

Supplementary Table S1. Strains, plasmids and primers used in the study.

Strain	Relevant characteristics	Source
<u>Streptococcus pyogenes</u>		
<u>WT</u>		
EC904	SF370 (M1 serotype) (WT)	ATCC 700294
<u>Δcas9</u>		
EC1788	EC904Δcas9	(16)
<u>Δrnc</u>		
EC1636	EC904Δrnc	(16)
<u>Δcas9 in SF370 + cas9 complementations in trans</u>		
EC2121	EC1788 + pEC714 (Pcas9(Spy)-cas9(Spy)-CtHis)	This study
EC2127	EC1788 + pEC710 (171 tracrRNA-Pcas9(Spy)-CtHis)	This study
EC2150	EC1788 + pEC553 (Pcas9(Spy)-cas9-HH983AA(Spy)-CtHis)	This study
EC2151	EC1788 + pEC554 (Pcas9(Spy)-cas9-D10A(Spy)-CtHis)	This study
EC2152	EC1788 + pEC555 (Pcas9(Spy)-cas9-H840A(Spy)-CtHis)	This study
EC2153	EC1788 + pEC556 (Pcas9(Spy)-cas9-N854A(Spy)-CtHis)	This study
EC2154	EC1788 + pEC557 (Pcas9(Spy)-cas9-N863A(Spy)-CtHis)	This study
EC2155	EC1788 + pEC558 (Pcas9(Spy)-cas9-D986A(Spy)-CtHis)	This study
EC2156	EC1788 + pEC559 (Pcas9(Spy)-cas9-E762A(Spy)-CtHis)	This study
EC2118	EC1788 + pEC518 (Pcas9(Spy)-cas9(Cje)-CtHis)	This study
EC2128	EC1788 + pEC538 (Pcas9(Spy)-cas9(Fno)-CtHis)	This study
EC2199	EC1788 + pEC544 (Pcas9(Spy)-cas9(Nme)-CtHis)	This study
EC2119	EC1788 + pEC520 (Pcas9(Spy)-cas9(Pmu)-CtHis)	This study
EC2111	EC1788 + pEC519 (Pcas9(Spy)-cas9(Smu)-CtHis)	This study
EC2112	EC1788 + pEC521 (Pcas9(Spy)-cas9(Sth*)-CtHis)	This study
EC2120	EC1788 + pEC522 (Pcas9(Spy)-cas9(Sth**)-CtHis)	This study
<u>Δrnc in SF370 + rnc complementations in trans</u>		
EC2076	EC1636 + pEC484 (Prnc(Spy)-rnc(Spy))	This study
EC2084	EC1636 + pEC505 (Prnc(Spy)-rnc-catalytically inactive(Spy))	This study
EC2083	EC1636 + pEC504 (Prnc(Spy)-rnc-RNA binding inactive(Spy))	This study
EC2078	EC1636 + pEC486 (Prnc(Spy)-rnc(Cje))	This study
EC2080	EC1636 + pEC492 (Prnc(Spy)-rnc(Eco))	This study
EC2126	EC1636 + pEC537 (Prnc(Spy)-rnc(Fno))	This study
EC2085	EC1636 + pEC506 (Prnc(Spy)-rnc(Nme))	This study
EC2077	EC1636 + pEC485 (Prnc(Spy)-rnc(Pmu))	This study
EC2086	EC1636 + pEC507 (Prnc(Spy)-rnc(Sau))	This study
EC2082	EC1636 + pEC494 (Prnc(Spy)-rnc(Smu))	This study
EC2131	EC1636 + pEC534 (Prnc(Spy)-rnc(Sth))	This study
<u>Campylobacter jejuni</u>		
EC437	NCTC 11168; ATCC 700819 (WT), CIP 107370	Pasteur Institute
<u>Francisella novicida</u>		
EC1041	U112 (WT)	Anders Sjöstedt
<u>Neisseria meningitidis</u>		
EC438	CIP 107858	Pasteur Institute
<u>Pasteurella multocida</u>		
EC439	Pm70 (WT), ATCC BAA-1113	Pasteur Institute
<u>Staphylococcus aureus</u>		
EC36	COL (WT)	Lab strain collection
<u>Streptococcus mutans</u>		
EC1293	UA159 (WT)	(16)
<u>Streptococcus thermophilus</u>		
EC810	LMD-9 (WT)	(16)
<u>E. coli</u>		
RDN204	TOP10, host for cloning	Invitrogen
EC1265	Rosetta	Novagen

^a Cje: *Campylobacter jejuni* NCTC 11168; Eco: *Escherichia coli* TOP10; Fno: *Francisella novicida* U112; Nme: *Neisseria meningitidis* A Z2491; Pmu: *Pasteurella multocida* Pm70; Sau: *Staphylococcus aureus* COL; Smu: *Streptococcus mutans* UA159; Spy: *Streptococcus pyogenes* SF370; Sth: *Streptococcus thermophilus* LMD-9.

Plasmid	Relevant characteristics	Source
Vectors for <i>S. pyogenes</i>		
pEC85	<i>repDEG</i> -pAMβ1, pJH1- <i>aphIII</i> , ColE1	Bernhard Roppenser
Plasmids for <i>cas9</i> domain functional and co-evolution analysis in <i>S. pyogenes</i> SF370		
pEC268	pEC85Ω171 <i>tracrRNA</i> (171 nt form)	(16)
pEC309	pEC85Ω <i>Pcas9</i> (Spy)- <i>cas9</i> (Spy)	(16)
pEC368	pEC85Ω171 <i>tracrRNA</i> - <i>Pcas9</i> (Spy)- <i>cas9</i> (Spy)	(16)
pEC710	pEC85Ω171 <i>tracrRNA</i> - <i>Pcas9</i> (Spy)-CtHis	This study
pEC714	pEC710Ω <i>cas9</i> (Spy)	This study
pEC553	pEC710Ω <i>cas9</i> -HH983AA(Spy)-CtHis	This study
pEC615	pEC553Ω <i>speM</i>	This study
pEC554	pEC710Ω <i>cas9</i> -D10A(Spy)-CtHis	This study
pEC659	pEC554Ω <i>speM</i>	This study
pEC555	pEC710Ω <i>cas9</i> -H840A(Spy)-CtHis	This study
pEC660	pEC555Ω <i>speM</i>	This study
pEC556	pEC710Ω <i>cas9</i> -N854A(Spy)-CtHis	This study
pEC661	pEC556Ω <i>speM</i>	This study
pEC557	pEC710Ω <i>cas9</i> -N863A(Spy)-CtHis	This study
pEC618	pEC557Ω <i>speM</i>	This study
pEC558	pEC710Ω <i>cas9</i> -D986A(Spy)-CtHis	This study
pEC662	pEC558Ω <i>speM</i>	This study
pEC559	pEC710Ω <i>cas9</i> -E762A(Spy)-CtHis	This study
pEC619	pEC559Ω <i>speM</i>	This study
pEC518	pEC710Ω <i>cas9</i> (Cje)-CtHis	This study
pEC538	pEC710Ω <i>cas9</i> (Fno)-CtHis	This study
pEC544	pEC710Ω <i>cas9</i> (Nme)-CtHis	This study
pEC520	pEC710Ω <i>cas9</i> (Pmu)-CtHis	This study
pEC519	pEC710Ω <i>cas9</i> (Smu)-CtHis	This study
pEC521	pEC710Ω <i>cas9</i> (Sth*)-CtHis	This study
pEC522	pEC710Ω <i>cas9</i> (Sth**)-CtHis	This study
Plasmids for <i>mc</i> co-evolution analysis in <i>S. pyogenes</i> SF370		
pEC483	pEC85Ω <i>Pmc</i> (Spy)	This study
pEC484	pEC85Ω <i>Pmc</i> (Spy)- <i>mc</i> (Spy)	This study
pEC505	pEC85Ω <i>Pmc</i> (Spy)- <i>mc</i> -catalytically inactive(Spy)	This study
pEC504	pEC85Ω <i>Pmc</i> (Spy)- <i>mc</i> -RNA binding inactive(Spy)	This study
pEC486	pEC85Ω <i>Pmc</i> (Spy)- <i>mc</i> (Cje)	This study
pEC492	pEC85Ω <i>Pmc</i> (Spy)- <i>mc</i> (Eco)	This study
pEC537	pEC85Ω <i>Pmc</i> (Spy)- <i>mc</i> (Fno)	This study
pEC506	pEC85Ω <i>Pmc</i> (Spy)- <i>mc</i> (Nme)	This study
pEC485	pEC85Ω <i>Pmc</i> (Spy)- <i>mc</i> (Pmu)	This study
pEC507	pEC85Ω <i>Pmc</i> (Spy)- <i>mc</i> (Sau)	This study
pEC494	pEC85Ω <i>Pmc</i> (Spy)- <i>mc</i> (Smu)	This study
pEC534	pEC85Ω <i>Pmc</i> (Spy)- <i>mc</i> (Sth)	This study
Plasmids for protospacer study <i>in vitro</i>		
pEC287	pEC85Ω <i>PspeM-speM</i> (10 bp downstream protospacer: GGGTATTGGG)	Lab plasmid collection
pEC691	pEC287 (10 bp downstream protospacer: TGGTATTGGG)	This study
pEC692	pEC287 (10 bp downstream protospacer: TGGTGTGGG)	This study
pEC693	pEC287 (10 bp downstream protospacer: GGGTGATTGG)	This study
pEC694	pEC287 (10 bp downstream protospacer: GGAGAATGGG)	This study
pEC696	pEC287 (10 bp downstream protospacer: GGGTCATAGG)	This study
pEC697	pEC287 (10 bp downstream protospacer: AGAAACAGGG)	This study
pEC698	pEC287 (10 bp downstream protospacer: AGAACCAGGG)	This study
pEC701	pEC287 (10 bp downstream protospacer: GTTTGATTGG)	This study
pEC706	pEC287 (10 bp downstream protospacer: GGAAAATGGG)	This study
Plasmids for <i>Cas9</i> overexpression		
pEC225	pET16b	Novagen
pEC621	pEC225 inserted with cassette harboring NotI, SacI, Sall site	This study
pEC626	pEC621Ω <i>cas9</i> (Spy)	This study
pEC627	pEC621Ω <i>cas9</i> -D10A(Spy)	This study
pEC628	pEC621Ω <i>cas9</i> -E762A(Spy)	This study
pEC629	pEC621Ω <i>cas9</i> -H840A(Spy)	This study
pEC630	pEC621Ω <i>cas9</i> -N854A(Spy)	This study
pEC631	pEC621Ω <i>cas9</i> -HH983AA(Spy)	This study
pEC632	pEC621Ω <i>cas9</i> (Cje)	This study
pEC633	pEC621Ω <i>cas9</i> (Pmu)	This study
pEC634	pEC621Ω <i>cas9</i> (Nme)	This study
pEC635	pEC621Ω <i>cas9</i> (Smu)	This study
pEC638	pEC621Ω <i>cas9</i> -N863A(Spy)	This study
pEC639	pEC621Ω <i>cas9</i> -D986A(Spy)	This study
pEC640	pEC621Ω <i>cas9</i> (Sth*)	This study
pEC641	pEC621Ω <i>cas9</i> (Sth**)	This study
pEC657	pEC621Ω <i>cas9</i> (Fno)	This study

Purpose	Primer	Sequence 5'-3' ^a	F/R ^b	Usage ^c
tracrRNA expression in <i>S. pyogenes</i> SF370				
tracrRNA	OLEC1014	GGACTAGCCTTATTTAACTTG	R	NB (3' probe)
crRNA (CRISPR01 (type II-A) expression in <i>S. pyogenes</i> SF370				
crRNA	OLEC1049	GGACCATTCAAAAACAGCATAGCTCTAAAAAC	R	NB (repeat)
Loading controls for Northern blots				
5S rRNA	OLEC288	CTAAGCGACTACCTTATCTCA	R	NB
His-tagged cas9 constructs (pEC85-based)				
pEC710	OLEC2151	GCAGGAATTCATCAGTGATGGTGATGGTGATGCCCGGGTTTGTGCGACCT CCTAAAAATAAAAAGTTTAAATTAATC	F	Cloning
	OLEC2066	GGTGGTCTGCAGGTTTGCAGTCAGAGTAGAATAGAAG	R	
pEC714	OLEC2096	ATGCAGGTCGACATGGATAAGAAATACTCAATAGGC	F	Expression cas9(Spy)
	OLEC2097	ATGCAGCCCGGGTACCTCTAGCTGACTCAATC	R	
speM	OLEC2867	ATGCAGCCTGCAGGGTGCAGAGAGAACTTGATTC AAC	F	Cloning of <i>speM</i> in other plasmids
	OLEC2868	ATGCAGCCTGCAGGCTTCGTTTAAAGTAAACATCAAAGTG	R	
pEC518	OLEC2104	ATGCAGGTCGACGTGGCAAGAAATTTGGCATTGG	F	Cloning cas9(Cje)
	OLEC2105	ATGCAGCCCGGGTTTTTAAATCTTCTCTTTGTC	R	
pEC538	OLEC2840	ATTAGTCGACATGAATTTCAAAATATTGCCAATAG	F	Cloning cas9(Fno)
	OLEC2841	ATTACCCGGGATTATTAGATGTTTCATTATAAATAC	R	
pEC544	OLEC2092	ATGCAGGTCGACATGGCTGCCTTCAAACCTAATCC	F	Cloning cas9(Nme)
	OLEC2093	ATGCAGCCCGGGACGGACAGGGGGCGTTTTTCAG	R	
pEC520	OLEC2100	ATGCAGGTCGACATGCAAAACAACAAATTTAAGTTA	F	Cloning cas9(Pmu)
	OLEC2101	ATGCAGCCCGGGACGCACAGGTTGCTTCTGCTGAG	R	
pEC519	OLEC2090	ATGCAGGTCGACATGAAAAAACCCTTACTCTATTGGAC	F	Cloning cas9(Smu)
	OLEC2091	ATGCAGCCCGGGTCTCCTCCTAACTATTGAGATC	R	
pEC521	OLEC2098	ATGCAGGTCGACATGACTAAGCCATACTCAATTGG	F	Cloning cas9(Sth*)
	OLEC2099	ATGCAGCCCGGGACCCCTCTCCTAGTTTGGCAAGGTC	R	
pEC522	OLEC2102	ATGCAGGTCGACATGAGTGACTTAGTTT TAGGACTTG	F	Cloning cas9(Sth**)
	OLEC2103	ATGCAGCCCGGGAAAACTAGCTTAGGCTTATCACC	R	
pEC553	OLEC2229	GTACGTGAGATTAACAATTACGCTGCTGCCCATGATGCGTATCTA	F	Mutagenesis cas9-HH983AA(Spy)
	OLEC2230	TAGATACGCATCATGGGCAGCAGCGTAATTGTTAATCTCACGTAC	R	
pEC554	OLEC2128	GAAATACTCAATAGGCTTAGCTATCGGCACAAATAGCGTCCG	F	Mutagenesis cas9-D10A(Spy)
	OLEC2129	CGACGCTATTTGTGCCGATAGCTAAGCCTATTGAGTATTTT	R	
pEC555	OLEC2223	TTTAAAGTGATTATGATGTCGATGCTGTTCCACAAGTTTCCCT	F	Mutagenesis cas9-H840A(Spy)
	OLEC2224	AGGAAACTTTGTGGAACAATGGCATCGACATCATAACTCACTTAAA	R	
pEC556	OLEC2225	CCTTAAAGACGATTCAATAGACGCTAAGGCTTAAACGGTTCTGA	F	Mutagenesis cas9-N854A(Spy)
	OLEC2226	TCAGAACGCGTTAAGACCTTAGCGTCTATTGATCGTCTTTAAGG	R	
pEC557	OLEC2227	GGTCTTAAACGCGTTCTGATAAAGCTCGTGGTAAATCGGATAACGT	F	Mutagenesis cas9-N863A(Spy)
	OLEC2228	ACGTTATCCGATTTACCACGAGCTTTATCAGAACGCGTTAAGACC	R	
pEC558	OLEC2231	GTAACAATTACCATCATGCCCTAGCTGCGTATCTAAATGCCGTCG	F	Mutagenesis cas9-D986A(Spy)
	OLEC2232	CGACGGCATTTAGATACGCAGCATGGGCATGATGGTAAATTGTTAC	R	
pEC559	OLEC2221	CAGAAAAATATCGTTATTGCAATGGCAGGTGAAATCAGACA	F	Mutagenesis cas9-E762A(Spy)
	OLEC2222	TGCTGTATTTTACAGTCCATTGCAATAACGATATTTTCTG	R	
rnc constructs (pEC85-based)				
pEC483	OLEC2149	ATGCAGGCATGCCTGTGATTTTGGCTTGTCTGATC	F	Cloning in pEC85
	OLEC3274	ATGCAGAGCTCCATGGAAAATCCCTTTCATATTTGTGAGTAGACC	R	
pEC484	OLEC2109	ATGCAGCCATGGAACAGCTTGAAGAGTTACTCTCAAC	F	Cloning <i>rnc</i> (Spy), SEQ
	OLEC1668	CTTTTAAAAACATCTAAACCTCAC	R	
pEC504	OLEC2109	ATGCAGCCATGGAACAGCTTGAAGAGTTACTCTCAAC	F	Cloning of <i>rnc</i> RNA binding inactive(Spy)
	OLEC2656	ATGCAGGAATTCCTACCCTTTTTCCACTGAGGAATC	R	
pEC505	OLEC2142	GAACGCTTGGAAATTTTAGGAGCCGCTGTTCACAAATGATTATT	F	Mutagenesis of <i>mc</i> catalytically inactive(Spy)
	OLEC2143	AATAATCAATTGTAGAACAGCGGCTCCTAAAAATCCAAGCGTTC	R	
pEC486	OLEC2116	ATGCAGCCATGGAAAACATTTGAAAAGCTAGAGCAGAG	F	Cloning <i>rnc</i> (Cje), SEQ
	OLEC2117	ATGCAGGAATTCCTATAAAGCTCCTAATTTCTCAAG	R	
pEC492	OLEC2124	ATGCAGCCATGGACCCATCGTAATTAATCGGCTTC	F	Cloning <i>rnc</i> (Eco), SEQ
	OLEC2125	ATGCAGGAATTCCTCATTCCAGTCCAGTTTTCACAG	R	
pEC537	OLEC2842	ATTACCATGGTTCTTGAATATTCACGATTTTATAAC	F	Cloning <i>rnc</i> (Fno), SEQ
	OLEC2843	ATTGAATTCCTATTTTTCATGTAAGCCTTGTGTG	R	
pEC506	OLEC2118	ATGCAGCCATGGAAAGACGATGTTTGAACAGCAGG	F	Cloning <i>rnc</i> (Nme), SEQ
	OLEC2119	ATGCAGGAATTCCTATTCTTTTCTTCTCAGCGGC	R	
pEC485	OLEC2114	ATGCAGCCATGGCTCAAATTTAGAAGCTTTTACAACG	F	Cloning <i>rnc</i> (Pmu), SEQ
	OLEC2115	ATGCAGGAATTCCTATTCTCATTCCAATAATGT	R	
pEC507	OLEC2126	ATGCAGCCATGGCTAAACAAAAGAAAGTGAGATAG	F	Cloning <i>rnc</i> (Sau), SEQ
	OLEC2127	ATGCAGGAATTCCTATTATTTGTTTAAATTTGCTTATAGG	R	
pEC494	OLEC2110	ATGCAGCCATGGAAACATTTAGAAAAAACTGGCAG	F	Cloning <i>rnc</i> (Smu), SEQ
	OLEC2111	ATGCAGGAATTCCTAAGAACCCTGTTGAAGTTTTC	R	
pEC534	OLEC2849	ATTACCATGGATCAACTTGAACAAAACTTGAACAGGACTTTGG	F	Cloning <i>rnc</i> (Sth), SEQ
	OLEC2850	ATTAGAATTCCTAATTACCTAGTTGTTCAAGGGCAGACTTCGC	R	
Cas9 overexpression (pEC621 based)				
pEC621	OLEC2978	TAGCGGCCGCGAGCTCCTCGAGCGC	F	Cassette inserting NotI, SacI, Sall site in pEC225
	OLEC2979	TAGCGTCCGAGCTCGCGGCCGC	R	

pEC626, 627, 628, 629, 630, 631, 638, 639	OLEC2097	ATGCAGGTCGACATGGATAAGAAATACTCAATAGGC	F	Cloning cas9(Spy and all mutants)
	OLEC2983	AGCTAGCGGCCGCTCAGTACCTCCTAGCTGACTCAAATC	R	
pEC632	OLEC2104	ATGCAGGTCGACGTGGCAAGAATTTGGCATTG	F	Cloning cas9(Cje)
	OLEC2986	ATGCAGCGGCCGCTCATTTTTTAAAACTTCTCTTTGTC	R	
pEC633	OLEC2100	ATGCAGGTCGACATGCAAAACAACAATTTAAGTTA	F	Cloning cas9(Pmu)
	OLEC2173	ATGACCGGCCGCTTAACGCACAGGTTGTCTTTGCTG	R	
pEC634	OLEC2092	ATGCAGGTCGACATGGCTGCCTTCAAACCTAATCC	F	Cloning cas9(Nme)
	OLEC2982	ATGACCGGCCGCTTAACGGACAGCGGGCGTTTTTCAG	R	
pEC635	OLEC2090	ATGCAGGTCGACATGAAAAAACCTTACTCTATTGGAC	F	Cloning cas9(Smu)
	OLEC2981	ATGACCGGCCGCTTAGTCTCCTCTAACTTATTGAG	R	
pEC640	OLEC2098	ATGCAGGTCGACATGACTAAGCCATACTCAATTGG	F	Cloning cas9(Sth*)
	OLEC2984	ATGACCGGCCGCTTAACCTCTCCTAGTTGGCAAG	R	
pEC641	OLEC2102	ATGCAGGTCGACATGAGTGACTTAGTTTTAGGACTG	F	Cloning cas9(Sth**)
	OLEC2985	ATGACCGGCCGCTTAAAAATCTAGCTTAGGCTTATCAC	R	
pEC657	OLEC2840	ATTAGTCGACATGAATTTCAAATAATTTGCCAATAG	F	Cloning cas9(Fno)
	OLEC2987	ATGCAGCGGCCGCTAATTATTAGATGTTTCATTATAAATAC	R	
Mutagenesis 10 bp downstream of <i>speM</i> protospacer				
pEC691	OLEC3140	CAACCACTAATTTCTAGAAAAATCTTCG	R	Mutagenesis on pEC287
	OLEC3141	CAATTTGTAAAAAATGGTATTGGGAATTC	F	
pEC692	OLEC3140	CAACCACTAATTTCTAGAAAAATCTTCG	R	Mutagenesis on pEC287
	OLEC3142	CAATTTGTAAAAAATGGTATTGGGAATTC	F	
pEC693	OLEC3140	CAACCACTAATTTCTAGAAAAATCTTCG	R	Mutagenesis on pEC287
	OLEC3144	CAATTTGTAAAAAAGGGTGATTGGGAATTC	F	
pEC694	OLEC3140	CAACCACTAATTTCTAGAAAAATCTTCG	R	Mutagenesis on pEC287
	OLEC3143	CAATTTGTAAAAAAGGAGAAATGGGAATTC	F	
pEC696	OLEC3194	CAACCACTAATTTT TAGAAAAATCTTCG	R	Mutagenesis on pEC693
	OLEC3197	CAATTTGTAAAAAAGGGTCATAGGGAATTC	F	
pEC697	OLEC3194	CAACCACTAATTTT TAGAAAAATCTTCG	R	Mutagenesis on pEC694
	OLEC3198	CAATTTGTAAAAAAGAAACAGGGGAATTC	F	
pEC698	OLEC3194	CAACCACTAATTTT TAGAAAAATCTTCG	R	Mutagenesis on pEC694
	OLEC3199	CAATTTGTAAAAAAGAACAGGGGAATTC	F	
pEC701	OLEC3194	CAACCACTAATTTT TAGAAAAATCTTCG	R	Mutagenesis on pEC693
	OLEC3204	CAATTTGTAAAAAAGTTTGATTGGGAATTC	F	
pEC706	OLEC3194	CAACCACTAATTTT TAGAAAAATCTTCG	R	Mutagenesis on pEC694
	OLEC3208	CAATTTGTAAAAAAGGAAATGGGAATTC	F	
In vitro tracrRNA and crRNA of <i>Streptococcus pyogenes</i> SF370 (<i>speM</i> spacer underlined)				
T7-tracrRNA	OLEC1521	GAAATTAATACGACTCCTATAGAAAACAGCATAGCAAGTTAAAAATAA	F	T7-tracrRNA 5'
	OLEC1522	AAAAAAGCACCAGACTCGGTGCCAC	R	T7-tracrRNA 3'
T7-crRNA (template)	OLEC2177	GAAATTAATACGACTCCTATAGGATAA ACTCAATTTGTAAAAAAGTTTT AGAGCTATGCTGTTTTG	F	crRNA <i>speM</i> 5'
	OLEC2179	CAAAACAGCATAGCTCTAAAAC TTTTTTACAAATTGAGTTAT CCTATAG TGAGTCGTATTAATTC	R	crRNA <i>speM</i> 3'
In vitro tracrRNA and crRNA of <i>Neisseria meningitidis</i> A Z2491 (<i>speM</i> spacer underlined)				
T7-tracrRNA (template)	OLEC3083	GAAATTAATACGACTCCTATAGGGAGAGCGAAATGAGAACCCTTGCTA CAATAAGGCCTCTGAAAAGATGTGCCGCAACGCTCTGCCCTTAAAGCT TCTGCTTTAAGGGGCATCGTTTTATT	F	T7-tracrRNA 5'
	OLEC3084	AATAAACGATGCCCTTAAAGCAGAAGCTTTAAGGGGCAGAGCGTTGCG GCACATCTTTTCAGACGCCTTATTGTAGCAACGGTTCTCATTTGCTCT CCTATAGTGAGTCGTATTAATTC	R	T7-tracrRNA 3'
T7-crRNA (template)	OLEC2209	GAAATTAATACGACTCCTATAGATGATAACTCAATTTGTAAAAAAGTT GTAGCTCCCTTTCTCATTT	F	crRNA <i>speM</i> 5'
	OLEC2214	AAATGAGAAAGGGAGTACAAC TTTTTTACAAATTGAGTTATCATCTAT AGTGAGTCGTATTAATTC	R	crRNA <i>speM</i> 3'
In vitro tracrRNA and crRNA of <i>Streptococcus mutans</i> UA159 (<i>speM</i> spacer underlined)				
T7-tracrRNA	OLEC3098	GAAATTAATACGACTCCTATAGGAAACAACACAGCAAGTTAAAAAAG	F	T7-tracrRNA 5'
	OLEC3099	AAATAAAAAAGCACCAGATCGG	R	T7-tracrRNA 3'
T7-crRNA (template)	OLEC3085	GAAATTAATACGACTCCTATAGGATAA ACTCAATTTGTAAAAAAGTTTT AGAGCTGTGTTGT	F	crRNA <i>speM</i> 5'
	OLEC3086	ACAACACAGCTCTAAAAC TTTTTTACAAATTGAGTTAT CCTATAGTGAG TCGTATTAATTC	R	crRNA <i>speM</i> 3'
In vitro tracrRNA and crRNA of <i>Campylobacter jejuni</i> NCTC 11168 (<i>speM</i> spacer underlined)				
T7-tracrRNA (template)	OLEC3128	GAAATTAATACGACTCCTATAGGAAGGGACTAAAAATAAGAGTTTGCG GGACTCTGCGGGGTACAATCCCTAAAACCGC	F	T7-tracrRNA 5'
	OLEC3129	GCGGTTTTAGGGGATTGTAAACCCGACAGTCCCGCAAACCTTTATTT TAGTCCCTTCC TATAGTGAGTCGTATTAATTC	R	T7-tracrRNA 3'
T7-crRNA (template)	OLEC3087	GAAATTAATACGACTCCTATAGGATAA ACTCAATTTGTAAAAAAGTTTT AGTCCCT	F	crRNA <i>speM</i> 5'
	OLEC3088	AGGGACTAAAAC TTTTTTACAAATTGAGTTAT CCTATAGTGAGTCGTAT TAATTC	R	crRNA <i>speM</i> 3'

