Supplementary Material

Supplementary Table 1. Principal bacteria, archaea, and fungi composing the human colonic microbiota

Phylum	Genus	Characteristics	Colonic abundance and observed effect on host health			Reference
			Infants	Adults	Older adults	
Bacillota	*Streptococcus*	Saccharolytic and proteolytic, produces lactate and acetate. Includes both beneficial species (e.g. *S. thermophilus*) and pathogens (e.g. *S. bovis*)	Infants delivered by C-section and formula-fed had an increased abundance of *Streptococcus* compared to other infants (n=27)	*Streptococcus* abundance was positively associated with coronary atherosclerosis (n=8973)	A higher abundance of *Streptococcus* was associated with unhealthy aging (n=32)	(190–192)
	Lactobacillus	Mainly saccharolytic, produces lactate and bacteriocins. Species are typically considered beneficial (e.g. *L. rhamnosus*)	Vaginally delivered infants had a higher abundance of *Lactobacillus* compared to those delivered via C-section during the first days of life (n=37)	A higher abundance of *Lactobacillus* was associated with type-2 diabetes (n=18) and obesity (n=20) in adults	Long-living older adults (aged 97-100) had increased *Lactobacillus* abundance compared to healthy older adults (aged 60-76) (n=20)	(193–196)
	Clostridium	Saccharolytic and proteolytic, produces acetate, propionate, and butyrate. Contains both beneficial species (e.g. *C. butyricum*) and pathogens (e.g. *C. difficile*)	Higher abundance of *Clostridium sensu stricto* in infants with food allergies (n=34)	A higher abundance of *Clostridium* was associated with obesity in adults (n=307)	Older adults with Parkinson's disease had a decreased abundance of *Clostridium* compared to healthy controls (n=45)	(197–199)
	Ruminococcus	Mainly saccharolytic, produces acetate. Degrades resistant starch contributing to butyrate production via cross-feeding (e.g. *R. bromii*)	Lower abundance of *Ruminococcus* in children and adolescents with Crohn's disease (n=64)	Lower abundance of *Ruminococcus* in adults with Crohn's disease compared to healthy controls (n=10)	Higher abundance of *Ruminococcus* in older adults with frailty and sarcopenia (n=18)	(200–202)
	Faecalibacterium	Mainly saccharolytic, produces SCFA, including butyrate. Typically considered beneficial, some species produce anti-inflammatory molecules (e.g. *F. prausnitzii*)	Lower abundance of *F. prausnitzii* in children with allergic asthma (n=92)	Lower abundance of *F. prausnitzii* in adults with Crohn's disease (n=68)	Lower abundance of *F. prausnitzii* in older adults with mild-cognitive impairment (n=15)	(203–205)
	Enterococcus	Saccharolytic and proteolytic, produces lactate and acetate. Some species raise concern due to capacity to acquire antibiotic resistance (e.g. *E. faecalis*)	Higher abundance of *Enterococcus* in infants with food allergies (n=34)	Higher abundance of *E. faecalis* in adults with colorectal cancer (n=25)	Higher abundance of *Enterococcus* in older adults with Parkinson's disease (n=24)	(199,206,207)
	Eubacterium	Chemoheterotroph, produces SCFAs, including butyrate.	Lower abundance of *E. rectale* in children with	Lower abundance of *Eubacterium* in adults with	Lower abundance of *Eubacterium* in older	(201,202,208,209)

