11 The Family *Coriobacteriaceae*

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Abstract
Coriobacteriaceae is a family within the order *Coriobacteriales* (phylum Actinobacteria), which includes 30 species belonging to 14 genera: *Adlercreutzia*, *Asaccharobacter*, *Atopobium*, *Collinsella*, *Coriobacterium* (type genus), *Cryptobacterium*, *Denitrobacterium*, *Eggerthella*, *Enterorhabdus*, *Gordonibacter*, *Olsenella*, *Paraeggerthella*, *Parvibacter*, and *Slackia*. These bacteria are normal dwellers of mammalian body habitats such as the oral cavity, the gastrointestinal tract, and the genital tract. In the gut, *Coriobacteriaceae* carry out functions of importance such as the conversion of bile salts and steroids as well as the activation of dietary polyphenols. However, they can also be considered as pathobionts, because their occurrence has been associated with a range of pathologies such as bacteremia, periodontitis, and vaginosis. *Coriobacteriaceae* are usually nonmotile, nonspore-forming, nonhemolytic, and strictly anaerobic bacteria that grow as small rods; stain Gram-positive; are negative for oxidase, urease, and indole production; and are characterized by a high G+C content of DNA (around 60 mol%). Many species are asaccharolytic and possess a variety of aminopeptidases. Typical cellular fatty acids are $C_{18:1}$w9c as well as saturated fatty acids ($C_{14:0}$, $C_{16:0}$, $C_{18:0}$) and derivatives thereof. The production of menaquinone-6 homologues of vitamin K_2 seems also to be an attribute of the family. Taking into account the aforementioned metabolic functions of *Coriobacteriaceae*, their clinical relevance and the fact that an increasing number of novel species have been described very recently, this bacterial family will surely gain an increasing attention in the field of host/bacteria interactions in the near future.

Taxonomy, Historical and Current

The proposal to create the family *Coriobacteriaceae* (Co.ri.o.bac.te.ri.a'ce.ae. M.L. neut. n. *Coriobacterium* type genus of the family; *-aceae* ending to denote a family; M.L. fern. pl. n. *Coriobacteriaceae* the *Coriobacterium* family) was first published in 1997 by Stackebrandt et al. who reported a novel hierarchic classification of the phylum Actinobacteria according to 16S ribosomal RNA (rRNA) gene-based phylogeny (Stackebrandt et al. 1997). The type genus of the family, *Coriobacterium*, includes only one species, *Coriobacterium glomerans*, originally cultured from the intestine of a red soldier bug (Haas and König 1988).

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Only five of the current members of the family were isolated before the advent of molecular phylogeny in the mid-1980s. All of them have been subjected to amended description: *Atopobium minutum* (formerly *Bacteroides minutum*, *Eubacterium minutum*, or *Lactobacillus minutus*) (Collins and Wallbanks 1992), *Atopobium parvulum* (formerly *Peptostreptococcus parvulus* or *Streptococcus parvulus*) (Collins and Wallbanks 1992), *Collinsella aerofaciens* (formerly *Bacteroides aerofaciens*, *Eubacterium aerofaciens*, or *Pseudobacterium aerofaciens*) (Kageyama et al. 1999a), *Eggerthella lenta* (formerly *Bacteroides lentus*, *Eubacterium lentum*, or *Pseudobacterium lentum*) (Wade et al. 1999), and *Slackia heliotrinireducens* (formerly *Peptococcus heliotrinreducans* or *Peptostreptococcus heliotrinreducens*) (Wade et al. 1999). The main phenotypic traits still used nowadays for the identification of most family members are as follows: Gram-positive staining; nonmotile (with the exception of *Gordonibacter pamelaeae*); nonspore-forming; nonhemolytic; mesophilic (typically with a relatively narrow range of growth temperatures around the optimum of 37 °C); usually neutrophilic and acidotolerant; strictly anaerobic, albeit some members reported to be aerotolerant (*Eggerthella lenta*, *Enterorhabdus*, and *Parvibacter* spp.) and others microaerophiles (*Olsenella* spp.) or facultative anaerobes (*Atopobium vaginae*); grow as small rods or coccobacilli that mostly occur as single cells, pairs, or chains (e.g., *Adlercreutzia equolifaciens*, *Collinsella aerofaciens*, *Collinsella tanakaei*, *Coriobacterium glomerans*, *Eggerthella* spp., *Olsenella umbonata*, *Paraeggerthella hongkongensis*); grow usually to low optical density in liquid medium (with the exception of *Atopobium*, *Collinsella*, and *Olsenella* spp.); enhanced growth in the presence of arginine (e.g., *Cryptobacterium*, *Eggerthella*, *Gordonibacter*, and *Slackia* spp.) or Tween 80 (e.g., *Atopobium* and *Olsenella* spp.); positive for arginine dihydrolase and a variety of aminopeptidases; and negative for indole production, oxidase, and urease. Many species are asaccharolytic or convert a very limited number of sugars, e.g., *Adlercreutzia equolifaciens*, *Asaccharobacter celatus*, *Eggerthella* spp., *Enterorhabdus* spp., *Paraeggerthella hongkongensis*, *Parvibacter caecicola*, and all *Slackia* species.

Researchers who isolated strains of *Coriobacteriaceae* in the early days focused mainly on the description of isolates from feces, wounds, abscesses, and gingival crevices, which drew attention to the pathogenic potential of these bacteria. To date, however, nearly all species within the *Coriobacteriaceae* are known as commensal members of mammalian microbiota. The last 5 years have seen a bloom in the number of newly described bacteria belonging to the family: 11 of the 30 known species with a standing name in nomenclature have been described since 2008 (Maruo et al. 2008; Minamida et al. 2008; Clavel et al. 2009, 2010, 2013; Matthies et al. 2009; Würdemann et al. 2009; Jin et al. 2010; Nagai et al. 2010; Kraatz et al. 2011). In light of these novel descriptions, chemotaxonomic features have emerged as important parameters for reliable taxonomic classification of isolates. Most members of the *Coriobacteriaceae* contain a high proportion of saturated cellular fatty acids (e.g., $C_{14:0}$, $C_{16:0}$, or $C_{18:0}$ and dimethyl acetal thereof) and/or $C_{18:1}$w9c. The major menaquinones hitherto reported are menaquinone-6 (MK-6) (e.g., in *Eggerthella lenta*, *Gordonibacter pamelaeae*, and *Paraeggerthella hongkongensis*), monomethylmenaquinone-6 (MMK-6) (e.g., in *Eggerthella sinensis*, *Enterorhabdus* spp., and *Parvibacter caecicola*), and dimethylmenaquinone-6 (DMMK-6) (e.g., in *Adlercreutzia equolifaciens*, *Eggerthella* spp., and *Enterorhabdus caecimuris*). The latter group of quinones seems to be unique to the *Coriobacteriaceae* (Würdemann et al. 2009). So far analyzed peptidoglycan structures are of type A4*a*, A4*b*, as well as A4*g* or A1*g* based on the presence of LL- or *meso*-diaminopimelic acid, respectively. In all species examined for the presence of polar lipids, phosphatidylglycerol and diphosphatidylglycerol as well as up to four glycolipids and three phospholipids were detected.

Molecular Analyses

Phylogenetic Structure of the Family and Its Genera

A 16S rRNA gene sequence-based phylogenetic tree of the 30 members of the family is shown in ❯ *Fig. 11.1*. The trees were reconstructed by using a subset of sequences representative of most closely related genera to stabilize the tree topology.

The first phylogenetic description of the family *Coriobacteriaceae* was published by Stackebrandt et al. (1997). Due to newly described species within the phylum Actinobacteria and the availability of their 16S rRNA gene sequences, an emended description of the family was recently published based on the analysis of 2,642 actinobacterial sequences with >1,300 unambiguous nucleotides (between position 100 and 1,400) (Zhi et al. 2009). The authors reported that the order *Coriobacteriales* (and thus *Coriobacteriaceae*, the sole family within this order) constitutes one of the deepest branches within the phylum Actinobacteria together with the lineages of the order *Rubrobacterales* (e.g., *Thermoleophilaceae*, *Conexibacteraceae*) and *Acidimicrobiales*. The pattern of 16S rRNA signatures of *Coriobacteriaceae* consists of nucleotides at positions 242 : 284 (C–G), 291 : 309 (C–G), 316 : 337 (U–G), 819 (A), 952 : 1229 (U–A), and 1115: 1185 (C–G). Before the first description of the family by Stackebrandt et al. (1997), 16S rRNA-based phylogeny had already played an important role for the sake of emended description of several misclassified member species, including *Lactobacillus minutus*, *Lactobacillus rimae*, and *Streptococcus parvulus* (Collins and Wallbanks 1992). The genus *Atopobium* has then served, together with *Coriobacterium*, as a phylogenetic core of the *Coriobacteriaceae* and has been used to demonstrate that the inclusion of a broad range of physiologically diverse bacteria and thoughtful selection of out-groups are essential prerequisites for drawing proper phylogenetic conclusion (Rainey et al. 1994; Stackebrandt and Ludwig 1994). Thereafter, 16S rRNA gene-based phylogenetic evidence has largely contributed to the reclassification of additional members of the *Coriobacteriaceae*, e.g., *Atopobium fossor*, *Collinsella aerofaciens*, *Eggerthella lenta*, *Slackia exigua*, and *Slackia heliotrinireducens* (Kageyama et al. 1999a, b; Wade et al. 1999).

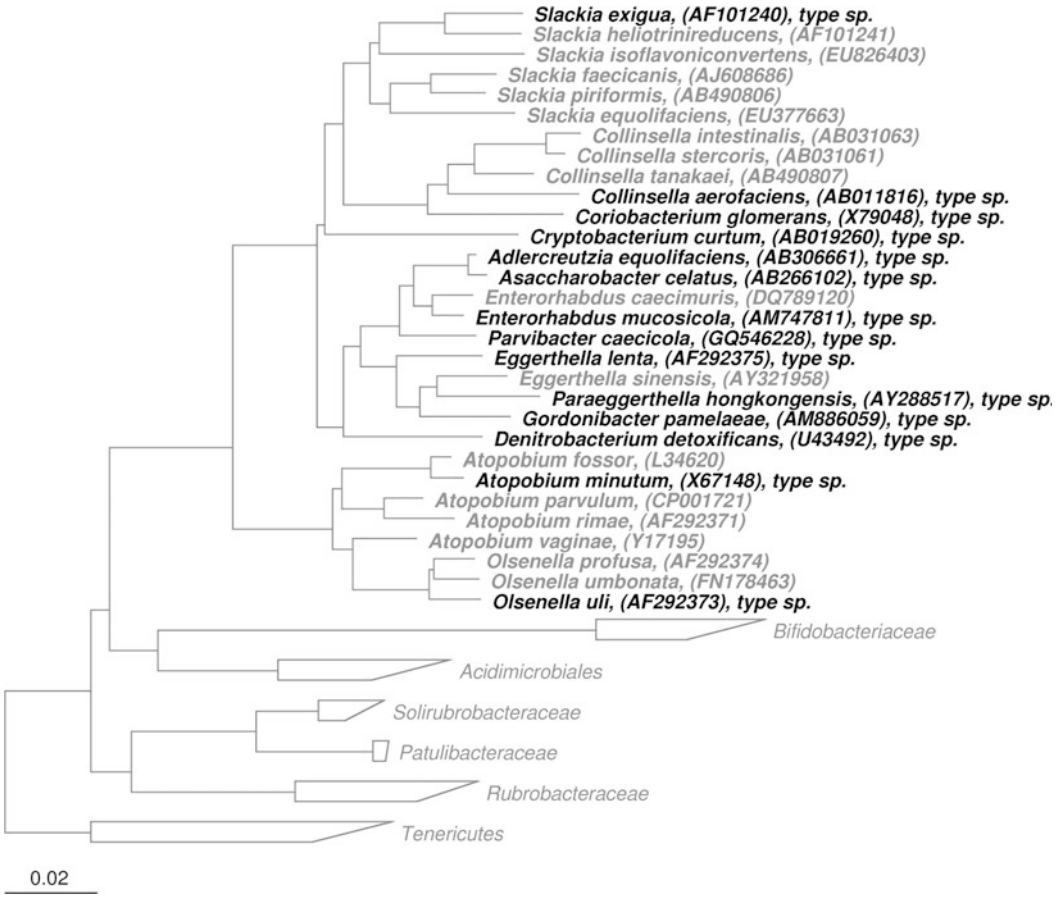

Fig. 11.1

Phylogenetic reconstruction of the family *Coriobacteriaceae* based on 16S rRNA and created using the neighbor-joining algorithm with the Jukes-Cantor correction. The sequence datasets and alignments were used according to the All-Species Living Tree Project (*LTP*) database (Yarza et al. 2010; http://www.arb-silva.de/projects/living-tree). The tree topology was stabilized with the use of a representative set of nearly 750 high-quality-type strain sequences proportionally distributed amongst the different bacterial and archaeal phyla. In addition, a 40 % maximum frequency filter was applied in order to remove hypervariable positions and potentially misplaced bases from the alignment. Scale bar indicates estimated sequence divergence

According to information retrieved from the Ribosomal Database Project, 749 isolates that relate to the *Coriobacteriaceae* family have been described (full and partial 16S rDNA length), most of them from the *Atopobium* genus (337) and unclassified *Coriobacteriaceae* (117), followed by *Olsenella* (94), *Collinsella* (63), *Cryptobacterium* (39), *Eggerthella* (25), *Slackia* (22), *Paraeggerthella* (20), *Coriobacterium* (10), *Adlercreutzia* (9), *Gordonibacter* (6), *Denitrobacterium* (4), *Enterorhabdus* (2), and *Asaccharobacter* (1). Even though the number of 16S rRNA operons varies greatly between species (from 1 operon to 7 in *Collinsella aerofaciens*), their average number is low (2.4) since most of the sequenced strains have only one to two 16S rRNA operons.

DNA-Based Analysis and Genome Comparison

With the exception of *Atopobium* spp. and *Cryptobacterium curtum*, family members are characterized by a high G+C content of DNA (approximately 60 mol% and above). All DNA-DNA relatedness values available in the literature for members of the *Coriobacteriaceae* are given in *Table 11.1*.

Table 11.2 gathers most relevant information on genome sequencing projects focused on members of the *Coriobacteriaceae*. Representative genomes are available for 24 species belonging to 8 of the *Coriobacteriaceae* genera: *Atopobium* ($n = 6$ genomes), including *Atopobium parvulum*, *Atopobium rimae*, and *Atopobium vaginae* (3 strains); *Collinsella* ($n = 4$ genomes), including *Collinsella aerofaciens*, *Collinsella intestinalis*, *Collinsella stercoris*, and *Collinsella tanakaei*; *Coriobacterium glomerans* ($n = 1$ genome); *Cryptobacterium curtum* ($n = 1$ genome); *Eggerthella lenta* ($n = 4$ genomes from 3 strains); *Gordonibacter pamelaeae* ($n = 1$ genome); *Olsenella* ($n = 2$ genomes), including *Olsenella uli* and *Olsenella* sp. oral taxon 809; *Slackia* ($n = 4$ genomes), including *Slackia exigua*, *Slackia heliotrinireducens*, and *Slackia piriformis* (2 strains); and unclassified *Coriobacteriaceae* ($n = 1$ genome; *Coriobacteriaceae* bacterium JC110).

Table 11.1
DNA-DNA homology between species of *Coriobacteriaceae*

Strain 1	Strain 2	%	Reference
Atopobium minutum VPI 9428^T	*Atopobium parvulum* VPI 0546^T	<16	Olsen et al. (1991)
Atopobium minutum VPI 9428^T	*Atopobium rimae* VPI D140H-11A^T	<11	Olsen et al. (1991)
Atopobium parvulum VPI 0546^T	*Atopobium rimae* VPI D140H-11A^T	16	Olsen et al. (1991)
Atopobium minutum VPI 9428^T	*Olsenella uli* VPI D76D-27C^T	4	Olsen et al. (1991)
Atopobium parvulum VPI 0546^T	*Olsenella uli* VPI D76D-27C^T	5	Olsen et al. (1991)
Atopobium rimae VPI D140H-11A^T	*Olsenella uli* VPI D76D-27C^T	8	Olsen et al. (1991)
Collinsella aerofaciens JCM 10188^T	*Collinsella intestinalis* RCA56-68^T	8	Kageyama and Benno (2000)
Collinsella aerofaciens JCM 10188^T	*Collinsella stercoris* RCA 55-54^T	8	Kageyama and Benno (2000)
Collinsella intestinalis RCA56–68^T	*Collinsella stercoris* RCA 55-54^T	<25	Kageyama and Benno (2000)
Cryptobacterium curtum 12–3^T	*Eggerthella lenta* ATCC 25559^T	<5	Nakazawa et al. (1999), Nakazawa and Hoshino (2004)
Cryptobacterium curtum 12–3^T	*Slackia exigua* ATCC 700122^T	4	Nakazawa and Hoshino (2004)
Cryptobacterium curtum 12–3^T	*Slackia heliotrinireducens* ATCC 29202^T	5	Nakazawa and Hoshino (2004)
Eggerthella lenta ATCC 25559^T	*Slackia exigua* ATCC 700122^T	<11	Poco et al. (1996), Nakazawa and Hoshino (2004)
Eggerthella lenta ATCC 25559^T	*Slackia heliotrinireducens* ATCC 29202^T	10	Nakazawa and Hoshino (2004)
Enterorhabdus caecimuris B7^T	*Enterorhabdus mucosicola* Mt1-B8^T	28	Clavel et al. (2010)
Olsenella profusa CCUG 45371^T	*Olsenella uli* CCUG 31166^T	33	Kraatz et al. (2011)
Olsenella profusa CCUG 45371^T	*Olsenella umbonata* lac31^T	50	Kraatz et al. (2011)
Olsenella uli CCUG 31166^T	*Olsenella umbonata* lac31^T	47	Kraatz et al. (2011)
Slackia exigua ATCC 700122^T	*Slackia heliotrinireducens* ATCC 29202^T	33	Nakazawa and Hoshino (2004)
Slackia isoflavoniconvertens HE8^T	*Slackia exigua* CCUG 44588^T	18	Matthies et al. (2009)
Slackia isoflavoniconvertens HE8^T	*Slackia faecicanis* DSM 17537^T	29	Matthies et al. (2009)
Slackia isoflavoniconvertens HE8^T	*Slackia heliotrinireducens* DSM 20476^T	22	Matthies et al. (2009)

A complete genome is available for eight of the sequenced organisms, whereas the others are whole genome shotgun under completion. Fourteen of the 24 sequenced species are human isolates; four of them were isolated from diseased patients (caries, periodontitis, or bacteremia). Genome size ranges from 1,418,601 (*Atopobium vaginae* DSM 15829^T) to 3,632,260 bp (*Eggerthella lenta* DSM 2243^T). No plasmids have been described. One chromosome has been described for each of the sequenced strains. The number of genes is lowest in the *Atopobium* genus and highest in *Eggerthella lenta* DSM 2243^T. On average, 73.2 % of genes can be assigned to Clusters of Orthologous Groups (COGs). This ranges from 66.5 % in *Collinsella* spp. (min. 60.0 % in *Collinsella stercoris*) to 80.7 % in *Coriobacterium glomerans* PW2. In *Eggerthella* sp. YY7918, Yokoyama et al. reported an incomplete carbohydrate metabolic pathway in KEGG, supporting the observation that members of this genus are known to be asaccharolytic (Yokoyama et al. 2011). Several phage-related genes have been described in the genomes of all members of the family (*Table 11.3*). The highest number of phage-related genes is observed in the genome of *Atopobium rimae* ATCC 49626 ($n = 20$) and *Collinsella stercoris* DSM 13279 ($n = 16$). However, no phages have been described to lyse or infect strains of the *Coriobacteriaceae*.

