

Supplementary Table Summary of bacterial taxa identified in four groups shown in Figure 4.

Group I: stage I > II > III

Bacterium	Metabolism and pathogenicity	Reference
<i>Bacteroides</i>	<i>Bacteroides</i> are dominant beneficial bacteria, which metabolize polysaccharides and oligosaccharides, providing nutrition and vitamins to the host and other intestinal microbial residents. Some strains, e.g. <i>Bacteroides fragilis</i> , produce <i>B. fragilis</i> toxin which causes Inflammatory bowel disease.	1, 2
<i>Prevotella</i>	Intestinal <i>Prevotella</i> colonization results in metabolic changes in the microbiota, which reduce IL-18 production and consequently exacerbate intestinal inflammation and potential systemic autoimmunity.	3
<i>Ruminococcus</i>	<i>Ruminococcus</i> belongs to probiotics and expresses mucus-, fucose-, and human milk oligosaccharides (HMO)-related degradation enzymes.	4

<i>Dorea</i>	Abundance of <i>Dorea</i> increases in dysbiosis of gut microbiota caused by other disease, such as esophageal cancer and nonalcoholic fatty liver disease.	5, 6
<i>Dialister</i>	<i>Dialister</i> is Gram-stain-negative in healthy faecal sample, and utilizes succinate and causes repetitive bartholinitis episodes.	7, 8
<i>Faecalibacterium</i>	<i>Faecalibacterium</i> plays a major role in the regulation of gut barrier, inflammation and metabolic functions.	9
<i>Coprococcus</i>	<i>Coprococcus</i> produces butyrate, and β -Glucan is a major growth substrate for <i>Coprococcus eutactus</i> .	10, 11
<i>Sutterella</i>	<i>Sutterella</i> is associated with gastrointestinal diseases. <i>Sutterella</i> does not induce substantial inflammation, but has a capacity to degrade IgA.	12
<i>Selenomonas</i>	<i>Selenomonas</i> is closely associated with CRC patients with hyperlipidaemia.	13
<i>Eubacterium</i>	Compared to healthy samples, abundance of <i>Eubacterium</i> decreases in patients with IBD and CRC.	14, 15

<i>Eggerthella</i>	<i>Eggerthella lenta</i> is involved in converting reaction of Plant-derived lignans in food to enterolignans ² .	16
<i>Phascolarctobacterium</i>	<i>Phascolarctobacterium</i> can produce short-chain fatty acids, including acetate and propionate, and is associated with the metabolic state and mood of the host.	17
<i>Desulfovibrio</i>	<i>Desulfovibrio</i> is commensal microbe colonising the mucus gel layer of the colon, metabolises the sulfate moiety of sulfated mucins, and has increased affinity to ulcerative colitis mucin.	18
<i>Comamonas</i>	<i>Comamonas</i> abundance changes when resistant starch intervention is used to reduce body fat.	19
<i>Anaerostipes</i>	<i>Anaerostipes</i> converts lactate-acetate and sugar to butyrate.	20
<i>Paraprevotella</i>	<i>Paraprevotella</i> is positively correlated with damaged gut integrity induced by major depressive disorder.	21
<i>Neisseria</i>	Anti-inflammatory microenvironment causes decreased <i>Neisseria</i> abundance.	22
<i>Slackia</i>	<i>Slackia</i> is gut-associated bacteria that play roles in host lipid and xenobiotic metabolism. <i>Slackia</i> may be free living in the lumen because it has low adhesion to cells.	23

Group II: stage I < II < III

Bacterium	Metabolism and pathogenicity	Reference
<i>Fusobacterium</i>	<i>Fusobacterium</i> has high abundance in intestine in CRC patients, and low abundance in health intestine.	24
<i>Delftia</i>	<i>Delftia</i> contains IMP-1 Metallo- β -Lactamase which is resistant to antibacterial activity against β -Lactams. <i>Delftia</i> is associated with Endophthalmitis and pneumonia with lung cavities formation.	25, 26, 27
<i>Citrobacter</i>	<i>Citrobacter</i> is able to induce colitis.	28
<i>Shewanella</i>	<i>Shewanella</i> is found in water environment and in patients, and can act as the originator of oxacillinase in Gram-negative bacteria.	29
<i>Klebsiella</i>	<i>Klebsiella</i> induces Pneumosepsis, produces cytotoxin, and is associated with necrotizing enterocolitis.	30, 31