		Typically associated with the promotion of colonic homeostasis (e.g. *E. rectale*)	ulcerative colitis (n=6) and in children with neurodevelopmental disorders (n=36)	Crohn's disease compared to healthy controls (n=10)	adults with frailty and sarcopenia (n=18)	
Bacteroidota	*Bacteroides*	Saccharolytic and proteolytic, produces acetate, propionate, and succinate. Contains both beneficial species (e.g. *B. thetaiotaomicron*) and pathogens (e.g. *B. fragilis*)	Decreased abundance of *Bacteroides* in infants delivered via C-section compared to infants vaginally delivered (n=9)	A meta-analysis reported lower abundance of *Bacteroides* in adults and adolescents with Crohn's disease and ulcerative colitis (n=706)	Higher abundance of *Bacteroides* in older adults was positively associated with increased risk of all-cause mortality (n=706)	(138,210,211)
	Prevotella	Saccharolytic and proteolytic, produces acetate and propionate. Contains species with potential role in promoting (e.g. *P. copri*) or suppressing inflammation (e.g. *P. histicola*)	Higher abundance of *Prevotella* in infants with food allergies (n=34)	Higher abundance of *Prevotella* in adults with hypertension (n=99). Increased abundance of *Prevotella* was associated with improved glucose metabolism in healthy adults (n=10)	A systematic review reported a lower abundance of *Prevotella* in frail older adults (n=912)	(199,212–214)
	Alistipes	Saccharolytic and proteolytic, produces acetate and propionate. Contains pathogenic species that produce pro-inflammatory toxins (e.g. *A. finegoldii*)	Lower abundance of *A. putredinis* in infancy was associated with neurodevelopmental disorders later in life (n=1748)	Lower abundance of *Alistipes* in adults with atrial fibrillation (n=50) and higher abundance in adults with chronic fatigue syndrome (n=25)	Higher abundance of *Alistipes* in older adults with frailty compared to healthy controls (n=47)	(215–218)
Actinomycetota	*Bifidobacterium*	Saccharolytic, produces acetate and lactate. Predominant in the infant colon. Typically considered beneficial (e.g. *B. breve* and *B. longum*)	Vaginally delivered and breastfed infants have higher *Bifidobacterium* abundance compared to those delivered via C-section and formula-fed (n=8)	Lower abundance of *Bifidobacterium* in obese women (n=15)	Higher abundance of *Bifidobacterium* in older adults with frailty compared to healthy controls (n=47)	(192,217,219)
Pseudomonadota	*Escherichia*	Saccharolytic and proteolytic. Contains pathogenic species that produce pro-inflammatory toxins (e.g. *E. coli*)	Higher abundance of *Escherichia* in children with non-alcoholic steatohepatitis (n=22)	A meta-analysis reported higher abundance of *E. coli* in adults with irritable bowel syndrome compared to healthy controls (n=1340)	Higher abundance of *Escherichia-Shigella* in critically ill older adults (n=72)	(220–222)
	Desulfovibrio	Reduces sulphate, producing hydrogen sulphide (excessive production is deleterious)	Higher abundance of *Desulfovibrio* in infants with stunting compared to healthy controls (n=10)	Higher abundance of *Desulfovibrio* in adults with systemic sclerosis (n=59)	Higher abundance of *Desulfovibrio* in older adults with Parkinson's disease (n=20)	(223–225)
Verrucomicrobiota	*Akkermansia*	Mucin degrader. Produces acetate, propionate, and butyrate. Assumed to promote colonic barrier integrity (e.g. *A. muciniphila*)	Lower abundance of *A. muciniphila* in overweight children (n=20)	Lower abundance of *A. muciniphila* in pregnant women (n=16) and patients with inflammatory bowel disease (n=46)	Higher abundance of *Akkermansia* in older adults with frailty compared to healthy controls (n=47)	(217,226–228)
Euryarchaeota	*Methanobrevibacter*	Archaea. Consumes hydrogen to produce methane, facilitating fermentation by anaerobic	Lower abundance of *Methanobrevibacter* in children with severe acute malnutrition (n=143)	Higher abundance of *Methanobrevibacter* in anorexic adults (n=20)	Abundance of *M. smithii* in older adults was positively associated with the severity of	(193,229,230)

		saccharolytic bacteria (e.g. *M. smithii*)			cognitive impairment (n=159)	
Ascomycota	*Candida*	Fungi. Converts simple carbohydrates into ethanol and acetate. Contains opportunistic pathogens (e.g. *C. albicans*)	Higher abundance of *Candida* in children with autism compared to neurotypical controls (n=40)	Higher abundance of *Candida* in adults with inflammatory bowel disease (n=235)	Higher abundance of *C. tropicalis* in older adults with Alzheimer's disease (n=88)	(231–233)
	Saccharomyces	Fungi. Converts simple carbohydrates into ethanol and carbon dioxide. Typically considered commensals (e.g. *S. cerevisiae*)	Higher abundance of *S. cerevisiae* in children with autism compared to neurotypical controls (n=29)	Higher abundance of *Saccharomyces* in adults with colorectal cancer (n=71). Lower abundance of *Saccharomyces* in adults with inflammatory bowel disease (n=235)	*Saccharomyces* abundance was positively associated with higher levels of circulating plasma triglycerides and very low-density lipoprotein in older adults (n=99)	(142,231,234,235)