The complete genomes of six sequenced strains were compared to the biggest genome of the family, i.e., *Eggerthella lenta* DSM 2243^T, using RAST (Aziz et al. 2008) (*Fig. 11.2*). Genes were annotated to proteins and results were computed using BLASTP (uni- and bidirectionally) to compare every protein in the reference genome (*Eggerthella lenta*) to every protein in the comparison genomes. Out of the 3,308 total proteins in *Eggerthella lenta*, 115 proteins were shared with the six other sequenced strains at a threshold of 60 % similarity. A major part of these genes were related to ribosomal proteins. Proteins that were not directly related to ribosomal proteins ($n = 73$) belonged to several COGs family, but originated mainly from the family J (translation, ribosomal structure, and biogenesis), L (DNA replication, recombination, and repair), O (posttranslational modification, protein turnover, chaperones), and R (general function prediction only). As expected, the genome of *Eggerthella* sp. YY7918 was the most closely related to that of *Eggerthella lenta*, followed by *Slackia heliotrinireducens*.

Phenotypic Analyses

Unless otherwise stated, all so far described species are Gram-positive, nonspore-forming, nonmotile, strictly anaerobic small rods or coccobacilli (*Fig.11.3*) that are negative for oxidase, urease, hemolysis, and indole production. The main

Table 11.2

***Coriobacteriaceae* family members for which the genome is completely or partially sequenced. Bacteria are listed according to their genome size. Data were extracted from the PATRIC resource (Gillespie et al. 2011). *Abbreviations*: *WGS* whole genome shotgun, *CDS* coding sequences**

Genome name	NCBI taxon Id	Genome status	Type strain	Publication (PMID)	GenBank accession	Genome length	GC content	RAST CDS
Atopobium vaginae DSM 15829	525256	WGS	Yes	Unpublished	ADNA00000000	1,418,601	42.7	1,214
Atopobium vaginae DSM 15829	525256	WGS	Yes	Unpublished	ACGK00000000	1,435,317	42.7	1,197
Atopobium vaginae PB189-T1-4	866774	WGS	No	Unpublished	AEDQ00000000	1,448,900		1,282
Atopobium parvulum DSM 20469	521095	Complete	Yes	21304653	CP001721	1,543,805	45.7	1,329
Cryptobacterium curtum DSM 15641	469378	Complete	Yes	21304644	CP001682	1,617,804	50.9	1,351
Atopobium rimae ATCC 49626	553184	WGS	No	Unpublished	ACFE00000000	1,626,291	49.3	1,480
Collinsella intestinalis DSM 13280	521003	WGS	Yes	Unpublished	ABXH00000000	1,809,497	62.5	1,537
Olsenella uli DSM 7084	633147	Complete	Yes	21304694	CP002106	2,051,896		1,805
Slackia sp. CM382	1111137	WGS	No	Unpublished	ALNO01	2,051,910	-	1,803
Slackia exigua ATCC 700122	649764	WGS	No	Unpublished	ACUX00000000	2,096,289	62.1	1,813
Slackia piriformis YIT 12062	742818	WGS	Yes	Unpublished	ADMD01	2,100,457	-	1,967
Coriobacterium glomerans PW2	700015	Complete	No	Unpublished	CP002628	2,115,681	60	1,936
Olsenella sp. oral taxon 809 str. F0356	661087	WGS	No	Unpublished	ACVE01	2,159,805	-	1,905
Coriobacteriaceae bacterium JC110	1034345	WGS	No	Unpublished	CAEM01	2,354,438	62.1	1,973
Atopobium sp. ICM58	1105030	WGS	No	Unpublished	ALIY01	2,390,495	-	1,968
Collinsella aerofaciens ATCC 25986	411903	WGS	Yes	Unpublished	AAVN00000000	2,439,869	60.5	2,110
Collinsella stercoris DSM 13279	445975	WGS	Yes	Unpublished	ABXJ00000000	2,475,429	63.2	1,805
Collinsella tanakaei YIT 12063	742742	WGS	Yes	Unpublished	ADLS01	2,482,197	–	2,190
Eggerthella sp. YY7918	502558	Complete	No	21914883	AP012211	3,123,671		2,715
Slackia heliotrinireducens DSM 20476	471855	Complete	Yes	Unpublished	CP001684	3,165,038	60.2	2,824
Eggerthella sp. HGA1	910311	WGS	No	Unpublished	AEXR00000000	3,362,931		3,021
Eggerthella sp. 1_3_56FAA	665943	WGS	No	Unpublished	ACWN00000000	3,453,272		3,045
Gordonibacter pamelaeae 7–10–1-b	657308	Complete	No	Unpublished	FP929047	3,608,022		3,083
Eggerthella lenta DSM 2243	479437	Complete	Yes	21304654	CP001726	3,632,260	64.2	3,212

discriminative features of *Coriobacteriaceae* at the genus level are listed in *Table 11.4*. Many species possess a range of amino-peptidases likely to be important for amino acid release from the environment, N cycling processes, ammonia production, and which are useful selective parameters for the classification of *Coriobacteriaceae*. Thus, information on arginine dihydrolase and amino acid arylamidases is summarized at the species level in *Table 11.5*.

Adlercreutzia Maruo et al. (2008)

Ad.ler.creut'zi.a. N.L. fem. n. *Adlercreutzia* named after H. Adlercreutz (Emeritus Professor, University of Helsinki, Finland), for his contributions to research on the effects of phytoestrogens on human health.

The genus is represented only by the type species *Adlercreutzia equolifaciens* (e.quo.li.fa'ci.ens. N.L. n. *equol-olis*

Table 11.3
Listing of phage-related genes in sequenced genomes of *Coriobacteriaceae*

Gene product name (sample locus tag)	*Atopobium vaginae* DSM 15829	*Atopobium vaginae* PB189-T1-4	*Atopobium rimae* ATCC 49626	*Atopobium parvulum* IPP 1246, DSM 20469	*Collinsella aerofaciens* ATCC 25986	*Collinsella stercoris* DSM 13279	*Collinsella intestinalis* DSM 13280	*Collinsella tanakaei* YIT 12063	*Cryptobacterium curtum* 12-3, DSM 15641	*Eggerthella* sp. HGA1	*Eggerthella* sp. 1_3_56FAA	*Eggerthella lenta* VPI 0255, DSM 2243	*Eggerthella* sp. YY7918	*Gordonibacter pamelaeae* 7-10-1-bT, DSM 19378	*Slackia heliotrinireducens* RHS1, DSM 20476	*Slackiaexigua* ATCC 700122	*Olsenella uli* VPI, DSM 7084	*Coriobacterium glomerans* PW2, DSM 20642
Conserved hypothetical phage AbiD protein (HMPREF0091_0188)	1																	
Holin, phage phi LC3 family (Apar_0594)			1	1	1	1			1									
Hypothetical membrane protein with similarity to phage infection protein (ATORI0001_0646)			1															
Integrase/recombinase, phage integrase family protein (HMPREF9404_4029)										1								
Lambda family phage portal protein (HMPREF9452_00397)								1										
Phage capsid family (GPA_22850)														1				
Phage DNA replication protein (predicted replicative helicase loader) (COLAER_00687)					1									1	1			
Phage family integrase (ATORI0001_0862)			1															
Phage integrase (HMPREF1023_00378)											4					2		
Phage integrase family protein (ATORI0001_1210)			1															
Phage integrase family (COLAER_00798)					2	3												
Phage integrase, N-terminal SAM domain protein (HMPREF9248_0962)		2								1								
Phage major capsid protein, HK97 family (Shel_08230)															1			
Phage major tail protein, -1 family (ATORI0001_0997)			1															
Phage major tail protein, phi13 family (COLSTE_02157)						1												
Phage minor capsid protein 2 (COLSTE_01119)						1												
Phage minor structural protein (Elen_2638)												1			1			
Phage minor structural protein, N-terminal region (COLSTE_01099)						2												
Phage *N*-6-adenine-methyltransferase (Elen_2611)											1	1						
Phage portal protein (ATORI0001_1181)			1															

Phage portal protein, HK97 family (Shel_08250)															1			
Phage portal protein, SPP1 family (ATORI0001_1007)			1															
Phage portal protein, SPP1 Gp6-like (COLAER_00274)					1									1				
Phage prohead protease, HK97 family (COLSTE_02163)	2					1									1			
Phage protein (ATORI0001_1002)			5															
Phage putative head morphogenesis protein, SPP1 gp7 family (COLAER_00268)					1													
Phage putative tail component, N-terminal domain (COLSTE_01100)						2												
Phage recombination protein Bet (Ccur_02960)					1	1			1									
Phage-related protein (ATORI0001_1186)			1															
Phage scaffold protein (ATORI0001_1003)			1															
Phage shock protein (HMPREF0762_01151)															1			
Phage shock protein A (IM30), suppresses sigma54-dependent transcription (GPA_11810)													2	1				
Phage shock protein C, PspC (Elen_0248)								1										
Phage SPO1 DNA polymerase-related protein (Corgl_0200)				1								1					1	1
Phage structural protein (ATORI0001_0992)			1															
Phage tail component (Elen_2637)											1							
Phage tail protein I (HMPREF1023_00258)										1								
Phage tail tape measure protein, family, core region (ATORI0001_1171)			1															
Phage tail tape measure protein, TP901 family (Ccur_02660)						1			1			1						
Phage tape measure protein (Apar_0588)				1														
Phage terminase-like protein, large subunit (GPA_22790)						1		1					1	1				
Phage terminase, large subunit, PBSX family (ATORI0001_1521)			1		1	1			1			1						
Phage terminase (COLINT_00860)							1											
Phage uncharacterized protein, XkdX family (COLAER_01621)					1													
Phage-associated deoxyribonuclease (HMPREF0762_01369)															1			
Phage-associated protein (EGYY_10090)												1						
Phage-related protein (COLINT_00124)						1	2											
Prophage LambdaCh01, site-specific recombinase, phage integrase family (HMPREF0762_01054)															1			
Putative phage head-tail adaptor (HMPREF9248_0591)		1																
Putative phage integrase (HMPREF0762_01085)															1			
Putative phage major tail protein (ATORI0001_1174)			1															
Putative phage *N*-6-adenine-methyltransferase (HMPREF9404_4960)										1								
Putative phage repressor (Corgl_1278)																		1
Putative phage terminase, large subunit (ATORI0001_1183)			1															
Site-specific recombinase, phage integrase family (HMPREF9248_0052)		1	1							2					1			
Total phage-related genes	3	4	20	3	9	16	3	3	4	5	6	6	1	6	7	7	1	2

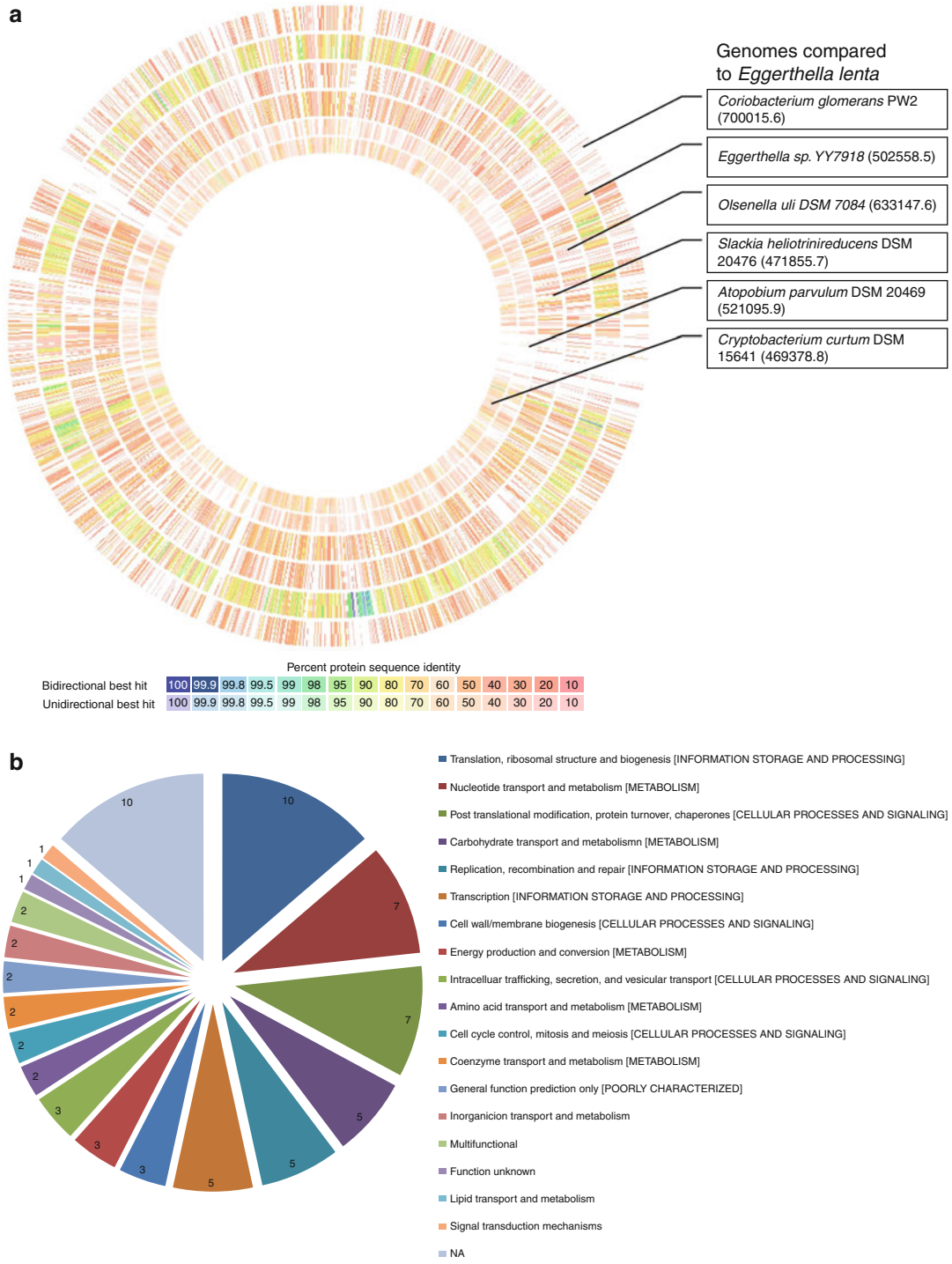

Fig. 11.2

Comparative genome analysis of *Coriobacteriaceae*. (a) Circular map of proteins encoded by the different compared genomes with percent similarity to the reference genome *Eggerthella lenta* (the order of proteins refers to the order of the contigs/genes in the reference genome). The amino acid identity of the query genomes relative to the reference is color coded on a logarithmic scale following the visible spectrum. (b) Functional category distribution of non-ribosomal proteins ($n = 73$) shared by the seven *Coriobacteriaceae* genomes

equol; L. part. adj. *faciens* making; N.L. part. adj. *equolifaciens* equol-producing). Cells are coccobacilli (0.6–0.7 × 1.5–2.7 μm) arranged in chains. Colonies on blood agar are 1–2 mm in diameter, grey to off-white grey, circular, entire, slightly convex, and smooth. The species does not grow in 20 % bile. It is asaccharolytic and positive for arginine dihydrolase as well as arginine and leucine arylamidase. No metabolic end product is detected in peptone-yeast extract medium

supplemented with glucose. Growth is stimulated by arginine. Nitrate is not reduced. *Adlercreutzia equolifaciens* converts the isoflavone daidzein into equol. Its cell wall contains A1*g*-type peptidoglycan with an (L-Ala)–D-Glu–m-Dpm peptide subunit. The diamino acid in the peptidoglycan is *meso*-diaminopimelic acid. The principal respiratory quinone is DMMK-6 (70–96 %). MMK-6 is a minor component (1–29 %). The major cellular fatty acid is $C_{18:1}$*cis*9. The G+C content of DNA is 64–67 mol% (64 mol% for the type strain). The description is based on the study of four strains: FJC-A10, FJC-B9, FJC-B20, and FJC-D53. The type strain is FJC-B9^T (= JCM 14793^T = DSM 19450^T = CCUG 54925^T).