***In vitro* tracrRNA and crRNAs of *Francisella novicida* U112 (*speM* spacer underlined)**

T7-tracrRNA	OLEC3102	GAAATTAATACGACTCACTATAG <i>GGTACCAAATAATTAATGCTCTG</i>	F	T7-tracrRNA 5'
	OLEC3103	<i>GTTATTCAGACGTGTCAAACAG</i>	R	T7-tracrRNA 3'
T7-crRNA (template)	OLEC3089	GAAATTAATACGACTCACTATAG <i>GATAACTCAATTTGTAAAAAGTTTC</i> <i>AGTTGCTGAATTATTTGGTAAAC</i>	F	crRNA <i>speM</i> 5'
	OLEC3090	<i>GTTTACCAAATAATTCAGCAACTGAACTTTTTTACAAATTGAGTTATC</i> CTATAGTGAGTCGTATTAATTC	R	crRNA <i>speM</i> 3'

***In vitro* tracrRNA and crRNAs of *Streptococcus thermophilus** LMD-9 (*speM* spacer underlined)**

T7-tracrRNA	OLEC3104	GAAATTAATACGACTCACTATAG <i>GAACAACACAGCGAGTTAAAAATAAGG</i>	F	T7-tracrRNA 5'
	OLEC3105	<i>AAAAAAAACACCGAATCGGTG</i>	R	T7-tracrRNA 3'
T7-crRNA (template)	OLEC3085	GAAATTAATACGACTCACTATAG <i>GATAACTCAATTTGTAAAAAGTTT</i> <i>AGAGCTGTGTTGT</i>	F	crRNA <i>speM</i> 5'
	OLEC3086	<i>ACAACACAGCTCTAAAACTTTTTTACAAATTGAGTTATCCTATAGTGAG</i> TCGTATTAATTC	R	crRNA <i>speM</i> 3'

In vitro* tracrRNA and crRNAs of *Streptococcus thermophilus LMD-9 (*speM* spacer underlined)**

T7-tracrRNA	OLEC3106	GAAATTAATACGACTCACTATAG <i>GCTTAAATCTGCAGAAGCTACAAAG</i>	F	T7-tracrRNA 5'
	OLEC3107	<i>AAATAACGAAAACACCCCTGCC</i>	R	T7-tracrRNA 3'
T7-crRNA (template)	OLEC3091	GAAATTAATACGACTCACTATAG <i>GATAACTCAATTTGTAAAAAGTTT</i> <i>TGTACTCTCAAGATTTA</i>	F	crRNA <i>speM</i> 5'
	OLEC3092	<i>TAAATCTTGAGAGTACAAAACTTTTTTACAAATTGAGTTATCCTATAG</i> TGAGTCGTATTAATTC	R	crRNA <i>speM</i> 3'

***In vitro* tracrRNA and crRNAs of *Pasteurella multocida* Pm70 (*speM* spacer underlined)**

T7-tracrRNA	OLEC3108	GAAATTAATACGACTCACTATAG <i>GCTGCGAAATGAGAGACGTTGCTAC</i>	F	T7-tracrRNA 5'
	OLEC3109	<i>AAAAACGATGCCCTTGAATTAAG</i>	R	T7-tracrRNA 3'
T7-crRNA (template)	OLEC3093	GAAATTAATACGACTCACTATAG <i>GATAACTCAATTTGTAAAAAGTTGT</i> <i>AGTTCCCTCTCTCATTTCGC</i>	F	crRNA <i>speM</i> 5'
	OLEC3094	<i>GCGAAATGAGAGGGGAACACAACTTTTTTACAAATTGAGTTATCCTA</i> TAGTGAGTCGTATTAATTC	R	crRNA <i>speM</i> 3'

Primers for sequencing analysis***cas9* *Streptococcus mutans* UA159**

<i>cas9</i> (Smu)	OLEC2792	<i>ATGAAAAAACCTTACTCTATTGGA</i>	F	SEQ
	OLEC2793	<i>GATTTTAAAAGCATTGAAATTA</i>	F	SEQ
	OLEC2794	<i>TACTTGCCAAATCAAAAAGTTCTT</i>	F	SEQ
	OLEC2795	<i>ATTATGGGACATCAACCTGAAAAAT</i>	F	SEQ
	OLEC2796	<i>TACCCACAATTGGAACCTGAATTT</i>	F	SEQ

***cas9* *Neisseria meningitidis* A Z2491**

<i>cas9</i> (Nme)	OLEC2797	<i>ATGGCTGCCTTCAAACCTAATCCA</i>	F	SEQ
	OLEC2798	<i>GTCAAAAAAATGTTGGGCATTGC</i>	F	SEQ
	OLEC2799	<i>ATCCATATTGAAACTGCAAGGGAA</i>	F	SEQ
	OLEC2800	<i>AACGCGTTTGACGGTAAAACCATA</i>	F	SEQ

***cas9* *Streptococcus thermophilus** LMD-9**

<i>cas9</i> (Sth*)	OLEC2807	<i>ATGACTAAGCCATACTCAATTGGA</i>	F	SEQ
	OLEC2808	<i>GATTTTAGGAAATGTTTTAATTTA</i>	F	SEQ
	OLEC2809	<i>TATTTGCCAGAAGAGAAGGTACTT</i>	F	SEQ
	OLEC2810	<i>GTAATGGGAGGAAGAAAACCCGAG</i>	F	SEQ
	OLEC2811	<i>GCAAGTCTTTACTTAAGAAATAC</i>	F	SEQ
	OLEC2812	<i>TTACTTTATCATGCTAAGAGAATA</i>	F	SEQ

cas9* *Streptococcus thermophilus LMD-9**

<i>cas9</i> (Sth**)	OLEC2817	<i>ATGAGTGACTTAGTTTTAGGACTT</i>	F	SEQ
	OLEC2818	<i>ATTTTTGGAATCTAATTGGGAAA</i>	F	SEQ
	OLEC2819	<i>GGAGACTTTGACAATATTGTCATC</i>	F	SEQ
	OLEC2820	<i>TTGAATTTGTGGAAAAACAAAAG</i>	F	SEQ
	OLEC2821	<i>CAGGAAAAATACAATGACATTAAG</i>	F	SEQ

***cas9* *Pasteurella multocida* Pm70**

<i>cas9</i> (Pmu)	OLEC2813	<i>ATGCAACAACAATAATTAAGTTAT</i>	F	SEQ
	OLEC2814	<i>ACGCATGAAAAAATGAGTTTAAA</i>	F	SEQ
	OLEC2815	<i>CTTGGGAAATCTTTTAAAGAACGT</i>	F	SEQ
	OLEC2816	<i>TATGAAATGGTGGATCAAGAAAGC</i>	F	SEQ

***cas9* *Campylobacter jejuni* NCTC 11168**

<i>cas9</i> (Cje)	OLEC2822	<i>GTGGCAAGAATTTGGCATTGAT</i>	F	SEQ
	OLEC2823	<i>GATGAAAAAAGAGCGCCAAAAAAT</i>	F	SEQ
	OLEC2824	<i>AACTACAAGGCCAAAAAAGACGCC</i>	F	SEQ
	OLEC2825	<i>AACAAAAGGAAGTTTTTGGAGCCT</i>	F	SEQ

***cas9* *Francisella novicida* U112**

<i>cas9</i> (Fno)	OLEC2869	<i>ATGAATTTCAAAATATTGCCAATA</i>	F	SEQ
	OLEC2870	<i>TTAGATACTCTTTAACTGATGAT</i>	F	SEQ
	OLEC2871	<i>TTAAAAGTCTTAAAGTCAAGTAAA</i>	F	SEQ
	OLEC2872	<i>GGTTCAGAAGATAAAAAAGGTAAT</i>	F	SEQ
	OLEC2873	<i>AGAATTTCTGCCTACGTGATCTT</i>	F	SEQ
	OLEC2874	<i>CCAATACTAATCCATAAAGAATA</i>	F	SEQ
	OLEC2875	<i>ACATCAAAAAATATTTTTGGCTG</i>	F	SEQ

^a *italic*, sequence annealing to the template; underlined, restriction site; **bold**, T7 promoter.

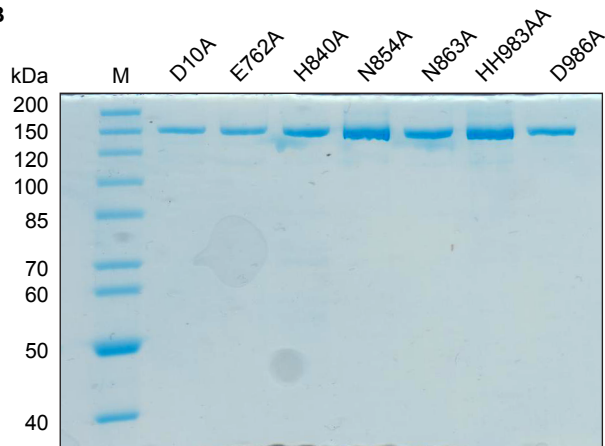
^b F, forward primer; R, reverse primer.

^c NB, probe for Northern blot; SEQ, sequencing

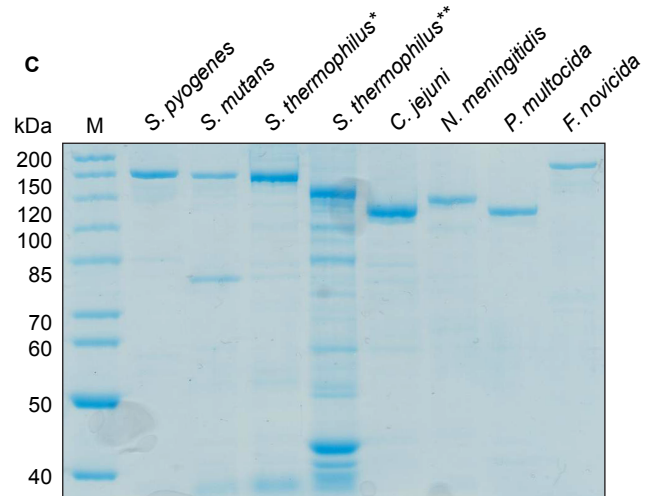
A

Strain ^a	GI accession number ^b	Amino acids (including purification-tag)	Molecular weight [kDa] (including purification-tag)	ϵ [$M^{-1} cm^{-1}$] ^c
<i>S. pyogenes</i> SF370	13622193	1368 (1392)	158.4 (161.2)	110470
<i>S. mutans</i> UA159	24379809	1345 (1369)	156.6 (159.4)	114190
<i>S. thermophilus</i> * LMD-9	116628213	1388 (1412)	161.0 (163.8)	128390
<i>S. thermophilus</i> ** LMD-9	116627542	1121 (1145)	129.4 (132.2)	103860
<i>C. jejuni</i> NCTC 11168	218563121	984 (1008)	114.9 (117.7)	78640
<i>N. meningitidis</i> A Z2491	218767588	1082 (1106)	124.3 (127.1)	101950
<i>P. multocida</i> Pm70	15602992	1056 (1080)	121.8 (124.6)	121460
<i>F. novicida</i> U112	118497352	1629 (1653)	190.4 (193.2)	189080

B



C



Supplementary Figure S1. Biochemical characteristics and SDS-PAGE analysis of Cas9 proteins purified in this study. (A) Overview of characteristics of Cas9 orthologous proteins ^aNote that the biochemical characteristics of *S. pyogenes* Cas9 WT and mutants are identical; ^bGenInfo (GI) Identifier; ^c ϵ , Extinction coefficient. (B) SDS PAGE analysis of purified mutants of Cas9 from *S. pyogenes*. (C) SDS PAGE analysis of purified Cas9 orthologs. M: PageRuler™ Unstained Protein Ladder (Thermo Scientific).

Supplementary Table S2. List of bacterial strains with identified Cas9 orthologs.

Cluster ^a	Strain ^b	Cas9 length (aa)	Cas9 GI	Cas1 GI ^c	Subtype ^d
	<i>Dolosigranulum pigrum</i> ATCC 51524	1332	375088882		
	<i>Enterococcus faecalis</i> ATCC 29200	1337	229548613		
	<i>Enterococcus faecalis</i> ATCC 4200	1337	256617555		
	<i>Enterococcus faecalis</i> D6	1337	257086028		
	<i>Enterococcus faecalis</i> E1Sol	1337	257080914		
	<i>Enterococcus faecalis</i> OG1RF	1337	384512368		
	<i>Enterococcus faecalis</i> TX0470	1337	312900261		
	<i>Enterococcus faecalis</i> TX4244	1337	422695652		
	<i>Enterococcus faecium</i> 1,141,733	1339	257888853		
	<i>Enterococcus faecium</i> 1,231,408	1340	257893735		
	<i>Enterococcus faecium</i> E1133	1339	430847551		
	<i>Enterococcus faecium</i> E3083	1340	431757680		
	<i>Enterococcus faecium</i> PC4.1	1340	293379700		
	<i>Enterococcus faecium</i> TX1330	1340	227550972		
	<i>Enterococcus faecium</i> TX1337RF	1340	424765774		
	<i>Enterococcus hirae</i> ATCC 9790	1336	392988474		
	<i>Enterococcus italicus</i> DSM 15952	1330	315641599		
	<i>Lactobacillus animalis</i> KCTC 3501	1314	335357451		
	<i>Listeria innocua</i> ATCC 33091	1337	423101383		
	<i>Listeria innocua</i> Clip11262	1334	16801805		
	<i>Listeria innocua</i> FSL S4-378	1103	422414122		
	<i>Listeria ivanovii</i> FSL F6-596	953	315305353		
	<i>Listeria monocytogenes</i> 10403S	1334	386044902		
	<i>Listeria monocytogenes</i> FSL J1-175	1099	255520581		
	<i>Listeria monocytogenes</i> FSL J1-194	1334	254825045		
	<i>Listeria monocytogenes</i> FSL J1-208	1334	422810631		
	<i>Listeria monocytogenes</i> FSL N3-165	1334	254829042		
	<i>Listeria monocytogenes</i> FSL R2-503	1334	254854201		
	<i>Listeria monocytogenes</i> str. 1/2a F6854	1334	47097148		
1	<i>Streptococcus agalactiae</i> 2603V/R	1370	22537057		Type II-A
	<i>Streptococcus agalactiae</i> 515	1377	77413160		
	<i>Streptococcus agalactiae</i> A909	1370	76788458		
	<i>Streptococcus agalactiae</i> ATCC 13813	1378	339301617		
	<i>Streptococcus agalactiae</i> CJB111	1370	77411010		
	<i>Streptococcus agalactiae</i> COH1	1370	77407964		
	<i>Streptococcus agalactiae</i> FSL S3-026	1370	417005168		
	<i>Streptococcus agalactiae</i> GB00112	1370	421147428		
	<i>Streptococcus agalactiae</i> H36B	1370	77405721		
	<i>Streptococcus agalactiae</i> NEM316	1377	25010965		
	<i>Streptococcus agalactiae</i> SA20-06	1370	410594450		
	<i>Streptococcus agalactiae</i> STIR-CD-17	1370	421532069		
	<i>Streptococcus anginosus</i> F0211	1345	315223162		
	<i>Streptococcus anginosus</i> SK1138	1386	421490579		
	<i>Streptococcus anginosus</i> SK52 = DSM 20563	1396	335031483		
	<i>Streptococcus bovis</i> ATCC 700338	1373	306833855		
	<i>Streptococcus canis</i> FSL Z3-227	1375	392329410		
	<i>Streptococcus constellatus</i> subsp. <i>constellatus</i> SK53	1345	418965022		
	<i>Streptococcus dysgalactiae</i> subsp. <i>equisimilis</i> AC-2713	1371	410494913		
	<i>Streptococcus dysgalactiae</i> subsp. <i>equisimilis</i> ATCC 12394	1371	386317166		
	<i>Streptococcus dysgalactiae</i> subsp. <i>equisimilis</i> GGS_124	1371	251782637		
	<i>Streptococcus dysgalactiae</i> subsp. <i>equisimilis</i> RE378	1371	408401787		
	<i>Streptococcus equi</i> subsp. <i>zooepidemicus</i> MGCS10565	1348	195978435		
	<i>Streptococcus equinus</i> ATCC 9812	1377	320547102		
	<i>Streptococcus gallolyticus</i> subsp. <i>gallolyticus</i> ATCC BAA-2069	1370	325978669		
	<i>Streptococcus gallolyticus</i> subsp. <i>gallolyticus</i> TX20005	1370	306831733		
	<i>Streptococcus gallolyticus</i> UCN34	1371	288905639		
	<i>Streptococcus infantarius</i> subsp. <i>infantarius</i> CJ18	1375	379705580		
	<i>Streptococcus iniae</i> 9117	1368	406658208		
	<i>Streptococcus macacae</i> NCTC 11558	1338	357636406		

Cluster ^a	Strain ^b	Cas9 length (aa)	Cas9 GI	Cas1 GI ^c	Subtype ^d
	<i>Streptococcus mitis</i> SK321	1392	307710946		
	<i>Streptococcus mutans</i> 11SSST2	1345	449165720		
	<i>Streptococcus mutans</i> 11SSST2	1345	449951835		
	<i>Streptococcus mutans</i> 11VS1	1345	449976542		
	<i>Streptococcus mutans</i> 14D	1345	450149988		
	<i>Streptococcus mutans</i> 15VF2	1355	449170557		
	<i>Streptococcus mutans</i> 15VF2	1355	449965974		
	<i>Streptococcus mutans</i> 1SM1	1345	449158457		
	<i>Streptococcus mutans</i> 1SM1	1345	449920643		
	<i>Streptococcus mutans</i> 24	1350	449247589		
	<i>Streptococcus mutans</i> 24	1350	450180942		
	<i>Streptococcus mutans</i> 2VS1	1345	449174812		
	<i>Streptococcus mutans</i> 2VS1	1345	449968746		
	<i>Streptococcus mutans</i> 3SN1	1345	449162653		
	<i>Streptococcus mutans</i> 3SN1	1345	449931425		
	<i>Streptococcus mutans</i> 4SM1	1345	449159838		
	<i>Streptococcus mutans</i> 4SM1	1345	449927152		
	<i>Streptococcus mutans</i> 4VF1	1345	449167132		
	<i>Streptococcus mutans</i> 4VF1	1345	449961027		
	<i>Streptococcus mutans</i> 5SM3	1345	449176693		
	<i>Streptococcus mutans</i> 5SM3	1345	449980571		
	<i>Streptococcus mutans</i> 66-2A	1359	449240165		
	<i>Streptococcus mutans</i> 66-2A	1359	450160342		
	<i>Streptococcus mutans</i> 8ID3	1345	449154769		
	<i>Streptococcus mutans</i> 8ID3	1345	449872064		
	<i>Streptococcus mutans</i> A19	1345	449187668		
	<i>Streptococcus mutans</i> A19	1345	450013175		
	<i>Streptococcus mutans</i> B	1345	450166294		
	<i>Streptococcus mutans</i> G123	1345	450029806		
	<i>Streptococcus mutans</i> GS-5	1345	397650022		
1	<i>Streptococcus mutans</i> LJ23	1345	387785882		Type II-A
(continued)	<i>Streptococcus mutans</i> M21	1345	449194333		
	<i>Streptococcus mutans</i> M21	1345	450036249		
	<i>Streptococcus mutans</i> M230	1345	449260994		
	<i>Streptococcus mutans</i> M230	1345	449903532		
	<i>Streptococcus mutans</i> M2A	1345	449209586		
	<i>Streptococcus mutans</i> M2A	1345	450074072		
	<i>Streptococcus mutans</i> N29	1345	449182997		
	<i>Streptococcus mutans</i> N29	1345	450003067		
	<i>Streptococcus mutans</i> N3209	1345	449210660		
	<i>Streptococcus mutans</i> N3209	1345	450077860		
	<i>Streptococcus mutans</i> N66	1345	449212466		
	<i>Streptococcus mutans</i> N66	1345	450083993		
	<i>Streptococcus mutans</i> NFSM1	1350	449202104		
	<i>Streptococcus mutans</i> NFSM1	1350	450051112		
	<i>Streptococcus mutans</i> NLML1	1345	450140393		
	<i>Streptococcus mutans</i> NLML4	1338	449202681		
	<i>Streptococcus mutans</i> NLML4	1338	450059882		
	<i>Streptococcus mutans</i> NLML9	1345	449209148		
	<i>Streptococcus mutans</i> NLML9	1345	450066176		
	<i>Streptococcus mutans</i> NMT4863	1355	449186850		
	<i>Streptococcus mutans</i> NMT4863	1355	450007078		
	<i>Streptococcus mutans</i> NN2025	1345	290580220		
	<i>Streptococcus mutans</i> NV1996	1345	450086338		
	<i>Streptococcus mutans</i> NVAB	1345	449181424		
	<i>Streptococcus mutans</i> NVAB	1345	449990810		
	<i>Streptococcus mutans</i> R221	1345	449258042		
	<i>Streptococcus mutans</i> R221	1345	449899675		
	<i>Streptococcus mutans</i> S1B	1345	449251227		
	<i>Streptococcus mutans</i> S1B	1345	449877120		
	<i>Streptococcus mutans</i> SF1	1345	450098705		
	<i>Streptococcus mutans</i> SF14	1345	449221374		

Cluster ^a	Strain ^b	Cas9 length (aa)	Cas9 GI	Cas1 GI ^c	Subtype ^d
1 (continued)	<i>Streptococcus mutans</i> SF14	1345	450107816		
	<i>Streptococcus mutans</i> SM1	1345	449245264		
	<i>Streptococcus mutans</i> SM1	1345	450176410		
	<i>Streptococcus mutans</i> SM4	1345	449246010		
	<i>Streptococcus mutans</i> SM4	1345	450170248		
	<i>Streptococcus mutans</i> SM6	1345	449223000		
	<i>Streptococcus mutans</i> SM6	1345	450112022		
	<i>Streptococcus mutans</i> ST6	1350	449227252		
	<i>Streptococcus mutans</i> ST6	1350	450123011		
	<i>Streptococcus mutans</i> UA159	1345	24379809	24379808	
	<i>Streptococcus mutans</i> W6	1345	450094364		
	<i>Streptococcus oralis</i> SK304	1373	421488030		
	<i>Streptococcus oralis</i> SK610	1371	419782534		
	<i>Streptococcus pseudoporcinus</i> LQ 940-04	1374	416852857		
	<i>Streptococcus pyogenes</i> SF370 (M1 GAS)	1368	13622193	13622194	
	<i>Streptococcus pyogenes</i> MGAS10270	1368	94543903		
	<i>Streptococcus pyogenes</i> MGAS10750	1371	94994317		
	<i>Streptococcus pyogenes</i> MGAS15252	1367	383479946		
	<i>Streptococcus pyogenes</i> MGAS2096	1368	94992340		
	<i>Streptococcus pyogenes</i> MGAS315	1368	21910213		Type II-A
	<i>Streptococcus pyogenes</i> MGAS5005	1368	71910582		
	<i>Streptococcus pyogenes</i> MGAS6180	1368	71903413		
	<i>Streptococcus pyogenes</i> MGAS9429	1368	94988516		
	<i>Streptococcus pyogenes</i> NZ131	1368	209559356		
	<i>Streptococcus pyogenes</i> SSI-1	1368	28896088		
	<i>Streptococcus rattus</i> FA-1 = DSM 20564	1370	400290495		
	<i>Streptococcus salivarius</i> K12	1385	421452908		
	<i>Streptococcus sanguinis</i> SK115	1377	422848603		
	<i>Streptococcus sanguinis</i> SK330	1392	422860049		
	<i>Streptococcus sanguinis</i> SK353	1370	422821159		
	<i>Streptococcus</i> sp. C300	1377	322375978		
	<i>Streptococcus</i> sp. F0441	1371	414157437		
	<i>Streptococcus</i> sp. M334	1375	322378004		
	<i>Streptococcus</i> sp. oral taxon 56 str. F0418	1371	339640839		
	<i>Streptococcus suis</i> ST1	1381	389856936		
	<i>Streptococcus thermophilus</i>	1388	343794781		
	<i>Streptococcus thermophilus</i> LMD-9	1388	116628213	116628212	
	<i>Streptococcus thermophilus</i> MN-ZLW-002	1388	387910220		
	<i>Streptococcus thermophilus</i> ND03	1388	386087120		
	2	<i>Campylobacter coli</i> 1098	984	419564797	
<i>Campylobacter coli</i> 111-3		984	419536531		
<i>Campylobacter coli</i> 132-6		987	419572019		
<i>Campylobacter coli</i> 151-9		984	419603415		
<i>Campylobacter coli</i> 1909		984	419576091		
<i>Campylobacter coli</i> 1957		965	419581876		
<i>Campylobacter coli</i> 2692		984	419553162		
<i>Campylobacter coli</i> 59-2		984	419578074		
<i>Campylobacter coli</i> 67-8		965	419587721		
<i>Campylobacter coli</i> 80352		965	419558307		
<i>Campylobacter coli</i> 80352		987	419559505		
<i>Campylobacter jejuni</i> subsp. <i>doylei</i> 269.97		984	153952471		Type II-C
<i>Campylobacter jejuni</i> subsp. <i>jejuni</i> 110-21		987	419676124		
<i>Campylobacter jejuni</i> subsp. <i>jejuni</i> 129-258		987	419619138		
<i>Campylobacter jejuni</i> subsp. <i>jejuni</i> 1336		987	283956897		
<i>Campylobacter jejuni</i> subsp. <i>jejuni</i> 140-16		984	419681578		
<i>Campylobacter jejuni</i> subsp. <i>jejuni</i> 1577		984	419685099		
<i>Campylobacter jejuni</i> subsp. <i>jejuni</i> 1854		987	419689467		
<i>Campylobacter jejuni</i> subsp. <i>jejuni</i> 1997-10		984	419666522		
<i>Campylobacter jejuni</i> subsp. <i>jejuni</i> 2008-1025		987	419650041		
<i>Campylobacter jejuni</i> subsp. <i>jejuni</i> 2008-872		984	419654778		
<i>Campylobacter jejuni</i> subsp. <i>jejuni</i> 2008-979		987	419660762		
<i>Campylobacter jejuni</i> subsp. <i>jejuni</i> 2008-988		965	419656328		

