

Appendix Table 1. Oral bacteria found in the gut of patients with gut pathology, with references

Gut pathology	Oral bacterial species § detected in the gut	Sample types	References
Irritable Bowel Syndrome (IBS)	<i>Streptococcus</i> spp.	Stool	Fourie et al. 2016; Kassinen et al. 2007; Malinen et al. 2005; Pittayanon et al. 2019; Rajilic-Stojanovic et al. 2011; Rigsbee et al. 2012; Saulnier et al. 2011; Si et al. 2004; Su et al. 2018; Tana et al. 2010; Vich Vila et al. 2018; Wyatt et al. 1988
	<i>Streptococcus thermophilus</i>	Stool	
	<i>Veillonella</i> spp.	Stool	
	<i>Haemophilus</i> spp.	Stool	
	<i>Prevotella</i> spp.	Stool	
	<i>Fusobacterium</i> spp.	Stool	
	<i>Dialister invisus</i>	Stool	
	Gammaproteobacteria (Class)	Stool	
Enterobacteriaceae (family)	Stool		
Inflammatory Bowel Disease (IBD)	Veillonellaceae (family)	Tissue	Atarashi et al. 2017; Burrello et al. 2019; Darfeuille-Michaud et al. 2004; Gevers et al. 2014; Ismail et al. 2012; Lupp et al. 2007; Mahendran et al. 2011; Man et al. 2010; Mottawea et al. 2016; Mukhopadhy a et al. 2011; Ohkusa et al. 2002; Ott et al. 2004; Pascal et al. 2017; Patwa et al. 2011; Pilarczyk-Zurek et al. 2013; Seksik et al. 2003; Sokol et al. 2017; Verma et al. 2010; Vich Vila et al. 2018; Willing et al. 2010
	Pasteurellaceae (family)	Tissue	
	Neisseriaceae (family)	Tissue	
	Peptostreptococcaceae (family)	Tissue	
	<i>Atopobium parvulum</i>	Tissue	
	Fusobacteriaceae (family)	Stool, Tissue	
	<i>Fusobacterium varium</i>	Tissue	
	<i>Campylobacter</i> spp.	Tissue	
	<i>Campylobacter concisus</i>	Stool, Tissue	
	<i>Aggregatibacter segnis</i>	Stool	
	<i>Streptococcus</i> spp.	Stool, Tissue	
	<i>Streptococcus anginosus</i>	Stool	
	Gemellaceae (family)	Stool, Tissue	
	Enterobacteriaceae (family)	Stool, Tissue	
<i>Escherichia coli</i>	Stool, Tissue		
Colorectal Cancer (CRC)	<i>Porphyromonas</i> spp.	Stool, Rectal swab	Ahn et al. 2013; Chen et al. 2012; Flemer et al. 2018; Guo and Li
	<i>Porphyromonas gingivalis</i>	Stool	

	<i>Porphyromonas uenonis</i>	Stool	2014; Herlyn et al. 1982; Komiya et al. 2019; Olsen and Yilmaz 2019; Thomas et al. 2019; Wirbel et al. 2019; Yachida et al. 2019; Zumkeller et al. 2006
	<i>Fusobacterium</i> spp.	Stool, tissue, rectal swab	
	<i>Fusobacterium nucleatum</i>	Stool, tissue	
	<i>Streptococcus</i> spp.	Stool	
	Peptostreptococcaceae (family)	Stool, Rectal swab	
	<i>Peptostreptococcus stomatis</i>	Stool	
	<i>Peptostreptococcus anaerobius</i>	Stool	
	<i>Prevotella</i> spp.	Stool	
	<i>Prevotella intermedia</i>	Stool	
	<i>Gemella morbillorum</i>	Stool, Rectal swab	
	<i>Solobacterium moorei</i>	Stool	
	<i>Atopobium parvulum</i>	Stool	
	<i>Actinomyces odontolyticus</i>	Stool	
	<i>Parvimonas micra</i>	Stool	
	<i>Escherichia coli</i>	Stool, Tissue	
	<i>Klebsiella</i> spp.	Stool	
	<i>Helicobacter pylori</i>	Tissue	
	<i>Mogibacterium</i>	Stool	
	<i>Dialister pneumosintes</i>	Tissue	
Celiac Disease	<i>Staphylococcus</i> spp.	Stool	Collado et al. 2008; Sanchez et al. 2013
	<i>Staphylococcus epidermidis</i>	Tissue	
	Enterobacteriaceae (family)	Tissue	
	<i>Klebsiella oxytoca</i>	Tissue	

The taxonomic rank is provided in parentheses only if the species information is not defined in the reference.