Supplementary Table 2. Principal metabolites produced by the human colonic microbiota

Category	Compound	Substrate or precursor	Major producing microbial taxa	Observed effect on host health			Reference
				Infants	Adults	Older adults	
Short-chain fatty acids (SCFAs)	Acetate	Primarily dietary fibre and resistant starch, but also amino acids	*Bifidobacterium, Lactobacillus, Prevotella, Ruminococcus, A. muciniphila*	Infants exclusively breastfed had a lower concentration of acetate, propionate, and butyrate (n=48)	A meta-analysis found an increased fecal concentration of acetate, propionate, and butyrate in obese adults (n=221)	Lower concentration of fecal acetate, propionate, and butyrate in older adults with Alzheimer's disease compared to healthy controls (n=27)	(236–238)
	Propionate		*Prevotella, Bacteroides, Propionibacterium*				
	Butyrate		*Clostridium, Roseburia, F. prausnitzii, E. rectale, B. fragilis, R. bromii, A. muciniphila*				
Branched-chain fatty acids (BCFAs)	Isobutyrate and isovalerate	Amino acids (valine, leucine, and isoleucine)	*Bacteroides, Clostridium*	Increased fecal levels of isobutyrate and isovalerate in formula-fed infants compared to breastfed infants (n=33)	Increased isobutyrate fecal levels in adults with non-alcoholic fatty liver disease (n=24) and increased isovalerate in adults with depression (n=34)	Increased fecal levels of isobutyrate and isovalerate in older adults with colorectal cancer (n=50)	(239–242)
Conjugated fatty acids	Conjugated linoleic acid	Linoleic acid	*Bifidobacterium, Enterobacter, Lactobacillus, Clostridium*	Conjugated linoleic acid supplementation in obese children decreased body fat and high-density lipoprotein compared to placebo (n=28)	Conjugated linoleic acid supplementation in adults decreased T lymphocyte activation (n=39)	Conjugated linoleic acid supplementation in adults older with type 2 diabetes reduced insulin sensitivity (n=16)	(243–245)
Vitamins	Complex B vitamins	Carbohydrates and amino acids	*Bifidobacterium, Lactobacillus, Bacteroides*	Deficiency of complex B vitamins in infants was linked with compromised brain development (n=6)	Decreased serum levels of vitamin B7 in adults were associated with obesity and type 2 diabetes (n=24)	Deficiency of complex B vitamins in older adults was linked with increased risk of dementia (n=228)	(246–248)
	Vitamin K family		*Bacteroides, Prevotella*	Vitamin K family deficiency in infants was linked with convulsions, hemorrhage, and death (n=30)	Serum vitamin K_1 levels were negatively associated with circulating inflammatory biomarkers in adults (n=1381)	Serum vitamin K_1 levels were negatively associated with circulating inflammatory biomarkers in older adults (n=662)	(249–251)
Gases	H_2	Carbohydrates	*Clostridium, Enterobacteriaceae*	Excessive H_2 production has been associated with the development of colic symptoms in infants (n=8)	Higher H_2 production from *in vitro* starch fermentation using fecal inoculum from adults with irritable bowel syndrome compared to healthy controls (n=14)	No differences in H_2 production from *in vitro* fermentation of different carbohydrates using fecal inoculum from older adults with pre-frailty compared to young controls (n=6)	(252–254)
	CO_2		*Clostridium*	No changes in CO_2 production were observed during *in vitro* incubation of fecal inoculum from infants fed soy-based infant formula,	CO_2 insufflation during colonoscopy in adults reduced the fecal abundance of colonic	CO_2 insufflation during colonoscopy in older adults was associated with less pain compared to air insufflation (n=66)	(255–257)