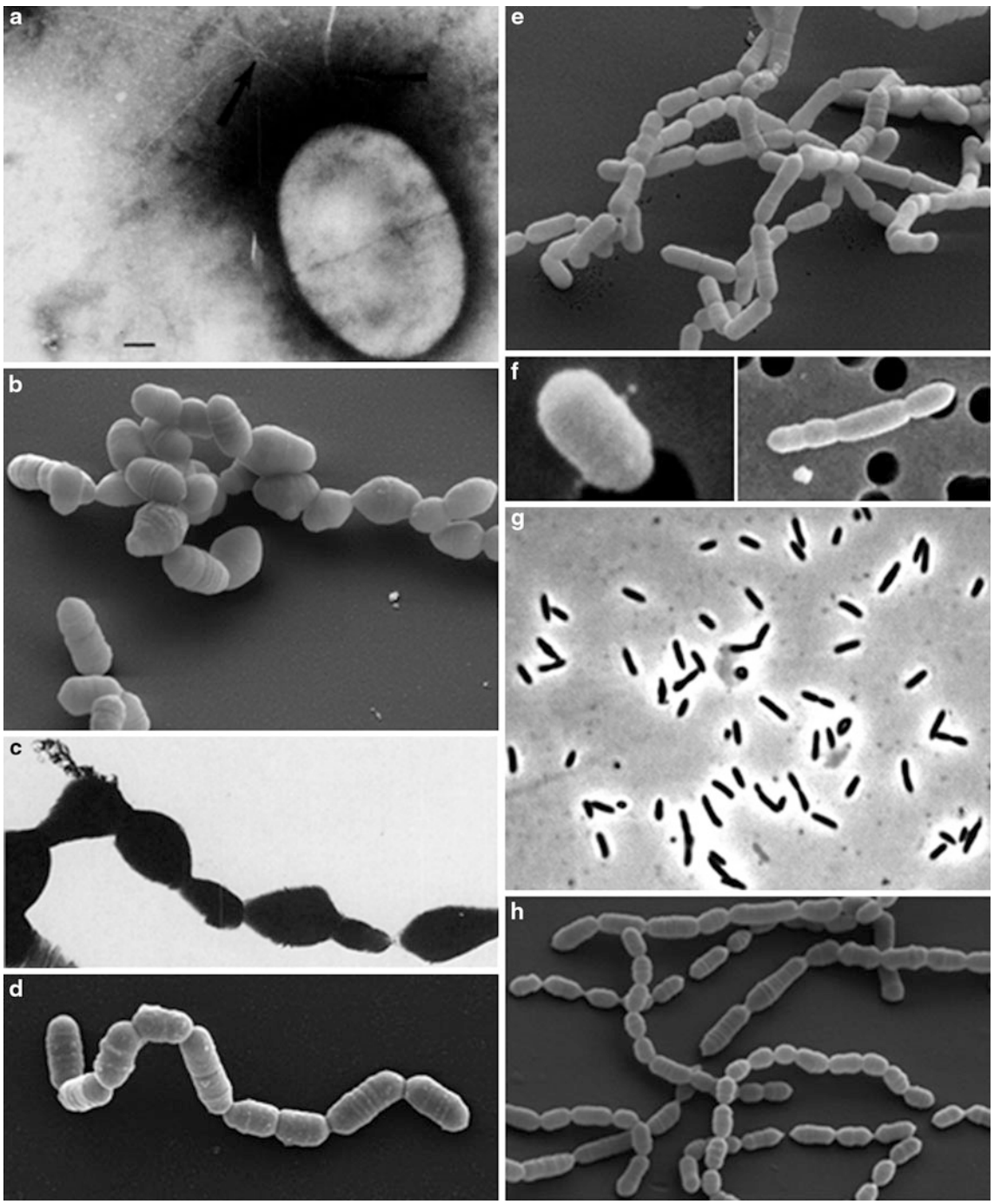

Fig. 11.3 (Continued)

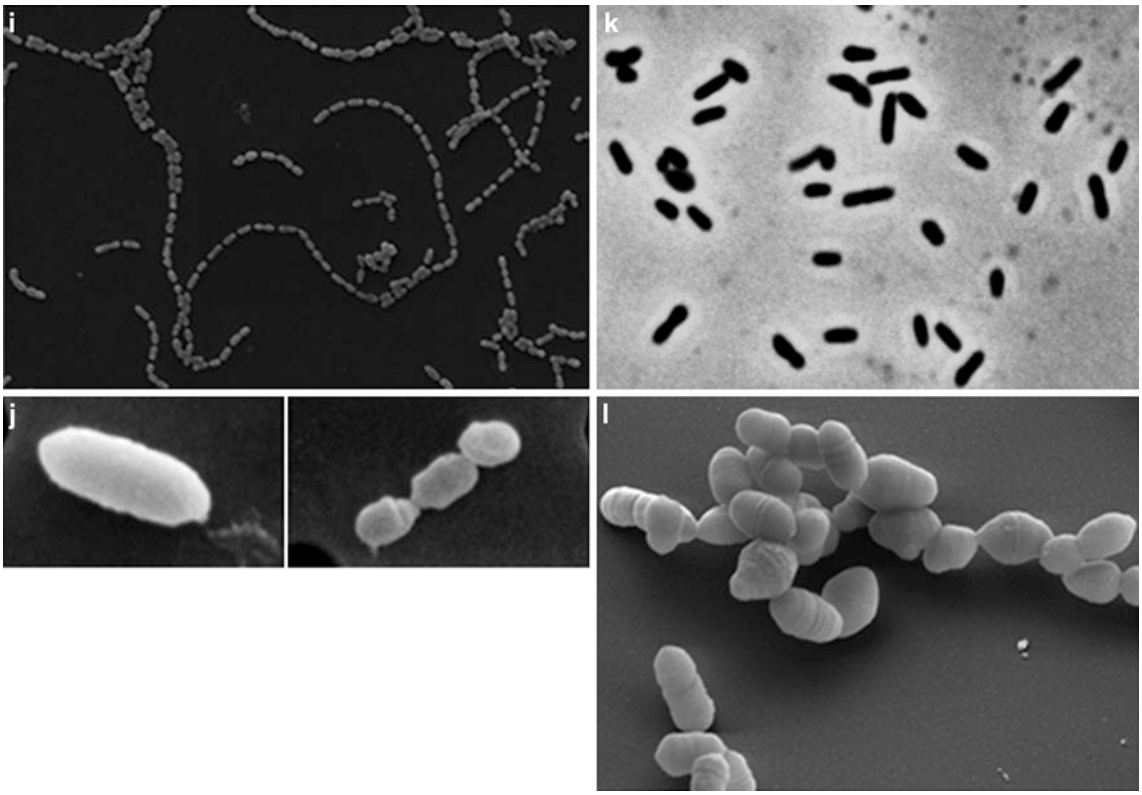

Fig. 11.3
Cell morphology of members of the *Coriobacteriaceae*. (a) *Atopobium fossor* (Bailey and Love 1986), (b) *Atopobium parvulum* (Copeland et al. 2009), (c) *Coriobacterium glomerans* (Haas and König 1988), (d) *Cryptobacterium curtum* (Mavrommatis et al. 2009), (e) *Eggerthella lenta* (Saunders et al. 2009), (f) *Eggerthella sinensis* (Lau et al. 2004b), (g) *Enterorhabdus mucosicola* (Clavel et al. 2009), (h) *Olsenella uli* (Goker et al. 2010), (i) *Olsenella umbonata* (Kraatz et al. 2011), (j) *Paraeggerthella hongkongensis* (Lau et al. 2004a), (k) *Parvibacter caecicola* (Clavel et al. 2013), (l) *Slackia heliotrinireducens* (Pukall et al. 2009)

Asaccharobacter Minamida et al. (2008)

A.sac.cha.ro.bac'ter. Gr. pref. *a-* not; Gr.n.*saccharon* sugar; N.L. masc. n. *bacter* a rod; N.L. masc. n. *Asaccharobacter* rod that does not digest sugar.

The genus is represented only by the type species *Asaccharobacter celatus* (ce.la'tus. L. masc. adj. *celatus* conceal, hide, keep secret). This species is phylogenetically closely related to *Adlercreutzia equolifaciens* FJC-B9^T and strain Julong 732 (>99 % similarity) based on partial 16S rRNA gene sequence analysis. DNA-DNA hybridization analysis of these three isolates has not been performed so far. In contrast to *Adlercreutzia equolifaciens*, *Asaccharobacter celatus* can grow in 20 % bile, is negative for leucine arylamidase, and is characterized by the presence of a dominant lipoquinone that is not MK, MMK, DMMK, ubiquinone, or rhodoquinone. Cells are rod-shaped (0.45 × 2.3–2.7 μm). Colonies are smooth, clear, and colorless on GAM agar, reaching 1 mm in diameter after 2 days at 37 °C. Growth is enhanced in the presence of arginine, but not Tween 80. The species does not reduce nitrate, is asaccharolytic, and produces trace amounts of organic acids (lactic, acetic, and succinic acid) in medium containing peptone, yeast extract, and glucose. It is capable of converting the isoflavone daidzein to equol. Cells do not produce acid from/show negative test results in the API 50 CH system with the following substrates: glycerol, glucose, erythritol, D-arabinose, L-arabinose, ribose, D-xylose, L-xylose, adonitol, methyl *b*-D-xyloside, galactose, fructose, mannose, sorbose, rhamnose, dulcitol, inositol, mannitol, sorbitol, methyl *a*-D-mannoside, methyl *a*-D-glucoside, *N*-acetylglucosamine, amygdalin, arbutin, esculin, salicin, cellobiose, maltose, lactose, melibiose, sucrose, trehalose, inulin, melezitose, raffinose, starch, glycogen, xylitol, gentiobiose, D-turanose, D-lyxose, D-tagatose, D-fucose, L-fucose, D-arabitol, L-arabitol, gluconate, 2-ketogluconate, and 5-ketogluconate. Cells show strong naphthol-AS-BI-phosphohydrolase activity, medium acid phosphatase activity, and weak alkaline phosphatase and esterase (C4) activities. The cell-wall peptidoglycan contains *meso*-diaminopimelic acid, alanine, and glutamic acid. The predominant cellular fatty acid is $C_{18:1}$*cis*9. The G+C content of DNA is 63 mol%. The type strain is do03^T (= JCM 14811^T = DSM 18785^T = AHU 1763^T).

Table 11.4

Comparison of selected characteristics of genera within the family *Coriobacteriaceae*

Characteristic	*Adlercreutzia*	*Asaccharobacter*	*Atopobium*	*Collinsella*	*Coriobacterium*
Growth requirement	Strictly anaerobic	Strictly anaerobic	Strictly or facultative anaerobic	Strictly anaerobic	Strictly anaerobic
Motility	–	–	–	–	–
Growth stimulated by arginine	+	+	–	ND	ND
Growth stimulated by Tween 80	–	–	+	+	ND
Nitrate reduction	–	–	–	–	–
Catalase	–	–	–	–	–
Esculin hydrolysis	ND	–	v	v	ND
Asaccharolytic	+	+	v	–	–
Lactate production	–	trace	+	trace	+
Main CFA	$C_{18:1}$w9c	$C_{18:1}$w9c	$C_{18:1}$w9c FAME/DMA	$C_{18:1}$w9c; $C_{18:1}$w9c DMA	ND
% saturated CFA (major sCFA)	67 ($C_{18:0}$ DMA)	20 ($C_{18:0}$)	14–16 ($C_{10:0}$ FAME; $C_{16:0}$ DMA)	3–30 ($C_{16:0}$ DMA; $C_{18:0}$ DMA)	ND
Major respiratory quinone	DMMK-6	Unidentified	ND	Not detected	ND
G+C mol%	64–67	63	39–46	60–64	60–61
Characteristic	***Cryptobacterium***	***Denitrobacterium***	***Eggerthella***	***Enterorhabdus***	***Gordonibacter***
Growth requirement	Strictly anaerobic	Strictly anaerobic	Strictly anaerobic	Strictly anaerobic	Strictly anaerobic
Motility	–	–	–	–	+
Growth stimulated by arginine	+	ND	+	ND	+
Growth stimulated by Tween 80	–	ND	–	ND	ND
Nitrate reduction	–	+	v	–	–
Catalase	–	–	+	–	+
Esculin hydrolysis	–	ND	–	v	ND
Asaccharolytic	+	+	+	+	–
Lactate production	–	ND	trace	ND	ND
Main CFA	ND	$C_{14:0}$ FAME; $C_{16:0}$ DMA	$C_{16:0}$ DMA	$C_{16:0}$	ai-$C_{15:0}$; $C_{16:0}$ DMA
% saturated CFA (major sCFA)	ND	87 ($C_{14:0}$ FAME; $C_{16:0}$ DMA)	61–76 ($C_{16:0}$ DMA)	70–71 ($C_{16:0}$)	89 (ai-$C_{15:0}$; $C_{16:0}$ DMA)
Major respiratory quinone	ND	ND	MK-6; MMK-6; DMMK-6	MMK-6	MK-6
G+C mol%	50–51	56–60	62–66	64–65	66

Table 11.4 (continued)

Characteristic	*Olsenella*	*Paraeggerthella*	*Parvibacter*	*Slackia*
Growth requirement	Microaerophilic or strictly anaerobic	Strictly anaerobic	Strictly anaerobic	Strictly anaerobic
Motility	−	−	−	−
Growth stimulated by arginine	−	ND	ND	+
Growth stimulated by Tween 80	+	ND	ND	−
Nitrate reduction	−	−	−	v
Catalase	−	+	−	−
Esculin hydrolysis	v	ND	ND	−
Asaccharolytic	−	+	+	+
Lactate production	+	ND	ND	−
Main CFA	$C_{14:0}$; $C_{18:0}$; $C_{18:1}$w9c; $C_{18:1}$w9c DMA	$C_{18:1}$w9c	$C_{16:0}$	$C_{18:1}$w9c; $C_{18:1}$w9c DMA
% saturated CFA (major sCFA)	54–100 ($C_{14:0}$; $C_{18:0}$)	49 ($C_{16:0}$ DMA)	75 ($C_{16:0}$)	16–42 ($C_{14:0}$; $C_{16:0}$DMA; $C_{18:0}$DMA)
Major respiratory quinone	ND	MK-6	MMK-6	ND or not detected
G+C mol%	63–64	61–62	63	58–64

Symbols and abbreviations: + positive, − negative, *ai* anteiso, *DMA* dimethyl acetal, *FAME* fatty acid methyl ester, *MK* menaquinone, *MMK* methylmenaquinone, *DMMK* dimethylmenaquinone, *ND* not determined, *v* variable depending on species, *CFA* cellular fatty acids

Table 11.5
Detection of aminopeptidase activity in *Coriobacteriaceae* species

Aminopeptidase	*Adlercreutzia equolifaciens*^{T}	*Asaccharobacter celatus*^{T}	*Atopobium minutum*^{T}	*Atopobium parvulum*	*Atopobium rimae*
Arginine dihydrolase	+	ND	v	−	−
Alanine arylamidase	ND	ND	v	+	−
Arginine arylamidase	+	ND	+	+	−
Cystine arylamidase	ND	−	ND	ND	ND
Glycine arylamidase	ND	ND	V	+	−
Histidine arylamidase	ND	ND	V	−	−
Leucine arylamidase	+	−	V	+	−
Leucyl glycine arylamidase	ND	ND	+	ND	ND
Lysine arylamidase	ND	ND	ND	ND	ND
Phenylalanine arylamidase	ND	ND	−	ND	ND
Proline arylamidase	ND	ND	v	−	−
Serine arylamidase	ND	ND	−	−	−
Tyrosine arylamidase	ND	ND	−	+	−
Valine arylamidase	ND	−	ND	ND	ND

Aminopeptidase	*Atopobium vaginae*	*Collinsella aerofaciens*^{T}	*Collinsella intestinalis*	*Collinsella stercoris*	*Collinsella tanakaei*
Arginine dihydrolase	+	+	+	+	+
Alanine arylamidase	−	−	−	+	−
Arginine arylamidase	+	+	+	+	+
Cystine arylamidase	ND	−	−	−	−
Glycine arylamidase	+	+	+	+	+
Histidine arylamidase	+	+	+	+	+
Leucine arylamidase	+	+	+	+	+

Table 11.5 (continued)

Aminopeptidase	*Atopobium vaginae*	*Collinsella aerofaciens*^{T}	*Collinsella intestinalis*	*Collinsella stercoris*	*Collinsella tanakaei*
Leucyl glycine arylamidase	ND	+	+	+	+
Lysine arylamidase	ND	ND	ND	ND	ND
Phenylalanine arylamidase	ND	–	–	–	–
Proline arylamidase	+	+	–	–	+
Serine arylamidase	+	–	–	+	–
Tyrosine arylamidase	–	–	–	+	–
Valine arylamidase	ND	–	–	–	–
Aminopeptidase	***Cryptobacterium curtum*^{T}**	***Eggerthella lenta*^{T}**	***Eggerthella sinensis***	***Enterorhabdus caecimuris***	***Enterorhabdus mucosicola*^{T}**
Arginine dihydrolase	+	+	+	+	+
Alanine arylamidase	ND	–	–	–	+
Arginine arylamidase	ND	v	+	–	–
Cystine arylamidase	ND	ND	ND	ND	ND
Glycine arylamidase	ND	–	–	–	+
Histidine arylamidase	ND	–	–	–	+
Leucine arylamidase	ND	–	–	–	+
Leucyl glycine arylamidase	ND	–	–	–	–
Lysine arylamidase	ND	ND	+	–	+
Phenylalanine arylamidase	ND	–	–	–	+
Proline arylamidase	ND	–	–	–	+
Serine arylamidase	ND	–	–	–	+
Tyrosine arylamidase	ND	–	–	–	+
Valine arylamidase	ND	ND	ND	ND	ND
Aminopeptidase	***Gordonibacter pamelaeae*^{T}**	***Olsenella profusa***	***Olsenella uli*^{T}**	***Olsenella umbonata***	***Paraeggerthella hongkongensis*^{T}**
Arginine dihydrolase	+	+	+	+	+
Alanine arylamidase	–	+	+	+	v
Arginine arylamidase	v	+	+	+	v
Cystine arylamidase	ND	+	+	+	ND
Glycine arylamidase	–	+	+	+	–
Histidine arylamidase	–	+	+	+	–
Leucine arylamidase	–	+	+	+	v
Leucyl glycine arylamidase	ND	+	+	+	–
Lysine arylamidase	ND	ND	ND	ND	v
Phenylalanine arylamidase	–	+	+	+	–
Proline arylamidase	–	+	+	+	–
Serine arylamidase	–	+	+	+	–
Tyrosine arylamidase	–	+	+	+	–
Valine arylamidase	ND	+	+	+	ND

Table 11.5 (continued)

Aminopeptidase	*Parvibacter caecicola*^{T}	*Slackia equolifaciens*	*Slackia exigua*^{T}	*Slackia faecicanis*	*Slackia heliotrinireducens*
Arginine dihydrolase	–	+	+	+	+
Alanine arylamidase	+	+	+	–	+
Arginine arylamidase	–	–	+	–	–
Cystine arylamidase	ND	ND	+	–	v
Glycine arylamidase	+	+	+	–	+
Histidine arylamidase	–	+	+	–	+
Leucine arylamidase	+	+	+	–	+
Leucyl glycine arylamidase	–	v	–	–	–
Lysine arylamidase	ND	ND	ND	ND	ND
Phenylalanine arylamidase	+	+	+	–	+
Proline arylamidase	+	+	+	–	+
Serine arylamidase	+	+	+	v	+
Tyrosine arylamidase	+	+	+	–	+
Valine arylamidase	ND	ND	+	–	+

Aminopeptidase	*Slackia isoflavoniconvertens*	*Slackia piriformis*
Arginine dihydrolase	+	+
Alanine arylamidase	–	+
Arginine arylamidase	–	–
Cystine arylamidase	–	+
Glycine arylamidase	–	+
Histidine arylamidase	–	+
Leucine arylamidase	–	+
Leucyl glycine arylamidase	–	–
Lysine arylamidase	ND	ND
Phenylalanine arylamidase	–	+
Proline arylamidase	–	+
Serine arylamidase	–	+
Tyrosine arylamidase	–	+
Valine arylamidase	–	+

Atopobium fossor, *Coriobacterium glomerans*, and *Denitrobacterium detoxificans* were not included in the table since, to the best of our knowledge, no information is available in the literature on any of the listed enzymes for these species

Symbols and abbreviations: + positive, – negative, *v* variable depending on strains, *ND* not determined

Atopobium Collins and Wallbanks (1992)

A.to.po'bi.um. Gr. adj. *atopos* having no place, strange; Gr. neu. part. used as noun; *bion* living thing; N.L. neu. n. *Atopobium* strange living thing.