<i>Granulicatella</i>	<i>Granulicatella</i> causes infective endocarditis and endophthalmitis.	32, 33
<i>Capnocytophaga</i>	<i>Capnocytophaga</i> causes infection in wound.	34
<i>Pseudomonas</i>	<i>Pseudomonas</i> produces exopolysaccharides and infection.	35, 36
<i>Pyramidobacter</i>	<i>Pyramidobacter</i> produces acetic and isovaleric acids.	37
<i>Acinetobacter</i>	<i>Acinetobacter</i> relates to carnitine metabolism.	38
TG5	Unknown	
<i>Moryella</i>	<i>Moryella</i> is weakly saccharolytic and produces indole, acetate, butyrate and lactate as major metabolic end products.	39
<i>Stenotrophomonas</i>	<i>Stenotrophomonas</i> is opportunistic emergent pathogen causing hospital-acquired infections.	40
<i>Megasphaera</i>	A butyrate-producing bacterium	41
<i>Eikenella</i>	<i>Eikenella</i> produces lysine decarboxylase.	42
<i>Vibrio</i>	<i>Vibrio</i> uses Lysine succinylation as post-translational modification to modulate host factors critical for infection.	43

<i>Turicibacter</i>	<i>Turicibacter</i> is an anaerobic, Gram-positive bacterium, isolated from human feces.	44
<i>Mycobacterium</i>	<i>Mycobacterium</i> infection is found in patients with metastatic colorectal cancer.	45
<i>Dickeya</i>	<i>Dickeya</i> relates to potato infection.	46
<i>Rubellimicrobium</i>	<i>Rubellimicrobium</i> exists in the soil.	47
<i>Plesiomonas</i>	<i>Plesiomonas</i> has several virulence factors, such as lysophospholipase, a twin-arginine translocation system and the type VI secretion effector Phospholipase A1, which relate to diarrhoeal disease.	48
<i>Rubrobacter</i>	<i>Rubrobacter</i> produces D-Amino Acid Oxidase.	49
<i>Erwinia</i>	<i>Erwinia</i> has high abundance in intestine of gastroenteritis patients.	50
<i>Dysgonomonas</i>	<i>Dysgonomonas</i> is Gram-stain negative cocci. It grows optimally at 37°C and is catalase positive but oxidase negative.	51
<i>Paludibacter</i>	A propionate-producing fermentative bacterium	52

Group III: stage I > II < III

Bacterium	Metabolism and pathogenicity	Reference
<i>Akkermansia</i>	Bacterial biomarker of colorectal cancer	53
<i>Sneathia</i>	<i>Sneathia amnii</i> produces a cytotoxin, named CptA for cytopathogenic toxin, component A, which is capable of permeabilizing chorionic trophoblasts and lysing human red blood cells.	54
<i>Morganella</i>	<i>Morganella</i> produces extended-spectrum β -lactamase, and causes wound infections after colorectal surgery.	55
<i>Parabacteroides</i>	<i>Parabacteroides</i> has higher abundance in tumor tissues than adjacent normal tissues in CRC patients.	56
<i>Ruminococcus</i>	Dietary α -ketoglutarate intervention may protect against inflammation-related CRC and increases <i>Ruminococcus</i> population.	57
<i>Porphyromonas</i>	<i>Porphyromonas gingivalis</i> is a keystone pathogen in periodontitis and promotes the proliferation of colorectal cancer cells by activating the MAPK/ERK signaling pathway.	58

<i>Bilophila</i>	<i>Bilophila</i> accesses sulfite from taurine to produce hydrogen sulfide.	59
<i>Gemella</i>	<i>Gemella</i> is associated with CRC. The risk of CRC is increased in patients with bacteremia from <i>Gemella</i> .	60
<i>Haemophilus</i>	<i>Haemophilus</i> was depleted in the transition from stage 0 to early-stage CRC.	61
<i>Leptotrichia</i>	<i>Leptotrichia</i> is significant co-occurrence within individual tumors.	62
<i>Odoribacter</i>	The relative abundance of <i>Odoribacter</i> is significantly increased in CRC gut flora after 5-Fluorouracil treatment	63
<i>Acidaminococcus</i>	Increased relative abundance of <i>Acidaminococcus</i> is associated with future linear growth deficits.	64
<i>Butyricimonas</i>	A closely interaction between <i>Butyricimonas</i> and <i>Clostridium</i> is observed in the microbiome network in CRC samples.	65
<i>Anaerotruncus</i>	The relative abundances of <i>Anaerotruncus</i> displayed significant relationships with both steroid biosynthesis and terpenoid and triterpenoid biosynthesis pathways.	66

<i>Christensenella</i>	The abundance of longevity related <i>Christensenella</i> species in gut microbiota increases after fasting and is inversely correlated with age as well as body mass index.	67
WAL_1855D	Unknown	

Group IV: stage I < II > III

Bacterium	Metabolism and pathogenicity	Reference
<i>Streptococcus</i>	<i>Streptococcus bovis</i> contributes to the development of CRC via recruiting CD11b ⁺ TLR-4 ⁺ cells, and should be investigated for early detection of colorectal pathology. <i>Streptococcus gallolyticus</i> subsp. <i>gallolyticus</i> (Sgg) infection has gained considerable attention for its strong association with CRC.	68, 69, 70
<i>Parvimonas</i>	Bacterial biomarker of colorectal cancer	53
<i>Peptostreptococcus</i>	Bacterial biomarker of colorectal cancer	53
<i>Oscillospira</i>	High <i>Oscillospira</i> abundance indicates constipation and low BMI.	71