				milk-based formula, or breastmilk (n=18)	pathogens compared to air insufflation (n=38)		
	CH_4	H_2, CO_2	*Methanobrevibacter smithii*	Higher breath methane in children with chronic constipation compared to healthy controls (n=75)	Higher breath methane in adults with multiple sclerosis compared to healthy controls (n=60)	Higher CH_4 production from *in vitro* fermentation of different carbohydrates using fecal inoculum from older adults with pre-frailty compared to young controls (n=6)	(254,258,259)
	H_2S	Sulphate	*Desulfovibrio*	Higher H_2S production was observed from *in vitro* incubation of fecal inoculum from infants fed soy-based infant formula compared to breastfed infants (n=5)	Higher H_2S production from *in vitro* starch fermentation using fecal inoculum from adults with irritable bowel syndrome compared to healthy controls (n=14)	A meta-analysis reported lower levels of circulating H_2S in older adults with chronic and degenerative diseases compared to healthy controls (n=1721)	(253,255,260)
Secondary bile acids	Deoxycholic acid, lithocholic acid	Primary bile acids	*Clostridium, Bifidobacterium, Lactobacillus, Bacteroides, M. smithii*	Higher fecal levels of secondary bile acid in critically ill children compared to healthy controls (n=39)	Higher levels of circulating lithocholic acid in adults with severe obstructive coronary heart disease compared to angiographically normal controls (n=150)	Higher levels of circulating unconjugated secondary bile acids were associated with a higher risk for cardiovascular diseases in older adults with type 2 diabetes (n=1234)	(261,262)
	Ursodeoxycholic acid	Primary bile acids	*Ruminococcus, Clostridium*	Higher levels of circulating ursodeoxycholate in formula-fed infants compared to breastfed infants (n=48)	Ursodeoxycholic acid use was associated with a reduced risk of colorectal cancer in adults (n=2557)	Ursodeoxycholic acid use was associated with a reduced risk of colorectal cancer in older adults (n=1911)	(263–265)
Neurotransmitters	Dopamine	Tyrosine, 3,4-dihydroxy-L-phenylalanine	*Bacillus, E. coli, Staphylococcus*	Higher circulating serotonin and serotonin transporter levels in children with autism compared to healthy control (n=60)	Higher plasma levels of dopamine and gamma-aminobutyric acid in adults with major depressive disorder compared to healthy controls (n=49)	Alterations in the dopamine system were associated with the progression of Alzheimer's disease in older adults (n= 144)	(266–268)
	Norepinephrine	Tyrosine	*Bacillus*				
	Serotonin	Tryptophan, 5-hydroxytryptophan	*Lactobacillus, Streptococcus, Clostridium*				
	Gamma-aminobutyric acid	Acetate, glutamate	*Bifidobacterium, Lactobacillus, Eubacterium, Bacteroides*				
Nitrogen-derivatives	Ammonia	Amino acids and peptides	*Clostridium, Fusobacterium, Bacteroides*	Hyperammonemia in infants was associated with liver failure and urea cycle defects (n=90)	Higher circulating levels of ammonia were associated with hepatic steatosis in adults (n=25)	Higher blood ammonia levels in patients with Alzheimer's disease compared to controls (n=3)	(269–271)
	p-cresol	Tyrosine	*Fusobacterium, Enterobacter, Clostridium*	Higher urinary levels of p-cresol in children with autism compared to healthy controls (n=33)	Higher circulating levels of p-cresol in adults undergoing hemodialysis were associated with increased risk for infection-	Higher circulating levels of p-cresol in older adults undergoing hemodialysis compared to non-hemodialysis controls (n=4)	(272–274)

					related hospitalizations (n=464)		
	Indole	Tryptophan	*Peptostreptococcus, Akkermansia, Clostridium*	Fecal levels of indole-3-lactic acid correlated positively with increased fecal abundance of *Bifidobacterium infants* in breastfed infants (n=18)	Lower serum levels of indole-3-pyruvic acid in adults with ulcerative colitis compared to healthy controls (n=15)	Lower fecal levels of indole-3-pyruvic acid in older adults with Alzheimer's disease compared to healthy controls (n=27)	(238,275,276)
Endotoxins	Lipopolysaccharide	Lipid A, oligosaccharide, O antigen	*Enterobacteriaceae, Bacteroidales*	Increased exposure to lipopolysaccharides in early infancy was associated with the development of autoimmune diseases (n=168)	Lipopolysaccharide exposure increased intestinal permeability in healthy adults (n=14)	Trend towards higher circulating levels of lipopolysaccharides in older adults with Alzheimer's disease compared to healthy controls (n=27)	(238,277,278)

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