The genus name *Atopobium* was initially proposed in 1992 following the pioneering 16S rRNA-based phylogenetic analysis of 40 lactic acid bacteria by Collins and Wallbanks. The genus was created to accommodate the species formerly classified as follows: (a) *Lactobacillus minutus* (synonyms: *Bacteroides minutum*, *Eubacterium minutum*) → *Atopobium minutum* comb. nov. (mi.nu'tum. L. neut. adj. *minutum* little, small); (b) *Lactobacillus rimae* → *Atopobium rimae* comb. nov. (L. gen. n. *rimae* of a fissure, here pertaining to the gingival crevice); and (c) *Streptococcus parvulus* (synonym: *Peptostreptococcus parvulus*) → *Atopobium parvulum* comb. nov. (L. neut. dim. adj. *parvulum* very small) (Collins and Wallbanks 1992). The genus also includes *Atopobium vaginae* (va.gi'nae. L. n. *vagina* vagina; L. gen. n. *vaginae* of the vagina) (Rodriguez Jovita et al. 1999) and *Atopobium fossor* (fos'sor. L.n. *fossor*, a digger, delver), originally described as [*Eubacterium fossor*] (Bailey and Love 1986; Kageyama et al. 1999b). The type species of the genus is *Atopobium minutum*. Of note, Olsen et al. published already in 1991 an amended description of [*Lactobacillus minutus*] and [*Streptococcus parvulus*] (Olsen et al. 1991), which were originally described in 1937 (Hauduroy et al. 1937; Weinberg et al. 1937). The transfer of [*Peptostreptococcus parvulus*] to the genus *Streptococcus* was published by Cato in 1983 (Cato 1983).

Table 11.6
Phenotypic features of *Atopobium* spp.

Characteristic	*Atopobium fossor*	*Atopobium minutum*^{T}	*Atopobium parvulum*	*Atopobium rimae*	*Atopobium vaginae*
Growth atmosphere	Strictly anaerobic	Strictly anaerobic	Strictly anaerobic	Strictly anaerobic	Facultative anaerobic
Esculin hydrolysis	–	–	+	v	–
b-Galactosidase	ND	–	+	–	–
Pyroglutamic acid arylamidase	ND	v	+	+	–
Growth in 6.5 % NaCl	ND	v (4/11)	v (6/67)	–	ND
G+C content of DNA (mol%)	43–46	44	39	45	44
Type strain	ATCC 43386 = CIP 106638 = JCM 9981 = NCTC 11919 = VPB 2127	VPI 9428 = ATCC 33267 = CCUG 31167 = DSM 20586 = JCM 1118 = LMG 9439 = NCIMB 702751 (NCFB 2751)	IPP 1246 = ATCC 33793 = CCUG 32760 = CIP 102970 = DSM 20469 = JCM 10300 = VPI 0546	VPI D140H-11A = ATCC 49626 = CCUG 31168 = DSM 7090 = IFO (now NBRC) 15546 = JCM 10299 = LMG 11476	ATCC BAA-55 = CCUG 38953 = CIP 106431

Symbols: *v* variable (number of positive strains/total number of strains tested)

The growth of *Atopobium* spp. is usually stimulated by the presence of Tween 80. Cells consist of short rods, often with central swellings, or small cocci that may appear to be elliptical. Cells occur singly, in pairs, or short chains. The major fermentation products from glucose are lactic acid, together with acetic and formic acid; trace amounts of succinic acid may also be formed. H_2 is not produced. Gelatin is not liquefied; meat is not digested. These bacteria are usually strictly anaerobic, but *Atopobium vaginae* can also grow under aerobic conditions (5 % CO_2). The G+C content of DNA is 35–46 mol%. Discriminative features of *Atopobium* spp. are shown in *Table 11.6*.

Collinsella Kageyama et al. (1999c), Emend. Kageyama and Benno (2000)

Col.lin.sel'la. M.L. fem. dim. ending *-ella*, M.L. fem. n. *Collinsella* named to honor Matthew D. Collins, a contemporary English microbiologist, for his outstanding contribution to microbial taxonomy and phylogeny.

The genus *Collinsella* was created in 1999 to accommodate [*Eubacterium*] *aerofaciens* (ae.ro.fa'ci.ens. Gr. n. *aer* gas; L. v. *facere* to make, to produce; M.L. part. adj. *aerofaciens* gas-producing), which had been previously published as *Bacteroides aerofaciens* (Eggerth 1935). The proposal to create *Collinsella* gen. nov. was based on 16S rRNA gene sequence analysis showing that three strains of [*Eubacterium*] *aerofaciens* (JCM 10188^T, JCM 7790, and JCM 7791) formed a cluster closest to *Atopobium* spp. and *Coriobacterium glomerans*. The three strains were also characterized by higher G+C content of DNA (60–61 vs. 45–47 mol%) when compared with *Eubacterium* sensu stricto (*Eubacterium limosum*, *Eubacterium barkeri*, *Eubacterium callanderi*). The genus currently comprises four species: *Collinsella intestinalis* (in'test.in.alis. N. L. adj. *intestinalis* pertaining to the intestine) (Kageyama and Benno 2000), *Collinsella stercoris* (ster'co.ris. L. n. *stercus* feces; L. gen. n. *stercoris* of feces, referring to the source of the isolate) (Kageyama and Benno 2000), *Collinsella tanakaei* (ta.na.ka'e.i. N.L. masc. gen. n. *tanakaei* of Tanaka, to honor Ryuichiro Tanaka, a Japanese microbiologist, for his contribution to increased knowledge about human intestinal microbiota and probiotics) (Nagai et al. 2010), and the type species *Collinsella aerofaciens*. *Collinsella* spp. occur in chains of rod-shaped cells (0.5–1.0 × 1–3 μm). Fermentation products of glucose are H_2, ethanol, formate, and lactate. All strains are positive for naphthol-AS-BI-phosphohydrolase, acid from glucose and D-mannose. They are negative for *a*-arabinosidase, *a*-fucosidase, *a*-galactosidase, *a*-mannosidase, chymotrypsin, esterase (C4), esterase lipase (C8), glutamic acid decarboxylase, glutamyl glutamic acid arylamidase, lipase (C14), pyroglutamic acid arylamidase and acid from L-arabinose, glycerol, D-mannitol, melezitose, raffinose, L-rhamnose, D-sorbitol, and D-xylose. It has been reported that the growth of *Collinsella* is stimulated by Tween 80 (Dewhirst et al. 2001; Maruo et al. 2008), but this characteristic is absent from the single description of all *Collinsella* species (Kageyama et al. 1999a; Kageyama and Benno 2000; Nagai et al. 2010). Cells of *Collinsella tanakaei* are resistant to 20 % bile (no data available for the other species). The cell wall contains a A4-type peptidoglycan. Respiratory quinones are not detected. The G+C content of DNA is

Table 11.7
Phenotypic features of *Collinsella* spp.

Characteristic	*Collinsella aerofaciens*^{T}	*Collinsella intestinalis*	*Collinsella stercoris*	*Collinsella tanakaei*
Acid produced from				
Cellobiose	–	+	+	+
Lactose	+	–	+	+
Maltose	+	–	+	+
Acid phosphatase	–	+	+	+
Alkaline phosphatase	–	+	+	+
b-Galactosidase	+	–	+	–
a-Glucosidase	+	–	–	–
b-Glucosidase	–	v	+	+
b-Glucuronidase	–	–	–	+
N-Acetyl *b*-glucosaminidase	–	+	+	–
6-phospho-*b*-galactosidase	–	+	–	–
Esculin hydrolysis	–	v	–	+
Peptidoglycan type	A4*b* [(L-Ala)-D-Glu-L-Orn-D-Asp]	A4*a* [(L-Ala)-D-Glu-L-Lys-D-Glu]	A4*b* [(L-Ala)-D-Glu-L-Orn-D-Asp]	ND
% saturated CFA	31	3	3	18
Type strain	VPI 1003 = ATCC 25986 = CCUG 28087 = DSM 3979 = JCM10188 = NCTC 11838	RCA56-68 = CCUG45296 = CIP 106914 JCM 10643 = DSM 13280	RCA55-54 = CCUG45295 = CIP 106913 = DSM 13279 = JCM 10641	YIT 12063 = DSM 22478 = JCM 16071

CFA cellular fatty acids

60–64 mol%. All strains were isolated from human feces. Discriminative features of the *Collinsella* spp. are shown in *Table 11.7*.

Coriobacterium Haas and König (1988)

Co.ri.o.bac.ter'i.um. Gr. fem. n. *koris* bug; Gr. neut. n. *bakterion* a small rod; M.L. neut. n. *Coriobacterium* rodlet associated with bugs.

The genus is represented only by the type species *Coriobacterium glomerans* (glo'me.rans. L. part. adj. *glomerans* agglomerating; the cells form flocculent, wooly sediments with a clear supernatant in fluid media). Cells grow as long chains (>150 μm) of pear-shaped to irregularly shaped rods (0.44–1.80 μm long). Spherical involution forms are common. The filamentous cell chains are attached to the epithelia in the intestine of bugs. The organisms grow on Columbia blood agar, supplemented Schaedler agar (BBL), and TPY agar at 25 and 30 °C. When grown in TPY medium, the fermentation products of glucose (−7.8 μmol/mL) are acetic acid (7.5 μmol/mL), L-lactic acid (6.5 μmol/mL), ethanol (6.1 μmol/mL), CO_2, and H_2. D-Lactic acid, formic acid, volatile short-chain alcohols, or other volatile fatty acids are not formed. The cells ferment glucose, L-arabinose, D-xylose, D-ribose, mannose, sucrose, maltose, cellobiose, mannitol, and salicin. Lactose, melibiose, raffinose, inulin, starch, and inositol are not fermented. The cells have an electron-dense Gram-positive 40-nm-wide cell wall. The peptidoglycan belongs to the Lys-Asp type. The G+C content of the DNA is 60–61 mol%. The type strain is PW2^T (= DSM 20642^T = ATCC 49209^T = JCM 10262^T). The species was originally reported to occur in the third bulbous midgut portion of all stages of the red soldier bug (*Pyrrhocoris apterus*), except the eggs. However, recent in situ hybridization experiments and sterilization of eggs revealed that vertical transmission of *Coriobacterium glomerans* occurs via the egg surface (Kaltenpoth et al. 2009).

Cryptobacterium Nakazawa et al. (1999)

Crypt.o.bac.te'ri.um. Gr. n. *kryptos* hidden; Gr. n. *bakterion* a small rod; M.L. neut. n. *Cryptobacterium* a hidden rod-shaped bacterium.

The genus is represented only by the type species *Cryptobacterium curtum* (cur'tum. L. neut. adj. *curtum*

shortened, a shortened cell of this organism). Cells are asaccharolytic short rods. On BHI-blood agar, minute, circular, convex, and translucent colonies less than 1 mm in diameter are formed, even after prolonged incubation. Growth in broth media is poor with or without carbohydrates. Starch is not hydrolyzed and no liquefaction of gelatin occurs. Ammonia is produced from arginine (Uematsu et al. 2006). Adonitol, amygdalin, arabinose, cellobiose, erythritol, fructose, galactose, glucose, glycogen, inositol, lactose, maltose, mannitol, mannose, melezitose, melibiose, rhamnose, ribose, salicin, sorbitol, starch, sucrose, trehalose, and xylose are not utilized. No metabolic end product is detected in peptone-yeast extract medium supplemented with glucose. Maruo et al. (2008) reported that growth is stimulated by arginine but not Tween 80, yet this statement is not found in the original description by Nakazawa et al., and no amended description has been proposed. The G+C content of DNA is 50–51 mol%. The type strain is 12-3^T (= ATCC 700863^T = DSM 15641^T).

Denitrobacterium Anderson et al. (2000)

De.nit.ro.bac.te'ri.um. L. pref. *de* from; L. n. *nitro* nitro-compound; Gr. neut. dim.n. *bakterion* a small rod; M.L. neut. n. *Denitrobacterium* nitro-compound-reducing rod.

The genus is represented only by the type species *Denitrobacterium detoxificans* (de.tox.if'i.cans. L. pref. *de* from; L. n. *toxicum* poison; L. neut. n. *detoxificans* poison reducer). Cells are chemoorganotrophic and rod-shaped (0.5–1.0 × 1.0–1.5 μm); bulbous ends may be present. The species grows equally well at 32, 37, and 39 °C. Growth occurs in media containing clarified rumen fluid, peptone, and a suitable electron acceptor, including nitrate, 3-nitropropanol, 2-nitropropanol, 3-nitropropionate, nitroethanol, nitroethane, 1-nitropropane, 2-nitrobutane, DMSO, trimethylamine oxide, hydrogen, formate, or (DL)-lactate. H_2S is not produced, and gelatin is not hydrolyzed. Little if any acid is produced during growth in medium with hydrogen or formate as electron donor. Acetate is the major product after growth on lactate; D-lactate is used more readily than L-lactate. The G+C content of DNA ranges from 56 to 60 mol % (thermal denaturation method). A *c*-type cytochrome was found in the type strain NPOH1^T (= ATCC 700546^T = CCUG 56741^T), isolated from a population of ruminal microbes enriched for enhanced metabolism of 3-nitropropanol, the toxic aglycone of miserotoxin (3-nitro-1-propyl-b- d-glucopyranoside) (Anderson et al. 1996). Strain NPOH1^T differs from other strains of the species (NPOH2 = ATCC 700547; NPOH3 = ATCC 700548; and MAJ1 = ATCC 700549) in that it has the ability to reduce nitrate.

Eggerthella Wade et al. (1999), Emend. Maruo et al. (2008), Emend. Würdemann et al. (2009)

Eg.ger.thel'la. L. dim. ending *-ella*; M.L. fem. n. *Eggerthella* named after Arnold H. Eggerth, an American microbiologist who was the first person to report the isolation of [*Eubacterium lentum*] from human feces in 1935 (Eggerth 1935).

The genus *Eggerthella* comprises two species: *Eggerthella sinensis* (M.L. gen. n. *sinae* of China; N.L. fem. adj. *sinensis* pertaining to China, the country where the bacterium was discovered) (Lau et al. 2004b) and the type species *Eggerthella lenta* (len'ta. L. fem. adj. *lenta* slow). *Eggerthella lenta* was originally referred to as *Eubacterium lentum* (Moore et al. 1971; Holdeman et al. 1977). Other synonyms of this species include [*Bacteroides lentus*] and [*Pseudobacterium lentum*]. The proposal to create the name *Eggerthella lenta* was first published in 1999 by Wade et al. on the basis of 16S rRNA gene-based phylogenetic evidence, which showed that [*Eubacterium lentum*], [*Eubacterium exiguum*], and [*Peptostreptococcus heliotrinreducens*] formed a coherent cluster closely related to *Atopobium* spp. and *Coriobacterium glomerans* but only distantly related to *Eubacterium limosum*, the type species of the genus *Eubacterium* (Wade et al. 1999). Kageyama et al. also published a similar study in 1999 and proposed to create the name *Eggerthella* gen. nov. to accommodate [*Eubacterium lentum*] (Kageyama et al. 1999c). However, the work by Wade et al. has priority. Kageyama et al. reported as well that the cell wall of *Eggerthella lenta* contains type A3 peptidoglycan, yet this information cannot be found in the original work by Schleifer and Kandler to which Kageyama et al. referred (Schleifer and Kandler 1972). In their amended description of the genus *Eggerthella*, Maruo et al. stated that the cell wall contains A4*g*-type peptidoglycan with an (L-Ala)–D-Glu–m-Dpm–D-Glu peptide subunit and an inter-peptide bridge that consists only of D-Glu (Maruo et al. 2008). In 2009, Saunders et al. published the genome sequence of the type strain of *Eggerthella lenta* and stated that its cell wall contains A1*g*-type peptidoglycan (Saunders et al. 2009). The latest description with standing in nomenclature is the one by Maruo et al. 2008. The major respiratory quinones are MK-6 (dominant in *Eggerthella lenta*) and MMK-6 (dominant in *Eggerthela sinensis*). DMMK-6 is also detected in *Eggerthella sinensis*. Polar lipids consist of two phospholipids, phosphatidylglycerol and diphosphatidylglycerol, and four glycolipids. The main cellular fatty acid is $C_{16:0}$ DMA. The proportion of saturated cellular fatty acids is 61–76 %. Growth is stimulated by arginine (Sperry and Wilkins 1976a). Cells are usually arranged in chains. They are catalase- and arginine dihydrolase-positive. Colonies on blood agar are as follows: 0.25–1.0 mm, circular, entire, slightly raised, smooth, grey, and translucent to semiopaque (*Eggerthella lenta*) and greyish white, 0.5 mm in diameter after 48 h at 37 °C (*Eggerthella sinensis*). *Eggerthella lenta* reduces nitrate and has been found to produce ammonia from arginine and to contain cytochromes *a*, *b*, and *c* and a carbon monoxide-binding pigment (Sperry and Wilkins 1976b). The G+C content of DNA is 61–64 mol% (*Eggerthella lenta*) and 65–66 mol% (*Eggerthella sinensis*). The type strain of *Eggerthella lenta* is DSM 2243^T (= ATCC 25559^T = CCUG 17323A^T = CIP 106637^T = JCM 9979^T = NCAIM B.01418^T = NCTC 11813^T). The type strain of *Eggerthella sinensis* is HKU14^T (= DSM 16107^T = JCM 14551^T = LMG 22123^T). Discriminative features of *Eggerthella* spp. are shown in Table 11.8.

Table 11.8
Phenotypic features of *Eggerthella* spp.

Characteristic	*Eggerthella lenta*^{T}	*Eggerthella sinensis*
Nitrate reduction	+	–
Major respiratory quinone	MK-6 (64 %)	MMK-6 (60 %)
Bile resistance	+	ND
Lysine arylamidase	ND	+

Abbreviations: *MK* menaquinone, *MMK* methylmenaquinone

Table 11.9
Phenotypic features of *Enterorhabdus* spp

Characteristic	*Enterorhabdus caecimuris*	*Enterorhabdus mucosicola*^{T}
Diamino pimelic acid	*meso*	LL
Respiratory quinone	MMK-6 (60 %); DMMK-6 (40 %)	MMK-6 (100 %)
Glucose in whole-cell sugars	+	–
Polar lipids	DPG, PG, 2 GL, 1PL, 1 L	DPG, PG, 4 GL, 3 PL
Aminopeptidases	–	+
Glutamic acid decarboxylase	+	–
Equol production	–	+

Abbreviations: *DPG* diphosphatidylglycerol, *GL* glycolipids, *L* unidentified lipid, *MMK* methylmenaquinone, *PG* phosphatidylglycerol, *PL* phospholipids

Enterorhabdus Clavel et al. (2009), Emend. Clavel et al. (2010)

En.te.ro.rhab'dus. Gr. n. *enteron* intestine; Gr. fem. n. *rhabdos* a rod; N.L. fem. n. *Enterorhabdus* a rod isolated from the intestine.

