGF-A, VEGF-E		[90]

Table S1C. Identified intratumoral microbiome-derived metabolites and their effects on distinct TME compartments in different types of malignancies

Microbial metabolite	Tumor type	Hypoxic TME	Acidic TME	Mechanical TME	Reference
Putrescine	GBM		Buffering the intracellular pH of myeloid lineage cells		[161]
Butyrate	Breast Cancer		↑MCT4 on cancer cells, lactate efflux		[163]
Butyrate	CRC	↓VEGF, ↓HIF-1α nuclear translocation	↑MCT1 on cancer cells, lactate influx	↓α2β1 integrin, ↓attachment to type I & IV collagen surfaces	[164, 171, 194]
Butyrate & propionate	CRC	↓HIF-2α			[172, 173]
Reuterin	CRC	↓HIF-2α			[172]
Biliverdin	CRC	↑VEGF-A			[175]

Table S1D. Identified intratumoral microorganisms and their effects on Metabolic TME compartment in different types of malignancies

Microorganism	Tumor type	Metabolic TME	Reference
<i>Lactobacillus</i> , <i>Muribaculaceae</i>	Gastric cancer	Altered glutathione, glucose or amino acid metabolic pathways	[178]
<i>Prevotella</i> , <i>Acinetobacter</i> , <i>Streptococcus</i>	Gastric cancer	Diacylglycerols, phosphatidylethanolamines synthesis	[177-179]
<i>Eshcherichia coli</i>	Breast cancer	Dysregulation of lipid, carbohydrate and amino acid metabolic pathways	[180]
Tenericutes	TNBC	↑Sphingomyelin, ceramide levels	[182]
Firmicutes, Bacteroidetes, Proteobacteria	TNBC	↑Lipid metabolites	[182]
Engineered <i>E. coli</i> Nissle 1917	CRC	↑L-arginine	[183]
<i>Clostridium butyricum</i> (effect mediated by butyrate)	PDAC	↑ROS, lipid droplets, triglycerides	[107]
<i>Lactobacillus reuteri</i> (effect mediated by reuterin)	CRC	↑Protein oxidation, impaired ribosomal biogenesis	[172]
<i>Akkermansia muciniphila</i>	Lung cancer	↓Lactate, nucleotide precursors, glutamine metabolites	[69]
<i>Acidobacteriales</i> , <i>Acidobacteriaceae</i>	Lung cancer	↑Lactate	[69]
Gammaproteobacteria	PDAC	↑Gemcitabine metabolism	[72]
<i>Escherichia coli</i>	CRC	↑5-fluorouracil metabolism	[185]
<i>Lactobacillus iners</i> (effect mediated by lactate)	Cervical cancer	↑Glycolysis, TCA cycle, DNA synthesis	[186]
<i>Paraburkholderia fungorum</i>	Cholangio-carcinoma	↑Alanine, aspartate, glutamate metabolites	[82]

Table S1E. Identified intratumoral microorganisms and their effects on Mechanical & Innervated TME compartments in different types of malignancies

Microorganism	Tumor type	Mechanical TME	Innervated TME	Reference
<i>Escherichia coli</i> str. K-12 substr. MG1655, butyrate-producing bacterium SM4/1	MIBC	↓E-cadherin		[191]
<i>Actinosynnema mirum</i> DSM 43827, <i>Burkholderia ambifaria</i> AMMD	MIBC	↓COL26A1, ↑Elastin		[191]
<i>Bifidobacterium adolescentis</i>	CRC	↑CD143+ CAFs		[192]
<i>Actinomyces</i>	CRC	↑αSMA+ stromal cells		[193]
<i>Porphyromonas gingivalis</i>	ESCC	↑MMP-9, ↓ E-cadherin		[197]
<i>Helicobacter pylori</i>	Gastric cancer	↑ VCAM-1 in CAFs		[198]
<i>Aspergillus flavus</i> , <i>Coccidioides immitis</i> RS, <i>Gaeumannomyces tritici</i> R3-111a-1, <i>Morchella esculenta</i>	HNSCC		↓Perineural invasion	[202]
<i>Solicoccozyma aeria</i>	Gastric cancer		↓Perineural invasion	[203]
<i>Delftia acidovorans</i> SPH-1	Prostate cancer		BDNF dysregulation	[142]