§ Oral bacteria are defined as following criteria; (i) bacteria identified as a constituent of the oral microbiome by the Human Oral Microbiome Database (Escapa IF *et al.* mSystems. 2018) and (ii) bacteria have higher abundance in the oral tissues than that in the gut samples in healthy individuals based on the NIH Human Microbiome Project (HMP1). In addition, some bacteria, which are previously reported as bacteria involved in oral pathology are also listed as possible oral bacteria, although they do not meet criterion (ii).

Appendix Table 2. Possible mechanisms of oral bacteria in the gut pathogenesis, with references

Oral bacteria	Target cells	Effector	Pathways in host cells		Pathological functions	References
			Receptor	Related signals		
<i>Fusobacterium nucleatum</i>	<i>Epithelial cells</i>	Fap2	Gal-GalNAc	-	Tumor binding and enrichment	Abed et al. 2016
	<i>Epithelial cells</i>	-	-	<i>metalloproteinases</i> <i>e</i> <i>collagenase</i>	Cellular migration and invasive properties	Uitto et al. 2005; Gursoy et al. 2008
	<i>Epithelial cells</i>	FadA	Ecad	<i>Wnt/β-catenin</i>	Tumor cell proliferation	Rubinstein et al. 2013
	<i>NK cells</i> <i>T cells</i>	Fap2	TIGIT	-	Immune evasion	Gur et al. 2015
	<i>Epithelial cells</i>	LPS	TLR4	<i>miR-4802</i> <i>miR-18a*</i>	Chemoresistance (Autophagy activation)	Yu et al. 2017
	<i>Epithelial cells</i>	LPS	TLR4	<i>Myd88</i> <i>miR-21</i>	Tumor cell proliferation	Yang et al. 2017
	-	-	-	-	Recruitment of tumor-infiltrating immune cells (MDSC, TAM, regDC)	Kostic et al. 2013
<i>Fusobacterium varium</i>	<i>Epithelial cells</i>	-	-	-	Adhesion and Invasion IL-8 and TNF-α production	Ohkusa et al. 2003; Ohkusa et al. 2009
<i>Porphyromonas gingivalis</i>	<i>Epithelial cells</i>	-	-	<i>Jak1/Akt/Stat3</i> <i>PI3K/Akt</i>	Cell survival (antiapoptotic)	Mao et al. 2007; Yilmaz et al. 2004
	<i>Epithelial cells</i>	-	-	<i>cyclin D & E</i> <i>PI3K</i>	Cell proliferation	Kuboniwa et al. 2008; Pan et al. 2014
	<i>Epithelial cells</i>	Gingipain	β-catenin destruction	<i>β-catenin</i>	Cell proliferation	Zhou et al. 2015