The genus *Enterorhabdus* comprises two species: *Enterorhabdus caecimuris* (ca.e.ci.mu'ris. L. n. *caecum* caecum; L. n. mus *muris* mouse; N.L. gen. n. *caecimuris* of the caecum of a mouse) and the type species *Enterorhabdus mucosicola* (mu.co.si'co.la. N.L. n. *mucosa* mucosa from L. adj. *mucosus -a -um* mucous; L. suff. *-cola* (from L. n. *incola*) inhabitant, dweller; N.L. n. *mucosicola* inhabitant of the intestinal mucosa). These species are mesophilic, aerotolerant anaerobes that grow as single short rods (0.5 × 2.0 μm) that do not produce glycosidases. Cultures in the stationary phase of growth in anoxic Wilkins-Chalgren-Anaerobe broth are characterized by stable pH (6.9–7.1) and a typically low turbidity (<0.5 McFarland standard). They grow well in the temperature range 30–40 °C. No growth occurs in the presence of 0.5 % (w/v) bile salts. *Enterorhabdus caecimuris* grows in the presence of 2 % (w/v) NaCl. Both species form pinpoint colonies on blood agar. The major cellular fatty acids are $C_{14:0}$, $C_{16:0}$, and $C_{16:0}$ DMA. Whole-cell sugars include galactose and ribose. The most dominant respiratory quinone is MMK-6. The G+C content is 64.2–64.5 mol%. The major polar lipids are diphosphatidylglycerol and two glycolipids. The type strain of *Enterorhabdus mucosicola* is Mt1B8^T(= DSM 19490^T = CCUG54980^T). The type strain of *Enterorhabdus caecimuris* is B7^T (= DSM 21839^T, =CCUG 56815^T). Discriminative features of *Enterorhabdus* spp. are shown in Table 11.9.

Gordonibacter Würdemann et al. (2009)

Gor.do'ni.bac'ter. N.L. masc. n. *Gordon* named after Jeffrey I. Gordon, MD, the Dr Robert J. Glaser Distinguished University Professor and Director of the Center for Genome Sciences at Washington University School of Medicine, St. Louis, MO, USA; N.L. masc. n. *bacter* a rod; N.L. masc.n. *Gordonibacter* a rod named after Jeffrey I. Gordon.

The genus is represented only by the type species *Gordonibacter pamelaeae* (pa.me'la.eae. N.L. fem. n. *pamelaeae* named after Dr Pamela Lee Oxley (née Fredericks), biochemist, environmentalist, teacher, mentor, and mother). Cells are catalase-positive coccobacilli (0.5–0.6 × 0.8–1.2 μm) with a conical cell apex. They are motile and characterized by the presence of a subpolarly inserted flagella when grown in BHI medium. Of note, one clinical isolate identified as *Gordonibacter pamelaeae* on the basis of 16S rRNA gene sequencing and phenotypic analysis was reported to be nonmotile (Woo et al. 2010). Growth is generally slow on BHI and Schaedler anaerobic media (Oxoid) supplemented with 5 % defibrinated horse blood, with pale-white, semitranslucent colonies forming after 48–72 h at 37 °C. Growth is enhanced by 1 % (w/v) arginine-HCl. Arabinose, glucose, mannose, raffinose, trehalose, xylose, L-methionine, L-phenylalanine, L-valine, L-valine plus L-aspartic acid, dextrin, and D-glucose 6-phosphate are not metabolized. Nitrate is not reduced. Only weak conversion of pyruvic acid and pyruvic acid methyl ester is observed. All other organic substrates included in the Biolog AN MicroPlate are not metabolized. Cellular fatty acids consist mainly (approximately 90 %) of saturated fatty acids (predominantly C_{15} and C_{16}). The major respiratory lipoquinone present is MK-6; MMK-6 is a minor component. The major polar lipids are phosphatidylglycerol, diphosphatidylglycerol, and four glycolipids. The G+C content of DNA is 66 mol%. The type strain is 7–10-1-b^T(= DSM 19378^T = CCUG55131^T).

Olsenella Dewhirst et al. (2001)

Ol.sen.el'la. L. fem. dim. ending *-ella*, N.L. fem. n. *Olsenella* of Olsen, named to honor Ingar Olsen, a contemporary Norwegian microbiologist, who first described *Lactobacillus uli*.

The genus currently comprises three species: (a) *Olsenella profusa* (pro.fus'a. L. adj. *profusus* profuse, referring to the good growth of the organism), (b) *Olsenella umbonata* (um.bo.na'ta. N.L. fem. adj. *umbonata* bossed, umbonate (from L. masc. n.

Table 11.10
Phenotypic features of *Olsenella* spp.

Characteristic	*Olsenella profusa*	*Olsenella uli*^{T}	*Olsenella umbonata*
Cell morphology	Single, pairs, or chains	Single, pairs, or chains	Short to very long serpentine chains
Acid produced from			
Mannitol	+	–	–
Lactose	+	v	–
Arabinose	+	–	–
Cellobiose	+	–	–
Raffinose	+	–	–
Alkaline phosphatase	+	–	–
b-Galactosidase	+	–	–
a-Glucosidase	+	–	+
b-Glucosidase	+	+	–
N-Acetyl-*b*-glucosaminidase	+	–	–
6-phospho-*b*-galactosidase	+	–	–
Growth stimulation by Tween 80	slight	+	+
Esculin hydrolysis	+	v	–
% saturated CFA (main)	93–97 (ai-$C_{14:0}$)	54–87 ($C_{18:0}$)	85–100 ($C_{14:0}$; $C_{18:0}$)
Type strain	D315A-29 = CCUG 45371 = CIP 106885 = DSM 13989 = JCM 14553	VPI D76D-27C = ATCC 49627 = CCUG 31166 = DSM 7084 = JCM 12494 = LMG 11480 = VPI D76D-27C	lac31 = CCUG 58604 = DSM 22620 = JCM 16156

Abbreviations: ai, anteiso, *CFA* cellular fatty acids

umbo, *umbonis* a shield boss), referring to the umbonate elevations of outgrown colonies on solid culture media) (Kraatz et al. 2011), and (c) the type species *Olsenella uli* (u'li.Gr. n. *oulon* the gum; N.L. gen. n. *uli* of the gum). Cells are microaerotolerantly (moderately obligately) anaerobic (less than 5 % O_2, v/v). They grow as small, elliptical rods that occur singly, in pairs, or short to very long serpentine chains. Convert a variety of sugars. Lactic acid is the major product from glucose. Minor products are formic and acetic acid. Able to grow on mucin from porcine stomach. All strains are negative for urease, *a*-galactosidase, *a*-arabinosidase, *b*-glucuronidase, *a*-mannosidase, *a*-fucosidase, raffinose fermentation, acidification of glycerol and melezitose, trypsin, *a*-chymotrypsin, reduction of nitrate, pyroglutamic acid arylamidase, glutamic acid decarboxylase, and glutamyl glutamic acid arylamidase. All strains are positive for mannose fermentation, acidification of glucose, and gelatin hydrolysis. Growth is stimulated by Tween 80 but not arginine. The cellular fatty acids consist mainly of saturated fatty acids. The G+C content of DNA is 63–64 mol%. Original values reported for [*Lactobacillus*] *uli* were $C_{18:1}$*cis*9 (major cellular fatty acid) and 53 mol% (G+C content of DNA) (Olsen et al. 1991). Göker et al. recently reported that *Olsenella uli* is characterized by the presence of a A4*b*-type peptidoglycan based on L-Orn-D-Asp (Goker et al. 2010). *Olsenella profusa* was previously designated *Eubacterium* group D52 (Holdeman et al. 1977). The description of *Olsenella umbonata* refers to the analysis of four strains (A2, lac 15, lac 16, and lac31^T). All lac strains were isolated from pig jejunal mucosa (Kraatz and Taras 2008), whereas strain A2 was isolated from sheep rumen as part of a study focusing on ammonia-producing bacteria (Eschenlauer et al. 2002). *Olsenella umbonata* was found to produce ammonium from peptone under anaerobic and unreduced microaerobic conditions (ca. 12 and 9 mmol/l, respectively). Growth of this species is positive in 20 % bile but absent in 6.5 % NaCl. Strain A2 (=CCUG 58212 = DSM 22619 = JCM 16157), which had been informally named [*Olsenella* (*Atopobium*) *oviles*] (Dewhirst et al. 2001; Eschenlauer et al. 2002), can be differentiated from the type strain lac31^T by a negative result for acidification of trehalose in the API 20 A strip. Discriminative features of *Olsenella* spp. are shown in *Table 11.10*.

Paraeggerthella Würdemann et al. (2009)

Pa'ra.eg.ger.thel'la. L. prep. *para* beside; N.L. fem. n. *Eggerthella* a bacterial genus name; N.L. fem. n. *Paraeggerthella* beside *Eggerthella*, named in recognition of the close relationship to the genus *Eggerthella*.

The genus is represented only by the type species *Paraeggerthella hongkongensis* (N.L. fem. adj. *hongkongensis*, pertaining to Hong Kong, the city where the bacterium was discovered). This species had been previously described as [*Eggerthella*] *hongkongensis* (Lau et al. 2004b), for which an emended description was published by Maruo et al. (2008). The type strain is HKU10^T (= DSM 16106^T = CCUG 49250^T), isolated in 1998 from the blood of a 30-year-old male patient suffering from alcoholic cirrhosis, portal hypertension, and epilepsy and diagnosed with perianal abscess (Lau et al. 2004a). Additional strains (HKU11, HKU12, HKU13) were isolated from blood cultures of a patient with an infected rectal tumor, a liver abscess, and acute appendicitis, respectively. These additional strains were not further studied in amended descriptions. The rationale for reclassifying [*Eggerthella*] *hongkongensis* into the novel genus *Paraeggerthella* was based on several major differences observed between strain HKU10^T and *Eggerthella* species: (a) 16S rRNA gene similarity values <95 %, (b) a lower amount of saturated cellular fatty acids (45 vs. 61–63 %), (c) the presence of $C_{18:1}$ w9c instead of $C_{16:0}$ DMA as major cellular fatty acid, (d) different polar lipid profiles (three instead of four glycolipids), and (e) the ability of *Paraeggerthella hongkongensis* to metabolize 3-methyl-D-glucose, palatinose, L-rhamnose, L-methionine, L-valine, L-valine plus L -aspartic acid, and uridine 5′-monophosphate. Physiological testing using Rapid ID32A and API 20A revealed just one positive reaction, for arginine dihydrolase. Lau et al. reported a positive reaction for *b*-glucosidase, which was not confirmed by Würdemann and colleagues. Results obtained with Biolog AN MicroPlates indicated that urocanic acid and L-threonine are metabolized. Weak conversion of rhamnose is observed. The other organic substrates included in the Biolog AN MicroPlate are not metabolized. No significant conversion of the flavonoids quercetin, rutin, genistein, and phloretin is observed. Cells are catalase-positive coccobacilli arranged in chains. They grow on blood agar as greyish white colonies of 0.5 mm in diameter after 48 h at 37 °C. The cell wall contains the A4*g*-type peptidoglycan. According to Würdemann et al., the major respiratory lipoquinone is MK-6 (68 %); MMK-6 is a minor component (32 %). Maruo et al. found that the principal respiratory quinone is MMK-6 and that minor menaquinones are MK-6 and DMMK-6. This discrepancy is likely due to growth conditions and technical issues, e.g., the fact that DMMK-6 can be difficult to detect using HPLC. Polar lipids consist of phosphatidylglycerol, diphosphatidylglycerol, and three glycolipids (GL1, GL2, andGL4). The G+C content of DNA of strain HKU10^T is 61–62 mol%.

Parvibacter Clavel et al. (2013)

Par.vi.bac'ter. L. adj. *parvus* small; N.L. masc. n. *bacter* rod; N.L. masc. n. *Parvibacter* small rod.

The genus is represented only by the type species *Parvibacter caecicola* (ca.e.ci'co.la. N.L. n. *caecum* blind pouch, caecum; L. suff. *-cola* (from L. n. *incola*), dweller, inhabitant; N.L. n. *caecicola* caecum dweller). Cells are aerotolerant small rods (0.5 × 1.5 μm) that grow only under strictly anoxic conditions in the temperature range from 25 to 37 °C. After 48 h at 37 °C on Wilkins-Chalgren-Anaerobe agar under anoxic conditions, colonies are circular, entire, pinpoint, and grey. Positive for proline, phenylalanine, leucine, tyrosine, alanine, glycine, and serine arylamidase. Negative for urease activity, arginine dihydrolase, *a*- and *b*-galactosidase, *a*- and *b*-glucosidase, *a*-arabinosidase, *b*-glucuronidase, *b*-*N*-acetylglucosamine, mannose and raffinose fermentation, glutamic acid decarboxylase, *a*-fucosidase, nitrate reduction, indole production, and alkaline phosphatase as well as arginine, leucyl glycine, pyroglutamic acid, histidine, and glutamyl glutamic acid arylamidase. The major cellular fatty acids are $C_{16:0}$ (26 %) and i-$C_{15:0}$ (11 %). Galactose, glucose, and ribose are detected as whole-cell sugars. The principal respiratory quinone is MMK-6. The diamino acid in the peptidoglycan is *meso*-diaminopimelic acid. The major polar lipids are diphosphatidylglycerol, phosphatidylglycerol, three phospholipids, four glycolipids, and one unidentified lipid. The G+C content of DNA is 62.5 %. The type strain is NR06^T (= DSM 22242^T = CCUG 57646^T).

Slackia Wade et al. (1999), Emend. Nagai (2010)

Slack'ia. M.L. fem. n. named to honor Geoffrey Slack, distinguished British microbiologist and dental researcher.

The rationale for creating the genus name *Slackia* was to accommodate [*Eubacterium exiguum*] (Poco et al. 1996) and [*Peptococcus heliotrinreducans*] (Lanigan 1976) on the basis of 16S rRNA phylogenetic evidence showing that these two species formed a distinct cluster within the *Coriobacteriaceae*. The genus *Slackia* currently comprises six species: (a) *Slackia equolifaciens* (e.quo.li.fa'ci.ens. N.L. n. *equol-olis* equol; L. part. adj. *faciens* making; N.L. part. adj. *equolifaciens* equol-producing) (Jin et al. 2010), (b) *Slackia faecicanis* (fae.ci.ca'nis. L. n. *faex, faecis* feces; L. gen. n. *canis* dog; N.L. gen. n. *faecicanis* from dog feces) (Lawson et al. 2005), (c) *Slackia heliotrinireducens* (he.li.o.trin.i.re.duc. ens. M.L. n. *heliotrinum* derived from heliotrine, a pyrrolizidine alkaloid; L.adj. *reducans* reducing M.L. adj. *heliotrinireducens* referring to the ability to bring about oxidative cleavage of the heliotrine molecule), (d) *Slackia isoflavoniconvertens* (i.so.fla.vo.ni.con.ver'tens. N.L. neut. n. *isoflavonum* isoflavone; L. part. adj. *convertens* converting; *isoflavoniconvertens* isoflavone-converting) (Matthies et al. 2009), (e) *Slackia piriformis* (pi.ri.for'mis. L. n. *pirum* pear; L. adj.

Table 11.11
Phenotypic features of *Slackia* spp.

Characteristic	*Slackia equolifaciens*	*Slackia exigua*^{T}	*Slackia faecicanis*	*Slackia heliotrinireducens*	*Slackia isoflavoniconvertens*	*Slackia piriformis*
Nitrate reduction	–	–	v	+	–	–
Bile resistance	ND	–	w[a]	–	ND	w[a]
% saturated CFA (main)	42 ($C_{14:0}$)	22–35 ($C_{14:0}$; $C_{16:0}$ DMA)	18–30 ($C_{14:0}$; $C_{18:0}$ DMA)	16 (i-$C_{14:0}$)	ND	26 ($C_{18:0}$ DMA)
G+C content of DNA (mol%)	61	60–64	61	61	58.5	58
Colony morphology (agar medium)	1–2 mm, translucent grey (GAM[b] + 0.5 % arginine-HCl)	<1 mm, circular, convex, translucent (BHI-blood)	1–2 mm, translucent to grey, uneven surface, irregular edges (anaerobic blood)	1–2 mm, effuse, entire edge, colorless, transparent (tryptone-yeast-mineral salts)	1 mm, smooth, translucent (Columbia blood)	0.1–1.0 mm, translucent to beige, circular, uneven surface, irregular edges (GAM[b])
Type strain	DZE (=CCUG 58231 = JCM 16059)	S-7 = ATCC 700122 = CIP 105133 = JCM 11022 = CCUG 44588	5WC12 = CCUG 48399 = CIP 108281 = JCM 14555 = DSM 17537	RHS1 = ATCC 29202 = CCUG 47954 = DSM 20476 = JCM 14554 = NCTC 11029	HE8 = CCUG57679 = DSM 22006 = JCM 16137	YIT 12062 = DSM 22477 = JCM 16070

Abbreviations: *BHI* brain-heart infusion, *DMA* dimethyl acetal, *i* iso, *ND* not determined, *w* weak
[a]*w* weak, cells grew on medium containing 2 % oxgall, but the number of colonies was decreased compared with control medium without oxgall (5 % and 50 % cfu for *Slackia faecicanis* and *Slackia piriformis*, respectively)
[b]General anaerobic medium, Nissui Pharmaceutical, Tokyo, Japan

suffix-*formis*-like, in the shape of; N.L. fem. adj. *piriformis* pear-shaped, referring to the cell shape) (Nagai et al. 2010), and (f) the type species *Slackia exigua* (ex.i.gu'a. L. adj. *exigua* scanty, small, referring to the scanty or poor growth of this organism). Cells are cocci, coccobacilli, or short bacilli, the growth of which is stimulated by 0.5 % arginine. Sugars are not fermented. Positive for naphthol-AS-BI-phosphohydrolase but negative for alkaline phosphatase, *a*-arabinosidase, *N*-acetyl-*b*-glucosaminidase, chymotrypsin, *a*-fucosidase, *a*-galactosidase, *b*-galactosidase, *a*-glucosidase, *b*-glucosidase, *b*-glucuronidase, glutamic acid decarboxylase, glutamyl glutamic acid arylamidase, lipase (C14), *a*-mannosidase, 6-phospho-*b*-galactosidase, pyroglutamic acid arylamidase, trypsin, urease, and esculin hydrolysis. The main cellular fatty acids are $C_{18:1}$w9c and $C_{18:1}$w9c DMA. Respiratory quinones have not been detected in *Slackia piriformis*, *Slackia exigua*, *Slackia heliotrinireducens*, and *Slackia faecicanis* (*Slackia equolifaciens* and *Slackia isoflavoniconvertens* have not been analyzed). *Slackia heliotrinireducens* was isolated for its ability to reductively cleave hepatotoxic pyrrolizidines found in forages. It also contains a *c*-type cytochrome. This species was originally published as *Peptococcus heliotrinreducans* (Lanigan 1976), before its transfer to the genus *Peptostreptococcus* as *Peptostreptococcus heliotrinreducens* in 1986 on the basis of its high G+C content of DNA and the presence of various aminopeptidases (Ezaki and Yabuuchi 1986). Discriminative features of *Slackia* spp. are shown in *Table 11.11*.