Cluster ^a	Strain ^b	Cas9 length (aa)	Cas9 GI	Cas1 GI ^c	Subtype ^d
2 (continued)	<i>Campylobacter jejuni</i> subsp. <i>jejuni</i> 2008-988	984	419655317		
	<i>Campylobacter jejuni</i> subsp. <i>jejuni</i> 260.94	961	86152042		
	<i>Campylobacter jejuni</i> subsp. <i>jejuni</i> 414	985	283953849		
	<i>Campylobacter jejuni</i> subsp. <i>jejuni</i> 51037	984	419674189		
	<i>Campylobacter jejuni</i> subsp. <i>jejuni</i> 51494	984	419619463		
	<i>Campylobacter jejuni</i> subsp. <i>jejuni</i> 53161	987	419647275		
	<i>Campylobacter jejuni</i> subsp. <i>jejuni</i> 60004	984	419629136		
	<i>Campylobacter jejuni</i> subsp. <i>jejuni</i> 81116	984	157415744		
	<i>Campylobacter jejuni</i> subsp. <i>jejuni</i> 84-25	984	88596565		
	<i>Campylobacter jejuni</i> subsp. <i>jejuni</i> 87459	984	419680124		
	<i>Campylobacter jejuni</i> subsp. <i>jejuni</i> ATCC 33560	984	419643715		
	<i>Campylobacter jejuni</i> subsp. <i>jejuni</i> CF93-6	987	86149266		
	<i>Campylobacter jejuni</i> subsp. <i>jejuni</i> CG8486	984	148925683		
	<i>Campylobacter jejuni</i> subsp. <i>jejuni</i> HB93-13	984	86152450		
	<i>Campylobacter jejuni</i> subsp. <i>jejuni</i> LMG 23210	987	419696801		Type II-C
	<i>Campylobacter jejuni</i> subsp. <i>jejuni</i> LMG 23211	984	419697443		
	<i>Campylobacter jejuni</i> subsp. <i>jejuni</i> LMG 23263	984	419628620		
	<i>Campylobacter jejuni</i> subsp. <i>jejuni</i> LMG 23264	984	419632476		
	<i>Campylobacter jejuni</i> subsp. <i>jejuni</i> LMG 23269	987	419634246		
	<i>Campylobacter jejuni</i> subsp. <i>jejuni</i> LMG 23357	987	419641132		
	<i>Campylobacter jejuni</i> subsp. <i>jejuni</i> NCTC 11168	984	218563121	218563120	
	<i>Campylobacter jejuni</i> subsp. <i>jejuni</i> NW	983	424845990		
	<i>Campylobacter jejuni</i> subsp. <i>jejuni</i> PT14	987	407942868		
	<i>Campylobacter lari</i>	1003	345468028		
	<i>Helicobacter canadensis</i> MIT 98-5491	1007	253828136		
	<i>Helicobacter cinaedi</i> ATCC BAA-847	1023	396079277		
<i>Helicobacter cinaedi</i> CCUG 18818	1023	313144862			
<i>Helicobacter cinaedi</i> PAGU611	1023	386762035			
3	<i>Catelicoccus marimammalium</i> M35/04/3	1140	424780480		
	<i>Lactobacillus farciminis</i> KCTC 3681	1126	336394701		
	<i>Listeriaceae bacterium</i> TTU M1-001	1087	381184145		
	<i>Streptococcus anginosus</i> 1_2_62CV	1125	319939170		
	<i>Streptococcus gallolyticus</i> UCN34	1130	288905632		
	<i>Streptococcus gordonii</i> str. Challis substr. CH1	1136	157150687		
	<i>Streptococcus infantarius</i> ATCC BAA-102	1129	171779984		
	<i>Streptococcus macedonicus</i> ACA-DC 198	1130	374338350		
	<i>Streptococcus mitis</i> ATCC 6249	1134	306829274		
	<i>Streptococcus mutans</i> NLML5	1128	449203378		
	<i>Streptococcus mutans</i> NLML5	1128	450064617		
	<i>Streptococcus mutans</i> NLML8	1125	449151037		
	<i>Streptococcus mutans</i> NLML8	1125	450133520		
	<i>Streptococcus mutans</i> ST1	1134	449228751		
	<i>Streptococcus mutans</i> ST1	1134	450114718		
	<i>Streptococcus mutans</i> U2A	1125	449232458		
	<i>Streptococcus mutans</i> U2A	1125	450125471		
	<i>Streptococcus oralis</i> SK1074	1121	418974877		Type II-A
	<i>Streptococcus oralis</i> SK313	1134	417940002		
	<i>Streptococcus parasanguinis</i> F0449	1140	419799964		
	<i>Streptococcus pasteurianus</i> ATCC 43144	1130	336064611		
	<i>Streptococcus salivarius</i> JIM8777	1127	387783792		
	<i>Streptococcus salivarius</i> PS4	1135	419707401		
	<i>Streptococcus</i> sp. BS35b	1026	401684660		
	<i>Streptococcus</i> sp. C150	1139	322372617		
	<i>Streptococcus</i> sp. GMD6S	1121	406576934		
	<i>Streptococcus suis</i> 89/1591	1122	223932525		
	<i>Streptococcus suis</i> D9	1122	386584496		
	<i>Streptococcus suis</i> ST3	1122	330833104		
	<i>Streptococcus thermophilus</i> CNRZ1066	1128	55822627		
	<i>Streptococcus thermophilus</i> JIM 8232	1121	386344353		
	<i>Streptococcus thermophilus</i> LMD-9	1121	116627542	116627543	
	<i>Streptococcus thermophilus</i> LMG 18311	1122	55820735		
	<i>Streptococcus thermophilus</i> MN-ZLW-002	1121	387909441		

Cluster ^a	Strain ^b	Cas9 length (aa)	Cas9 GI	Cas1 GI ^c	Subtype ^d
3 (continued)	<i>Streptococcus thermophilus</i> MTCC 5460	1122	445374534		Type II-A
	<i>Streptococcus thermophilus</i> ND03	1121	386086348		
	<i>Streptococcus vestibularis</i> ATCC 49124	1128	322517104		
4	<i>Actinobacillus minor</i> NM305	1056	240949037		Type II-C
	<i>Actinobacillus pleuropneumoniae</i> serovar 10 str. D13039	1054	307256472		
	<i>Actinobacillus succinogenes</i> 130Z	1062	152978060		
	<i>Actinobacillus suis</i> H91-0380	1054	407692091		
	<i>Haemophilus parainfluenzae</i> ATCC 33392	1054	325578067		
	<i>Haemophilus parainfluenzae</i> CUG 13788	1052	359298684		
	<i>Haemophilus parainfluenzae</i> T3T1	1052	345430422		
	<i>Haemophilus sputorum</i> HK 2154	1052	402304649		
	<i>Kingella kingae</i> PYKK081	1060	381401699		
	<i>Neisseria bacilliformis</i> ATCC BAA-1200	1077	329117879		
	<i>Neisseria cinerea</i> ATCC 14685	1082	261378287		
	<i>Neisseria flavescens</i> SK114	1081	241759613		
	<i>Neisseria lactamica</i> 020-06	1082	313669044		
	<i>Neisseria meningitidis</i> 053442	1082	161869390		
	<i>Neisseria meningitidis</i> 2007056	1082	433531983		
	<i>Neisseria meningitidis</i> 63049	1082	433514137		
	<i>Neisseria meningitidis</i> 8013	1082	385324780		
	<i>Neisseria meningitidis</i> 92045	1082	421559784		
	<i>Neisseria meningitidis</i> 93003	1081	421538794		
	<i>Neisseria meningitidis</i> 93004	1081	421541126		
	<i>Neisseria meningitidis</i> 96023	1082	433518260		
	<i>Neisseria meningitidis</i> 98008	1081	421555531		
	<i>Neisseria meningitidis</i> alpha14	1082	254804356		
	<i>Neisseria meningitidis</i> alpha275	1082	254672046		
	<i>Neisseria meningitidis</i> ATCC 13091	1082	304388355		
	<i>Neisseria meningitidis</i> N1568	1081	416164244		
	<i>Neisseria meningitidis</i> NM140	1081	421545139		
	<i>Neisseria meningitidis</i> NM220	1082	418291220		
	<i>Neisseria meningitidis</i> NM233	1082	418288950		
	<i>Neisseria meningitidis</i> WUE 2594	1082	385337435		
	<i>Neisseria meningitidis</i> Z2491	1082	218767588	218767587	
	<i>Neisseria</i> sp. oral taxon 14 str. F0314	1089	298369677		
<i>Neisseria wadsworthii</i> 9715	1097	350570326			
<i>Pasteurella multocida</i> subsp. <i>gallicida</i> X73	1058	425063822			
<i>Pasteurella multocida</i> subsp. <i>multocida</i> str. P52VAC	1056	421263876			
<i>Pasteurella multocida</i> subsp. <i>multocida</i> str. Pm70	1056	15602992	15602991		
<i>Simonsiella muelleri</i> ATCC 29453	1063	404379108			
5	<i>Lactobacillus brevis</i> subsp. <i>gravesensis</i> ATCC 27305	1377	227509761		Type II-A
	<i>Lactobacillus buchneri</i> CD034	1371	406027703		
	<i>Lactobacillus buchneri</i> NRRL B-30929	1371	331702228		
	<i>Lactobacillus casei</i> BL23	1361	191639137		
	<i>Lactobacillus casei</i> Lc-10	1361	418010298		
	<i>Lactobacillus casei</i> M36	1363	417996992		
	<i>Lactobacillus casei</i> str. Zhang	1361	301067199		
	<i>Lactobacillus casei</i> T71499	1360	417999832		
	<i>Lactobacillus casei</i> UCD174	1366	418002962		
	<i>Lactobacillus casei</i> W56	1389	409997999		
	<i>Lactobacillus coryniformis</i> subsp. <i>coryniformis</i> KCTC 3167	1354	333394446		
	<i>Lactobacillus curvatus</i> CRL 705	1368	354808135		
	<i>Lactobacillus fermentum</i> 28-3-CHN	1313	260662220		
	<i>Lactobacillus fermentum</i> ATCC 14931	1381	227514633		
	<i>Lactobacillus florum</i> 2F	1327	408790128		
	<i>Lactobacillus gasserii</i> JV-V03	1391	300361537		
	<i>Lactobacillus hominis</i> CRBIP 24.179	1386	395244248		
	<i>Lactobacillus jensenii</i> 269-3	1391	238854567		
	<i>Lactobacillus jensenii</i> 27-2-CHN	1395	256852176		
	<i>Lactobacillus johnsonii</i> DPC 6026	1375	385826041		
<i>Lactobacillus mucosae</i> LM1	1382	377831443			
<i>Lactobacillus paracasei</i> subsp. <i>paracasei</i> 8700:2	1362	239630053			

Cluster ^a	Strain ^b	Cas9 length (aa)	Cas9 GI	Cas1 GI ^c	Subtype ^d
5 (continued)	<i>Lactobacillus pentosus</i> IG1	1382	339637353		
	<i>Lactobacillus pentosus</i> KCA1	1361	392947436		
	<i>Lactobacillus pentosus</i> MP-10	1358	334881121		
	<i>Lactobacillus plantarum</i> ZJ316	1358	448819853		
	<i>Lactobacillus rhamnosus</i> GG	1363	258509199	258509198	
	<i>Lactobacillus rhamnosus</i> HN001	1361	199597394		
	<i>Lactobacillus rhamnosus</i> R0011	1361	418072660		
	<i>Lactobacillus ruminis</i> ATCC 25644	1375	323340068		Type II-A
	<i>Lactobacillus salivarius</i> SMXD51	1339	418960525		
	<i>Lactobacillus sanfranciscensis</i> TMW 1.1304	1331	347534532		
	<i>Lactobacillus</i> sp. 66c	1419	408410332		
	<i>Pediococcus acidilactici</i> DSM 20284	1364	304386254		
	<i>Pediococcus acidilactici</i> MA18/5M	1366	418068659		
<i>Psychroflexus torquus</i> ATCC 700755	1509	408489713			
6	<i>Anaerophaga</i> sp. HS1	1552	371776944		
	<i>Anaerophaga thermohalophila</i> DSM 12881	1515	346224232		
	<i>Bacteroides coprophilus</i> DSM 18228	1509	224026357		
	<i>Bacteroides coprosuis</i> DSM 18011	1504	333031006		
	<i>Bacteroides dorei</i> DSM 17855	1504	212694363		
	<i>Bacteroides eggerthii</i> 1_2_48FAA	1509	317474201		
	<i>Bacteroides faecis</i> 27-5	1526	380696107		
	<i>Bacteroides fluxus</i> YIT 12057	1509	329965125		
	<i>Bacteroides nordii</i> CL02T12C05	1512	393788929		
	<i>Bacteroides</i> sp. 20_3	1517	301311869	301311870	Type II-C
	<i>Bacteroides</i> sp. D2	1510	383115507		
	<i>Bacteroides uniformis</i> CL03T00C23	1508	423303159		
	<i>Bacteroides vulgatus</i> CL09T03C04	1504	423312075		
	<i>Capnocytophaga gingivalis</i> ATCC 33624	1436	228473057		
	<i>Capnocytophaga</i> sp. CM59	1437	402830627		
	<i>Capnocytophaga</i> sp. oral taxon 324 str. F0483	1471	429756885		
	<i>Capnocytophaga</i> sp. oral taxon 326 str. F0382	1450	429752492		
	<i>Capnocytophaga</i> sp. oral taxon 412 str. F0487	1450	393778597		
	<i>Chryseobacterium</i> sp. CF314	1419	399023756		
	<i>Fibrobacter succinogenes</i> subsp. <i>succinogenes</i> S85	1512	261414553		
	<i>Flavobacteriaceae</i> bacterium S85	1516	372210605		
	<i>Flavobacterium columnare</i> ATCC 49512	1459	365960762		
	<i>Fluviicola taffensis</i> DSM 16823	1458	327405121		
	<i>Mucilagibacter paludis</i> DSM 18603	1473	373954054		
	<i>Myroides odoratus</i> DSM 2801	1466	374597806		
	<i>Ornithobacterium rhinotracheale</i> DSM 15997	1535	392391493		
	<i>Prevotella bivia</i> JCVIHMP010	1485	282858617		Type II-C
	<i>Prevotella buccae</i> ATCC 33574	1457	315607525		
	<i>Prevotella nigrescens</i> ATCC 33563	1506	340351024		
	<i>Prevotella</i> sp. MSX73	1483	402307189		
	<i>Prevotella timonensis</i> CRIS 5C-B1	1487	282881485		
	<i>Prevotella veroralis</i> F0319	1496	260592128		
<i>Sphingobacterium spiritivorum</i> ATCC 33861	1426	300771242			
<i>Weeksella virosa</i> DSM 16922	1440	325955459			
7	<i>Bacteroides fragilis</i> 638R	1436	375360193		
	<i>Bacteroides fragilis</i> NCTC 9343	1436	60683389	60683388	
	<i>Bacteroides</i> sp. 2_1_16	1436	265767599		
	<i>Bacteroides</i> sp. 3_1_19	1424	298377533		
	<i>Bacteroides</i> sp. D2	1436	383110723		
	<i>Bacteroidetes</i> oral taxon 274 str. F0058	1434	298373376		
	<i>Belliella baltica</i> DSM 15883	1352	390944707		
	<i>Bergeyella zoohelcum</i> CCUG 30536	1430	406673990		Type II-C
	<i>Capnocytophaga canimorsus</i> Cc5	1430	340622236		
	<i>Capnocytophaga ochracea</i> DSM 7271	1426	256819408		
	<i>Capnocytophaga</i> sp. oral taxon 329 str. F0087	1435	332882466		
	<i>Capnocytophaga</i> sp. oral taxon 335 str. F0486	1426	420149252		
	<i>Capnocytophaga</i> sp. oral taxon 380 str. F0488	1432	429748017		
	<i>Capnocytophaga sputigena</i> Capno	1426	213962376		

Cluster ^a	Strain ^b	Cas9 length (aa)	Cas9 GI	Cas1 GI ^c	Subtype ^d
7 (continued)	<i>Flavobacterium psychrophilum</i> JIP02/86	1354	150025575		
	<i>Galbibacter</i> sp. ck-12-15	1391	408370397		
	<i>Indibacter alkaliphilus</i> LW1	1354	404451234		
	<i>Joostella marina</i> DSM 19592	1397	386818981		
	<i>Kordia algicida</i> OT-1	1391	163754820		
	<i>Marinilabilia</i> sp. AK2	1345	410030899		
	<i>Myroides injenensis</i> M09-0166	1401	399927444		
	<i>Niabella soli</i> DSM 19437	1426	374372722		
	<i>Parabacteroides johnsonii</i> DSM 18315	1443	218258638		
	<i>Parabacteroides</i> sp. D13	1424	256840409		Type II-C
	<i>Prevotella histicola</i> F0411	1375	357042839		
	<i>Prevotella intermedia</i> 17	1380	387132277		
	<i>Prevotella nigrescens</i> F0103	1380	445119230		
	<i>Prevotella oralis</i> ATCC 33269	1391	323344874		
	<i>Prevotella</i> sp. oral taxon 306 str. F0472	1375	383811446		
	<i>Riemerella anatipestifer</i> RA-CH-1	1405	407451859		
	<i>Riemerella anatipestifer</i> RA-GD	1400	386321727		
	<i>Zunongwangia profunda</i> SM-A87	1388	295136244		
	8	<i>Actinomyces coleocanis</i> DSM 15436	1105	227494853	
<i>Actinomyces georgiae</i> F0490		1113	420151340		
<i>Actinomyces naeslundii</i> str. Howell 279		1101	400293272		
<i>Actinomyces</i> sp. ICM47		1144	396585058		
<i>Actinomyces</i> sp. oral taxon 175 str. F0384		1095	343523232		
<i>Actinomyces</i> sp. oral taxon 181 str. F0379		1103	429758968		
<i>Actinomyces</i> sp. oral taxon 848 str. F0332		1120	269219760		
<i>Actinomyces turicensis</i> ACS-279-V-Col4		1114	405979650		
<i>Bifidobacterium dentium</i> Bd1		1138	283456135		
<i>Bifidobacterium longum</i> DJO10A		1187	189440764	189440765	
<i>Bifidobacterium longum</i> subsp. <i>longum</i> 2-2B		1124	419852381		
<i>Bifidobacterium longum</i> subsp. <i>longum</i> KACC 91563		1138	384200944		
<i>Bifidobacterium</i> sp. 12_1_47BFAA		1151	317482066	317482065	
<i>Corynebacterium accolens</i> ATCC 49725		1099	227502575		
<i>Corynebacterium accolens</i> ATCC 49726		1099	306835141		
<i>Corynebacterium diphtheriae</i> 241		1084	375289763		
<i>Corynebacterium diphtheriae</i> 31A		1084	376283539		Type II-C
<i>Corynebacterium diphtheriae</i> BH8		1084	376286566		
<i>Corynebacterium diphtheriae</i> bv. <i>intermedius</i> str. NCTC 5011		1084	419861895		
<i>Corynebacterium diphtheriae</i> C7 (beta)		1084	376289243		
<i>Corynebacterium diphtheriae</i> HC02		1084	376292154		
<i>Corynebacterium diphtheriae</i> NCTC 13129		1084	38232678		
<i>Corynebacterium diphtheriae</i> VA01		1084	376256051		
<i>Corynebacterium matruchotii</i> ATCC 14266		1089	305681510		
<i>Corynebacterium matruchotii</i> ATCC 33806		1069	225021644		
<i>Gardnerella vaginalis</i> 1500E		1186	415717744		
<i>Gardnerella vaginalis</i> 284V		1186	415703177		
<i>Gardnerella vaginalis</i> 5-1	1186	298252606			
<i>Mobiluncus curtisii</i> subsp. <i>holmesii</i> ATCC 35242	1123	315656340			
<i>Mobiluncus mulieris</i> 28-1	1091	269977848			
<i>Mobiluncus mulieris</i> FB024-16	1091	307700167			
<i>Scardovia inopinata</i> F0304	1178	294790575			
9	<i>Bacillus cereus</i> BAG4X12-1	1068	423439645		
	<i>Bacillus cereus</i> BAG4X2-1	1078	423445130		
	<i>Bacillus cereus</i> Rock1-15	1069	229113166		
	<i>Bacillus smithii</i> 7_3_47FAA	1088	365156657	365156658	
	<i>Bacillus thuringiensis</i> serovar <i>finitimus</i> YBT-020	1069	384183447		Type II-C
	<i>Brevibacillus laterosporus</i> GI-9	1092	421874297	421874296	
	<i>Clostridium perfringens</i> C str. JGS1495	1065	169343975		
<i>Clostridium perfringens</i> D str. JGS1721	1065	182624245			
<i>Sporolactobacillus vineae</i> DSM 21990 = SL153	1084	404330915			
10	<i>Gemella haemolysans</i> ATCC 10379	1392	241889924		
	<i>Gemella morbillorum</i> M424	1385	317495358		Type II-A
	<i>Megasphaera</i> sp. UPII 135-E	1352	342218215		

Cluster ^a	Strain ^b	Cas9 length (aa)	Cas9 GI	Cas1 GI ^c	Subtype ^d
10 (continued)	<i>Veillonella atypica</i> ACS-134-V-Col7a	1398	303229466	303229394	Type II-A
	<i>Veillonella parvula</i> ATCC 17745	1398	282849530		
	<i>Veillonella</i> sp. 6_1_27	1395	294792465		
	<i>Veillonella</i> sp. oral taxon 780 str. F0422	1120	342213964		
11	<i>Treponema denticola</i> AL-2	1395	449103686	42525844	Type II-A
	<i>Treponema denticola</i> ASLM	1395	449106292		
	<i>Treponema denticola</i> ATCC 35405	1395	42525843		
	<i>Treponema denticola</i> H1-T	1395	449118593		
	<i>Treponema denticola</i> H-22	1395	449117322		
	<i>Treponema denticola</i> OTK	1395	449125136		
	<i>Treponema denticola</i> SP37	1395	449130155		
12	<i>Mycoplasma canis</i> PG 14	1233	384393286	384393287	Type II-A
	<i>Mycoplasma canis</i> PG 14	1233	419703974		
	<i>Mycoplasma canis</i> UF31	1233	384937953		
	<i>Mycoplasma canis</i> UF33	1233	419704625		
	<i>Mycoplasma canis</i> UFG1	1233	419705269		
	<i>Mycoplasma canis</i> UFG4	1233	419705920		
	<i>Mycoplasma cynos</i> C142	1239	433625054		
13	<i>Enterococcus faecalis</i> Fly1	1150	257084992	315149831	Type II-A
	<i>Enterococcus faecalis</i> R508	1150	424761124		
	<i>Enterococcus faecalis</i> T11	1150	257419486		
	<i>Enterococcus faecalis</i> TX0012	1150	315149830		
	<i>Enterococcus faecalis</i> TX0012	1150	422729710		
	<i>Enterococcus faecalis</i> TX1342	1150	422701955		
	<i>Facklamia hominis</i> CCUG 36813	1142	406671118		
14	<i>Gluconacetobacter diazotrophicus</i> PAI 5	1003	209542524	296446028	Type II-C
	<i>Gluconacetobacter diazotrophicus</i> PAI 5	1050	162147907		
	<i>Methylocystis</i> sp. ATCC 49242	1080	323139312		
	<i>Methylosinus trichosporium</i> OB3b	1082	296446027		
	<i>Rhodopseudomonas palustris</i> BisB18	1066	90425961		
	<i>Rhodopseudomonas palustris</i> BisB5	1064	91975509		
	<i>Tistrella mobilis</i> KA081020-065	1049	389874754		
15	<i>Francisella</i> cf. <i>novicida</i> 3523	1646	387824704	118497352	Type II-B
	<i>Francisella</i> cf. <i>novicida</i> Fx1	1629	385792694		
	<i>Francisella novicida</i> FTG	1629	208779141		
	<i>Francisella novicida</i> GA99-3548	1629	254374175		
	<i>Francisella novicida</i> U112	1629	118497352		
	<i>Francisella tularensis</i> subsp. <i>novicida</i> GA99-3549	1629	254372717		
16	<i>Acidovorax avenae</i> subsp. <i>avenae</i> ATCC 19860	1045	326315085	330822846	Type II-C
	<i>Alicyclophilus denitrificans</i> BC	1029	319760940		
	<i>Alicyclophilus denitrificans</i> K601	1029	330822845		
	gamma proteobacterium HdN1	1025	304313029		
	<i>Nitrosomonas</i> sp. AL212	1044	325983496		
	<i>Verminephrobacter eiseniae</i> EF01-2	1068	121608211		
17	<i>Mycoplasma gallisepticum</i> NC95_13295-2-2P	1269	401767318	284931711	Type II-A
	<i>Mycoplasma gallisepticum</i> NY01_2001.047-5-1P	1224	401768851		
	<i>Mycoplasma gallisepticum</i> str. F	1269	284931710		
	<i>Mycoplasma gallisepticum</i> str. F	1269	385326554		
	<i>Mycoplasma gallisepticum</i> str. R(low)	1270	294660600		
18	<i>Prevotella buccalis</i> ATCC 35310	1218	282878504	282880052	Type II-C
	<i>Prevotella ruminicola</i> 23	1204	294674019		
	<i>Prevotella stercorea</i> DSM 18206	1216	359406728		
	<i>Prevotella tanneriae</i> ATCC 51259	1234	258648111		
	<i>Prevotella timonensis</i> CRIS 5C-B1	1218	282880052		
	<i>Phascolarctobacterium succinatutens</i> YIT 12067	1087	323142435		
19	<i>Roseburia intestinalis</i> L1-82	1140	257413184	225377803	Type II-C
	<i>Roseburia intestinalis</i> M50/1	1128	291537230		
	<i>Roseburia inulinivorans</i> DSM 16841	1152	225377804		
	<i>Subdoligranulum</i> sp. 4_3_54A2FAA	1084	365132400		
20	<i>Coriobacterium glomerans</i> PW2	1384	328956315	328956316	Type II-A
	<i>Eggerthella</i> sp. YY7918	1380	339445983		