			complex degradation			
	<i>Epithelial cells</i>	-	-	-	Immune evasion (B7-H1 and B7-DC upregulation)	Groeger et al. 2011
	<i>Epithelial cells</i>	Gingipain	PAR	<i>NF-kB, ERK1/2, p38</i>	Tumor invasiveness (MMPs expression↑)	Ha et al. 2015; Inaba et al. 2015; Inaba et al. 2014
	<i>Epithelial cells and others</i>	-	-	-	Epithelial disruption Proinflammatory cytokine induction Gut dysbiosis	Arimatsu et al. 2014; Nakajima et al. 2015
	<i>Epithelial cells and others</i>	-	-	-	Epithelial disruption Immune activation Gut dysbiosis	Sato et al. 2017; Flak et al. 2019
	<i>Neutrophils</i>	-	TLR1-TLR2	<i>Myd88</i>	Impaired antimicrobial response Impaired killing activity	Hajishengallis 2015
	<i>Mø and DC</i>	Fimbrial proteins (FimA & Mfa1)	CR3 or DC-SIGN	MMP and C1q	Hijack and direct host immune cells (Distant tissue destruction)	Hajishengallis 2015
<i>Klebsiella pneumoniae Klebsiella aerogenes (Klebsiella aeromobilis)</i>	<i>Epithelial cells</i>	-	TLR	<i>IL18 MyD88</i>	Th1 cell generation	Atarashi et al. 2017
<i>Atopobium parvulum</i>	<i>Unknown</i>	H ₂ S			Mitochondrial dysfunction in host with impaired H ₂ S detoxification	Mottawea et al. 2016

<i>Campylobacter concisus</i>	<i>Epithelial cells</i>				Epithelial disruption	Nielsen et al. 2011
<i>Staphylococcus aureus</i>	<i>Epithelial cells</i> <i>T cells</i>	enterotoxins	-	-	Epithelial disruption Immune activation	Edwards et al. 2012

Appendix Table 3. Potential factors associated with gut colonization of oral bacteria, with references

(Corresponding to Fig.1)

Oral bacterial dissemination into bloodstream after dental activities		
Factors	Oral bacteria detected in the "blood"	References
General activity (e.g., chewing, brushing)	<i>Streptococcus</i> spp.	Bhanji et al. 2002; Forner et al. 2006; Hartzell et al. 2005; Kinane et al. 2005; Lockhart et al. 2008; Lucas and Roberts 2000; Sconyers et al. 1973
	<i>Streptococcus mitis</i>	
	<i>Streptococcus anginosus</i>	
	<i>Streptococcus intermedius</i>	
	<i>Streptococcus sanguinis</i>	
	<i>Staphylococcus epidermidis</i>	
	<i>Staphylococcus warneri</i>	
	<i>Stenotrophomonas maltophilia</i>	
	<i>Propionibacterium acnes</i>	
	<i>Acinetobacter Iwoffii</i>	
	<i>Acinetobacter calcoaceticus</i>	
	<i>Actinobacillus actinomycetemcomitans</i>	
	<i>Peptostreptococcus micros</i>	
	<i>Veillonella parvula</i>	
<i>Actinomyces naeslundii</i>		
Periodontal procedures (e.g., probing, root planing, extraction)	<i>Streptococcus</i> spp.	Aitken et al. 1995; Allison et al. 1993; Assaf et al. 2007; Bender et al. 2003; Cherry et al. 2007;
	<i>Streptococcus sanguinis</i>	Daly et al. 1997; Daly et al. 2001; Debelian et al. 1995; Diz Dios et al. 2006; Erverdi et al. 2001;
	<i>Streptococcus mutans</i>	Erverdi et al. 2000; Flood et al. 1990; Hall et al. 1996; Hunter et al. 1989; Khairat 1966; Lafaurie et al. 2007; Lamey et al. 1985; Lockhart et al. 2004; Lockhart et al. 2008; Lucas et al. 2007;
	<i>Streptococcus oralis</i>	Lucas et al. 2002; Macfarlane et al. 1984; Rahn et al. 1995; Rajasuo et al. 2004; Roberts et al. 2006; Roberts et al. 1998; Rosa et al. 2005;
	<i>Streptococcus milleri</i>	
	<i>Streptococcus anginosus</i>	
	<i>Streptococcus constellatus</i>	
	<i>Streptococcus cristatus</i>	
	<i>Streptococcus gordonii</i>	
	<i>Streptococcus intermedius</i>	
<i>Streptococcus mitis</i>		

Streptococcus salivarius

Savarrio et al. 2005; Sweet et al. 1978; Tomas et

Actinomyces spp.

al. 2007a; Tomas et al. 2007b; Waki et al. 1990;

Actinomyces meyeri

Yamalik et al. 1992

Actinomyces odontolyticus

Actinomyces naeslundii

Staphylococcus spp.