Isolation, Enrichment, and Maintenance Procedures

It is striking that all members of the *Coriobacteriaceae* have been so far isolated only from body habitats of mammals and insects, which hints at evolutionary driving forces that made these bacteria best suited for efficient colonization and survival in such environments. The first cultivable representatives of the family, i.e., *Collinsella aerofaciens* and *Eggerthella lenta*, were recovered from human feces (Eggerth 1935). All strains of so far described species have been isolated by chance using either nonselective rich media or selective media and isolation procedures targeting specific metabolic functions or bacterial populations, e.g., conversion of isoflavones (*Asaccharobacter celatus*, *Slackia equolifaciens*, *Slackia isoflavoniconvertens*), mucosa-associated bacteria

(*Gordonibacter pamelaeae*, *Enterorhabdus mucosicola*, *Olsenella umbonata*), reduction of nitro-compounds (*Denitrobacterium detoxificans*), or ammonia production (*Olsenella umbonata*, *Slackia heliotrinireducens*). For this reason, and due as well to the metabolic versatility of the 30 species of the family, there is to date no selective medium available for exhaustive enrichment of *Coriobacteriaceae*. The efficacy of blood, arginine, or Tween 80 to stimulate growth as well as the resistance towards bile and antibiotics has hitherto not been tested for all species. Moreover, while strictly anoxic culture techniques are suited for cultivation of most species, *Olsenella* spp. grow under microaerophilic conditions and *Atopobium vaginae* is a facultative anaerobe. The isolation and maintenance conditions reported for the 30 species of the family are summarized in Table 11.12.

Ecology

The family *Coriobacteriaceae* includes a large majority of strictly anaerobic strains with fastidious growth requirements. They frequently coexist with a number of other microorganisms in complex ecosystems. As a result, the ecology of this family (as in the sense of the occurrence and functions of its members) was poorly studied until the emergence (and affordability) of culture-independent techniques such as polymerase chain reaction (PCR), sequencing of 16S rRNA genes as well as metabolomics and system biology approaches (Woo et al. 2008; Claus et al. 2011). It is now becoming clear that these previously understudied bacterial species carry out important physiological functions within their hosts.

Habitat and Occurrence

At the time of writing, the family accommodates 14 genera, 13 of which originate from the gastrointestinal tract of mammals (human, mouse, rat, dog, cow, and sheep). *Coriobacterium glomerans*, the type species of the family, has been so far retrieved only from the gut of insects (Haas and König 1988; Kaltenpoth et al. 2009). The diversity and composition of the human intestinal microbiota varies greatly between individuals (Qin et al. 2010). Nevertheless, *Coriobacteriaceae* can be considered as prevalent and dominant dwellers of the human intestine (and by extension of the mammalian intestine in general). Dominant means that certain species can be found at cell densities above 10^8 cells per gram intestinal content. Still, actinobacteria, and thus *Coriobacteriaceae*, represent usually a minor fraction of gut bacterial diversity (<2–5 % of total 16S rRNA gene sequences) when compared with members of the phyla Bacteroidetes and Firmicutes.

Culture-independent studies have demonstrated that the genus *Collinsella* is the most abundant human gut taxon of the family (Kageyama et al. 2000). The species *Collinsella aerofaciens* seems to be a member of the core human gut microbiome, i.e., "a set of bacterial molecular species that are altogether dominant and prevalent within the fecal microbiota of healthy humans" (Tap et al. 2009; Qin et al. 2010). Based on the use of specific 16S rRNA-targeted oligonucleotide probes for fluorescence in situ hybridization, Harmsen et al. found that the *Collinsella* and *Atopobium* phylogenetic groups were part of the dominant microbiota in 26 of 33 adult subjects, with cell counts $>10^9$ cell/g dry feces (Harmsen et al. 2000). In another similar study, mean proportions of the *Atopobium* group were >3 % of dominant bacteria in 39 postmenopausal women (Clavel et al. 2005). Thus, *Atopobium* spp. also seem to be predominant in human feces. However, it is important to note that the specificity of 16S probes warrants detection of relatively broad phylogenetic groups rather than specific species (e.g., the *Atopobium* probe S-*-Ato-0291-a-A-17 targets also other *Coriobacteriaceae*). In one study based on the use of quantitative PCR, *Slackia* spp. were detected in 16 of 40 fecal samples from healthy Japanese adults at a mean population density of $\log_{10}$ 6.4 ± 2.4 cell/g wet weight (Tsuji et al. 2010). PCR-based assays have been used as well to assess the occurrence of *Eggerthella lenta* in human feces, revealing that this species is detected in 30–40 % of tested samples (Schwiertz et al. 2000; Kageyama and Benno 2001). In fact, part of the aforementioned molecular data confirmed the pioneering culture-based work by W. E. C. Moore, S. M. Finegold, and L. V. Holdeman, who readily isolated a number of strains of [*Eubacterium*] *aerofaciens* and [*Eubacterium lentum*] from feces of healthy human adults. These isolates were usually recovered from 50 % of analyzed subjects at mean densities of $>10^9$ cfu/g dry weight (Moore and Holdeman 1974; Finegold et al. 1983). Some *Coriobacteriaceae* have also been detected in sewage samples using massively parallel pyrosequencing of hypervariable regions in microbial rRNA genes (McLellan et al. 2010). The genus *Collinsella* was detected at 0.27 % and 1.07 % total sequences in sewage and human fecal samples, respectively, but not in surface water. The presence of fecal microbial taxa in sewage water appears to be the consequence of human fecal pollution of the wastewater treatment plants rather than such environmental samples being the natural habitat of *Coriobacteriaceae*.

Regarding more recently described taxa within the family, *Enterorhabdus* spp. have been repeatedly found in high-throughput 16S rRNA gene sequence datasets from the mouse, human, and bovine intestinal tract (Benson et al. 2010; Werner et al. 2011; Hristov et al. 2012; Martinez et al. 2012). This speaks in favor of a widespread occurrence in various gut ecosystems, yet most likely at lower population densities. With respect to specific niches occupied by *Coriobacteriaceae* in the gut, it is worth noting that some members may be well suited for colonization of mucosal surfaces, as suggested by (a) the isolation of strains from mucosal samples or using selective culture media containing mucin (*Enterorhabdus mucosicola*, *Gordonibacter pamelaeae*, *Olsenella umbonata*), (b) the symbiotic relationship they may have with their hosts (*Coriobacterium glomerans*), and (c) their detection in mucosal samples using molecular-based techniques (*Atopobium* and *Collinsella* spp.) (Collado and Sanz 2007a, b; Nadal et al. 2007; Lyra et al. 2012).

Table 11.12

Origin, isolation, and growth conditions of type strains of *Coriobacteriaceae*

	Adlercreutzia equolifaciens	*Asaccharobacter celatus*	*Atopobium fossor*	*Atopobium minutum*	*Atopobium parvulum*
Publication	2008	2008	1986	1937[a]	1937[a]
Sample type	Feces of a 25-year-old healthy woman	Caecal content (frozen glycerol stock) of a male Sprague–Dawley rat[b]	Pharyngeal tonsillar surface of normal horses	Human oral cavity	Human oral cavity
Agar medium	BL[c] + 5 % horse blood	GAM[c] + 2 g Fujiflavone P10[d]	Sheep blood (5 %) + vitamin K-hemin + formate-fumarate[e]	Nonselective D4[f]	Nonselective D4[f]
Incubation	3 d, 37 °C	2 d, 37 °C	NR (d), 37 °C	5 d, NR (t°C)	5 d, NR (t°C)
Atmosphere	Anaerobic[g]	$N_2/H_2/CO_2$ (85:5:10)	$N_2/H_2/CO_2$ (80:10:10)	$N_2/H_2/CO_2$ (85:3:12)	$N_2/H_2/CO_2$ (85:3:12)
Additional maintenance media	GAM[c] + 0.5 % arginine, pH 7.0	GAM[c]	Tryptose agar[h]	/	/
References	Maruo et al. (2008)	Minamida et al. (2008)	Bailey and Love (1986)	Moore et al. (1982), Moore et al. (1983)	Moore et al. (1982), Moore et al. (1983)
	Atopobium rimae	*Atopobium vaginae*	*Collinsella aerofaciens*	*Collinsella intestinalis*	*Collinsella stercoris*
Publication	1991	1999	1935	2000	2000
Sample type	Human gingival crevice	Human vagina	Human feces	Human feces	Human feces
Medium	NR	NR	Beef-heart infusion agar[i]	EG agar[j]	EG agar[j]
Incubation	NR	NR	5–6 d, NR (t°C)	2 d, 37 °C	2 d, 37 °C
Atmosphere	NR	NR	Anaerobic[g] As for Adlercreutzia	100 % CO_2	100 % CO_2
Additional maintenance media	Reduced and unreduced PYG (DSMZ medium 104)	Columbia CNA (Difco) + 5 % horse blood; 37 °C; 5 % CO_2 in air	Liver infusion agar	/	/
References	Olsen et al. (1991)	Rodriguez Jovita et al. (1999)	Eggerth (1935)	Kageyama and Benno (2000)	Kageyama and Benno (2000)
	Collinsella tanakaei	*Coriobacterium glomerans*	*Cryptobacterium curtum*	*Denitrobacterium detoxificans*	*Eggerthella lenta*
Publication	2010	1988	1999	1996	1935
Sample type	Human feces	Intestinal tract of a red soldier bug (*Pyrrhocoris apterus*)	Human periodontal pocket	Rumen content, cow #1 reared at NADC[k] and fed an alfalfa/corn (9:1) diet	Human feces
Medium	GAM[c] + 1 % (w/v) NaCl + fosfomycin (60 μg/mL)	Blood agar (BD)	NR	Enrichment in medium A[l]	Beef-heart infusion agar[i]
Incubation	3 d, 37 °C	10–20 d, 25–30 °C	NR	24 h of consecutive batch cultures; 39 °C	5–6 d, NR (t°C)

Table 11.12 (continued)

	Collinsella tanakaei	*Coriobacterium glomerans*	*Cryptobacterium curtum*	*Denitrobacterium detoxificans*	*Eggerthella lenta*
Atmosphere	$N_2/H_2/CO_2$ (88:7:5)	N_2/CO_2 (80:20)	NR	H_2/CO_2 (50:50)	Anaerobic (Eggerth 1935)
Additional maintenance media	GAM[c]	TPY medium (11) + Na2S + cysteine-HCl (each 0.45 g/l)	BHI-blood agar; 3 d, 37 °C; $N_2/H_2/CO_2$ (80:10:10)	Medium B and C[m]	Liver infusion agar
References	Nagai et al. (2010)	Haas and König (1988)	Sato et al. (1998), Nakazawa et al. (1999)	Anderson et al. (1996), Anderson et al. (2000)	Eggerth (1935)
	Eggerthella sinensis	*Enterorhabdus caecimuris*	*Enterorhabdus mucosicola*	*Gordonibacter pamelaeae*	*Olsenella profusa*
Publication	2004	2010	2009	2009	2001
Sample type	Blood of a 59-year-old female patient with acute proctitis and a history of cervical carcinoma	Caecum of a C3H/HeJBir mouse	Ileal mucosa of a 12-week-old female heterozygous $TNF^{deltaARE}$ C57BL/6 mouse with ileitis	Sigmoid region of the colon of a 33-year-old male patient suffering from active Crohn's disease[n]	Human subgingival plaque in adults with periodontitis
Medium	BACTEC 9240 blood culture system (Becton Dickinson, Sparks, MD, USA)	ATCC medium 602E	Mucin-containing medium[o]	Schaedler basal agar (Oxoid) with 5 % defibrinated horse blood	NR
Incubation	NR	3 d, 37 °C	9 d, 37 °C	37 °C	NR
Atmosphere	Anaerobic[g]	$N_2/H_2/CO_2$ (90:5:5)	AnaeroGen catalyzer (Oxoid)	$N_2/H_2/CO_2$ (80:10:10)	NR
Additional maintenance media	Blood agar	BHI (BD 211059) +2 g/l each yeast extract and glucose + 0.05 % (w/v) cysteine; 100 % N_2	BHI (BD 211059) + 2 g/l each yeast extract and glucose + 0.05 % (w/v) cysteine; 100 % N_2	Pre-reduced BHI + 1 % (w/v) arginine-HCl	Fastidious anaerobe agar (LabM) with 5 % horse blood
References	Lau et al. (2004a), Lau et al. (2004b)	Duck et al. (2007)	Clavel et al. (2009)	Würdemann et al. (2009)	Holdeman et al. (1977), Dewhirst et al. (2001)
	Olsenella uli	*Olsenella umbonata*	*Paraeggerthella hongkongensis*	*Parvibacter caecicola*	*Slackia equolifaciens*
Publication	1991	2011	2004	2013	2010
Sample type	Human gingival crevice	Jejunal mucosa of a healthy 62-day-old pig	Blood of a 30-year-old male patient[p]	Caecal content of a 25-week-old male heterozygous $TNF^{deltaARE}$ C57BL/6 mouse with ileitis	Human fecal enrichment in GAM broth + 0.1 mM daidzein
Medium	NR	LAB selective medium with porcine gastric mucin (type III; Sigma)[q]	BACTEC 9240 blood culture system (Becton Dickinson, Sparks, MD, USA)	WCA +1 % (v/v) autoclaved rumen fluid, 0.05 % (w/v) cysteine and 0.02 % DTT	GAM[c] agar
Incubation	NR	7–14 d, 37 °C	NR	6 d, 37 °C	3 d, 37 °C
Atmosphere	NR	Anaerocult A (Merck)	Anaerobic[g]	$N_2/H_2/CO_2$ (85:5:10)	100 % CO_2

Table 11.12 (continued)

	Olsenella uli	*Olsenella umbonata*	*Paraeggerthella hongkongensis*	*Parvibacter caecicola*	*Slackia equolifaciens*
Additional maintenance media	Reduced and unreduced PYG (DSMZ medium 104)	Reduced and unreduced PYG (DSMZ medium 104)	Blood agar	WCA with cysteine and DTT; 100 % N_2	GAM[c] + 0.5 % arginine-HCl
References	Olsen et al. (1991)	Eschenlauer et al. (2002), Kraatz and Taras (2008)	Lau et al. (2004a), Lau et al. (2004b)	Clavel et al. (2013)	Jin et al. (2010)

	Slackia exigua	*Slackia faecicanis*	*Slackia heliotrinireducens*	*Slackia isoflavoniconvertens*	*Slackia piriformis*
Publication	1996	2005	1976	2009	2010
Sample type	Human deciduous teeth with endodontic lesions	Feces of a healthy male Labrador dog	Sheep rumen	Feces of a healthy 37-year-old woman	Human feces
Medium	BHI-blood agar	*Bacteroides* agar[r]	Rich medium with rumen fluid and heliotrine (2 mg/mL)	BHI + 100 μM daidzein + 10 μg/mL tetracyclin	GAM + 6 % Bacto oxgall (Difco)
Incubation	7 d, 37 °C	2 d, 37 °C	7d, 38 °C	Enrichment by limiting dilution; cycles of 37 °C, 72 h	3 d, 37 °C
Atmosphere	$N_2/H_2/CO_2$ (80:10:10)	$N_2/H_2/CO_2$ (80:10:10)	CO_2	CO_2/H_2(80:20)	$N_2/H_2/CO_2$ (88:7:5)
Additional maintenance media	/	Chocolate or blood agar	/	BHI or Columbia agar	GAM
References	Sato et al. (1993), Poco et al. (1996)	Lawson et al. (2005)	Lanigan (1976)	Matthies et al. (2009)	Nagai et al. (2010)

Abbreviations: *BHI* brain-heart infusion, *d* days, *GAM* general anaerobic medium, *NR* not reported, *PYG* peptone-yeast-glucose

[a]The isolation procedure in the table refers to the work by Moore et al. 1982, 1983

[b]SLC Japan, Tokyo; the rat was fed an AIN-93G casein diet for 3 weeks

[c]Nissui Pharmaceutical, Tokyo, Japan

[d]Fujicco, Kobe, Japan

[e]Smibert and Holdeman (1976), Holdeman et al. (1977)

[g]Details on gas phase were not provided

[f]Per L, 37 g brain-heart infusion, 5 g yeast extract, 5 mL 6 % (w/v) ammonium formate solution, 0.5 g cysteine-HCl, 5 mg hemin, 2.5 mg resazurin, 1 mg vitamin K_1, 4 % rabbit blood, pH 7.0

[h]Per L, 5 g NaCl, 15 g agar, 20 g tryptose, 2.5 g tryptone, 1 g yeast extract, 1 g of glucose, pH 7.4–7.6

[i]1.5 % agar, 1 % Parke Davis peptone, 0.4 % Na_2HPO_4. $12H_20$, 5 % blood, 0.15 % glucose, pH 7.6

[j]Per L: 3 g beef extract, 5 g yeast extract, 10 g peptone, 1.5 g glucose, 0.5 g L-cysteine. HCl, 0.2 g L-cystine, 4 g Na_2HPO_4, 0.5 g soluble starch, 0.5 g Tween 80, 0.5 g silicone, 15 g agar, 5 % horse blood, pH 7.7

[k]The National Animal Disease Center in Ames (IA, USA)

[l]Contained Na_2CO_3, resazurin, L-cysteine-HCl, and vitamins at concentrations that were the same as in the complete medium of Bryant and Robinson (Bryant and Robinson 1961). Also contained (in 1 L) 800 mg phytone peptone, 5 μg lipoic acid, 2 μg vitamin B_{12}, 40 % (v/v) clarified rumen fluid, and the same minerals as in the non-rumen fluid medium of Dawson et al. (Dawson et al. 1980). Supplemented for enrichment with milk vetch or alfafa forage + 4.2 mM nitropropanol

[m]Same as medium A with 8 and 0 % rumen fluid, respectively

[n]Treated with azathioprine, mutaflor and cortisone

[o]Per L, 5 g mucin (Sigma M1778), 0.5 % (v/v) ethanol, 500 mg L-cysteine, 1 mg yeast extract, 20 mg folic acid, 20 mg vitamin B_{12}, 50 mmol $NaHCO_3$, 10 mmol sodium acetate, 5 mmol Na_2HPO_4, 5 mmol NaCl, 3 mmol KH_2PO_4, 1 mmol $CaCl_2$, 1 mmol $MgCl_2$, 10 mmol $FeCl_3$, 1 % (w/v) agar, pH 7.7

[p]Suffered from alcoholic cirrhosis, portal hypertension, and epilepsy and diagnosed with perianal abscess

[q]Per L, 10.0 g mucin, 0.01 g peptone, 0.01 g yeast extract, 0.01 g glucose, 0.3 g NaCl, 0.1 g $CaCl_2$, 6.0 g KH_2PO_4, 5 mL Rogosa's salt solution, 1 mL modified (lacking elements already included in Rogosa's salt solution) Pfennig's SL8 trace element solution, 0.2 mL vitamin solution, 0.5 mg resazurin, 4–7.5 g agar, pH 5 (Kraatz and Taras 2008)

[r]Holdeman et al. (1977)

A number of species of the family have also been isolated from mammalian body habitats other than the gut. However, their prevalence in these other environments has not been investigated, apart from *Atopobium* spp. in the mouth and vagina (Zhou et al. 2004; Ravel et al. 2011; Belda-Ferre et al. 2012; Liu et al. 2012; Santiago et al. 2012). The other body origins of *Coriobacteriaceae* include:

(a) The blood: *Atopobium rimae* (Angelakis et al. 2009), *Eggerthella sinensis* and *Paraeggerthella hongkongensis* (Lau et al. 2004b), and *Gordonibacter pamelaeae* (Woo et al. 2010).
(b) The perineum region and vagina: *Atopobium minutum* (Hauduroy et al. 1937; Collins and Wallbanks 1992) and *Atopobium vaginae* (Rodriguez Jovita et al. 1999). The latter species is usually found in biofilms adherent to the vaginal mucosa rather than in the vaginal fluid (Verhelst et al. 2004; Swidsinski et al. 2005; Polatti 2012).
(c) The oral cavity and respiratory tract: *Atopobium fossor* (Bailey and Love 1986; Kageyama et al. 1999b), *Atopobium parvulum* and *Atopobium rimae* (Weinberg et al. 1937; Olsen et al. 1991; Collins and Wallbanks 1992), *Cryptobacterium curtum* (Nakazawa et al. 1999), *Olsenella profusa* and *Olsenella uli* (Dewhirst et al. 2001), and *Slackia exigua* (Poco et al. 1996; Wade et al. 1999). Using 16S rRNA gene sequencing, Dewhirst et al. identified *Olsenella uli* and *Olsenella profusa* from subgingival plaques in patients with severe periodontal disease, suggesting that, similarly to other *Coriobacteriaceae* in the gut and vaginal mucosa, *Olsenella uli* and *Olsenella profusa* favor an adherent mode of growth. However, in sheep rumen, *Olsenella umbonata* was isolated from ruminal fluid, indicating variability in the mode of growth of this genus (Kraatz et al. 2011).