Cluster ^a	Strain ^b	Cas9 length (aa)	Cas9 GI	Cas1 GI ^c	Subtype ^d
20 (continued)	<i>Gordonibacter pamelaee</i> 7-10-1-b	1371	295106015		Type II-A
	<i>Olsenella uli</i> DSM 7084	1399	302336020		
21	<i>Fusobacterium nucleatum</i> subsp. <i>vincentii</i> ATCC 49256	1374	34762592	34762593	Type II-A
	<i>Fusobacterium</i> sp. 1_1_41FAA	1367	294782278		
	<i>Fusobacterium</i> sp. 3_1_27	1367	294785695		
	<i>Fusobacterium</i> sp. 3_1_36A2	1367	256845019	256845020	
22	<i>Finegoldia magna</i> ACS-171-V-Col3	1347	302380288		Type II-A
	<i>Finegoldia magna</i> ATCC 29328	1348	169823755	169823756	
	<i>Finegoldia magna</i> SY403409CC001050417	1348	417926052		
	<i>Helcococcus kunzii</i> ATCC 51366	1338	375092427		
23	<i>Prevotella denticola</i> CRIS 18C-A	1422	325859619		Type II-C
	<i>Prevotella micans</i> F0438	1425	373501184		
	<i>Prevotella</i> sp. C561	1424	345885718	345885719	
24	<i>Leuconostoc gelidum</i> KCTC 3527	1355	333398273		Type II-A
	<i>Oenococcus kitaharae</i> DSM 17330	1389	366983953	366983954	
	<i>Oenococcus kitaharae</i> DSM 17330	1389	372325145		
25	<i>Anaerococcus tetradius</i> ATCC 35098	1361	227501312		Type II-A
	<i>Lactobacillus iners</i> LactinV 11V1-d	1369	309803917		
	<i>Peptoniphilus duerdenii</i> ATCC BAA-1640	1364	304438954	304438953	
	<i>Coprococcus catus</i> GD/7	1338	291520705	291520706	
26	<i>Dorea longicatena</i> DSM 13814	1340	153855454		Type II-A
	<i>Ruminococcus lactaris</i> ATCC 29176	1341	197301447		
	<i>Staphylococcus pseudintermedius</i> ED99	1334	323463801	323463802	
27	<i>Staphylococcus pseudintermedius</i> ED99	1334	386318630		Type II-A
	<i>Staphylococcus simulans</i> ACS-120-V-Sch1	1112	414160476		
	<i>Dinoroseobacter shibae</i> DFL 12	1079	159042956	159042957	
28	<i>Sphingobium</i> sp. AP49	1110	398385143		Type II-C
	<i>Sphingomonas</i> sp. S17	1090	332188827		
	<i>Flavobacterium branchiophilum</i> FL-15	1473	347536497	no <i>cas1</i>	
29	<i>Flavobacterium columnare</i> ATCC 49512	1535	365959402		Type II-C
	<i>Bifidobacterium bifidum</i> S17	1420	310286728	310286727	
30	<i>Scardovia wiggisiae</i> F0424	1471	423349694		Type II-A
	<i>Burkholderiales</i> bacterium 1_1_47	1428	303257695		
31	<i>Parasutterella excrementihominis</i> YIT 11859	1428	331001027	331001028	Type II-B
32	<i>Streptococcus sanguinis</i> SK49	1421	422884106	422884107	Type II-A
	<i>Streptococcus</i> sp. oral taxon 71 str. 73H25AP	1420	306826314		
33	<i>Eubacterium</i> sp. AS15	1391	402309258		Type II-A
	<i>Eubacterium yurii</i> subsp. <i>margaretiae</i> ATCC 43715	1391	306821691	306821690	
34	<i>Legionella pneumophila</i> 130b	1372	307608922		Type II-B
	<i>Legionella pneumophila</i> str. Paris	1372	54296138	54296139	
35	<i>Acidaminococcus intestini</i> RyC-MR95	1358	352684361		Type II-A
	<i>Acidaminococcus</i> sp. D21	1358	227824983	227824982	
36	<i>Lactobacillus farciminis</i> KCTC 3681	1356	336394882	336394883	Type II-A
	<i>Lactobacillus versmoldensis</i> KCTC 3814	1289	365906066		
37	<i>Mycoplasma synoviae</i> 53	1304	144575181		Type II-A
	<i>Mycoplasma synoviae</i> 53	1314	71894592	71894593	
38	<i>Elusimicrobium minutum</i> Pei191	1195	187250660	187250661	Type II-C
	uncultured Termite group 1 bacterium phylotype Rs-D17	1032	189485059		
39	<i>Clostridium spiroforme</i> DSM 1552	1116	169349750		Type II-A
	<i>Eubacterium dolichum</i> DSM 3991	1096	160915782	160915783	
40	<i>Eubacterium rectale</i> ATCC 33656	1114	238924075	238924076	Type II-A
	<i>Eubacterium ventriosum</i> ATCC 27560	1107	154482474		
41	<i>Staphylococcus aureus</i> subsp. <i>aureus</i>	1053	403411236		Type II-A
	<i>Staphylococcus lugdunensis</i> M23590	1054	315659848	315659847	
42	<i>Ignavibacterium album</i> JCM 16511	1688	385811609	385811610	Type II-C
43	<i>Odoribacter laneus</i> YIT 12061	1498	374384763	374384762	Type II-C
44	<i>Caenispirillum salinarum</i> AK4	1442	427429481	427429479	Type II-C
45	<i>Sutterella wadsworthensis</i> 3_1_45B	1422	319941583	319941582	Type II-B
46	<i>Bergeyella zoohelcum</i> ATCC 43767	1415	423317190	423317188	Type II-C
47	<i>Wolinella succinogenes</i> DSM 1740	1409	34557932	34557933	Type II-B

Cluster ^a	Strain ^b	Cas9 length (aa)	Cas9 GI	Cas1 GI ^c	Subtype ^d
48	<i>gamma proteobacterium</i> HTCC5015	1397	254447899	no <i>cas1</i>	Type II-B
49	<i>Filifactor alocis</i> ATCC 35896	1365	374307738	374307737	Type II-A
50	<i>Planococcus antarcticus</i> DSM 14505	1333	389815359	389815358	Type II-A
51	<i>Catenibacterium mitsuokai</i> DSM 15897	1329	224543312	224543313	Type II-A
52	<i>Solobacterium moorei</i> F0204	1327	320528778	320528779	Type II-A
53	<i>Fructobacillus fructosus</i> KCTC 3544	1323	339625081	339625080	Type II-A
54	<i>Mycoplasma ovipneumoniae</i> SC01	1265	363542550	363542551	Type II-A
54	<i>Streptobacillus moniliformis</i> DSM 12112	1259	269123826		
55	<i>Mycoplasma mobile</i> 163K	1236	47458868	47458867	Type II-A
56	<i>Porphyromonas</i> sp. oral taxon 279 str. F0450	1197	402847315	402847305	Type II-C
57	<i>Actinomyces</i> sp. oral taxon 180 str. F0310	1181	315605738	315605739	Type II-C
58	<i>Sphaerochaeta globus</i> str. Buddy	1179	325972003	325972002	Type II-C
59	<i>Rhodospirillum rubrum</i> ATCC 11170	1173	83591793	83591790	Type II-C
60	<i>Azospirillum</i> sp. B510	1168	288957741	288957738	Type II-C
61	<i>Nitrobacter hamburgensis</i> X14	1166	92109262	no <i>cas1</i>	Type II-C
62	<i>Ruminococcus albus</i> 8	1156	325677756	325677757	Type II-C
63	<i>Barnesiella intestinihominis</i> YIT 11860	1153	404487228	404487227	Type II-C
64	<i>Alicyclobacillus hesperidum</i> URH17-3-68	1146	403744858	403744859	Type II-C
65	<i>Acidothermus cellulolyticus</i> 11B	1138	117929158	117929157	Type II-C
66	<i>Nitratifactor salsuginis</i> DSM 16511	1132	319957206	319957207	Type II-C
67	<i>Acidovorax ebreus</i> TSPY	1131	222109285	222109284	Type II-C
67	<i>Francisella tularensis</i> subsp. <i>tularensis</i> WY96-3418	1125	134302318		
68	<i>Lactobacillus coryniformis</i> subsp. <i>torquens</i> KCTC 3535	1119	336393381	336393380	Type II-C
69	<i>Alcanivorax</i> sp. W11-5	1113	407803669	407803668	Type II-C
70	<i>Akkermansia muciniphila</i> ATCC BAA-835	1101	187736489	187736488	Type II-C
71	<i>Ilyobacter polytropus</i> DSM 2926	1092	310780384	310780383	Type II-C
72	<i>Bradyrhizobium</i> sp. BTAi1	1064	148255343	no <i>cas1</i>	Type II-C
73	<i>Ralstonia syzygii</i> R24	1062	344171927	344171926	Type II-C
74	<i>Treponema</i> sp. JC4	1062	384109266	384109265	Type II-C
75	<i>Wolinella succinogenes</i> DSM 1740	1059	34557790	34557789	Type II-C
76	<i>Rhodovulum</i> sp. PH10	1059	402849997	402849996	Type II-C
77	<i>Aminomonas paucivorans</i> DSM 12260	1052	312879015	312879014	Type II-C
77	<i>Bacteroides</i> sp. 3_1_33FAA	1055	265750948		
78	<i>Parvibaculum lavamentivorans</i> DS-1	1037	154250555	154250554	Type II-C
79	<i>Candidatus Puniceispirillum marinum</i> IMCC1322	1035	294086111	294086112	Type II-C
80	<i>Blastopirellula marina</i> DSM 3645	1027	87307579		
80	<i>Helicobacter mustelae</i> 12198	1024	291276265	291276264	Type II-C
81	<i>Clostridium cellulolyticum</i> H10	1021	220930482	220930481	Type II-C
82	<i>Lactobacillus crispatus</i> FB077-07	857	423321767		
82	uncultured delta proteobacterium HF0070_07E19	1011	297182908	no <i>cas1</i>	Type II-C
	<i>Acetobacter acetii</i> NBRC 14818	240	340779894		
	<i>Acetobacter acetii</i> NBRC 14818	376	340779669		
	<i>Acetobacter acetii</i> NBRC 14818	400	340779439		
	<i>Actinobacillus ureae</i> ATCC 25976	239	322514756		
	<i>Actinobacillus ureae</i> ATCC 25976	400	322514772		
	<i>Bacillus cereus</i> BAG2X1-3	333	423408783		
	<i>Bacteroides cellulosilyticus</i> DSM 14838	206	224535831		
	<i>Bacteroides cellulosilyticus</i> DSM 14838	1219	224535832		
	<i>Bacteroides coprosuis</i> DSM 18011	349	333031028		
	<i>Bacteroides oleiciplenus</i> YIT 12058	653	427387687		
	<i>Bacteroides oleiciplenus</i> YIT 12058	779	427387686		
	<i>Bacteroides</i> sp. 9_1_42FAA	1055	237710146		
	<i>Bacteroides uniformis</i> CL03T12C37	286	423308124		
	<i>Bacteroides uniformis</i> CL03T12C37	1210	423308121		
	<i>Bifidobacterium bifidum</i> IPLA 20015	1281	421736922		
	<i>Bifidobacterium dentium</i> ATCC 27678	1121	171742822		
	<i>Bifidobacterium longum</i> subsp. <i>longum</i> 1-6B	182	419848319		
	<i>Bifidobacterium longum</i> subsp. <i>longum</i> 1-6B	354	419847807		
	<i>Bifidobacterium longum</i> subsp. <i>longum</i> 1-6B	441	419848320		
	<i>Bifidobacterium longum</i> subsp. <i>longum</i> 44B	166	419856168		

Cluster ^a	Strain ^b	Cas9 length (aa)	Cas9 GI	Cas1 GI ^c	Subtype ^d
	<i>Bifidobacterium longum</i> subsp. <i>longum</i> 44B	967	419856216		
	<i>Butyrivibrio fibrisolvens</i> 16/4	103	291518094		
	<i>Butyrivibrio fibrisolvens</i> 16/4	177	291518096		
	<i>Butyrivibrio fibrisolvens</i> 16/4	765	291518097		
	<i>Campylobacter coli</i> 2685	933	419548338		
	<i>Campylobacter jejuni</i> subsp. <i>jejuni</i> 2008-894	666	419652996		
	<i>Campylobacter jejuni</i> subsp. <i>jejuni</i> 305	190	317510779		
	<i>Campylobacter jejuni</i> subsp. <i>jejuni</i> 305	759	317510780		
	<i>Campylobacter jejuni</i> subsp. <i>jejuni</i> 327	462	415747744		
	<i>Campylobacter jejuni</i> subsp. <i>jejuni</i> 327	512	415747743		
	<i>Campylobacter jejuni</i> subsp. <i>jejuni</i> CG8421	721	205356639		
	<i>Campylobacter jejuni</i> subsp. <i>jejuni</i> M1	861	384442103		
	candidate division TM7 single-cell isolate TM7c	372	167957190		
	<i>Capnocytophaga ochracea</i> F0287	303	315224863		
	<i>Capnocytophaga ochracea</i> F0287	1117	315224862		
	<i>Coprococcus comes</i> ATCC 27758	686	226325213		
	<i>Diplosphaera colitermitum</i> TAV2	210	225164109		
	<i>Enterococcus faecalis</i> TX1467	921	422867931		
	<i>Enterococcus faecalis</i> TX4248	936	307270261		
	<i>Enterococcus faecium</i> E2620	892	431752788		
	<i>Enterococcus</i> sp. 7L76	116	295113136		
	<i>Francisella tularensis</i> subsp. <i>holarctica</i> 257	878	254367943		
	<i>Francisella tularensis</i> subsp. <i>holarctica</i> FSC022	158	254369498		
	<i>Francisella tularensis</i> subsp. <i>holarctica</i> FSC022	244	254369502		
	<i>Francisella tularensis</i> subsp. <i>holarctica</i> FSC022	292	254369497		
	<i>Francisella tularensis</i> subsp. <i>holarctica</i> FSC022	393	254369499		
	<i>Francisella tularensis</i> subsp. <i>holarctica</i> FSC022	501	254369496		
	<i>Francisella tularensis</i> subsp. <i>holarctica</i> LVS	158	89256630		
	<i>Francisella tularensis</i> subsp. <i>holarctica</i> LVS	393	89256631		
	<i>Francisella tularensis</i> subsp. <i>holarctica</i> URFT1	53	290953529		
	<i>Francisella tularensis</i> subsp. <i>holarctica</i> URFT1	285	290953528		
	<i>Francisella tularensis</i> subsp. <i>tularensis</i> SCHU S4	1123	56707712		
	<i>Gemella haemolysans</i> M341	1258	329766883		
	<i>Haemophilus pittmaniae</i> HK 85	121	343519651		
	<i>Haemophilus pittmaniae</i> HK 85	203	343519677		
	<i>Haemophilus pittmaniae</i> HK 85	650	343519679		
	<i>Helicobacter hepaticus</i> ATCC 51449	131	32266975		
	<i>Helicobacter pullorum</i> MIT 98-5489	344	242308998		
	<i>Helicobacter pullorum</i> MIT 98-5489	702	242309214		
	<i>Kingella kingae</i> ATCC 23330	1000	333374624		
	<i>Lactobacillus buchneri</i> ATCC 11577	1239	227512703		
	<i>Lactobacillus casei</i> 21/1	234	417984225		
	<i>Lactobacillus casei</i> 21/1	1128	417984226		
	<i>Lactobacillus casei</i> CRF28	566	417994652		
	<i>Lactobacillus casei</i> CRF28	700	417993346		
	<i>Lactobacillus casei</i> UW1	315	418005912		
	<i>Lactobacillus casei</i> UW1	330	418005913		
	<i>Lactobacillus casei</i> UW1	412	418005908		
	<i>Lactobacillus casei</i> UW4	236	418008739		
	<i>Lactobacillus casei</i> UW4	330	418008740		
	<i>Lactobacillus crispatus</i> 214-1	534	293381764		
	<i>Lactobacillus crispatus</i> CTV-05	298	312978192		
	<i>Lactobacillus crispatus</i> FB049-03	206	423318602		
	<i>Lactobacillus crispatus</i> FB049-03	347	423318603		
	<i>Lactobacillus crispatus</i> FB049-03	857	423318600		
	<i>Lactobacillus crispatus</i> JV-V01	278	227878395		
	<i>Lactobacillus crispatus</i> JV-V01	544	227878705		
	<i>Lactobacillus crispatus</i> MV-1A-US	277	256850790		
	<i>Lactobacillus crispatus</i> MV-1A-US	538	256850346		
	<i>Lactobacillus crispatus</i> MV-3A-US	279	262048056		
	<i>Lactobacillus delbrueckii</i> subsp. <i>bulgaricus</i> 2038	544	385815564		
	<i>Lactobacillus delbrueckii</i> subsp. <i>bulgaricus</i> 2038	669	385815562		

Cluster ^a	Strain ^b	Cas9 length (aa)	Cas9 GI	Cas1 GI ^c	Subtype ^d
	<i>Lactobacillus iners</i> LactinV 09V1-c	255	309804524		
	<i>Lactobacillus iners</i> LactinV 09V1-c	343	309804534		
	<i>Lactobacillus iners</i> LactinV 09V1-c	447	309804536		
	<i>Lactobacillus iners</i> SPIN 2503V10-D	270	309809475		
	<i>Lactobacillus iners</i> SPIN 2503V10-D	667	309809480		
	<i>Lactobacillus ruminis</i> ATCC 25644	1352	417973941		
	<i>Lactobacillus salivarius</i> ACS-116-V-Col5a	629	301299400		
	<i>Lactobacillus salivarius</i> CECT 5713	897	385839899		
	<i>Lactobacillus salivarius</i> UCC118	1149	90961083		
	<i>Leptospira inadai</i> serovar Lyme str. 10	125	398345609		
	<i>Leptospira inadai</i> serovar Lyme str. 10	418	398341884		
	<i>Leptospira inadai</i> serovar Lyme str. 10	907	398345610		
	<i>Leuconostoc pseudomesenteroides</i> 4882	468	399517481		
	<i>Leuconostoc pseudomesenteroides</i> 4882	883	399517482		
	<i>Listeria ivanovii</i> FSL F6-596	232	315301622		
	<i>Listeria ivanovii</i> FSL F6-596	849	315301624		
	<i>Listeria monocytogenes</i> FSL F2-208	782	422410878		
	<i>Listeria monocytogenes</i> FSL J1-208	300	255024093		
	<i>Listeria seeligeri</i> FSL N1-067	874	313631816		
	<i>Listeria seeligeri</i> FSL N1-067	874	422420175		
	<i>Maritimibacter alkaliphilus</i> HTCC2654	997	84685065		
	<i>Mycoplasma iowae</i> 695	226	350547050		
	<i>Mycoplasma iowae</i> 695	933	350546886		
	<i>Neisseria lactamica</i> ATCC 23970	408	269215119		
	<i>Neisseria lactamica</i> ATCC 23970	666	269215120		
	<i>Neisseria lactamica</i> Y92-1009	241	422110930		
	<i>Neisseria lactamica</i> Y92-1009	828	422110931		
	<i>Neisseria meningitidis</i> NM3001	67	421568320		
	<i>Neisseria meningitidis</i> NM3001	976	421568319		
	<i>Neisseria mucosa</i> C102	220	319639577		
	<i>Neisseria</i> sp. oral taxon 20 str. F0370	392	429743981		
	<i>Neisseria</i> sp. oral taxon 20 str. F0370	701	429743980		
	<i>Neisseria subflava</i> NJ9703	587	284799897		
	<i>Nitritalea halalkaliphila</i> LW7	79	390445315		
	<i>Nitrobacter hamburgensis</i> X14	641	92118334		
	<i>Oribacterium sinus</i> F0268	653	227873236		
	<i>Parabacteroides merdae</i> ATCC 43184	103	154493351		
	<i>Parabacteroides merdae</i> CL03T12C32	84	423346601		
	<i>Parabacteroides merdae</i> CL09T00C40	82	423723156		
	<i>Pasteurella bettyae</i> CCUG 2042	398	387770127		
	<i>Pasteurella bettyae</i> CCUG 2042	610	387770112		
	<i>Pasteurella multocida</i> subsp. <i>multocida</i> str. Anand1_buffalo	199	421253447		
	<i>Pasteurella multocida</i> subsp. <i>multocida</i> str. Anand1_cattle	53	421259752		
	<i>Pasteurella multocida</i> subsp. <i>multocida</i> str. Anand1_cattle	63	421259756		
	<i>Pasteurella multocida</i> subsp. <i>multocida</i> str. Anand1_cattle	134	421259749		
	<i>Pediococcus acidilactici</i> 7_4	1229	270290729		
	<i>Pediococcus lolii</i> NGRI 0510Q	270	427443367		
	<i>Pediococcus lolii</i> NGRI 0510Q	1016	427441502		
	<i>Peptoniphilus</i> sp. oral taxon 386 str. F0131	1341	299144352		
	<i>Porphyromonas catoniae</i> F0037	211	429741290		
	<i>Porphyromonas catoniae</i> F0037	1009	429741242		
	<i>Prevotella denticola</i> F0289	1218	327314511		
	<i>Prevotella disiens</i> FB035-09AN	443	303235616		
	<i>Prevotella disiens</i> FB035-09AN	795	303237415		
	<i>Prevotella melaninogenica</i> D18	1354	288802595		
	<i>Prevotella multiformis</i> DSM 16608	129	325268382		
	<i>Prevotella multiformis</i> DSM 16608	535	325268383		
	<i>Prevotella oulorum</i> F0390	691	345881543		
	<i>Prevotella oulorum</i> F0390	774	345881542		
	<i>Prevotella saccharolytica</i> F0055	242	429739781		
	<i>Prevotella</i> sp. oral taxon 317 str. F0108	593	288929745		
	<i>Prevotella</i> sp. oral taxon 317 str. F0108	1174	288930149		

Cluster ^a	Strain ^b	Cas9 length (aa)	Cas9 GI	Cas1 GI ^c	Subtype ^d
	<i>Prevotella</i> sp. oral taxon 472 str. F0295	241	260910968		
	<i>Prevotella</i> sp. oral taxon 472 str. F0295	992	260910970		
	<i>Pseudoramibacter alactolyticus</i> ATCC 23263	586	315926102		
	<i>Pseudoramibacter alactolyticus</i> ATCC 23263	770	315926103		
	<i>Rhizobium etli</i> GR56	103	218671711		
	<i>Riemerella anatipestifer</i> ATCC 11845 = DSM 15868	1145	383485594		
	<i>Sphingobacterium spiritivorum</i> ATCC 33300	116	227540450		
	<i>Sphingobacterium spiritivorum</i> ATCC 33300	1306	227540451		
	<i>Staphylococcus massiliensis</i> S46	475	425737243		
	<i>Staphylococcus massiliensis</i> S46	581	425737242		
	<i>Staphylococcus simulans</i> ACS-120-V-Sch1	1112	410878248		
	<i>Streptococcus agalactiae</i> 18RS21	773	76799343		
	<i>Streptococcus downei</i> F0415	994	312866154		
	<i>Streptococcus dysgalactiae</i> subsp. <i>equisimilis</i> SK1249	538	417753185		
	<i>Streptococcus dysgalactiae</i> subsp. <i>equisimilis</i> SK1250	1155	417926916		
	<i>Streptococcus mutans</i> SA38	1229	449253007		
	<i>Streptococcus mutans</i> SA38	1229	449880497		
	<i>Streptococcus oralis</i> SK255	550	417794716		
	<i>Streptococcus oralis</i> SK255	670	417793840		
	<i>Streptococcus pseudoporcinus</i> SPIN 20026	1326	313890160		
	<i>Streptococcus pyogenes</i> M49 591	1052	56808315		
	<i>Streptococcus sanguinis</i> VMC66	1167	323351495		
	<i>Streptococcus</i> sp. BS35b	93	401683465		
	<i>Streptococcus</i> sp. GMD4S	206	419816637		
	<i>Streptococcus</i> sp. GMD4S	317	419819606		
	<i>Streptococcus thermophilus</i> CNCM I-1630	302	418027683		
	<i>Streptococcus thermophilus</i> CNCM I-1630	595	418027684		
	<i>Streptococcus thermophilus</i> MTCC 5461	39	445389093		
	<i>Streptococcus vestibularis</i> F0396	97	312863468		
	<i>Streptococcus vestibularis</i> F0396	1038	312863582		
	<i>Sutterella parvirubra</i> YIT 11816	406	378822098		
	<i>Sutterella parvirubra</i> YIT 11816	951	378821855		
	<i>Sutterella wadsworthensis</i> 2_1_59BFAA	389	422348538		
	<i>Tannerella</i> sp. 6_1_58FAA_CT1	976	365118488		
	<i>Treponema denticola</i> ATCC 33520	631	449107910		
	<i>Treponema denticola</i> ATCC 33520	769	449107911		
	<i>Treponema denticola</i> F0402	357	422340642		
	<i>Treponema denticola</i> F0402	370	422340641		
	<i>Treponema denticola</i> F0402	631	422340640		
	<i>Treponema phagedenis</i> F0421	591	320536383		
	<i>Treponema phagedenis</i> F0421	738	320536384		
	<i>Treponema vincentii</i> ATCC 35580	281	257456747		
	<i>Treponema vincentii</i> ATCC 35580	992	257456748		
	uncultured bacterium	600	406975829		
	uncultured bacterium	1017	406999582		
	uncultured bacterium T3_7_42578	675	411001094		
	uncultured Termite group 1 bacterium phylotype Rs-D17	166	189485058		
	uncultured Termite group 1 bacterium phylotype Rs-D17	1032	189485225		
	<i>Verminephrobacter aporrectodeae</i> subsp. <i>tuberculatae</i> At4	983	347820874		

^aCas9 sequences are grouped according to the BLASTClust clustering program. Truncated sequences were not selected for the clustering and are listed at the bottom of the table without any cluster number (see Materials and Methods).

^bBacterial strains harboring a *cas9* orthologous gene are listed; GI, GenInfo Identifier. Bold, cluster representatives chosen for the alignment and tree reconstruction (Supplementary Figures S1 and S2). Grey, discarded, incomplete Cas9 sequences (see Materials and Methods). Note that the incomplete sequences were all confirmed to be truncated Cas9 orthologs based on the presence of conserved motifs and/or similarity to other Cas9 orthologs.

^cCas1 GenInfo Identifier of the representative sequences chosen for the alignment and tree reconstruction are given (Supplementary Figures S2 and S3). Grey, discarded, incomplete sequences. Whenever possible, an alternative Cas1 sequence from the same cluster as that of the discarded Cas1 sequence was selected (clusters 8, 9 and 21, in bold).

^dSubtype of the CRISPR-Cas loci belonging to a same Cas9 cluster as inferred from the representative Cas1 and Cas9 tree topology.