<i>Blautia</i>	<i>Blautia</i> is inversely associated with visceral fat area.	72
<i>Bifidobacterium</i>	A possible role of <i>Bifidobacteria</i> in determining distinct tumor characteristics or as an indicator of dysfunctional mucosal barrier in CRC. <i>Bifidobacterium longum</i> suppresses colorectal carcinogenesis.	73, 74
<i>Campylobacter</i>	<i>Campylobacter jejuni</i> produces a genotoxin, cytolethal distending toxin, which has DNase activity and causes DNA double-strand breaks and promotes colorectal tumorigenesis.	75
<i>Roseburia</i>	<i>Roseburia</i> produces butyrate and shows a significant reduction in the gut microbiota of CRC rats.	76
<i>Collinsella</i>	<i>Collinsella</i> is proinflammatory bacterium, and is associated with biopsy-proven nonalcoholic steatohepatitis.	77
<i>Bulleidia</i>	<i>Bulleidia</i> is an anaerobic Gram-positive pathogen identified within oral and gastroenterological ecological niches.	78
<i>Megamonas</i>	<i>Megamonas</i> is associated with lymph node metastasis status.	79
<i>Veillonella</i>	<i>Veillonella</i> is more abundant in the proximal segments than in the distal segments of the colon.	80

<i>Prevotella</i>	<i>Prevotella</i> produces butyrate and reduces abundance in CRC patients.	81
Enterococcus	Some literatures suggest <i>Enterococcus</i> has a harmful role, whereas other papers report <i>Enterococcus faecalis</i> as an important probiotic microorganism with great applicability in food products.	82
<i>Clostridium</i>	<i>Clostridium</i> causes clostridium difficile infection after colorectal surgeries.	83
<i>Lactobacillus</i>	As a probiotic, <i>Lactobacillus</i> prevents dimethylhydrazine-induced colorectal cancers.	84
<i>Serratia</i>	Prodigiosin isolated from cell wall of <i>Serratia marcescens</i> alters expression of apoptosis-related genes and increases apoptosis in colorectal cancer cells.	85
<i>Actinomyces</i>	<i>Actinomyces</i> is significantly increased in multiple polypoid adenomas and intramucosal carcinomas.	86
<i>Epulopiscium</i>	Unknown	
<i>Bradyrhizobium</i>	<i>Bradyrhizobium</i> has higher abundance in off-tumor site of CRC intestine than on-tumor site or healthy person.	15

<i>Anaerococcus</i>	<i>Anaerococcus</i> is significantly increased in moderately severe acute pancreatitis.	87
<i>Dethiosulfatibacter</i>	<i>Dethiosulfatibacter</i> has higher abundance in on-tumor site of CRC intestine than off-tumor site or healthy person.	15
<i>Peptoniphilus</i>	<i>Peptoniphilus</i> is a Gram-positive anaerobic coccus mainly involved in polymicrobial infections, and is reported in a case of peritoneal infection in a patient with intestinal occlusion	88
<i>Lachnospira</i>	<i>Lachnospira</i> shows a negative association with asthma risk under 4 years of age.	89
<i>Mogibacterium</i>	<i>Mogibacterium</i> causes IL8/IFN γ /TNF α pro-inflammatory effect.	90
<i>Schwartzia</i>	<i>Schwartzia</i> shows higher abundance in off-tumor site of CRC intestine than on-tumor site or healthy person.	15
<i>Proteus</i>	<i>Proteus</i> induces a 2-fold increase of VIM gene expression within Caco2 cells after cocultivation with <i>Proteus vulgaris</i> , suggesting that <i>Proteus vulgaris</i> promotes epithelial-mesenchymal transition.	91

<i>Corynebacterium</i>	<i>Corynebacterium</i> has relative abundance in the invasive CRC group compared with early CRC group.	92
<i>Aggregatibacter</i>	<i>Aggregatibacter</i> is positively correlated with visceral fat, fasting plasma insulin, and HOMA-IR in non-alcoholic fatty liver disease.	93
<i>Catenibacterium</i>	Compared to normal samples, <i>Catenibacterium</i> is only detected in CRC tumor samples	94
<i>Ralstonia</i>	Harmful bacteria for intestine	95
<i>Methylobacterium</i>	<i>Methylobacterium</i> shows higher abundance in off-tumor site of CRC intestine than on-tumor site or healthy person.	15
<i>Sphingomonas</i>	<i>Sphingomonas</i> shows high abundance in pro-inflammatory intestinal microenvironment.	96

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