Staphylococcus epidermidis

Staphylococcus warneri

Staphylococcus aureus

Neisseria spp.

Neisseria elongata

Neisseria flavescens

Neisseria mucosa

Neisseria sicca

Neisseria pharyngis

Capnocytophaga sp.

Eikenella corrodens

Fusobacterium nucleatum

Fusobacterium fusiforme

Granulicatella adiacens

Haemophilus aphrophilus

Lactobacillus rhamnosus

Lactobacillus casei

Lactobacillus salivarius

Porphyromonas gingivalis

Prevotella spp.

Prevotella denticola

Prevotella melaninogenica

Prevotella oralis

Propionibacterium acnes

Veillonella parvula

	<i>Enterobacter aerogenes</i>	
	<i>Eubacterium lentescens</i>	
	<i>Capnocytophaga</i> spp.	
	<i>Micromonas micros</i>	
Oral diseases (e.g., gingivitis, periodontitis)	<i>Staphylococcus epidermidis</i>	Raber-Durlacher et al. 2013
	<i>Streptococcus mitis</i>	
	<i>Streptococcus oralis</i>	
	<i>Streptococcus acidominimus</i>	

Impaired gastric barrier function

Factors	Oral bacteria detected in the "gut"	References
Gastric hypochlorhydria (e.g., proton pump inhibitor, surgery)	<i>Streptococcus</i> spp. <i>Veillonella</i> spp. <i>Haemophilus</i> spp. <i>Megasphaera</i> spp. <i>Actinomyces</i> spp. <i>Granulicatella</i> spp. <i>Enterobacteriaceae</i> spp. <i>Escherichia coli</i> <i>Klebsiella pneumoniae</i> <i>Veillonella</i> spp. <i>Veillonella parvula</i> <i>Veillonella dispar</i> <i>Pseudomonas</i> spp.	Castaner et al. 2018; Graessler et al. 2013; Jackson et al. 2016; Paganelli et al. 2019; Takagi et al. 2018; Tremaroli et al. 2015

Disruption of gut colonization resistance

Factors	Oral bacteria detected in the "gut"	References
Antibiotics (e.g., vancomycin)	<i>Klebsiella pneumoniae</i> <i>Escherichia coli</i> <i>Veillonella</i> spp. <i>Streptococcus mitis</i> <i>Lactobacillus salivarius</i>	Reijnders et al. 2016
	<i>Fusobacterium nucleatum</i>	

Dietary components (e.g., high fat, artificial sweetener)	<i>Aggregatibacter aphrophilus</i> <i>Streptococcus</i> spp. <i>Staphylococcus</i> spp. <i>Peptostreptococcaceae</i> spp.	Bian et al. 2017; David et al. 2014; Mehta et al. 2017; Palma et al. 2012
Environmental factors (e.g., smoking, aging)	<i>Porphyromonadaceae</i> <i>Neisseria</i> spp. <i>Streptococcus</i> spp. <i>Veillonella dispar</i> <i>Prevotella intermedia</i> <i>Prevotella tannerae</i> <i>Corynebacterium</i> spp. <i>Mogibacterium</i> spp. <i>Peptococcaceae</i> spp. <i>Pseudoramibacter_Eubacterium</i> <i>Bulleidia</i> spp. <i>Campylobacter</i> spp. <i>TM7</i> spp. <i>Megasphaera</i> spp.	Iwauchi et al. 2019; Lee et al. 2018; Odamaki et al. 2016; Shanahan et al. 2018
Host genetics (e.g., HLA, SNP)	<i>Staphylococcus</i> spp. <i>Klebsiella</i> spp. <i>Streptococcus sanguinis</i> <i>Streptococcus thermophilus</i> <i>Streptococcus australis</i> <i>Veillonella</i> spp. <i>Veillonella atypica</i>	Kolde et al. 2018; Palma et al. 2012; Russell et al. 2019
Gut Diseases (e.g., IBD, CRC)	Please see an appendix table 1	

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