227494853 *Actinomyces coleoscanis* DSM 15436#
227824983 *Coriobacterium glomerans* FW2
303229466 *Acidimandibularium* sp. D21
303229466 *Veillonella atypica* ACS-134-V-Col7a
374362592 *Fusobacterium nucleatum* ATCC 49256
374307738 *Filifactor aloccis* ATCC 35896
320528778 *Solobacterium moorei* F0204
291520705 *Coprococcus catus* GJ-7
42525843 *Tronema denitratia* ATCC 35405
304338954 *Peptoniphilus durdenii* ATCC BAA-1640
224543312 *Catenibacterium mitsukoi* DSM 15897
116628213 *Streptococcus thermophilus* LMD-9
24379809 *Streptococcus mutans* UA159
13622193 *Streptococcus pyogenes* SF370
310286728 *Bifidobacterium bifidum* S17
42525843 *Streptococcus kitasatoii* ATCC 17330
422848106 *Streptococcus sanguinis* SK49
339625081 *Fructobacillus fructuosus* KCTC 3544
306281691 *Eubacterium yurii* ATCC 43715
336394882 *Lactobacillus farcininus* KCTC 3681
324363801 *Staphylococcus pseudintermedius* ED99
389815359 *Planococcus antarcticus* DSM 14505
336394882 *Planococcus ammannus* ATCC 35896
169823755 *Finogoldia magna* ATCC 29328
Jnet
227501312
47458868 *Mycoplasma mobile* 163K
284931710 *Mycoplasma gallisepticum* str. F
71894592 *Mycoplasma synoviae* 53
363542550 *Mycoplasma ovipneumoniae* SC01
363542550 *Mycoplasma pneumoniae* SC01
238924075 *Eubacterium rectale* ATCC 33656
315149830 *Enterococcus faecalis* XJ0012
116627542 *Streptococcus thermophilus* LMD-9
315659848 *Staphylococcus lugdunensis* M23590
160915782 *Eubacterium dolichum* DSM 3991
325677756 *Ruminococcus albus* 8
374362592 *Streptococcus thermophilus* LMD-9
336393381 *Lactobacillus coryniformis* KCTC 3535
310780384 *Llyobacter polytropus* DSM 2926
301311869 *Bacteroides* sp. 20 3
385811609 *Ignavibacterium album* JCM 16511
60683389 *Bacteroides fragilis* NCTC 9343
319957206 *Nitratifactor saluspinis* DSM 16511
187250660 *Elusimicrobium minutum* Pe191
325972003 *Sphaerochaeta globus* str. Buddy
296446027 *Methylosinus trichosporium* Ob3b
374362497 *Flavobacterium branchiophilum* Fl-15
345885718 *Prevotella* sp. c561
282880052 *Prevotella timonensis* CRIS 5C-B1
312879015 *Aminomonas paucivirans* DSM 12260
340089611 *Paracoccus luteus* ATCC 35461
330828845 *Alicyclyphillus denitrificans* K601
344171927 *Ralstonia szygii* R24
159042956 *Dinoroseobacter shibae* DFL 12
83591793 *Rhodospirillum rubrum* ATCC 11170
288957741 *Azospirillum* sp. B510
442729481 *Cenozoopirillum salinarum* AK4
92109252 *Nitrobacter hamburgensis* X14
148255343 *Bradyrhizobium* sp. B2A11
34557790 *Wolinella succinogenes* DSM 1740
218563121 *Campylobacter jejuni* NCTC 11168
218563121
Jnet
221276265 *Helicobacter mustelae* 12198
422109285 *Acidovorax ebbeus* TFSY
315605738 *Acidovorax* sp. oral 17FAA
220930482 *Clostridium cellulolyticum* H10
297182908 *uncultured delta proteobact.* HF000 07E19
154250555 *Parvibaculum lavamentivorans* DS-1
218767588 *Neisseria meningitidis* Z2491
156022992 *Pasteurella multocida* str. Em70
187736489 *Akkermansia muciniphila* ATCC BAA-835
315605738 *Actinomyces* sp. oral 17FAA
117929158 *Acidothermus cellulolyticus* 11B
189440764 *Bifidobacterium longum* DJO10A
403744858 *Alicyclobacillus hesperidum* URH17-3-68
403780669 *Alcanivorax* sp. W11-5
423317190 *Bergeyella zoohelium* ATCC 43767
282847315 *Porphyromonas* sp. oral tatum 279 str. F0450
42525843 *Francisella tularensis* str. Paris
374384763 *Odoribacter lanicus* YIT 12061
384109266 *Tronema* sp. JC4
402849997 *Rhodovulum* sp. PH10
331001027
Jnet
331001027 *Parasutterella excrementihominis* YIT 11859
345577932 *Wolinella succinogenes* DSM 1740
42525843 *Francisella tularensis* str. Paris
319941583 *Sutterella wadsworthensis* 3 1 45B
254447899 *gamma proteobact.* HTCC5015
118497352 *Francisella novicida* U112

Motifs
informative positions
5 RuvC I (RRR)

Supplementary Figure S2. Multiple sequence alignment of representative Cas9 sequences (following Table S2 and Material and Methods). The rows described as Jnet with following GI identifier of a selected Cas9 sequence provide the predicted secondary structure of Cas9 within the corresponding subgroups (sequences indicated below each Jnet). Conserved motifs are marked below the alignment and the mutated amino acid residues are highlighted. Asterisks indicate informative positions chosen for the Cas9 tree reconstruction.

227494853 Actinomyces colocoensis DSM 15436#
328956315 Coriobacterium glomerans FW2
227824983 Acidaminococcus sp. D21
303229466 Veillonella atypica ACS-134-V-Col7a
34762592 Fusobacterium nucleatum ATCC 49256
374307738 Filifactor alovis ATCC 35896
320528778 Coprobacterium moorei F0204
291520705 Symbiobacterium GD-7
42525843 Treponema denticola ATCC 35405
304438954 Peptoniphilus duerdenii ATCC BAA-1640
224543312 Catenibacterium mitsuokai DSM 15897
116628213 Streptococcus thermophilus LMD-9
24379809 Streptococcus mutans UA159
13622193 Streptococcus pyogenes SF370
310286728 Bifidobacterium bifidum S17
364983953 Omococcus kitaharae DSM 17330
422884106 Streptococcus sanguinis SK49
339625081 Fructobacillus fructosus KCTC 3544
306821691 Eubacterium yurii ATCC 43715
336394882 Lactobacillus farciminus KCTC 3681
323463801 Staphylococcus pseudintermedius EP99
389815359 Planococcus antarcticus DSM 14505
258509199 Lactobacillus rhamnosus GG
169823755 Finegoldia magna ATCC 29328
Jnet
227501312
47458868 Mycoplasma mobile 163K
284931710 Mycoplasma gallisepticum str. F
71894592 Mycoplasma synoviae 53
363542550 Mycoplasma canis SC01
384392826 Mycoplasma canis FC 14
238924075 Eubacterium rectale ATCC 33656
315149830 Enterococcus faecalis TX0012
116627542 Streptococcus thermophilus LMD-9
315659848 Staphylococcus lugdunensis M23590
160915782 Eubacterium dolichum DSM 3991
325677756 Ruminococcus albus 9
225377804 Roseburia inulinivorans DSM 16841
336393381 Lactobacillus coryniformis KCTC 3535
310780384 Ilyobacter polytropus DSM 2926
Bacteroides sp. 20 3
301311869 Ignavibacterium album JCM 16511
60683389 Bacteroides fragilis NCTC 9343
311987206 Nitrosifactor saulspis DSM 16511
187250660 Elusimicrobium minutum Pe191
325972003 Sphaerochaeta globus str. Buddy
296446027 Methylosinus trichosporium OB3b
347536497 Flavobacterium brachiophilum FL-15
345885718 Prevotella sp. C561
282880052 Prevotella limonenensis CRIS 5C-B1
312879015 Aminomonas pascuiphila DSM 12260
294086111 Candidatus Puniceispirillum marinum IMCC1322
330822845 Alicyclophilus denitrificans K601
344171927 Ralstonia syzygii R24
159042956 Dinoroseobacter shibae DFL 12
83591793 Rhodospirillum rubrum ATCC 11170
288957741 Azospirillum sp. B510
427429481 Caenospirillum salinarum AK4
92109262 Nitrobacter hamburgensis X14
148255343 Bradyrhizobium sp. BTA11
34557790 Wolinella succinogenes DSM 1740
218563121 Campylobacter jejuni NCTC 11168
Jnet
218563121
291276265 Helicobacter mustelae 12198
222109285 Acidovorax ebrensens TP5Y
365156657 Bacillus smithii 7 3 47FAA
220930482 Clostridium cellulolyticum H10
297182908 uncultured delta proteobact. HF0070 07E19
154250555 Parvibaculum lavamentivorans DS-1
218767588 Neisseria meningitidis Z2491
15602992 Pasteurella multocida str. Em70
347736489 Akkermansia muciniphila ATCC 2749-835
315605738 Actinomyces sp. oral taxon 180 str. F0310
117929158 Acidothermus cellulolyticus 11B
189440764 Bifidobacterium longum DJO10A
403744858 Alicyclobacillus hesperidum URH17-3-68
407803669 Alcanivorax sp. W11-5
423317190 Bergeyella zoohelium ATCC 43767
402847315 Parviphysomonas sp. oral taxon 279 str. F0450
404487228 Bacteriella intestinihominis YIT 11860
374384763 Odoribacter lanus YIT 12061
384109266 Treponema sp. JC4
402849997 Rhodovulum sp. PH10
Jnet
331001027
331001027 Parasutterella excrementihominis YIT 11859
Wolinella succinogenes DSM 1740
54296138 Legionella pneumophila str. Paris
319941583 Sutterella wadsworthensis 3 1 45B
254447899 gamma proteobact. HTCC5015
118497352 Francisella novicida U112

Motifs
Informative positions

E R

227494853 *Actinomyces coleocanis* DSM 15436#

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227824983 *Acidaminococcus* sp. D21

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374307738 *Filifactor aloicis* ATCC 35896

320528778 *Solobacterium moorei* F0204

291520705 *Coprococcus catus* GD-

42525843 *Treponema dentitcola* ATCC 35405

304438954 *Peptoniphilus duerdenii* ATCC BAA-1640

224543312 *Catenibacterium mitsuokai* DSM 15897

116628213 *Streptococcus thermophilus* LMD-9

24379809 *Streptococcus mutans* UAL159

13622193 *Streptococcus pyogenes* SF370

310286728 *Bifidobacterium bifidum* B17

366983953 *Streptococcus kitaharae* ATCC 17330

422884106 *Streptococcus sanguinis* SK49

339625081 *Fructobacillus fructosus* KCTC 3544

306821691 *Eubacterium yurii* ATCC 43715

336394882 *Lactobacillus farciminis* KCTC 3681

323463801 *Staphylococcus pseudintermedius* ED99

389815359 *Planococcus antarcticus* DSM 14505

408509195 *Lactobacillus tharogus* G6

169823755 *Finegoldia magna* ATCC 29328

Jnet 227501312

47458868 *Mycoplasma mobile* 163K

284931710 *Mycoplasma gallisepticum* str. F

71894592 *Mycoplasma synoviae* 53

363542550 *Mycoplasma ovipneumoniae* SC01

384393284 *Mycoplasma fermentans* 14

238924075 *Eubacterium rectale* ATCC 33656

315149830 *Enterococcus faecalis* TX0012

116627542 *Streptococcus thermophilus* LMD-9

315659848 *Staphylococcus lugdunensis* M23590

160915782 *Eubacterium dolichum* DSM 3991

325677756 *Ruminococcus albus* 8

225377804 *Roseburia inulinivora* DSM 16841

336393381 *Lactobacillus coryniformis* KCTC 3535

310780384 *Ilyobacter polytropus* DSM 2926

301311869 *Bacteroides* sp. 20 3

385811609 *Ignavibacterium album* JCM 16511

60683389 *Bacteroides fragilis* NCTC 9343

319957206 *Nitratifactor salisuginis* DSM 16511

187250660 *Elusimicrobium mitum* Pei191

325972003 *Sphaerochaeta globus* str. Buddy

296446027 *Methylosinus trichosporium* CB3b

347536497 *Flavobacterium branchiophilum* FL-15

345885718 *Prevotella* sp. C561

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294086111 *Cardiatus Functispirillum marinum* IMCC1322

330822845 *Alicyclophilus denitrificans* K601

344171927 *Ralstonia szygii* R24

159042956 *Dinoroseobacter shibae* DFL 12

83591793 *Rhodospirillum rubrum* ATCC 11170

288957741 *Azospirillum* sp. B510

427429481 *Caenispirillum salinarum* AK4

92109262 *Nitrobacter hamburgensis* X14

148255343 *Bradyrhizobium* sp. BTA11

34557790 *Wolinella succinogenes* DSM 1740

218563121 *Campylobacter jejuni* NCTC 11168

Jnet 218563121

291276265 *Helicobacter mustelae* 12198

222109285 *Acidovorax ebursus* TFSY

365156657 *Bacillus smithii* 7 3 47FAA

220930482 *Clostridium cellulolyticum* H10

297182908 *uncultured delta proteobact.* HF0070 07E19

154250555 *Parvibaculum lavamentivorans* DS-1

218767588 *Neisseria meningitidis* Z2491

15602992 *Pasteurella multocida* str. Pm70

187736489 *Akkermansia muciniphila* ATCC BAA-835

315605738 *Actinomyces* sp. oral taxon 180 str. F0310

117929158 *Acidothermus cellulolyticus* 11B

189440764 *Bifidobacterium longum* DJ010A

403744858 *Alicyclobacillus hesperidum* URH17-3-68

407803669 *Alcanivorax* sp. W11-5

423317190 *Bergeyella zoohelcum* ATCC 43767

282847315 *Porphyromonas* sp. oral taxon 279 str. F0450

404487228 *Francisella tularensis* YIT 11860

374384763 *Odoribacter laneus* YIT 12061

384109266 *Treponema* sp. Jc4

402849997 *Rhodovulum* sp. PH10

Jnet 331001027

331001027 *Parasutterella excrementihominis* YIT 11859

34557932 *Wolinella succinogenes* DSM 1740

54296128 *Levinsella pneumophila* str. Paris

319941583 *Sutterella wadsworthensis* 3 1 45B

254447899 *gamma proteobact.* HTCC5015

118497352 *Francisella novicida* U112

TSAARKAS-----GFE-----SR-----

SHDFAR-----ELV-----KC-----

SSDFRHEP-----GLV-----KS-----

VSDFRHNN-----NFI-----KV-----

ASSFREMP-----DFI-----KV-----

VSDFRKPL-----NYL-----KS-----

VSEFRNRKD-----KELP-----KF-----

VSNFRQTY-----ELL-----KV-----

VSMFRKPT-----DFV-----KC-----

ASRFRQEP-----DII-----KC-----

SHEFRVKN-----HIY-----KN-----

VSQFRKDF-----ELY-----KV-----

VSNFRKEF-----ELY-----KV-----

VSDFRKDF-----QFY-----KV-----

TREMHYLY-----GFS-----HK-----

TADMFRYV-----DII-----KC-----

ITNFRNTE-----HIA-----K-----

TADMRLLV-----GIK-----K-----

VSEFRHKEF-----ELF-----K-----

STAFRRKALSGQDDTYHFHFP-----ELV-----K-----

VSEFRKFF-----DIP-----K-----

VSKFRFFS-----ELP-----K-----

SQRLRQEL-----DFP-----KC-----

ASDLRQDM-----NTL-----KS-----

HHHHHH-----

TSNLRNQIAFVGIKNNKETEREW-KRPEGFK-----SI-----

TSFLRKNFD-----DSVYA-----KK-----

TSFLRKSMM-----RKN-----EE-----

TKYFRKPVQRKNGPNEN-----LNKK-----PE-----

TSFLRKNF-----SYDN-----K-----

THQMRGNL-----KLD-----KN-----

THTLRKKW-----GAD-----LD-----

TSQLRRHW-----GIE-----KT-----

TDYLRRKW-----KFK-----KE-----

TNAFRKRI-----NLK-----KD-----

TSMFRRW-----LN-----EK-----

TSYLRRKW-----GLM-----K-----

TSKLRSSW-----GFL-----KV-----

TAQLRARW-----RLN-----KV-----

TDRLKRDW-----GIN-----DVMNKIVLPRFIRL-----

TSELKITW-----GLN-----GVWKDLRPRFKRL-----

TDKLRDWD-----QLI-----DV-----M-----

TSKFRSLL-----GIK-----SK-----

TSFLRKNF-----GLM-----K-----

TSLLRKA-----NLQ-----GI-----

TDRLRRAW-----GLQ-----WM-----

VAEFRKII-----GIQ-----ES-----

TAKFRKIL-----GIQ-----SV-----

TAEFRKMW-----GLQ-----SE-----

TAFLRQKW-----GLH-----KN-----

TSFLRKNF-----GLM-----K-----

TALLRCKE-----GLN-----DV-----

TAMLRKAW-----GLN-----RV-----

TEMLRRHW-----GLN-----SL-----

TGLLRRAW-----DITTPGAPRDLPTPRDALRDDTAARRFLDGLTFFPLAKAVEGAVQ-----

TALLRRRW-----GID-----AI-----

ISRVFRVW-----GSVTMHLRQLLRQDRKNDYQTHHAEDACLLLAGFA-----

TSMLRKKW-----GLN-----K-----

TALLRATW-----ELN-----DL-----

TSVLRQW-----GLE-----SK-----

TSALRHTW-----GFS-----AK-----

HHHHHH-----

TSMRSFW-----GVO-----EK-----

TFLRARW-----GLT-----KV-----

TAMLRSSW-----DFN-----KN-----

TAQLRSSW-----GLN-----KN-----

TGYLRKOW-----GLE-----

TAQLRKLW-----TLN-----NI-----

TNLLRGFW-----GLR-----KV-----

TALLRSRW-----GLI-----KA-----

TAEVRKAW-----DVF-----GV-----

TACARRAK-----HVD-----KR-----

TAEARRWL-----DISIE-----RL-----

TASARRAA-----GIE-----GK-----

TAYMRARW-----GLT-----KD-----

TAELRRRW-----GLD-----TVIPOVRFESG-MPVVDEEGAEI-----TPEEFKFRLOWEGRVTRMRTDRR-----

TDYLRNHW-----GLT-----DKFKLLHERY-EALLESEKFLAEYDNYKDFDRKRKEYEKEVLFEBQELTREEPTKEYKENYIRYKKNKLIIGWS-----

TARLSRLW-----GYG-----KILHTLNLDRY-DSMGTERV-----SREGATEEELHTNWS-----

TKLRRKRW-----GND-----EVLHRLNDRY-KKVGTEVIEV-----NHSSVIRERQKWS-----

TAELRLHLW-----GLN-----NLQSAPDIFPLPVSAATENHREYVITNEQWIRLFRKQGETPRTEKCELLTGEVEKRVFKPCGMQEPQDVSQDKYWRRLKLSVSSVWSPLFAPKPIADGQIVLKGRIKGVFVNCQKQKLTGPDGYSMIL-----

TKLRDKW-----EMD-----

TGLLRARW-----GLN-----SIL-----

HHHHHH-----HHHHHHHHHHHH-----EEEEEE-----HHHHHHHHHHHH-----HEE-----

AMFVRSIF-SKVRQALAAWQETGNELIFDAISVPA-----ADSEMRKRPAEYRPEFRK-----

KYLAKIQ-EKLTML-----FNKHLSPFLADA-----TEVSELRQPARQNPFLAK-----

KFLSKRIM-EFLSTLA-----DSKQLQELFISQITP-----EVLHRLNDRY-KKVGTEVIEV-----NHSSVIRERQKWS-----

INMKLNLA-NKLRREEQNWCKTNNRHLFQAANTV-----SDAKNLRKLAQNQDFEK-----

AWLAKIA-SLLAEHL-----DKGRDYLSAHDIDP-----WSVSKQRKMLSAEPIWAK-----

RYFAEVLN-NNIYLRN-KKENLNTDKISFDYFGIPTGNG-----RGLAETRLQLEKVDSDIQAYAK-----

Motifs
informative positions

R

227494853 Actinomyces coelestis DSM 154366
329956315 Coriobacterium glomerans FW2
227824983 Acidaminococcus sp. D21
303229466 Veillonella atypica ACS-134-V-Col7a
34762592 Fusobacterium nucleatum ATCC 49256
374307738 Filifactor aloccis ATCC 35896
320528778 Solobacterium moorei F0204
321520705 Coprococcus catus G0-
42525843 Treponema dentale ATCC 35405
304438954 Peptoniphilus duerdenii ATCC BAA-1540
224543312 Catenibacterium mitsuoaii DSM 15897
116628213 Streptococcus thermophilus LMD-9
24379809 Streptococcus mutans UAl59
13622193 Streptococcus pyogenes SF370
310286728 Bifidobacterium bifidum B17
364983953 Clostridium kluyveri DSM 17330
422894106 Streptococcus sanguinis SK49
339625081 Fructobacillus fructosus KCTC 3544
306821691 Eubacterium yurii ATCC 43715
336394882 Lactobacillus farcinimus KCTC 3681
323463801 Streptococcus pseudintermedius ED99
389815359 Planococcus antarcticus DSM 14505
385691832 Lactobacillus helveticus G6
169823755 Finegoldia magna ATCC 29328
Jnet 227501312
47458868 Mycoplasma mobile 163K
284931710 Mycoplasma gallisepticum str. F
71894592 Mycoplasma synoviae 53
363542550 Mycoplasma pneumoniae SC01
384393286 Mycoplasma chlamydii F014
238924075 Eubacterium rectale ATCC 33656
315149830 Enterococcus faecalis TX0012
116627542 Streptococcus thermophilus LMD-9
315659848 Streptococcus lugdunensis M23590
160915782 Eubacterium dolichum DSM 3991
325677756 Ruminococcus albus 8
225377804 Roseburia inulinivans DSM 16841
336393381 Lactobacillus coryniformis KCTC 3553
310780384 Ilyobacter polytropus DSM 2926
301311869 Bacteroides sp. 20 3
385811609 Ignavibacterium album JCM 16511
60683389 Bacteroides fragilis NCTC 9343
319957206 Nitratifactor saaluginis DSM 16511
187250460 Elusimicrobium mitium Pei191
325972003 Sphaerochaeta globosa str. Buddy
296446027 Methylosinus trichosporium CB3b
347536497 Flavobacterium branchophilum FL-15
345858718 Prevotella sp. C561
282800052 Prevotella timonensis CRIS 5C-1
312879015 Aminomonas paucivorans DSM 12260
294086111 Clostridium butyricum DSM IMCC1322
330828245 Alicyclophillus denitrificans K601
344171927 Ralstonia syygii R24
159042956 Dinoroseobacter shibae DFL 12
83591793 Rhodospirillum rubrum ATCC 11170
288957741 Azospirillum sp. B510
427429481 Caenospirillum salinarum AK4
92109262 Nitrobacter hamburgensis X14
148255343 Bradyrhizobium sp. BTAA1
34557790 Wolinella succinogenes DSM 1740
218563121 Campylobacter jejuni NCTC 11168
Jnet 218563121
291276265 Helicobacter mustelae 12198
222109285 Acidovorax ebrewus TFSY
365156657 Bacillus smithii 7 3 47PA
220930482 Clostridium cellulolyticum H10
291782908 uncultured delta proteobact. HF0070 07E19
154255055 Parvibaculum lavamentivorans DS-1
218767588 Neisseria meningitidis Z2491
15602992 Pasteurella multocida str. Pm70
187736489 Akkermansia muciniphila ATCC BAA-835
315605738 Actinomyces sp. oral taxon 180 str. F0310
117929158 Acidothermus cellulolyticus 11B
189440764 Bifidobacterium longum DJo10A
403744858 Alicyclobacillus hesperidum URH17-3-68
Alcanivorax sp. W11-5
423317190 Bergyella zoohelcum ATCC 43767
402847315 Porphyromonas sp. oral taxon 279 str. F0450
404487228 Bartonella pneumophila str. Paris
374384763 Odoiribacter laneus YIT 12061
384109266 Treponema sp. Jc4
402849997 Rhodovulum sp. PH10
331001027 Jnet 331001027
331001027 Parasuterrella excrementihominis YIT 11859
34557932 Wolinella succinogenes DSM 1740
54296138 Lactonella pneumophila str. Paris
319941583 Sutterella wadswothensis 3 1 45B
254447899 gamma proteobact. HTCC5015
118497352 Francisella novicida U112

---TKLQMHVGDWSLVEIDRAST---FALWALCALTR---QPDFFWRQDGL---PANEEDRTIIVNGTHYGLDVRGVTF---GKAASALVVRGG---SVDIGISA
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KGETSNE1S1IKPKLYDGRDNKL---NEKYGYTS1KAAYF1VVEHEKNNK---KVKTFER1TRIDST1LNKEK1LK---KVKTFER1TRIDST1LNKEK1LK---KVKTFER1TRIDST1LNKEK1LK
---QNKNGNSVSLKGLD---VKYGGVFSANTYSFSLIEF---EDKGDNRARH---1IGVPIYIANN---ERSLETVYIK---DVELYLDQFIK---YCESV---LGLKEPQ
---VFKRGQFP1KQGRD---IEKYGVNKL5SAAF1FAVEYIGKRRAR---E1RTIETVPFL---Y1KQI0E1NH8E---SATQYLAQREKNDK---PEILLSEK
---MKRGQG1P1HGNDRLEAD---IEKYGVNKL5SAAF1FAVEYIGKRRAR---E1RTIETVPFL---Y1KQI0E1NH8E---SATQYLAQREKNDK---PEILLSEK
---MKRGQGF1P1HGNDRLEAD---IEKYGVNKL5SAAF1FAVEYIGKRRAR---E1RTIETVPFL---Y1KQI0E1NH8E---SATQYLAQREKNDK---PEILLSEK
---MRNGQT1P1KQENTNKSN---TSLYGGFSNKAFAV1VLESKQ---KTRLNVNMGQ---EYSLLDGRFSD---DELKRYLAKRKE---YARANIL
SNDHADHAGKVTAV1P1VFNKNSD---VHKYGGFSGLYQTVIAEGQKRRKQ---KTLVVKISGV1PLHKAASINEKI---KTLVVKISGV1PLHKAASINEKI---KTLVVKISGV1PLHKAASINEKI
---KPKNSNEMLVGAKEYL---PKYGGVYAG1SNSTFV1KGT1EIKG---AKK1TNVLEFQGIS1LDRINRYK---AKK1TNVLEFQGIS1LDRINRYK---AKK1TNVLEFQGIS1LDRINRYK
---LPGNSDKL1PRKTKFYWD---TKKYGGFSD1V1AVS1LVIADIEKG---KSKLKT1KVVLGV1T1EMKTFER---KSKLKT1KVVLGV1T1EMKTFER---KSKLKT1KVVLGV1T1EMKTFER
---LPKNSDKL1LARKDWD---PKYGGFSD1V1AVS1V1AVKVEKG---KSKLKS1V1KELLG1T1MERSSFEK---KSKLKS1V1KELLG1T1MERSSFEK---KSKLKS1V1KELLG1T1MERSSFEK
---ATDPKRG1FG1PFDGAKDQ---TSLYGGFSNKAFAV1VLESKQ---KTRLNVNMGQ---EYSLLDGRFSD---DELKRYLAKRKE---YARANIL
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Jnet 227501312
47458868 Mycoplasma mobile 163K
284931710 Mycoplasma gallisepticum str. F
71894592 Mycoplasma synoviae 53
363542550 Mycoplasma pneumoniae SC01
384393286 Mycoplasma chlamydii F014
238924075 Eubacterium rectale ATCC 33656
315149830 Enterococcus faecalis TX0012
116627542 Streptococcus thermophilus LMD-9
315659848 Streptococcus lugdunensis M23590
160915782 Eubacterium dolichum DSM 3991
325677756 Ruminococcus albus 8
225377804 Roseburia inulinivans DSM 16841
336393381 Lactobacillus coryniformis KCTC 3553
310780384 Ilyobacter polytropus DSM 2926
301311869 Bacteroides sp. 20 3
385811609 Ignavibacterium album JCM 16511
60683389 Bacteroides fragilis NCTC 9343
319957206 Nitratifactor saaluginis DSM 16511
187250460 Elusimicrobium mitium Pei191
325972003 Sphaerochaeta globosa str. Buddy
296446027 Methylosinus trichosporium CB3b
347536497 Flavobacterium branchophilum FL-15
345858718 Prevotella sp. C561
282800052 Prevotella timonensis CRIS 5C-1
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294086111 Clostridium butyricum DSM IMCC1322
330828245 Alicyclophillus denitrificans K601
344171927 Ralstonia syygii R24
159042956 Dinoroseobacter shibae DFL 12
83591793 Rhodospirillum rubrum ATCC 11170
288957741 Azospirillum sp. B510
427429481 Caenospirillum salinarum AK4
92109262 Nitrobacter hamburgensis X14
148255343 Bradyrhizobium sp. BTAA1
34557790 Wolinella succinogenes DSM 1740
218563121 Campylobacter jejuni NCTC 11168
Jnet 218563121
291276265 Helicobacter mustelae 12198
222109285 Acidovorax ebrewus TFSY
365156657 Bacillus smithii 7 3 47PA
220930482 Clostridium cellulolyticum H10
291782908 uncultured delta proteobact. HF0070 07E19
154255055 Parvibaculum lavamentivorans DS-1
218767588 Neisseria meningitidis Z2491
15602992 Pasteurella multocida str. Pm70
187736489 Akkermansia muciniphila ATCC BAA-835
315605738 Actinomyces sp. oral taxon 180 str. F0310
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Alcanivorax sp. W11-5
423317190 Bergyella zoohelcum ATCC 43767
402847315 Porphyromonas sp. oral taxon 279 str. F0450
404487228 Bartonella pneumophila str. Paris
374384763 Odoiribacter laneus YIT 12061
384109266 Treponema sp. Jc4
402849997 Rhodovulum sp. PH10
331001027 Jnet 331001027
331001027 Parasuterrella excrementihominis YIT 11859
34557932 Wolinella succinogenes DSM 1740
54296138 Lactonella pneumophila str. Paris
319941583 Sutterella wadswothensis 3 1 45B
254447899 gamma proteobact. HTCC5015
118497352 Francisella novicida U112