Metabolic Activities

Conversion of Cholesterol-Derived Host Metabolites

The potential of *Coriobacteriaceae* to modulate host metabolism in vivo has been recently brought to light by reports of significant correlations between their occurrence and altered metabolic parameters, including (a) higher intestinal cholesterol absorption and higher levels of plasma non-high-density lipoprotein (non-HDL) cholesterol in hamsters (Martinez et al. 2009, 2012) and (b) energy metabolism via decreased glycogenesis and enhanced triglycerides synthesis as well as hepatic detoxification pathways (higher 2*b*- and 6*b*-hydroxylase activity) in mice (Claus et al. 2011). Moreover, a recent metagenomic analysis of fecal samples from approximately 350 human subjects indicated that the prevalence of *Eggerthella lenta* is linked to type-2 diabetes (Qin et al. 2012). However, these data are descriptive and there is yet no direct proof of molecular mechanisms underlying the impact of *Coriobacteriaceae* on host metabolism. In other words, research on bacteria/host interactions with respect to *Coriobacteriaceae* is in its infancy.

The best studied metabolic functions of *Coriobacteriaceae* are the dehydrogenation and dehydroxylation of cholesterol-derived host factors (Ridlon et al. 2006). The type and various strains of *Eggerthella lenta* and *Collinsella aerofaciens* possess hydroxysteroid dehydrogenases (HSDH), which are responsible for stereospecific oxidation and epimerization (change from *a* to *b* configuration or vice versa) of bile acids, thereby generating stable oxo-bile acid intermediates. Hitherto detected dehydrogenases include both 3*a*- and 12*a*-HSDH in *Eggerthella lenta* and 7*b*-HSDH in *Collinsella aerofaciens* (Eyssen and Verhulst 1984; Ridlon et al. 2006). This hints at metabolic chains between *Coriobacteriaceae* and other bacteria, since the combined activity of two position-specific, stereochemically distinct HSDH (e.g., 3*a* and 3*b*) is required for epimerization of bile salts (Ridlon et al. 2006).

Although early work reported that *Eubacterium* spp., especially strain VPI 12708, were also capable of dehydroxylating free primary bile acids (cholic and chenodeoxycholic acid) into secondary bile acids (deoxycholic and lithocholic acid) (White et al. 1988; Takamine and Imamura 1995), deeper taxonomic assignment revealed that these bacteria actually belong to the genus *Clostridium* (Kitahara et al. 2000). There is to date no report on bile acid dehydroxylase activity in *Eggerthella lenta* or other *Coriobacteriaceae*. One paper referred to 7*a*-dehydroxylation by one isolate related to [*Eubacterium lentum*] without standing in nomenclature (Hirano and Masuda 1982). Bacterial dehydroxylation renders bile acids more hydrophobic, thereby favoring passive reabsorption in the proximal colon (enterohepatic circulation). However, secondary bile salts may also contribute to the pathogenesis of cholesterol gallstones and colon cancer (Ridlon et al. 2006). Altered bile acid metabolism has also been associated with chronic intestinal inflammation (Gnewuch et al. 2009; Devkota et al. 2012; Duboc et al. 2012).

Transformation of bile salts by HSDH and dehydroxylases is believed to serve as an energy source for the bacteria and reduce the levels of bile acids with antimicrobial activities (Ridlon et al. 2006). Several *Coriobacteriaceae* are reported to be bile resistant, e.g., *Asaccharobacter celatus*, *Eggerthella lenta*, *Olsenella umbonata*, and *Slackia piriformis*. Additionally, the favorable generation of oxo-bile acids by *a*-HSDH at higher redox potentials such as those encountered at mucosal surfaces may be one additional reason for the colonization of these areas by some *Coriobacteriaceae* (Ridlon et al. 2006). Finally, *Eggerthella lenta* is also able to dehydroxylate corticoids such as deoxycorticosterone to form progesterone via 21-dehydroxylase activity (Bokkenheuser et al. 1977). This species also carries a corticoid-converting 16*a*-dehydroxylase (Bokkenheuser et al. 1980) and a 3*a*-HSDH (Bokkenheuser et al. 1979). Strikingly, despite the apparent implication for the host of this bacterial rearrangement of hormonal networks in the gut, related functional studies in experimental animal models have not yet been performed.

Polyphenol Metabolism

One of the most peculiar enzymatic properties of *Coriobacteriaceae* is the conversion of food polyphenols, especially the activation of the isoflavone daidzein to the bioactive metabolite equol (Clavel and Mapesa 2013). Isoflavones are dietary phytoestrogens that are abundant in soybean and soy-derived products. They share structural similarities with steroid hormones such as 17-*b*-estradiol and thus have low binding affinity to estrogen receptors (Kuiper et al. 1998; Kostelac et al. 2003). Equol is known to be the most potent isoflavone metabolite, e.g., it has stronger affinity to estrogen receptors than its substrate (Clavel and Mapesa 2013). The biological properties of equol have been given attention since the 1930s when reproductive failures started to affect sheep grazing on clover containing high amounts of isoflavones and later in the 1980s in captive cheetahs fed a soy-based diet (Setchell et al. 1987; Messina 2010). Since then, equol has been associated with protective effects against cardiovascular diseases, bone disorders, prostate and breast cancer, and other hormone-related conditions, even though gold-standard randomized control trials are urgently needed to substantiate results (Clavel and Mapesa 2013). In humans, only 30–50 % of individuals are able to produce equol from daidzein, possibly due to the absence of specific equol-producing bacteria in the rest of the population (Xu et al. 1995; Rowland et al. 2000).

Evidence of intestinal microbial equol production dates back from the early 1980s (Axelson and Setchell 1981). However, it was only in 2005 that the first equol-producing isolate, strain Julong 732, was cultured from human feces (Wang et al. 2005). To date, only ten bacterial strains capable of producing equol from daidzein have been isolated from intestinal samples of pigs, rodents, and humans. Nearly all of them ($n = 9$) fall into the family *Coriobacteriaceae* based on 16S rRNA gene sequence analysis. These strains include five type strains, which have been fully described and assigned valid names (human isolates are marked with stars in the following list): (1) *Adlercreutzia equolifaciens** FJC-B9^T (=DSM 19450^T) (GenBank accession AB306661) (Maruo et al. 2008), (2) *Asaccharobacter celatus* do03^T (=DSM 18785^T) (AB266102) (Minamida et al. 2006, 2008), (3) *Enterorhabdus mucosicola* Mt1B8^T (=DSM 19490^T) (AM747811) (Matthies et al. 2008; Clavel et al. 2009), (4) strain Julong 732* (AY310748) (Wang et al. 2005), (5) '*Eggerthella*' sp. YY7918* (AB379693) (Yokoyama and Suzuki 2008), (6) *Slackia equolifaciens** DZE^T (=CCUG 58231^T) (EU377663) (Jin et al. 2010), (7) *Slackia isoflavoniconvertens** HE8^T (=DSM 22006^T) (EU826403) (Matthies et al. 2009), (8) '*Slackia*' sp. NATTS* (AB505075) (Tsuji et al. 2010), and (9) strain D1 (DQ904563) (Yu et al. 2008). Of note, *Adlercreutzia equolifaciens*, *Asaccharobacter celatus*, and strain Julong 732 share >99 % similarity based on 16S rRNA-based phylogeny (Maruo et al. 2008). One additional equol-producing isolate, strain D2, seems not to belong to the *Coriobacteriaceae* based on 16S rRNA gene sequencing (DQ904564) (Yu et al. 2008). Interestingly, the production of equol from daidzein by '*Slackia*' sp. NATTS was found to be two to fourfold higher after addition of 1 g/L autoclaved adonitol, arabinose, galactose, lactitol, inositol, melezitose, ribose, sorbitol, sorbose, trehalose, or xylose to the culture medium(Tsuji et al. 2010). Conversely, the addition of fructooligosaccharides, galactooligosaccharides, inulin, lactose, raffinose, or sucrose inhibited equol production. This may fit with the observation that resistant polysaccharides do not enhance equol production in vivo (Larkin et al. 2007; Mathey et al. 2007).

In addition to isoflavones, dietary lignans are phytoestrogens that can also be activated by *Coriobacteriaceae*. Conversion of plant lignans (pinoresinol, lariciresinol, secoisolariciresinol, matairesinol, and corresponding glycosides) by gut bacteria involves two to five different reactions (deglycosylation, reduction, demethylation, dehydroxylation, and dehydrogenation) to form the enterolignans enterodiol and enterolactone (Clavel et al. 2006). Enterolignans were actually thought to be new steroid hormones after their first detection in urine samples from female primates and human adults (Setchell et al. 1980; Stitch et al. 1980). Their bacterial origin was highlighted shortly thereafter (Setchell et al. 1981; Borriello et al. 1985). Several strains of *Eggerthella lenta* were found to reduce and dehydroxylate plant lignans and intermediate metabolites thereof (Clavel 2006). Thus, beyond the metabolism of host-derived bile acids and steroid hormones, the species *Eggerthella lenta* is also involved in metabolic chains leading to the production of bioactive molecules from plant substrates in the gut. Recently, this species was also found to reductively cleave the heterocyclic C-ring of the flavanols epicatechin and catechin (Kutschera et al. 2011). Most importantly, the successful isolation and cultivation of phytoestrogen-converting strains open ways to assess the effects of bacterial metabolites on host health in detail using, for instance, gnotobiotic approaches (i.e., colonization of germfree animals with specific strains of interest) (Woting et al. 2010; Becker et al. 2011; Mabrok et al. 2012).

Pathogenicity, Clinical Relevance

As seen above, members of the *Coriobacteriaceae* carry out functions of importance for their hosts. However, several members of the genera *Atopobium*, *Eggerthella*, *Gordonibacter*, *Olsenella*, and *Paraeggerthella* have been also implicated in the development of various clinical pathologies including abscesses, intestinal diseases and tumors, periodontitis, vaginosis, and bacteremia. *Coriobacteriaceae* can thus be considered as pathobionts, i.e., potentially pathogenic commensal species of host body microbiota (Chow et al. 2011). However, one can say that nearly all published studies on *Coriobacteriaceae* refer to descriptive work, for instance, the enumeration of bacteria in diseased versus healthy tissues/subjects or the isolation of bacteria from clinical specimens. Hence, fundamental knowledge on how and when *Coriobacteriaceae* start to be detrimental to their hosts is lacking. The antimicrobial susceptibility profile of some family members has been well defined in various studies and is summarized in *Table 11.13*.

Table 11.13
Antimicrobial susceptibility profiles of *Coriobacteriaceae*

Antibiotic class	Antibiotic	*Atopobium parvulum*	*Atopobium rimae*	*Atopobium vaginae*	*Collinsella aerofaciens*	*Eggerthella lenta*	*Eggerthella sinensis*	*Enterorhabdus caecimuris*	*Enterorhabdus mucosicola*	*Olsenella uli*	*Paraeggerthella hongkongensis*	*Parvibacter cecicola*	*Slackia exigua*
Penicillins	Amoxicillin					1							
	Ampicillin	0.125	0.023	<0.016–0.94	≤0.03–1	0.5–2							0.094–0.19
	Oxacillin							36	4.667			6	
	Penicillin		0.064	0.008–0.25	≤0.03–2	1–4	0.5			≤0.03–1	0.25–2		0.064–0.125
	Piperacillin					1–16							
Tetracyclines	Doxycycline			0.19–0.75									
	Minocycline	0.25											
	Tetracycline				0.06–8	6		0.12	0.115	0.125–32		0.069	
	Tigecycline					0.12–25					0.06–0.25		
Macrolides	Azithromycin		<0.016	<0.016–0.32	≤0.03–0.25								
	Clarithromycin	<0.004						<0.016	<0.016			< 0.016	
	Erythromycin		<0.016		≤0.03–0.25	3		<0.016	0.048			< 0.016	0.016–0.023
Aminoglycosides	Kanamycin			8–16									
	Tobramycin							4.333	2.667			0.6	
Quinolones	Ciprofloxacin		0.06	0.023–0.25	≤0.5–2			0.305	>32	≤0.5– > 8		0.061	
	Levofloxacin	0.25–0.5			≤0.06–2	0.5				0.25–8			
	Moxifloxacin			0.06–1		0.25– > 32					0.25–4		
	Nalidixic acid			>256									
	Nemofloxacin					0.25– > 32					0.5–2		
	Nifuratel			0.125–1									
	Trovafloxacin			<0.015–2									
Polypeptides	Bacitracin			1–4									
	Colistin			>1,024					>256			> 256	
Lincosamides	Clindamycin	1		<0.016–2	≤0.03–0.25	<0.06– > 32		0.105	<0.016	≤0.03– > 32	4	< 0.016	0.016–0.023

Oxazolidinones	Linezolid			0.016–0.25		0.5–4					1		
Sulfonamide	Trimethoprim/ sulfamethoxazole												>32
Carbapenems	Doripenem					0.25					0.25		
	Ertapenem												0.016–2
	Imipenem	0.25	0.032	<0.015–0.5	≤0.03–0.25	0.06–8					0.5–1		
	Meropenem			<0.015–0.5		0.5					0.5		
Cephems	Cefalexin				0.25 –8					0.25– > 32			
	Cefepime			1									
	Cefmetazole	2				16–32					8–16		
	Cefotaxime					0.5– > 256	0.25	>32	1.25		>32	4.167	
	Cefotetan					8–128							
	Cefoxitin			2–3									0.5–3
	Ceftriaxone	0.5		0.25–2		1– > 128							0.002–0.25
	Cefuroxime			0.016–0.25									
	Flomoxef					8–16					8–16		
B-Lactam/B-lactamase inhibitor combinations	Amoxicillin/ clavulanic acid		0.012		≤0.015–0.25	1–4				≤0.015–2			0.094–0.25
	Ampicillin-sulbactam			0.032–0.25		4					2–4		
	Piperacillin-tazobactam				≤0.03–16	32–64					16–64		
Glycopeptides	Vancomycin	2	1.25	1–4	0.25–2	0.5–2	3	1.5	1.333		0.75–2	0.585	0.032–0.5
	Teicoplanin					0.06–0.5							
Lipopeptides	Daptomycin				0.06– > 32	0.25–0.5					0.25		
Macrocyclic antibiotics	Fidaxomicin					0.015–0.25					0.12–0.25		
Nitroimidazoles	Metronidazole	2		0.12– >256	≤0.03–2	0.25–2	0.25	0.016	0.034	0.125–>32	0.25–4	0.069	0.064–0.38
Phenicols	Chloramphenicol					8–16							

Table 11.13 (continued)

Antibiotic class	Antibiotic	*Atopobium parvulum*	*Atopobium rimae*	*Atopobium vaginae*	*Collinsella aerofaciens*	*Eggerthella lenta*	*Eggerthella sinensis*	*Enterorhabdus caecimuris*	*Enterorhabdus mucosicola*	*Olsenella uli*	*Paraeggerthella hongkongensis*	*Parvibacter cecicola*	*Slackia exigua*
Rifamycin	Rifampicin			<0.002									
Streptogramins	Quinupristin/ dalfopristin				0.06–8	0.25–2							
References		a, b	c	d, e, f, g, h, i	j, k	a, l, m, n, o, p	q	r	s	k	q, m	t	u

The shaded boxes show antimicrobial resistance according to the 2012 CLSI MIC breakpoints for anaerobes (M100-S22)

References (when more than one strain was analyzed, the number of strains is shown within brackets after the corresponding reference):

[a]Tanaka et al. (2006)

[b]Hirokawa et al. (2008)

[c]Angelakis et al. (2009)

[d]Knoester et al. (2011)

[e]Salimnia et al. (2008)

[f]Polatti (2012)

[g]Ferris et al. (2004) (3)

[h]De Backer et al. (2006) (9)

[i]Chan et al. (2012)

[j]Goldstein et al. (2003) (9)

[k]Merriam et al. (2006) (7)

[l]Liderot et al. (2010)

[m]Lee et al. (2012) (8)

[n]Mosca et al. (1998) (29)

[o]Sneath et al. (1986) (12)

[p]Credito and Appelbaum (2004) (10)

[q]Lau et al. (2004b)

[r]Clavel et al. (2010)

[s]Clavel et al. (2009)

[t]Clavel et al. (2013)

[u]Kim et al. (2010) (6)

Bacteremia

Five of the 14 genera of the family include species which have been already isolated from blood samples of human patients: *Atopobium*, *Eggerthella*, *Gordonibacter*, *Olsenella*, and *Paraeggerthella*. There seems to be a consensus about the reservoir of infection as being the natural habitats of *Coriobacteriaceae*, i.e., the mouth and the gastrointestinal or genital tract, or acutely infected organs (Lau et al. 2004a; Salimnia et al. 2008; Angelakis et al. 2009; Woo et al. 2010; Thota et al. 2011).