Motifs
informative positions

16130662 Escherichia coli str. K-12 substr. MG1655
11500011 Archaeoglobus fulgidus DSM 4304
18977490 Pyrococcus furiosus DSM 3638
46447796 Desulfovibrio vulgaris str. Hildenborough
54296139 Legionella pneumophila str. Paris
331001028 Parasutterella excrementihominis YIT 11859
319941582 Sutterella wadsworthensis 3 1 45B
118497353 Francisella novicida U112
34557933 Wolinella succinogenes DSM 1740
187736488 Akkermansia muciniphila ATCC BAA-835
407803668 Alcanivorax sp. W11-5
325972002 Sphaerochaeta globus str. Buddy
187250661 Elusimicrobium minutum Peil191
47458867 Mycoplasma mobile 163K
363542551 Mycoplasma ovipneumoniae SC01
71894593 Mycoplasma synoviae 53
384393287 Mycoplasma canis PG 14
284931711 Mycoplasma gallisepticum str. F
117929157 Acidothermus cellulolyticus 11B
317482065 Bifidobacterium sp. 12 1 47BFAA
315605739 Actinomyces sp. oral taxon 180 str. F0310
294086112 Candidatus Punciceispirillum marinum IMCC1322
282800533 Prevotella timonensis CRIS 5c-B1
374384762 Odoribacter lanus YIT 12061
423317188 Bergeyella zoohelcum ATCC 43767
385811610 Ignavibacterium album JCM 16511
402847305 Porphyromonas sp. oral taxon 279 str. F0450
345885719 Prevotella sp. C561
404487227 Barnesella intestihominis YIT 11860
301311870 Bacteroides sp. 20 3
60683388 Bacteroides fragilis NCTC 9343
402849966 Rhodovulum sp. PH10
154250554 Parvibaculum lavamentivorans DS-1
159042957 Dinoroseobacter shibae DFL 12
288957740 Azospirillum sp. B510
330822846 Alicyclophagus denitrificans K601
344171926 Ralstonia snyderii R24
319957207 Nitratifactor salusginis DSM 16511
315149831 Enterococcus faecalis TX0012
116627543 Streptococcus thermophilus LMD-9
238924076 Eubacterium rectale ATCC 33656
218563120 Campylobacter jejuni NCTC 11168
291276264 Helicobacter mustelae 12198
325677757 Ruminoecoccus albus 8
296446028 Methylosinus trichosporium OB3b
34557789 Wolinella succinogenes DSM 1740
222109284 Acidovorax ebrens TPSY
336393380 Lactobacillus coryniformis KCTC 3535
218767587 Neisseria meningitidis Z2491
15602991 Pasteurella multocida Pm70
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403744859 Alicyclobacillus hesperidum URH17-3-68
421874296 Brevibacillus laterosporus GI-9
220930481 Clostridium cellulolyticum H10
225377803 Roseburia inulinivorans DSM 16841
315659847 Staphylococcus lugdunensis M23590
160915783 Eubacterium dolichum DSM 3991
323463802 Staphylococcus pseudintermedius ED99
389815358 Planococcus antarcticus DSM 14505
328956316 Coriobacterium glomerans PW2
422884107 Streptococcus sanguinis SK49
116628212 Streptococcus thermophilus LMD-9
24379808 Streptococcus mutans UR159
13622194 Streptococcus pyogenes SP370
227824982 Acidaminococcus sp. D21
169823756 Finegoldia magna ATCC 29328
320528779 Solobacterium moorei F0204
303229394 Veillonella atypica ACS-134-V-Col7a
304438953 Peptoniphilus duerdenii ATCC BAA-1640
374307737 Fliifactor aloicis ATCC 35896
256845020 Fusobacterium sp. 3 1 36A2
306821690 Eubacterium yurii ATCC 43715
42525844 Treponema denticola ATCC 35405
291520706 Coprococcus catus GD-7
285809198 Lactobacillus rhamnosus GG
336394883 Lactobacillus farciminius KCTC 3681
339625080 Fructobacillus fructosus KCTC 3544
310286727 Bifidobacterium bifidum S17
366983954 Oenococcus oeni DSM 17330

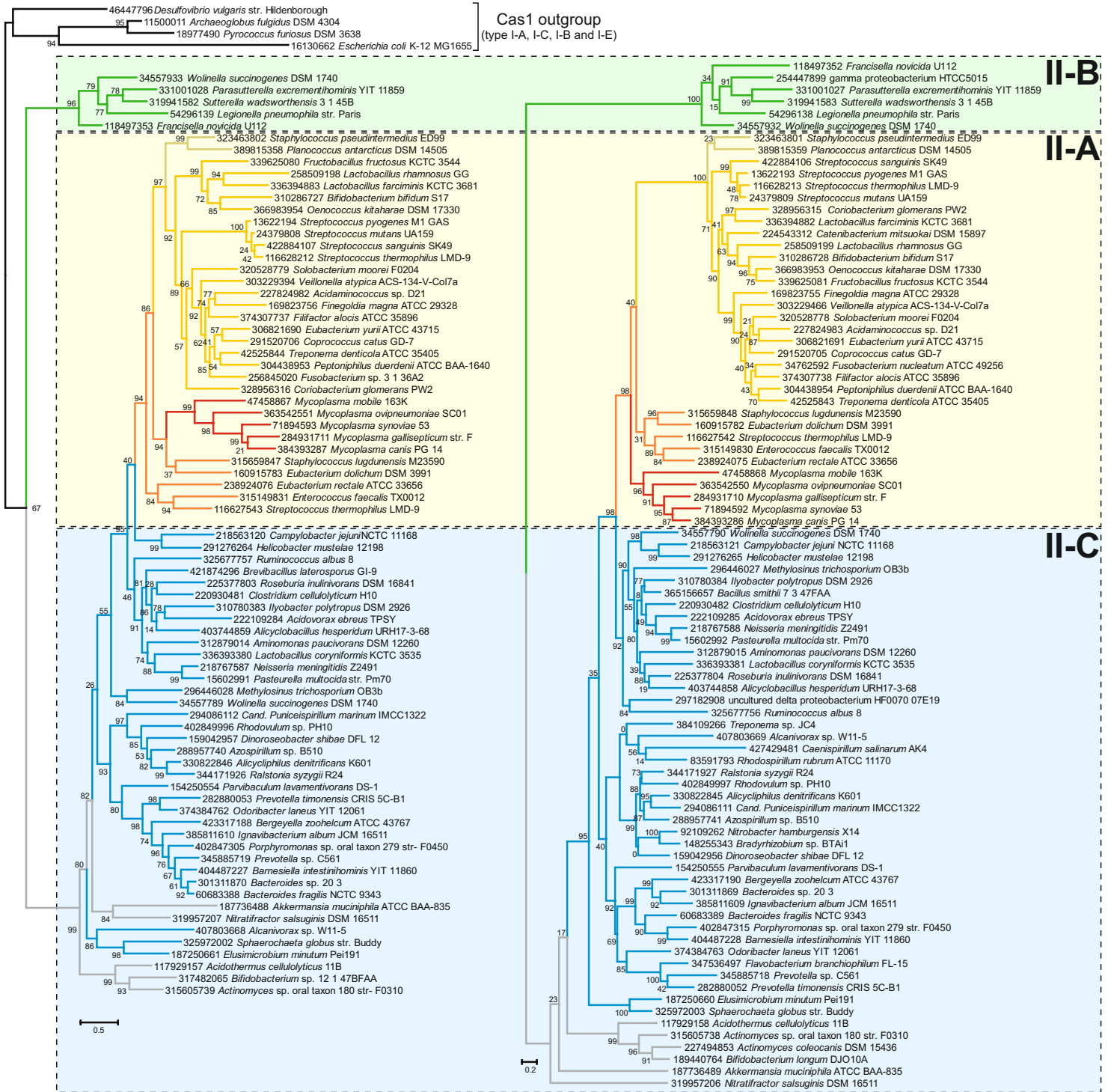
informative positions

S-----KTLAKLPLIEDVLAAGEIQPPAFPEDAQ---PVAIPLPVLGDAGHRSS-----
RLEKTVKHKLNKRVYSYQRIIRLECYKLVKHFVAKR---YSPFMMW-----
ELEKTVKHKPLKGVTRRIRLREYAKI IKHLVGVVE---YSLPVMV-----
RKQDEIVHPFLNKRIPGLVHFVQAMLMARLKGDLDD---GYP-PPVVK-----
PL-----PYHKRRISLESI IQRVQVYHLVAVFSGEK---YKGYLFWK-----
TMST--KINYSQKQCKLENALQRVQVYLKAGAVBEGR---YRGIRFKW-----
TMAN--AVSWGQKSVRLLENALQRAYRLAGTVVDGKR---YKSIKFRW-----
TIARKY--LYNGKRLKLEHI IQRVYLSGGFPAGEBN---YKPIYFKW-----
TMNK--KHLNKNRNLGQVMQRYVRLVGFAPQQR---YKSIYFKW-----
SV-----MYRDKQLPKAAVEAVCSFRKAVLAGQS---EYEPWLMATTIKWAG---
TV-----CLNGQDFRPLPAIRKTVASVYLRILEAGG---GRRRKLPEPCF---
EV-----VFEEQVDFSYALRVLVLSLPSLFRNRD---AIQFPKYRYAVAV---
NL-----YFEDGAPNLTAGIQKYQSYIAFLEREN---RIIFPAILK-----
KV-----IYKGYFYVNDFFDQIADNLVNRKSWVWV---ELWD-----
HI-----EYNGKRLKLEHI IQRVYLSGGFPAGEBN---YKPIYFKW-----
KI-----LHAKNSVSNVEYICKLEBNFVSNVYK---YKSIYFKW-----
KI-----AIKNTKLSVNEYIDKIVKSVINNNLICED---FIIKWS-----
FI-----FPNGKN--LNQVIDMLKAI INNKINERD---FNIDWS-----
QF-----DASGATVG--TAVERFAQQQVGRVVEGIR---SLRPAMPALSHA---
Q-----FNGSLGTPSSSLNDFAQQFGLYCEKGDID---RLQVEYVVGES---
-----RFDGQGHGIPVAEALAQSFGRVVEGGDID---RLCVLAWQSPSSVAVED---
-----AVVGRSIFLQRMSSQYSYLWNLNLDGKT---TMPMPQLPELEIAMVBSBC---
DP-----YFNVRPLPSVGLTMMVAQVYVYAKR---KISLPLLK-----
DT-----YFENTRPLMVLGSLQTLARCFSGEQK---KMVYEPFK-----
DV-----KIDQVRPLLVAVKSTVSSLKYCTYGEKR---QISYPKML-----
DV-----FIEQKRLPMIAVORTSSLAKCFSGNQK---KIIYVPFRL-----
DV-----EIEGQRPLMLAATQATSLRRCFTGEAR---RLAYPLLSCEPSA---
DV-----YIGGRSPLMIAAGLTASLAKCYNGEAR---EISYPSFL-----
EV-----GIQGRSPLMVAVAGTASLRCFNGELR---KIIYPSFL-----
EV-----KIQGRSPLMIAVAGTASLRCFNGELR---RIVYPSFL-----
EV-----IIGGRSPLMVAVAGTASLRCFNGELR---RISYPSFL-----
DF-----ATSDGRPLSNVLRARLAVLAQVTRERR---GLAFPETLVPPLTAEDDGSANETAHVAHVSDLV---
TV-----LVGGRMPLLLALHSAASLRCALTGGEA---ALALPEGMPLAPDLLNDGEG---
DL-----PLGDSLTPVSVVALGLAI SLGQSFESGTL---DLALPAPPDALTLAGLGA---
DM-----LTAQQTTPIGTVLIRLAGSLAQVVEGKG---DLDLPLALDRPAMPLEWPAAPPAGGETGC---
DM-----GTSVQVTPVPMQVRLCSLAQVLYGERT---KLELQGLPLALSSSESD---
DM-----PSPQITPVMQVRLCSLAQVLYGERK---ELEDLPLCTPDLAAMPVPLA---
EYL-----YDAGRSTLRTVATRYIQGFKAVRSRKI---ENLHFFITDFGALRECF---
KI-----KVNKLIYMQAMSEYVAAFVAMETGDF---ENVQKILHVNMLEGK---
KI-----KYGKETCSVTVAMDKYVKGFKYIKSEKDS---SKFPCPVSSLEWRK---
KI-----MYREKMYMCMNIENYIQOYASLIMKRTD---NIVFPDYNLIGEEYG---
PI-----NFDGQNYPLNRAIMHYVANFNKALLYEDE---LKIYFDD-----
KV-----LLQGRSPLMVAVAGTASLRCFNGELR---KLELQGLPLALSSSESD---
KI-----KMGKKTTRVRYADKYISLSLSAIEKNDP---GLLQPLTIQIDEMFEDDEDG---
NA-----RVGKEIVSLVASEKAEGLVQAMSGSA---AILKLPFFVTPKSSP---
SC-----IMTERYETLLSATQIIRLSLVSAGQKES---RRLI-LPVMGEDDVQGEVYEAADGV---
DV-----AMPGRQMSVLASIEQAASLRLVYDGGSE---QVLELPLRIGLRQVFEI---
EV-----RIDGEPHLSNAVHKLVSSTYTCRNNNSA---AGLKLPELIPVLAHEYE---
QT-----SIEQGHSTLAAIDKMSQFAGVTDKNA---KQLKLPPELPLKYEQYE---
QM-----SFQETFSVLAARIDRVGFSQALITPNA---NLLKLPPELPLKHEQYE---
DV-----KLTRKYSVNI SIDEVIKRYTKICRGGG---NLLPSIPIQEHRYV---
RM-----EIQGRHTLIRGTALCAEFGAAACREKNP---DLLALPALISPDG---
MV-----WLENERYDLTASIEAMVSSFNASTEDP---SALQPLRTEVQMGVYE---
QV-----ELEGRYSNRAIEEMKSYVTACTRSMY---ERLRTPLTLLKLIHSYE---
EC-----VFBGKI I IRSIAIEKVISFSSSCKANDY---SLLKLPPIPLVPHANE---
DM-----SVKDMRIVSNIDMLIASYSSALQGNRT---ELEDLPELQVPHSYE---
RI-----EIDKMGITIRAEIMIQSIIYFKNGHL---DIVKFNLRKQVYFEL---
KI-----EIDKGLQVFNANVEVSEILKVIETGKI---TDFKPSPHVDVYDL---
KL-----KIDNKYFVFNAVEIYVDSLKFKVLSNGNR---EVKIPWTYV---
KV-----QIRNSKQFLQAAVQVYLDLQVYLDGKH---EKLLFPILDFPKAR---
CI-----AYRDGYKTSVVISLVQDCLNANLKRKA---IDELDPPDIV---
TF-----HYNGKIDMYLSNIVSDYTKVVIQALNQPEK---GVPEFRI---
TV-----LYNGKEMVLSNIVSDYTKVVIQALNQPEK---EIPFRI---
TY-----LYNGKEMVLSNIVSDYTKVVIQALNQPEK---GVPEFRI---
TF-----SYNGKEMVLSNIVSDYTKVVIQALNQPEK---GVPEFRI---
IL-----YIDSRQFLANAIYANSIQALKEKCDT---SKIKIYEI---
EV-----FIGKTRYTLNANVEYCKSVFLALEKGE---QLKFDYEL---
KV-----SIMGREYMLNAIEIYVKSILDAISSENP---SLIKFVVEYFCTYESDVL---
DV-----KINDTIQTFSAARVYICKSVFDALVQAAA---NEIRFIEYEL---
FV-----TIDNKYCRINQALMIEYIRSVFDALNNDI---SLLRFPYSEL---
EV-----RIDKSVYVNNAKIKKISFEALHYETD---SYLKFYVTEL---
KF-----RINNHNHYSIDIKIYKISFDALSANDL---SLVRFPEDEL---
SV-----IINGRTEVLTNAVKIYCKSIFDALQKDI---SLIRFYNEF---
KV-----LNNKHYLNKAIIFVHSIFDALNEKDI---SQINRYNEL---
EV-----RIDGKQVYVNNAKIKKISFEALSDSDS---ALIRFYKIEL---
EI-----TFNGKALLQNAVADHVENCLAPLDGKAKVCRIVKFPDVEVSHANDHV---
EI-----SYGSKFTLKNALSQYIRCCSYLDSNQE---VELKQVGFDEE---
EI-----TMSKRELVQVQVYKQVCKYKLSGSDI---ELRMEFEL---
D-----VDELGTITITQISVFRDALRVLSEGEK---LPELGVRCQTELCF---
EV-----GYLQQTAVNSAIEYVRNADLVLCGRP---EVAVSVAI---

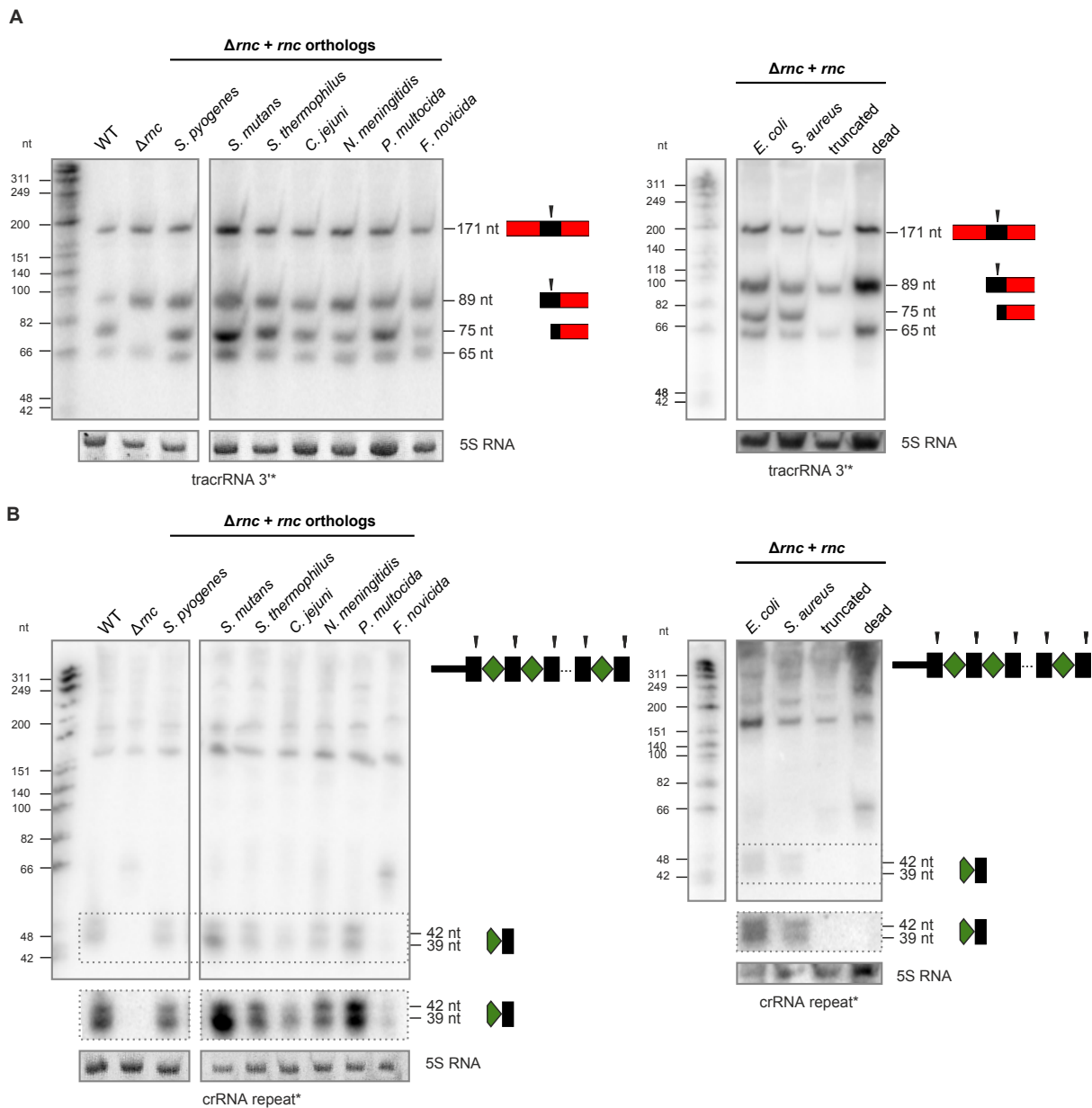
* *****

Cas1

Cas9



Supplementary Figure S4. Phylogenetic analysis of representative Cas9 and Cas1 sequences. Phylogenetic trees of Cas1 (left) and Cas9 (right) reconstructed from selected, informative positions of Cas1 and Cas9 multiple sequence alignments are shown (see Figure 1 and Supplementary Figures S2 and S3). The Cas1 tree is rooted to the outgroup of selected Cas1 orthologs of type I CRISPR-Cas systems. The Cas1 and Cas9 orthologs of the types classified as II-A, II-B and II-C are highlighted with shaded boxes. The same branch colors were used for each bacterial strain on both trees. Each protein is represented by the GenInfo (GI) identifier followed by the bacterial strain name. The bootstrap values are given for each node (see Materials and Methods). The scale bars for the branch length are given as the estimated number of amino acid substitution per site. Note the similarity of the trees topology and monophyletic clusters of subtypes II-A and II-B on both trees supported by high bootstrap values.



Supplementary Figure S5. RNase III is a general executioner of tracrRNA:pre-crRNA processing in type II CRISPR-Cas. Northern blot analysis of total RNA from *S. pyogenes* WT, Δrnc and Δrnc complemented with *rnc* orthologs or *rnc* mutants probed with (A) tracrRNA and (B) crRNA repeat (Supplementary Table S1). The dashed-line boxes represented below the Northern blots in (B) show the area of the blots with enhanced exposure. All RNase III orthologs can co-process *S. pyogenes* tracrRNA and pre-crRNA. No mature forms of tracrRNA and crRNAs could be observed in Δrnc complemented with the truncated version or catalytically inactive (dead) mutant of RNase III.

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*
15674631 Streptococcus pyogenes SF370 -----MKQLEELLSTSF-----DIQFNDLTLLETAFTHTSYANEHRLLNVSHNERLEPLGDAVLQLIISEYLFAPKPKTEGDMSKLRSMIVREESLAGFSRFCSDAYIKLGKGEKSGGRRRDTILGDLFEAFGLALLDQGLDAVR
24379904 Streptococcus mutans UA159 -----MKTLEKKLAEDF-----KIVFSDKELLETAFTHTSYANEHRLLNISHNERLEPLGDAVLQTIISHYLPDKYQKAEGLSKMRSMIVREESLAGFSRNCHFDRIYIKLGKGEKSGGRRDITILGDLFEAFGLALLDAGLKAVE
116628032 Streptococcus thermophilus LMD-9 -----MNLEQKLEQDF-----GIVFSDKLELLETAFTHTSYANEHRLLNISHNERLEPLGDAALQLVIVSVLYNRYPNKPEGEMSKMRSTIVREESLAGFTKACGFEQYIRLKGKGEKSGGRRERATILGDLWEAFGLALYLDQGLPAVE
57651802 Staphylococcus aureus COL -MSKQKKSEIVNRFKRFPDKMTELGFYQNIIDLYQQAFSHSSFINDFNMNRDLHNERLEPLGDAVLELTVSRVLPDKHPNLPENLTKMRATIVCEPSLVI FANKIGLNEMILLGKGEKSGGRRTRPRLISDAFEAFIGALYLDQGLDIWV
118498035 Francisella novicida U112 -----MVPEYSRFFYNIL-----GYNFKDYTLIRALTHRSTTK-----NYERLEPLGDSVLSFVIAEVLVYKQFTDLAEGKLSQLRSLKLVGTTLAQLASSLKMDEYIILGASEQ--GGHKREKILEDVFEAVIGAIYLDSDPATVK
218767809 Neisseria meningitidis Z2491 MKDDVLKQQAHAAIQKKL-----GYAFRDISLLRQALTHRSHAK-----HNERFEPVGD SILNYTVARMLPDAFPKLTTEGELSRLRASLVNEGVLAEMAEMNVGDGLYL GAGELKSGGFRPRLADAMEAMFAVVSFDADFNAT
15601926 Pasteurella multocida Pm70 -----MTQNLERLQRQI-----GYQFNQFALLKQALTHRSAVK-----HNERLEPLGDAILNFIIEAALYHQFPKCNEGELSRMRATLVREPTLASLARQFELG DYLSLGPGEKSGGFRRESILADCV EAIIGAI SLDSDLATTT
218563224 Campylobacter jejuni NCTC 11168 -----MKNIEKLEQSL-----TYEFKDKNLLIHALTHKSPKKS-----NNERLEPLGDAVLDLVVGEYLFHKFAKDAEGDLSKLRALVNEKSFAKIANSNLNGDFILMSVAEENNGGKPKSILSDAEAIIGAIHLEAGFEFAK
16130492 Escherichia coli K-12 -----MNPIVINRLEQRKL-----GYTFNHQELLQALTHRSAVK-----HNERLEPLGDSILSYVIANALYHRPPRVDEGDMSTRMATLVRGNTLAE LAREFELGECLELRGPGEKSGGFRRESILADTVEALIGGVFLDSDIQTVE

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Motifs [_____ Cutting domain _____]

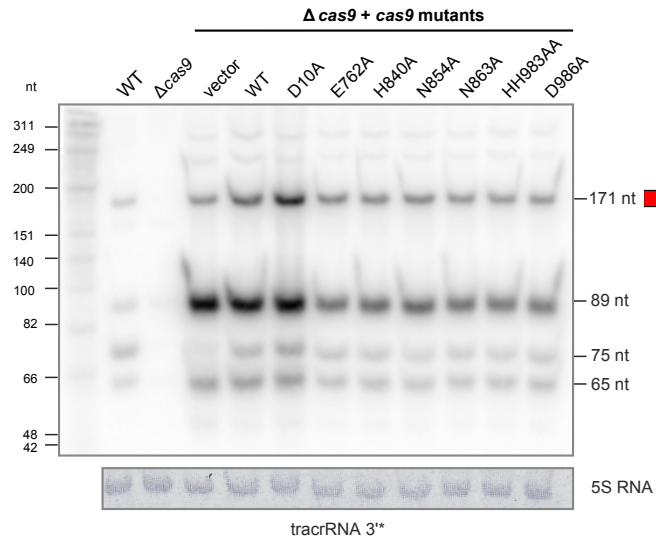
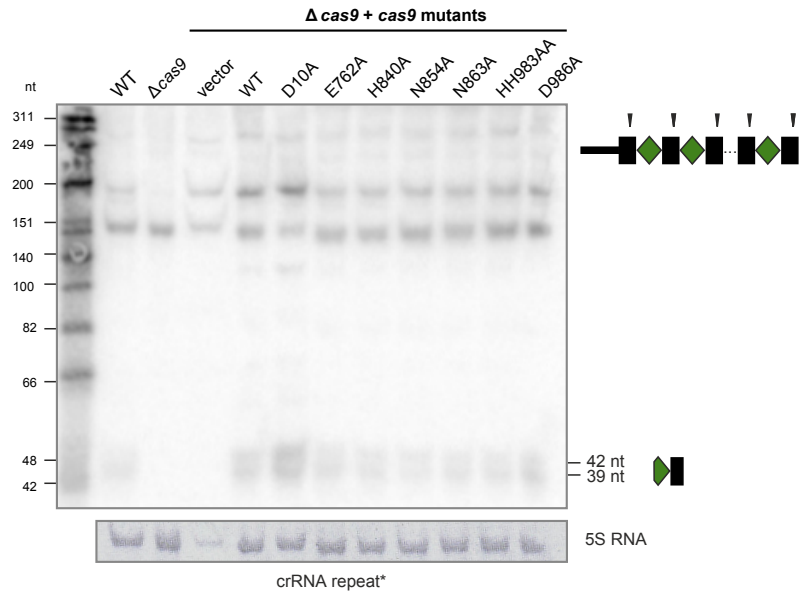
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15674631 Streptococcus pyogenes SF370 RFLKQVMIPQVEKGNFE--RVKDYKTCLEFLQTKGDAIDYQVISEKGAHAKQFEVSI VVNG-AVLSKGLGKSKKLAEQDAAKNALAQ LSEV-----
24379904 Streptococcus mutans UA159 AFLNQVVI PKVENNNYE--RVTDYKTALQELLQVDGDLIDYEVLKE SGPAAKCFEVAVSMNH-EKLSSTGKSKKLAEQEAAKNAL EKLQGRS-----
116628032 Streptococcus thermophilus LMD-9 KFLNQVMIPQVEKGNFD--RVIDYKTALQERLQVNGKVDITYTVIDESGPAHAKFEFTMQVAVDG-KELSTGFGKSKKLAEQAAKSALEQLGN-----
57651802 Staphylococcus aureus COL KFAEKVIFPHVEQNELL--GVVDFKTFQFQYVHQNKQNGDVTYNIKEEGPAHHR LFTSEVILQG-EAIAEGKGTKKESQRAAESAYKQLKQIK-----
118498035 Francisella novicida U112 KVILKWPQI IISSINLDTIKVKDSKSKLQEI LLQNALSLPEYSIETIDGKDHEQQFTVAMSKDLNLRVKAQGT SRKKAQEQA AEKMIEMLSQQGLHEKK--
218767809 Neisseria meningitidis Z2491 KVVRLHFAERVRRVDFQN-QAKDGKTALQEALQARRPALPKYRIEEQIGHANDS MFVISC DLGELGPFVCRAGT SRKKAQEQA AEKAEKALWLEEKLP LK KKKK
15601926 Pasteurella multocida Pm70 KIVQHWYQAQLKIQPGD-NQKDKPTRLQEYLQGRRLPLPTYNVVEIKGEAHCQTF TVECYVKNIDRTFMGSGASRRKAEQA AAEKILQLLEMK-----
218563224 Campylobacter jejuni NCTC 11168 TIALRLIEKNFPQIDAKI-LIKDYKTKLQEIITQGGIGQTPQYETVRAF GPDLKQFBIALMLDG-KELARAIAGSKKEAQQMAAKIALEKLGAL-----
16130492 Escherichia coli K-12 KLILNWPQTRLDEISPGD-KQKDKPTRLQEYLQGRHLPLPTYL VVQVGEAHDQEFTHCQVSGLS EFPVVTGSSRRKAEQA AAEQALKKLELE-----

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Motifs [_____ dsRNA binding domain _____]

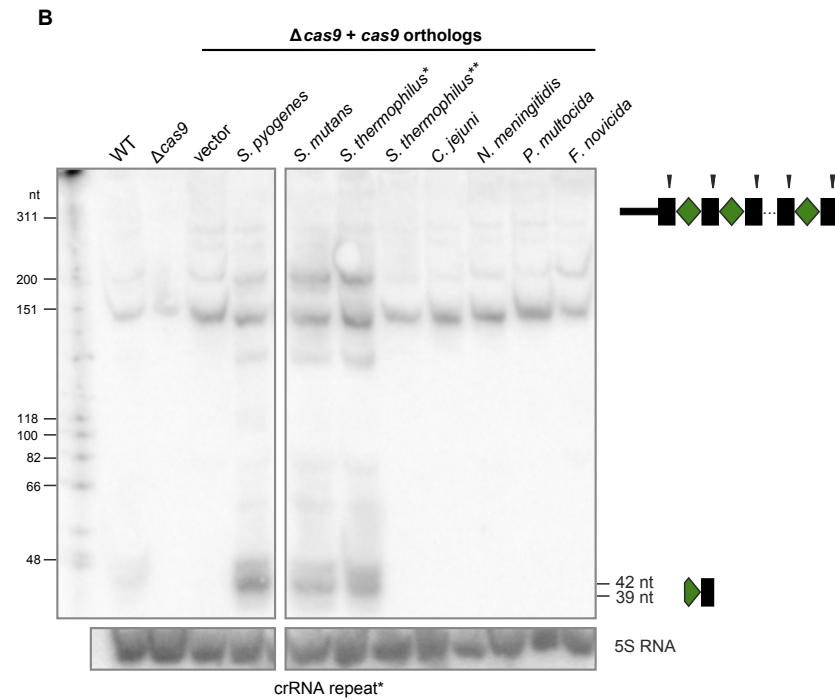
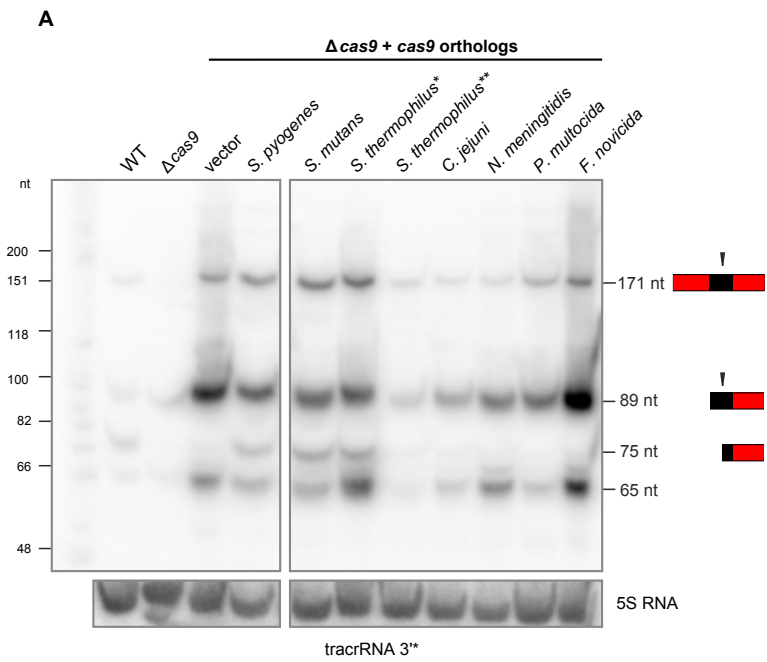
Supplementary Figure S6. Multiple sequence alignment of bacterial endoribonucleases III used in the study. Domains indicated below the alignment are according to the domains identified in RNase III from *E. coli* (58, 59). The conserved catalytic aspartate residue mutated in the catalytically inactive “*mc dead*” mutant and the last amino acid of the truncated *mc* mutant are indicated above the alignment with an asterisk and an arrow, respectively.

A**B**

Supplementary Figure S7. Conserved catalytic amino acid residues of Cas9 are not involved in dual-RNA processing by RNase III. Northern blot analysis of total RNA extracted from *S. pyogenes* WT, $\Delta cas9$ and $\Delta cas9$ complemented with pEC342 (backbone vector containing tracrRNA-171 nt and the native *cas* operon promoter from *S. pyogenes*) or pEC342-derived plasmids encoding Cas9 WT or mutants, hybridized with (A) tracrRNA or (B) crRNA repeat probe (Supplementary Table S1). tracrRNA:crRNA co-processing is observed in all strains encoding Cas9 point mutants. Note that in a previous study, we observed low abundance of tracrRNA in the *cas9* deletion mutant (16). For this reason, plasmids used in *cas9* complementation studies were designed to encode tracrRNA in addition to *cas9*.

Supplementary Figure S8. Cas9 and tracrRNA:crRNA co-evolved.

Northern blot analysis of total RNA extracted from *S. pyogenes* WT, $\Delta cas9$ and $\Delta cas9$ complemented with pEC342 or pEC342-derived plasmids encoding Cas9 WT or mutants, hybridized with (A) tracrRNA or (B) crRNA repeat probe (Supplementary Table S1). Only *S. pyogenes* Cas9 WT and closely related Cas9 orthologs from *S. mutans* and *S. thermophilus** (CRISPR3) can contribute to co-processing of *S. pyogenes* tracrRNA:pre-crRNA.



Supplementary Table S3. Overview of type II CRISPR-Cas spacer sequences from selected bacterial strains with BLAST candidate protospacers and their downstream sequence.

Strain ^a	Number of spacers	CRISPR Spacer ^b	Spacer sequence	Blast candidate ^c	% Identity ^d	10 bp downstream protospacer ^e	
<i>Streptococcus pyogenes</i> SF370 (Accession: NC_002737)	1		TGC GCTGGTTGATTTCTTCTTGC GCTTTTT	<i>S. pyogenes</i> MGAS1882 (MGAS1882_1116), MGAS8232 (spyM18_0769), MGAS10394 (M6_Spy0995, M6_Spy1349), SSI-1 (SPs0926), ΦP9 endopeptidase gene	100	TGGCTTTTTTC	
				<i>S. pyogenes</i> MGAS2096 (MGAS2096_Spy1450), A20 (A20_1472c), M1 476 (M1GAS476_1503), MGAS9429 (MGAS9429_Spy1426), MGAS5005 (M5005_Spy1424) endopeptidase gene	97	TGGCTTTTTTC	
				<i>S. pyogenes</i> M1 GAS (SPy_0700), MGAS2096 (MGAS2096_Spy0592) endopeptidase gene	97	TTGCTTTTTTC	
				<i>S. pyogenes</i> MGAS6180 (M28_Spy1234); NIH1 (NIH1.1_43), SSI-1 (SPs0647), MGAS315 (SpyM3_0930, SpyM3_1215) phage related gene	100	TGACTTTTTTC	
	6	2		TTATATGAACATAACTCAATTTGTA AAAAA	gene for pyrogenic exotoxin M (<i>speM</i>) of several Streptococci strains	100	GGCTATTGGG
					<i>S. pyogenes</i> MGAS8232 (spyM18_0742), MGAS10750 (MGAS10750_Spy0588), MGAS10270 (MGAS10270_Spy0563) adenine specific methylase gene	100	TGGTATGTTG
					<i>S. pyogenes</i> Manfredo (SpyM50653) adenine specific methylase gene	97	TGGTATGTTG
					<i>S. pyogenes</i> Alab49 (SPYALAB49_001176), MGAS10750 (MGAS10750_Spy1285), MGAS9429 (MGAS9429_Spy0843), MGAS10394 (M6_Spy1203), SSI-1 (SPs0763), MGAS315 (SpyM3_1101), ΦH4489A (<i>hylP</i>) hyaluronoglucosaminidase gene	100	TGGCGCATT A
4		AGTGCCGAGGAAAAATTAGGTGCGCTTGCC	<i>S. pyogenes</i> MGAS8232 (spyM18_1254), NZ131 (Spy49_0785) hyaluronoglucosaminidase gene	97	TGGCGCATT A		

Strain ^a	Number of spacers	CRISPR Spacer ^b	Spacer sequence	Blast candidate ^c	% Identity ^d	10 bp downstream protospacer ^e
		5	TAAATTTGTTTTAGCAGGTAAACCGTGCTTT	<i>S. pyogenes</i> MGAS10750 (MGAS10750_Spy0839), MGAS10270 (MGAS10270_Spy0546, MGAS10270_Spy0804), SSI-1 (SPs0517, SPs0888), MGAS1882 (MGAS1882_1156), MGAS8232, NZ131(Spy49_1511c), MGAS315 (SpyM3_0965, SpyM3_1347) phage protein gene or intergenic region	100	TGGTTATAATC
<i>Streptococcus mutans</i> UA159 (Accession: NC_004350)	5	3	CTAACTATGATGACACAACAGCTTTTAGCG	ΦM102 (orf13) putative tail protein gene	100	TTGAAATTC
<i>Streptococcus mutans</i> LJ23 (Accession: NC_017768)	8	2	TGAAGTGCAAGCTTACGTGACTGACTCGCG	ΦM102 (orf15) putative minor structural protein	90	AGGTATGCAG
<i>Streptococcus mutans</i> GS-5 (Accession: NC_018089)	21	3	TAATAGCAATCGTGACGGACGTATTGATTT	ΦM102 (orf15) putative minor structural protein	97	AGGTGAAATT
		5	GTTGAGTGCAACAGCTAGCTAATAGCTTTT	ΦM102	100	AGGCTGGCAC
		16	AGGCATTTTCTGATTGAGATTTTCGATATT	ΦM102 (orf3) putative large terminase gene	93	TGGAAAGATG
		18	TATAGCTAATATGTGTATACTGACAGCGCA	ΦM102 (orf7) putative DNA packaging protein gene	100	AGAAAGATTG
<i>Streptococcus mutans</i> NN2025 (Accession: NC_013928)	69	2	GATTGTGCCCGCTAGTAAACCGCCTCGCGC	ΦM102 (orf20) putative endolysin gene	93	TGCAGATTTG
		6	GATTGTATCAGTAATCGAACTTCTGCTTAT	ΦM102 (orf38, orf39) hypothetical protein gene	93	GGGATTTGAC
		8	TGGTCCAAAGTGCAGAGCCAAAGAAAAACA	ΦM102 (orf11) putative major tail protein gene	97	AACCGGTCTT
		9	ATTGTCAATCGCCGTTCTGCGCTTGCACG	ΦM102 (orf17) hypothetical protein gene	90	CGGTTTTGAA
		17	GCTTGAATATAATTGTGTATCCGCAATGA	ΦM102 (orf21) putative replisome organizer gene	93	CGAATTACGA

Strain ^a	Number of spacers	CRISPR Spacer ^b	Spacer sequence	Blast candidate ^c	% Identity ^d	10 bp downstream protospacer ^e
		23	AAAAAGAAACGCCTTTTGATTGACCAATC	ΦM102 (orf14) putative receptor-binding protein gene	90	AAGCAAGA
		29	AGTTATTAATATCTATGACAGTCTCAAAGA	ΦM102 (orf14) putative receptor-binding protein gene	93	GGCTACAGA
		37	TTCTGGCTGTCTTTCAGAGTGATAAGCGCA	ΦM102 (orf2) putative small terminase gene	100	GGATTTTCA
		40	TGCAAGTTATCTTGCTATGTGGACGAATTG	ΦM102 (orf9) hypothetical protein gene	93	GGAAACAATC
		43	GCAATTTAGTTTTATTCCGTGGGAGCAGCA	ΦM102 (orf3) putative large terminase gene	93	AGGCTCCATT
		48	AGAGTATAGCCAGTGTTCACAGGCTTTTA	ΦM102 (orf12) putative tape measure protein gene	93	GTGGTGACAA
		49	CGCAACAATGACTATTAATATCAACGGTGG	ΦM102 (orf15) putative minor structural protein gene	93	CGGAGCAAT
		56	AATCGCTTCTTTGCTAACCACAATTTGTGC	ΦM102 (orf26) putative RecT family single-strand annealing protein gene	93	AGGCGCAGAG
		60	AAATGCTCTTGAAGAACCTGATAGATGACA	ΦM102 (orf3) putative large terminase gene	93	GAGACGAAAA
		66	TGCAAAAGATGGCCTCGAGCAATTATCGCA	ΦM102 (orf33) hypothetical protein gene	100	TGGATTAAGC
<i>Streptococcus thermophilus</i> LMD-9 CASS4 locus (Accession: NC_008532)	8	2	TCAATGAGTGGTATCCAAGACGAAACTTA	<i>Streptococcus thermophilus</i> plasmid pSt106 putative resolvase gene	100	TGGCAAGTT
		3	CCTTGTCGTGGCTCTCCATACGCCATATA	<i>Streptococcus thermophilus</i> plasmid pND103	100	AGGGCGGGT
		4	TGTTTGGGAAACCGCAGTAGCCATGATTAA	Φ7201 (orf33)	100	AGGTCTCGCT

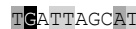

Strain ^a	Number of spacers	CRISPR Spacer ^b	Spacer sequence	Blast candidate ^c	% Identity ^d	10 bp downstream protospacer ^e	
<i>Streptococcus thermophilus</i> LMD-9 CASS4a locus (Accession: NC_008532)	5		ACAGAGTACAATATTGTCCTCATTGGAGACAC	Φ TP-J34 (orf11) hypothetical protein gene	94	TGGGCTAGGA	
				ΦSfi19 (orf1626) minor tail protein gene	100	TGGTGCTAAT	
	6		CTCATATTCGTTAGTTGCTTTTGCATAAA	ΦYMC 2011 (Ssal_phage00063) putative minor tail protein gene	90	GGGTGCTAAC	
				Φ7201 (orf33)	90	TGGTGCTAGA	
	2		CTTCACCTCAAATCTTAGAGCTGGACTAAA	Φ7201 (orf39)	100	GTAGAAATAGA	
	3		ATGTCTGAAAATAACCGACCATCATTACT	Φ TP-J34 (orf49), ΦSfi11 (orf669) putative minor structural protein gene	93	CCAGAAATGTC	
	4		GAAGCTCATCATGTTAAGGCTAAAACCTAT	ΦALQ13.2 (orf35) helicase gene	90	CTAAAAATTA	
	16				ΦSfi11 (orf443), ΦSfi18 (orf443), ΦSfi21 (orf443), ΦSfi19 (orf443), ΦO1205 (orf10) putative helicase gene	90	CTCAAAATTA
					Φ1033, Φ 1042 nonfunctional host specificity protein gene	97	ATAAAATTCATCA
					ΦDT1.1 (orf18), ΦDT1.2 (orf18), ΦDT1.3 (orf18), ΦDT1.4 (orf18), ΦDT1.5 (orf18), ΦMD4 (orf18) host specificity protein gene	93	ATAAAATTCATCA
					pSt08 plasmid	97	CCGAAAAATA
					ΦALQ13.2 (orf25), Φ858 (orf30), ΦST3 (orf253) endonuclease gene	90	TGAAAAATTA
	7				ΦJ1 (orf253), ΦS3b (orf253) endonuclease gene	90	TGAAAGATTA
13						AACTACCAAGCAAATCAGCAATCAATAAGT	ΦSfi11

Strain ^a	Number of spacers	CRISPR Spacer ^b	Spacer sequence	Blast candidate ^c	% Identity ^d	10 bp downstream protospacer ^e
				ΦYMC-2011 (Ssal_phage00051) predicted clp-protease gene	93	TTAAGAACAT
				ΦSfi21 (orf221) clp-protease gene	90	TCAAAGAATAT
				Φ858 (orf22)	93	AAAAAAACT
		16	AACAGTTACTATTAATCACGATTCCAACGG	Φ2972 (orf21) structural protein gene	93	AAAAAAACT
				ΦAbc2 (orf17) tail protein gene	93	TAAAAAGACT
<i>Campylobacter jejuni</i> subsp. <i>jejuni</i> NCTC 11168 (Accession: NC_002163)	5	1-5		no significant BLAST hits		
<i>Campylobacter jejuni</i> subsp. <i>jejuni</i> CF93-6 (Accession: AANJ00000000)	5	3	TCATCATCACTTAAACCTTAAATTTACC	<i>C. jejuni</i> RM1221 (CJE1445) hypothetical protein gene	93	ATAACGCAAG
<i>Campylobacter jejuni</i> subsp. <i>jejuni</i> HB93-13c_jejuni_subsp_jejunihb_13_42 (Accession: AANQ00000000)	9	1	GCATTGCTTTACTACATAGCCAGTCGTGTA	<i>C. jejuni</i> subsp. <i>doylei</i> 269.97 (JJD26997_1148) conserved hypothetical protein gene	100	TCACACACGC
<i>Campylobacter jejuni</i> subsp. <i>jejuni</i> NW	5	2	TTATTTTTGTCGCTAATTGCACCTAAAGAC	<i>C. jejuni</i> subsp. <i>doylei</i> 269.97 (JJD26997_0867) putative primase gene	97	TCCAACACAT

Strain ^a	Number of spacers	CRISPR Spacer ^b	Spacer sequence	Blast candidate ^c	% Identity ^d	10 bp downstream protospacer ^e
genomic scaffold Mich_State_Univ:Contig3 (Accession: JH376989 REGION: 13521..15062)		5	GGGACACGAGGAATCCTGTCTGAATCCGGG	<i>C. jejuni</i> subsp. <i>jejuni</i> PT14 (A911_r08426, A911_r08428, A911_r08430), NCTC 11168-BN148 (BN148_r02, BN148_r05, BN148_r08), S3 (CJS3_1811, CJS3_1817, CJS3_1830), ICDCCJ07001 (ICDCCJ07001_29, ICDCCJ07001_396, ICDCCJ07001_718), M1 (CJM1_0031, CJM1_0413, CJM1_0727), IA3902 (CJSA_Cj23SA, CJSA_Cj23SB, CJSA_Cj23SAC), BABS091400, 81116 (C8J_Cj23SA, C8J_Cj23SB, C8J_Cj23SC), 81-176 (CJJ81176_1714, CJJ81176_1727, CJJ81176_1707), NCTC 11168; <i>C. jejuni</i> DSM 4688, UNSW091300, strain 100, RP0001, 102-27 (rrlC, rrlB, rrlA), 69-30 (rrlC, rrlB, rrlA), 140-16 (rrlC, rrlB, rrlA), 110-21 (rrlC, rrlB, rrlA), RM1221 (CJE_Cj23SA, CJE_Cj23SB, CJE_Cj23SC), TGH9011_ATCC43431 (rrl); <i>C. coli</i> 59-2 (rrlC, rrlB, rrlA); <i>C. jejuni</i> subsp. <i>doylei</i> 269.97 (JJD26997_0040, JJD26997_1264, JJD26997_1520) 23S rRNA gene	100	TCGACCACGA
<i>Campylobacter jejuni</i> subsp. <i>doylei</i> 269.97 (Accession: NC_009707)	5	2	CTAAGCAATCTTATTTTACCATCTTTTTTA	<i>C. jejuni</i> strain TGH 9011 (Tgh093) <i>C. jejuni</i> RM1221 (CJE1099) hypothetical protein gene	97 93	TAAACACTT TAAACACTT
<i>Campylobacter jejuni</i> subsp. <i>jejuni</i> 1336 (Accession: NZ_CM000854 NZ_ADGL01000000)	2	1	TTACTGATATTAATAAATAACTCCATAATTT	<i>C. jejuni</i> 00-3477 (cje0227), <i>C. jejuni</i> subsp. <i>jejuni</i> S3 (CJS3_0723), ΦCGC-2007 prophage related genes	100	GCTGCCATTA
		2	ATAAAGCTAATGCAAAAGTTGAAAACAAA	<i>C. jejuni</i> NCTC 13255 (putative CJIE1-2-like prophage), 99-7046 (putative CJIE1-3-like prophage), 00-2425 (putative CJIE1 prophage), RM1221 (CJE0227) <i>C. jejuni</i> subsp. <i>jejuni</i> ICDCCJ07001 (ICDCCJ07001_691) major tail sheath protein	93	GCTGCCATTA
		2	TTTATCTGCATCCATAATGGCAATGAGTGA	<i>C. jejuni</i> NCTC 13255 (putative CJIE1-2-like prophage), 99-7046 (putative CJIE1-3-like prophage), 00-3477 (putative CJIE1-4 Mu-like prophage), 00-2425 (putative CJIE1 prophage), RM1221 (CJE0238), <i>C. jejuni</i> subsp. <i>jejuni</i> S3 (CJS3_0704), ICDCCJ07001, <i>C. hyoilei</i> hypothetical protein gene	100	AGAGCTATAA
<i>Campylobacter jejuni</i> subsp. <i>jejuni</i> 414 (Accession: NZ_CM000855 NZ_ADGM01000000)	33	2	TTTATCTGCATCCATAATGGCAATGAGTGA	<i>C. jejuni</i> subsp. <i>jejuni</i> PT14 (A911_03310), NCTC 11168-BN148 (BN148_0680c), S3 (CJS3_0675), ICDCCJ07001 (ICDCCJ07001_619), M1 (CJM1_0650), IA3902 (CJSA_0644), 81116 (C8J_0632), 81-176 (CJJ81176_0703), NCTC 11168 (Cj0680c), P694a (Cj0680c), P569a (Cj0680c), P179a (Cj0680c), H73020 (Cj0680c), H704a (Cj0680c), <i>C. jejuni</i> RM1221 (CJE0778), <i>C. jejuni</i> subsp. <i>doylei</i> 269.97 (JJD26997_1327) excinuclease ABC subunit B gene	97	AACTTCAGGC