The best documented cases of *Coriobacteriaceae*-driven bacteremia relate to *Eggerthella* spp. and closely related species. In Hong Kong, between 1998 and 2001, *Eggerthella lenta* was associated with five of 16 clinically relevant cases of bacteremia, whereas five additional cases were associated with the presence of its relatives *Eggerthella sinensis* and *Paraeggerthella hongkongensis* (Lau et al. 2004a, b). Lee et al. very recently published 10 additional cases of bacteremia due to *Eggerthella lenta* and *Paraeggerthella hongkongensis* in Taiwanese subjects hospitalized between 2001 and 2010 (Lee et al. 2012). Landais et al. also reported two cases of bacteremia in France that were associated with the presence of *Eggerthella lenta* based on 16S rRNA gene sequencing of isolates (the authors erroneously cited the genus name as '*Eggerthela*') (Landais et al. 2007). In this study, patient 1 was admitted to the hospital with fecal peritonitis related to intestinal perforation, whereas patient 2 had acute appendicitis. They received imipenem (1.5 g/day for 3 weeks) and amoxicillin/clavulanic acid (3 g/day), respectively, with favorable outcomes. Two additional clinically relevant strains of *Eggerthella lenta* have been reported, including one strain identified on the basis of the VITEK system after isolation from the blood of a 21-year-old African-American woman diagnosed with Crohn's disease who developed bacteremia after ileocaecal resection (Chan and Mercer 2008; Thota et al. 2011). This case of *Eggerthella lenta* bacteremia was successfully treated with a combination of meropenem, metronidazole, and vancomycin. Finally, one case of polymicrobial bloodstream infection with *Eggerthella lenta* and *Desulfovibrio desulfuricans* was reported in Sweden in one 86-year-old woman who was successfully treated with cefuroxime and amoxicillin (Liderot et al. 2010). Of note, a rather broad range of diseases may underlie translocation of *Eggerthella* spp. from the gut to the blood stream, since patients positive for these species in blood cultures were hospitalized for a variety of reasons (pelvic inflammatory disease, infected bed sore, perianal abscess, infected rectal tumor, liver abscess, acute appendicitis, and proctitis) and suffered from a variety of chronic diseases (lung, cervical and colon cancer, alcoholic cirrhosis, diabetes, cardiovascular disorders, recurrent pyogenic cholangitis) (Lau et al. 2004a; Landais et al. 2007). Finally, *Eggerthella lenta* was also isolated from (a) the pus of a hepatic abscess from a 42-year-old patient who was treated favorably with a course of metronidazole (1.5 g/day) (Landais et al. 2007) and (b) bone biopsy samples of the spine in one 82-year-old Chinese women with spondylodiscitis who was treated with trimethoprim/sulfamethoxazole and metronidazole (Bok and Ng 2009).

The genus *Atopobium* also gained attention following the isolation of strains from clinical samples (Olsen et al. 1991; Kumar et al. 2005). *Atopobium rimae*, together with *Streptococcus gordonii*, was recently associated with a case of septic shock in a 77-year-old woman in France, from whom two isolates were recovered from blood cultures on two separate occasions during hospitalization for pneumonia (Angelakis et al. 2009). Treatment of the patient with intravenous amoxicillin-clavulanate (2 g/200 mg) led to full recovery within 7 days. Beforehand, *Atopobium rimae* had been already identified in blood samples from a 47-year-old man with liver cirrhosis, who was treated with success using metronidazole and imipenem (Chung et al. 2007). Another *Atopobium* species phylogenetically closely related to *Atopobium rimae* (98 % 16S rRNA gene sequence identity) has also been associated with bacteremia (Salimnia et al. 2008). This species, provisionally named "*Atopobium detroiti*", was isolated from the blood of a 38-year-old paraplegic male patient hospitalized for presumed sepsis and characterized by a necrotic decubitus ulcer of the hip and poor oral hygiene after physical examination. Finally, the species *Atopobium vaginae* has also been identified in the context of intrauterine infection leading to fetal death and maternal bacteremia in a 40-year-old woman undergoing transcervical chorionic villus sampling (Knoester et al. 2011). Unlike *Eggerthella lenta*, *Atopobium vaginae* has been associated with metronidazole resistance (Ferris et al. 2004; De Backer et al. 2006; Knoester et al. 2011), and successful treatment of *Atopobium vaginae* bacteremia usually involves a course of *b*-lactam antibiotics alone or in combination with *b*-lactamase inhibitors or clindamycin (Knoester et al. 2011; Chan et al. 2012).

Less frequently reported cases of *Coriobacteriaceae*-driven bacteremia relate to bacteria other than *Eggerthella* and *Atopobium*. One isolate identified as *Gordonibacter pamelaeae* based on 16S rRNA gene sequencing and phenotypic description was recently recovered from the blood of an 82-year-old Chinese man diagnosed to have rectosigmoid carcinoma with lung metastasis (Woo et al. 2010). In contrast to the type strain of the species, this isolate was found to be nonmotile and positive for arginine arylamidase. The patient was successfully treated with a course of intravenous amoxicillin-clavulanate for 9 days. Finally, one case of bacteremia associated with a strain of *Olsenella uli* obtained from the blood of one 43-year-old male subject suffering from acute cholangitis has been reported (Lau et al. 2004a).

In summary, when compared with bacteremia due to usual suspects such as *Bacteroides fragilis*, enterobacteria, enterococci, or staphylococci, cases of *Coriobacteriaceae*-driven bacteremia seem to be relatively rare, but are very often clinically relevant. More research effort is needed to identify environmental factors and molecular mechanisms that favor initial colonization and survival of *Coriobacteriaceae* in the blood. Of note, only three genera within the family are positive for catalase activity: *Eggerthella*, *Gordonibacter*, and *Paraeggerthella*. All three have been associated with cases of bacteremia. The presence of catalase may help these organisms coping with oxidative stress during infection.

Gastrointestinal Pathologies

Although there are an increasing number of studies investigating the gut microbiota in colorectal cancer (CRC), the exact contribution of bacteria to molecular mechanisms underlying disease remains unclear. Intestinal bacteria are proposed to play a role in CRC via two main mechanisms: (1) the production of metabolites such as hydrogen sulfide or ammonia, which can have detrimental effects on host cell functions (Blaut and Clavel 2007), and (2) the alteration of innate immune mechanisms (Rakoff-Nahoum and Medzhitov 2007).

The role of a variety of bacteria such as enterotoxigenic *Bacteroides fragilis*, *Enterococcus faecalis*, *Fusobacterium* spp., *Prevotella* spp., and *Streptococcus bovis* in CRC has already been discussed (Wu et al. 2009; Al-Jashamy et al. 2010; Sobhani et al. 2011; Kostic et al. 2012). *Coriobacteriaceae* have gained attention in this field very recently. The occurrence of *Collinsella*, *Eggerthella*, *Olsenella*, and *Slackia* spp. was significantly higher on tumor site versus adjacent nonmalignant tissue in six Dutch patients who underwent resection for primary colon adenocarcinoma (Marchesi et al. 2011). Other recent studies on bacterial diversity in CRC patients found an increased prevalence of 16S rRNA gene sequences classified as *Actinobacteria*, including *Collinsella* spp., in feces from CRC versus healthy control subjects (Chen et al. 2012; Wang et al. 2012). In the study by Chen et al., the prevalence of sequences assigned to the *Coriobacteriaceae* was 1.19 % in CRC patients versus 0.74 % in healthy individuals. Still, these data refer only to the density of bacterial populations, and there is no indication that *Coriobacteriaceae* have overall positive or negative effects on tumorigenesis. *Coriobacteriaceae* have recently been referred to as "passenger" bacteria in CRC, in contrast to "driver" bacteria such as *Bacteroides fragilis* which seem to be involved in the initiation of disease (Tjalsma et al. 2012). Passenger bacteria are proposed to be best suited for colonization of disturbed microenvironments in the vicinity of tumors. In that context, the effect of local production of equol by *Slackia* spp. that colonize tumor sites in the gut may be worth investigating considering the biological properties of this bacterial product (Magee et al. 2006; Choi 2009). The effects of ammonia production by, for instance, *Olsenella* spp. or *Eggerthella lenta* may be worth investigating too (Eschenlauer et al. 2002; Kraatz et al. 2011).

Apart from cancer, the role of *Coriobacteriaceae* in other pathologies associated with gastrointestinal dysfunctions is ill defined. Isolates of *Eggerthella lenta* identified on the basis of fermentation and biochemical reactions were recovered in 44 % of 41 appendix tissue samples from children with suspected acute appendicitis (Rautio et al. 2000). Moreover, although clinical case reports and targeted isolation procedures hint at the relevance of *Coriobacteriaceae* in inflammatory bowel diseases, there is to date no corresponding quantitative or functional data available (Clavel et al. 2009, 2013; Würdemann et al. 2009; Joossens et al. 2011; Thota et al. 2011). Finally, there is an increasing body of evidence pointing at the involvement of gut bacteria in host energy balance and metabolic disorders (Backhed et al. 2004; Qin et al. 2012). *Coriobacteriaceae* have been detected in the feces of 14 overweight and obese human volunteers with no history of gastrointestinal disease (Walker et al. 2011). As previously reported in healthy individuals (Harmsen et al. 2000; Kageyama et al. 2000; Tap et al. 2009), *Collinsella aerofaciens* was amongst the most abundant taxonomic units (3.7 % of 16S rRNA clones) after *Faecalibacterium prausnitzii* (8.0 %), *Eubacterium rectale* (4.4 %), and *Clostridium clostridioforme* (3.8 %) in the fecal sample from six of the 14 volunteers. The proportion of *Collinsella aerofaciens* was significantly reduced to 0.6 % after consumption of a protein-rich, fat, and carbohydrate-reduced weight-loss diet. In another study, the number of 16S rRNA gene sequences assigned to *Coriobacteriaceae* in the feces of three obese subjects was found to be higher than in lean controls and in subjects after gastric bypass-induced weight loss (Zhang et al. 2009). Based on these descriptive findings on the dominance of *Coriobacteriaceae* in the gut and considering their metabolic potential with regard to hepatic functions and lipid homeostasis (see metabolic activities), their role in the regulation of host metabolic disorders is worth investigating in more details.

Allergy

Commensal gut microbial communities are known to influence host immune responses beyond the gut. For instance, they have been implicated in the regulation of molecular mechanisms underlying allergies (Hormannsperger et al. 2012). A molecular study comparing the fecal microbiota in <12-month-old infants with cow's milk protein allergy versus nonallergic infants ($n = 46$ each) found higher median counts of the *Atopobium* group in allergic infants (0.6 vs. 0.0 % of total bacteria) (Thompson-Chagoyan et al. 2011). Of note, in a former study, the *Atopobium* and *Collinsella* group represented a substantial proportion of the gut microbiota in the feces of formula-fed infants when compared with breast-fed infants (>17 vs. 0.5 % of total bacteria; $n = 6$ each) (Harmsen et al. 2000). Breast-feeding is proposed to have protective effects on the development of atopic disorders, although more data are needed to reach consensus in results (Mimouni Bloch et al. 2002; Batchelor et al. 2010; Brew et al. 2011).

Dental Caries and Abscess

In the human oral cavity, *Coriobacteriaceae*, including *Atopobium parvulum*, *Atopobium rimae*, and *Olsenella profusa*, have been detected during the final phase of caries extension in dental pulp with established and advanced infection (Nadkarni et al. 2010). The spatial distribution of these bacteria suggested an intricate association with members of the *Bacteroidetes* in tightly concentrated biomass, even though underlying reasons were unclear. Identification of bacterial pathogens by 16S rRNA gene-targeted PCR in the oral cavity of 21 patients suffering from primary or persistent endodontic infections revealed that some *Coriobacteriaceae* were amongst the most prevalent phylotypes: *Olsenella uli*,

Olsenella profusa, and *Atopobium parvulum* were identified in 33, 9.5, and 5 % of cases of infection, respectively (Siqueira and Rocas 2005). *Olsenella uli* was also identified in persistent endodontic infections in this study. This species was also found to be one of the most prevalent species in root canals from 139 teeth with apical periodontitis (Dewhirst et al. 2001; Chavez de Paz et al. 2004). A number of additional papers reported the detection of *Coriobacteriaceae*, especially *Atopobium* and *Olsenella* spp., in oral clinical samples (Kumar et al. 2003, 2005; Aas et al. 2008; Preza et al. 2008; Subramanian and Mickel 2009; Lima et al. 2011). In one additional study, high-throughput sequencing of 16S rRNA genes allowed the identification of *Coriobacteriaceae* in the oral cavity, infected root canal, and periapical abscess of eight patients (Hsiao et al. 2012). The genus *Atopobium* was mostly found in root canal samples, whereas the genus *Collinsella* was significantly overrepresented in abscess samples. Other *Coriobacteriaceae*, including *Olsenella*, *Slackia*, *Cryptobacterium*, and *Eggerthella* were seldom identified in oral cavity samples.

Bacterial Vaginosis

Bacterial vaginosis is a frequently reported polymicrobial infection in which the commensal microbiota usually dominated by lactobacilli is replaced by obligate anaerobes (Danielsson et al. 2011). The type strain of *Atopobium vaginae* was isolated from the vagina of a healthy woman (Rodriguez Jovita et al. 1999). The pathogenic potential of this species was highlighted in 2003 by a case of tubo-ovarian abscess following transvaginal oocyte recovery (Geissdorfer et al. 2003). Clinical isolates have also been recovered in the context of uterine endometritis (Yamagishi et al. 2011) and intrauterine infection (Knoester et al. 2011). Thanks to molecular techniques, this bacterium has been frequently detected in vaginal infections and is thought to be involved in 55–95 % of cases and responsible for therapeutic failures (Ferris et al. 2004; Verhelst et al. 2004; Polatti 2012). A recent evaluation of the microbiota in vaginal swabs from 220 women using pyrosequencing of 16S rRNA gene amplicons showed that women with vaginosis are characterized by diverse heterogeneous communities with a high prevalence of *Atopobium vaginae* and *Eggerthella* species (Srinivasan et al. 2012).

Atopobium vaginae is commonly identified alongside *Gardnerella vaginalis* in clinical samples, and their association appears to provide a reliable diagnosis (Lamont et al. 2011; Srinivasan et al. 2012). Fluorescence in situ hybridization analysis of vaginal biopsies provided further evidence of the strong co-occurrence of these species, which accounts for more than 90 % of the biofilm mass on vaginal epithelial surfaces (Swidsinski et al. 2005). The biofilm-forming properties of *Atopobium vaginae* and *Gardnerella vaginalis* contribute to the recalcitrance of infection by conferring a protective environment against both antibacterial therapies and immune responses. A 5-day treatment of polymicrobial *Gardnerella*, *Atopobium*, and *Lactobacillus* spp. biofilm using 400 mg/day moxifloxacin in women with bacterial vaginosis showed a significant decrease in *Atopobium* and *Gardnerella* coupled to an increase in lactobacilli in biofilms (Swidsinski et al. 2011). However, despite short-term clinical efficacy, moxifloxacin (similarly to metronidazole and clindamycin) fails to prevent the recurrence of vaginosis (Swidsinski et al. 2011; Bradshaw et al. 2012).

The antibiotic susceptibility profile of *Atopobium vaginae* reveals resistance to the antibiotics nalidixic acid and colistin with MIC values higher than 256 and 1,024 μg/mL, respectively, while metronidazole resistance was reported for a number of strains (Ferris et al. 2004; De Backer et al. 2006; Polatti 2012). Also, *Atopobium vaginae* was found to be susceptible to a range of antibiotics including clindamycin, the antibiotic of choice for bacterial vaginosis, as well as ampicillin, ampicillin-sulbactam, azithromycin, ceftriaxone, ciprofloxacin, imipenem, linezolid, meropenem, moxifloxacin, penicillin, rifampicin, and trovafloxacin (Ferris et al. 2004; De Backer et al. 2006). It was recently suggested that the nitrofuran derivative, nifuratel, provides an alternative therapy for bacterial vaginosis involving the common pathogens *Atopobium vaginae* and *Gardnerella vaginalis*, without affecting the commensal microbiota of the vagina (Togni et al. 2011; Polatti 2012).

Application

Due to the recent description of a substantial number of *Coriobacteriaceae* species and to the even more recent reports that highlight some of their physiologically and clinically relevant functions, the use of these bacteria for application purposes has been very limited so far, but is at favorable odds for the near future.

The ability of *Coriobacteriaceae* to convert dietary isoflavones into the bioactive product equol is of particular interest for potential nutraceutical or pharmaceutical applications. The observation that two thirds of the human population cannot produce equol has spurred considerable interest on applied microbiological approaches aimed at triggering equol production in non-equol producers, along with the hypothesis that people hosting equol-producing *Coriobacteriaceae* are more likely to benefit from potentially beneficial health effects of soyfood and isoflavone intake. However, most attempts fell short of their target. First, there is to date no official nutritional recommendation on the benefit of dietary soy isoflavones on human health and state-of-the-art intervention trials are needed (Clavel and Mapesa 2013). Second, a number of animal and human studies examined the use of probiotic strains to boost equol production but failed to establish clear evidence (Larkin et al. 2007; Clavel and Mapesa 2013). Finally, the intake of *Coriobacteriaceae* themselves as probiotic strains in human subjects is for obvious safety issues not sound. However, the use of already isolated and characterized *Coriobacteriaceae* can be of great value in several ways: (1) for gathering functional evidence that equol is indeed directly linked to beneficial health effects using gnotobiotic mouse models of diseases colonized with, for instance, equol-producing or steroid-dehydroxylating versus

non-active strains (Woting et al. 2010; Becker et al. 2011), (2) for studying the production and effects of so far unknown isoflavone products such as 5-hydroxy-equol (Matthies et al. 2008), and (3) for large-scale affordable production of equol, for instance, for the sake of intervention trials that require large quantity of pure material. With respect to the latter point, the enantiospecificity of equol production is noteworthy. Gut bacteria are known to produce exclusively the *S*-enantiomer of equol, which seems to be more biologically active than its counterpart *R*-equol (Setchell et al. 2005; Wang et al. 2005, 2007; Shinkaruk et al. 2010). Patents related to the bacterial or synthetic production of enantiomeric equol and to the isolation of involved bacterial enzymes have already been registered (Setchell et al., US2009/7528267, Shimada et al., US2010/0330627; Isono et al., US2011/0189134; Tsuji et al., US2011/0318309). *Coriobacteriaceae*-based applications for the sake of metabolite production are also valid with respect to secondary bile acids, as recently studied using a 7*b*-HSDH from *Collinsella aerofaciens* (Braun et al. 2012).

The aforementioned use of *Coriobacteriaceae* in gnotobiotic mouse models can actually be extended to the study of host metabolic functions. Such experiments would help deciphering, for instance, the health implication of *Eggerthella*-encoded bile acid and steroid dehydroxylases as well as the role of these bacteria on hepatic functions, e.g., lipid metabolism and detoxification pathways (Ridlon et al. 2006; Claus et al. 2011; Martinez et al. 2012). In addition, one member of the *Coriobacteriaceae* isolated from the bovine rumen, *Denitrobacterium detoxificans*, is capable of metabolizing the nitrotoxins 3-nitro-1-propanol and 3-nitro-1-propionate found in forages, thereby providing potential industrial application for clearance of nitrocompounds from environmental samples or enhancement of tolerance towards environmental toxins in cattle (Anderson et al. 2000, 2005). *Slackia heliotrinireducens* may also be of interest for the reduction of pyrrolizidine alkaloid poisoning in cattle (Hovermale and Craig 2002).

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