Strain ^a	Number of spacers	CRISPR Spacer ^b	Spacer sequence	Blast candidate ^c	% Identity ^d	10 bp downstream protospacer ^e
<i>Neisseria meningitidis</i> serogroup A strain Z2491 (Accession: NC_003116)	2		CTTCTGCCTTTTTACAAGCTCGCTTTCTTT	<i>N. gonorrhoeae</i> (NGU65994, PivNG), FA 1090 (NGO1137, NGO1164, NGO1262) invertase related genes, phage associated protein genes	97	CGCCGACCGG
				<i>N. meningitidis</i> NZ-05/33 (NMBNZ0533_1722), M04-240196 (NMBNZ0533_1722), M01-240149 (NMBH4476_1701), H44/76 (NMBH4476_1701) hypothetical proteins upstream of transposase gene	100	GTCTGATTTT
	3		TTTGGTAAAGGTTTCTGTTGCGACCCGAAT	<i>N. lactamica</i> isolate 3207487 (plasmid pNL3.2), <i>N. lactamica</i> (plasmid pNL9)	97	GTCTGATTTT
				<i>N. gonorrhoeae</i> TDCD-NG08107, NCCP11945 intergenic region (putative phage proteins)	93	GGCTGTTTTT
				<i>N. gonorrhoeae</i> NCCP11945 (NGK_1948, NGK_1990, NGK_2023) hypothetical protein genes	93	GTCTGATTTT
				<i>N. gonorrhoeae</i> intergenic region PivNG	93	GTCTGATTTT
				<i>N. gonorrhoeae</i> FA 1090 numerous intergenic regions in prophages	93	GTCTGATTTT
				<i>N. gonorrhoeae</i> TDCD-NG08107, <i>N. gonorrhoeae</i> NCCP11945 intergenic region (putative phage proteins)	97	GGACGATTTT
	7		AAATTCGTTTCAGATAGCAAACGCAGTAGT	<i>N. lactamica</i> plasmid pNL9	93	TGCGGCCATA
				<i>N. meningitidis</i> plasmid pJS-B	100	TACGAACATT
	12		GGGTAGCCAGTGCTAAAACCGCACCCGCTT	<i>N. lactamica</i> plasmid pNL9	93	AGCTGCTTTG
				<i>N. meningitidis</i> plasmid pJS-B	97	AGCCGCTTTG
	13		CCAAATAGAAATACATACGCCGAGTAATTA	<i>N. lactamica</i> plasmid pNL9	93	AGCTGCTTTG
				<i>N. meningitidis</i> plasmid pJS-B	97	AGCCGCTTTG
14		TTTCTTTTTGTAATTGTTCTGCCTTTTTTA	<i>N. lactamica</i> plasmid pNL9	100	ATTGGATTTT	

Strain ^a	Number of spacers	CRISPR Spacer ^b	Spacer sequence	Blast candidate ^c	% Identity ^d	10 bp downstream protospacer ^e
				<i>N. meningitidis</i> plasmid pJS-B	100	ATTGGATTIT
		15	TACCCACGGCGGAAACCATTGCCACAAAAC	<i>N. meningitidis</i> strain alpha522 draft genome (NMALPHA522_0671), H44/76 (NMBH4476_0684), 053442 (NMCC_0153), <i>N. meningitidis</i> serogroup C FAM18 (NMC1864) hypothetical protein gene	100	CCATGATTAC
				<i>N.meningitidis</i> M04-240196 (NMBM04240196_0048, NMBM04240196_0749) putative membrane protein gene	100	CCATGATTAC
<i>Pasteurella multocida</i> str. Pm70 (Accession: NC_002663)	5	1-5		no significant BLAST hits		
<i>Pasteurella multocida</i> subsp. <i>gallicida</i> X73 (Accession: CM001580 AMBP01000000)	20	9	AAAGAATACACCCCTTATTCCAAAAAGTTTG	<i>P. multocida</i> 1.8 kb plasmid	100	GCGACAGATG
		15	GTCTGAACAGTATTAACTTCCTGTTTCT	<i>P. multocida</i> subsp. <i>multocida</i> str. HN06(PMCN06_2098) hypothetical protein gene	97	GATGCTACT
<i>Francisella tularensis</i> subsp. <i>novicida</i> U112 (Accession: NC_008601)	13	1-13		no significant BLAST hits		
<i>Francisella novicida</i> FTG FTG_scaffold1 genomic scaffold (Accession: NZ_DS995363 NZ_ABXZ01000000)	22	15	ATCTCAAAGCAGCTCTTTCGCGTGTAATATCGTT	<i>F. cf. novicida</i> 3523 (FN3523_1002) phage protein gene	91	TGGATTAGAT
		19	CTATCTAAGAGAACTTACAAGACAAGAGAAAATACT	<i>F. cf. novicida</i> 3523 (FN3523_0993) hypothetical protein gene	94	TGGTGGTAAA
<i>Francisella tularensis</i>	10	2	AGCCCTATCAGAAATATATGCAAGTTTGAATATAG	<i>F. cf. novicida</i> 3523 (FN3523_1009) phage-related baseplate assembly protein gene	89	AGGTTGTAGC

Strain ^a	Number of spacers	CRISPR Spacer ^b	Spacer sequence	Blast candidate ^c	% Identity ^d	10 bp downstream protospacer ^e
subsp. <i>novicida</i> GA99-3548 supercont1.3 (Accession: DS264589 ABAH01000000)	3		AGATAACTCTTATATTGATTTGTATATTGAAGATA	<i>F. cf. novicida</i> 3523 (FN3523_1006) hypothetical protein gene	94	
	4		CGCAAAAAGGCGAATTTGAGCAGAAAATTTGGGC	<i>F. cf. novicida</i> 3523 (FN3523_0999) hypothetical protein gene	91	

^aSelected strains used in this study. No potential protospacers were found for *Streptococcus mutans* UA159, *Campylobacter jejuni* subsp. *jejuni* NCTC 11168, *Pasteurella multocida* str. Pm70 and *Francisella tularensis* subsp. *novicida* U112. Therefore, closely related strains were analyzed for the presence of type II CRISPR-Cas arrays. Spacer sequences from selected arrays were then used to search for protospacer candidates.

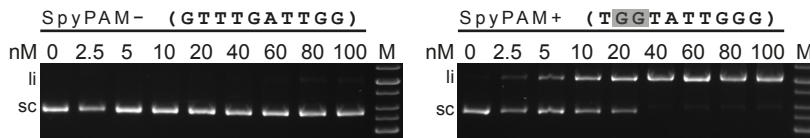
^bNumbering of spacers starts from the leader proximal end based on RNAseq data (15). Spacers with no significant protospacer BLAST hit are not listed in the table.

^cA BLAST candidate was considered a potential protospacer when the identity to the spacer was $\geq 90\%$ and when the protospacer originated either from phage, plasmid or genomic DNA related to the analyzed species. For each identified protospacer, the strain name, the protospacer-containing gene locus and the potential function of the gene are given.

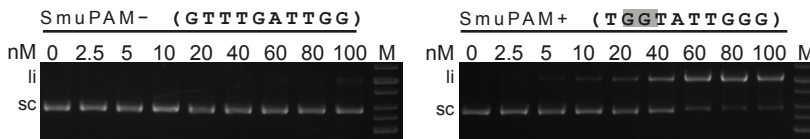
^dPercentage identity between spacer and protospacer sequence.

^e10 nt sequence located directly 3' of the protospacer sequence. The identified sequences for each bacterial species were aligned using GeneDoc (<http://www.nrbsc.org/gfx/genedoc/>). The degree of conservation is indicated with a color code (black: 100%, dark grey: $\geq 80\%$, light grey: $\geq 60\%$). These sequences were used to create the logo plot represented in Figure 5.

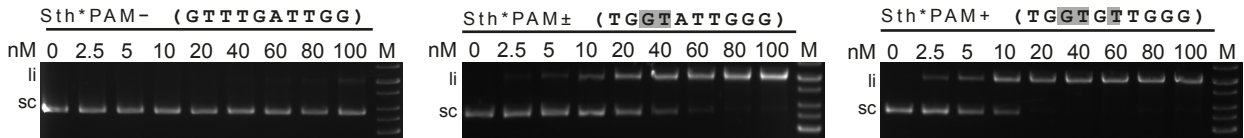
■ ***S. pyogenes* dual-RNA:Cas9**



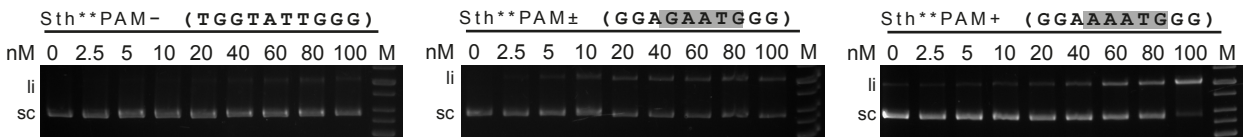
■ ***S. mutans* dual-RNA:Cas9**



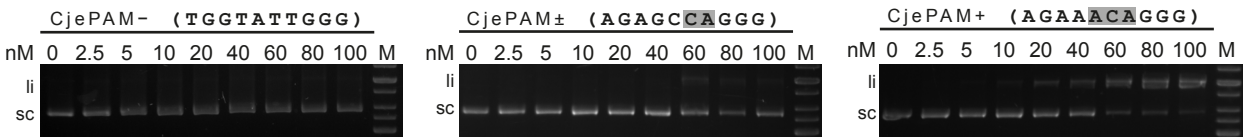
■ ***S. thermophilus** dual-RNA:Cas9**



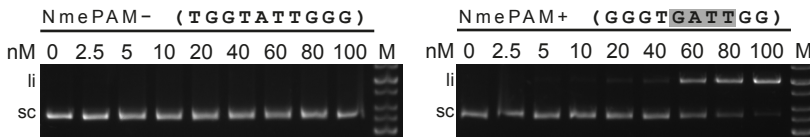
■ ***S. thermophilus*** dual-RNA:Cas9**



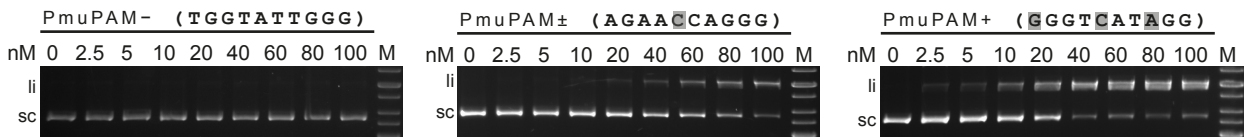
■ ***C. jejuni* dual-RNA:Cas9**



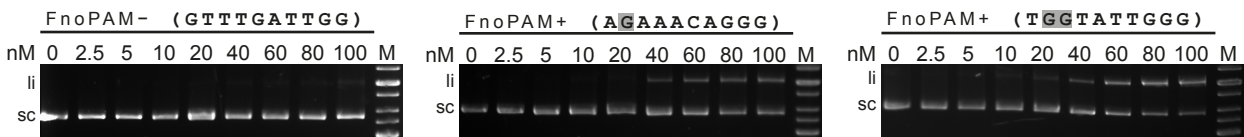
■ ***N. meningitidis* dual-RNA:Cas9**



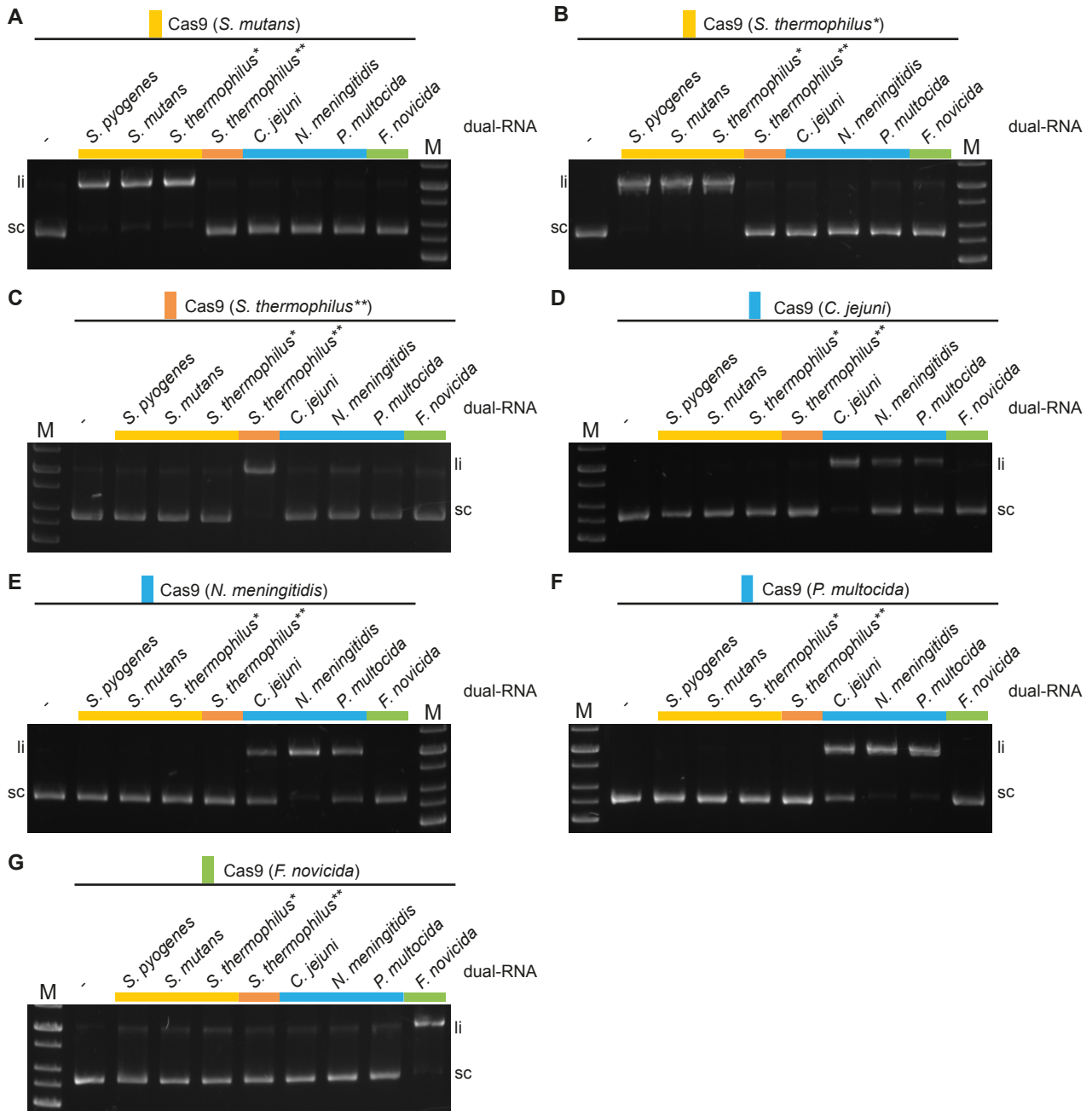
■ ***P. multocida* dual-RNA:Cas9**



■ ***F. novicida* dual-RNA:Cas9**



Supplementary Figure S9. Cas9 orthologs cleave plasmid DNA in the presence of their cognate dual-RNA and specific PAM. Agarose gel electrophoresis analysis of dual-RNA:Cas9 titration (0-100 nM dual-RNA-Cas9 complex) on plasmid DNA (5 nM) containing *speM* protospacer and adjacent WT PAM (PAM+), imperfect PAM (PAM±) or no PAM (PAM-). For *S. pyogenes*, *S. mutans*, *S. thermophilus**, *S. thermophilus*** and *N. meningitidis*, the PAM sequence has already been published (27,28,53,54). For the other bacterial species, PAMs were predicted based on the downstream sequence of protospacer identified in the investigated or related strains (see Supplementary Table S2 and Materials and Methods). The 10 bp sequence located directly downstream of the crRNA-targeted *speM* protospacer is shown. The nucleotide(s) predicted to belong to the PAM sequence are shaded in grey. li: linear cleavage product, sc: supercoiled plasmid DNA, M: 1 kb DNA ladder.



Supplementary Figure S10. Summary of *in vitro* plasmid cleavage assays of Cas9 orthologs in combination with dual-RNAs. Agarose gel electrophoresis of cleavage assays. (A) *S. mutans* Cas9 (50 nM), (B) *S. thermophilus** Cas9 (25 nM), (C) *S. thermophilus*** Cas9 (100 nM), (D) *C. jejuni* Cas9 (100 nM), (E) *N. meningitidis* Cas9 (100 nM), (F) *P. multocida* Cas9 (25 nM), (G) *F. novicida* Cas9 (100 nM) in complex with equimolar concentrations of each of the dual-RNA orthologs were incubated with plasmid DNA (5 nM) containing *speM* protospacer sequence and the PAM sequence specific to the Cas9 ortholog analyzed. li: linear cleavage product, sc: supercoiled plasmid DNA, M: 1 kb DNA ladder.

Supplementary Table S4. Cas9 is present in bacteria from 12 different phyla and diverse habitats.

Strain ^a	Class	Isolation/habitat ^b
Actinobacteria		
Actinobacteridae		
<i>Acidothermus cellulolyticus</i> 11B	<i>Acidothermaceae</i>	extremophile (hot water spring)
<i>Actinomyces coleocanis</i> DSM 15436	<i>Actinomycetaceae</i>	dog genital tract
<i>Actinomyces georgiae</i> F0490	<i>Actinomycetaceae</i>	oral cavity
<i>Actinomyces naeslundii</i> str. Howell 279	<i>Actinomycetaceae</i>	oral cavity
<i>Actinomyces</i> sp. ICM47	<i>Actinomycetaceae</i>	ND
<i>Actinomyces</i> sp. oral taxon 175 str. F0384	<i>Actinomycetaceae</i>	oral cavity
<i>Actinomyces</i> sp. oral taxon 180 str. F0310	<i>Actinomycetaceae</i>	oral cavity
<i>Actinomyces</i> sp. oral taxon 181 str. F0379	<i>Actinomycetaceae</i>	oral cavity
<i>Actinomyces</i> sp. oral taxon 848 str. F0332	<i>Actinomycetaceae</i>	oral cavity
<i>Actinomyces turicensis</i> ACS-279-V-Col4	<i>Actinomycetaceae</i>	genital tract
<i>Bifidobacterium bifidum</i> S17	<i>Bifidobacteriaceae</i>	gastrointestinal tract/feces
<i>Bifidobacterium dentium</i> Bd1	<i>Bifidobacteriaceae</i>	oral cavity
<i>Bifidobacterium longum</i> DJO10A	<i>Bifidobacteriaceae</i>	gastrointestinal tract/feces
<i>Bifidobacterium</i> sp. 12_1_47BFAA	<i>Bifidobacteriaceae</i>	gastrointestinal tract/feces
<i>Corynebacterium accolens</i> ATCC 49726	<i>Corynebacterineae</i>	wound
<i>Corynebacterium diptheriae</i> NCTC 13129	<i>Corynebacterineae</i>	oral cavity
<i>Corynebacterium matruchotii</i> ATCC 14266	<i>Corynebacterineae</i>	oral cavity
<i>Gardnerella vaginalis</i> 5-1	<i>Bifidobacteriaceae</i>	genital tract
<i>Mobiluncus curtisii</i> ATCC 35242	<i>Actinomycetaceae</i>	genital tract
<i>Mobiluncus mulieris</i> 28-1	<i>Actinomycetaceae</i>	genital tract
<i>Scardovia inopinata</i> F0304	<i>Bifidobacteriaceae</i>	oral cavity
<i>Scardovia wiggisiae</i> F0424	<i>Bifidobacteriaceae</i>	oral cavity
Coriobacteridae		
<i>Coriobacterium glomerans</i> PW2	<i>Coriobacteriaceae</i>	invertebrate (red soldier bug)
<i>Eggerthella</i> sp. YY7918	<i>Coriobacteriaceae</i>	gastrointestinal tract/feces
<i>Gordonibacter pamelaiae</i> 7-10-1-b	<i>Coriobacteriaceae</i>	gastrointestinal tract/feces
<i>Olsenella uli</i> DSM 7084	<i>Coriobacteriaceae</i>	oral cavity
Bacteroidetes		
Bacteroidia		
<i>Anaerophaga</i> sp. HS1	<i>Marinilabiliaceae</i>	extremophile (hot water spring)
<i>Anaerophaga thermohalophila</i> DSM 12881	<i>Marinilabiliaceae</i>	environmental sample (oil residue)
<i>Bacteroides cellulosityticus</i> DSM 14838	<i>Bacteroidaceae</i>	gastrointestinal tract/feces
<i>Bacteroides coprophilus</i> DSM 18228	<i>Bacteroidaceae</i>	gastrointestinal tract/feces
<i>Bacteroides coprosuis</i> DSM 18011	<i>Bacteroidaceae</i>	pig feces
<i>Bacteroides dorei</i> DSM 17855	<i>Bacteroidaceae</i>	gastrointestinal tract/feces
<i>Bacteroides eggerthii</i> 1_2_48FAA	<i>Bacteroidaceae</i>	gastrointestinal tract/feces
<i>Bacteroides faecis</i> MAJ27	<i>Bacteroidaceae</i>	gastrointestinal tract/feces
<i>Bacteroides fluxus</i> YIT 12057	<i>Bacteroidaceae</i>	gastrointestinal tract/feces
<i>Bacteroides fragilis</i> NCTC9343	<i>Bacteroidaceae</i>	gastrointestinal tract/feces
<i>Bacteroides nordii</i> CL02T12C05	<i>Bacteroidaceae</i>	gastrointestinal tract/feces
<i>Bacteroides oleiciplenus</i> YIT 12058	<i>Bacteroidaceae</i>	gastrointestinal tract/feces
<i>Bacteroides</i> sp. 2_1_16	<i>Bacteroidaceae</i>	gastrointestinal tract/feces
<i>Bacteroides</i> sp. 203	<i>Bacteroidaceae</i>	gastrointestinal tract/feces
<i>Bacteroides</i> sp. 3_1_19	<i>Bacteroidaceae</i>	gastrointestinal tract/feces
<i>Bacteroides</i> sp. 3_1_33FAA	<i>Bacteroidaceae</i>	gastrointestinal tract/feces
<i>Bacteroides</i> sp. 9_1_42FAA	<i>Bacteroidaceae</i>	gastrointestinal tract/feces
<i>Bacteroides</i> sp. D2	<i>Bacteroidaceae</i>	gastrointestinal tract/feces
<i>Bacteroides uniformis</i> CL03T00C23	<i>Bacteroidaceae</i>	gastrointestinal tract/feces
<i>Bacteroides vulgatus</i> CL09T03C04	<i>Bacteroidaceae</i>	gastrointestinal tract/feces
<i>Bacteroidetes</i> oral taxon 274 str. F0058	<i>Bacteroidaceae</i>	oral cavity
<i>Barnesiella intestinhominis</i> YIT 11860	<i>Bacteroidaceae</i>	gastrointestinal tract/feces

Strain ^a	Class	Isolation/habitat ^b
Bacteroidia (continued)		
<i>Marinilabilia</i> sp. AK2	<i>Marinilabiliaceae</i>	extremophile (solar saltern)
<i>Odoribacter laneus</i> YIT 12061	<i>Porphyromonadaceae</i>	gastrointestinal tract/feces
<i>Parabacteroides johnsonii</i> DSM 18315	<i>Bacteroidaceae</i>	gastrointestinal tract/feces
<i>Parabacteroides</i> sp. D13	<i>Bacteroidaceae</i>	gastrointestinal tract/feces
<i>Porphyromonas catoniae</i> F0037	<i>Porphyromonadaceae</i>	oral cavity
<i>Porphyromonas</i> sp. oral taxon 279 str. F0450	<i>Porphyromonadaceae</i>	oral cavity
<i>Prevotella bivia</i> JCVIHMP010	<i>Prevotellaceae</i>	genital tract
<i>Prevotella buccae</i> ATCC 33574	<i>Prevotellaceae</i>	oral cavity
<i>Prevotella buccalis</i> ATCC 35310	<i>Prevotellaceae</i>	oral cavity
<i>Prevotella denticola</i> F0289	<i>Prevotellaceae</i>	oral cavity
<i>Prevotella disiens</i> FB035-09AN	<i>Prevotellaceae</i>	oral cavity
<i>Prevotella histicola</i> F0411	<i>Prevotellaceae</i>	oral cavity
<i>Prevotella intermedia</i> 17	<i>Prevotellaceae</i>	oral cavity
<i>Prevotella melaninogenica</i> D18	<i>Prevotellaceae</i>	oral cavity/rumen
<i>Prevotella micans</i> F0438	<i>Prevotellaceae</i>	oral cavity
<i>Prevotella multififormis</i> DSM 16608	<i>Prevotellaceae</i>	oral cavity
<i>Prevotella nigrescens</i> ATCC 33563	<i>Prevotellaceae</i>	oral cavity
<i>Prevotella oralis</i> ATCC 33269	<i>Prevotellaceae</i>	oral cavity
<i>Prevotella oulorum</i> F0390	<i>Prevotellaceae</i>	oral cavity
<i>Prevotella ruminicola</i> 23	<i>Prevotellaceae</i>	rumen
<i>Prevotella saccharolytica</i> F0055	<i>Prevotellaceae</i>	oral cavity
<i>Prevotella</i> sp. C561	<i>Prevotellaceae</i>	oral cavity
<i>Prevotella</i> sp. MSX73	<i>Prevotellaceae</i>	oral cavity
<i>Prevotella</i> sp. oral taxon 306 str. F0472	<i>Prevotellaceae</i>	oral cavity
<i>Prevotella</i> sp. oral taxon 317 str. F0108	<i>Prevotellaceae</i>	oral cavity
<i>Prevotella</i> sp. oral taxon 472 str. F0295	<i>Prevotellaceae</i>	oral cavity
<i>Prevotella stercorea</i> DSM 18206	<i>Prevotellaceae</i>	gastrointestinal tract/feces
<i>Prevotella tanneriae</i> ATCC 51259	<i>Prevotellaceae</i>	oral cavity
<i>Prevotella timonensis</i> CRIS 5C-B1	<i>Prevotellaceae</i>	wound (breast abscess)
<i>Prevotella veroralis</i> F0319	<i>Prevotellaceae</i>	oral cavity
<i>Tannerella</i> sp. 6_1_58FAA_CT1	<i>Porphyromonadaceae</i>	gastrointestinal tract/feces
Cytophagia		
<i>Belliella baltica</i> DSM 15883	<i>Cyclobacteriaceae</i>	environmental sample (groundwater)
<i>Indibacter alkaliphilus</i> LW1	<i>Cyclobacteriaceae</i>	extremophile (soda lake)
<i>Nitritalea halalkaliphila</i> LW7	<i>Cyclobacteriaceae</i>	extremophile (saline soda lake)
Flavobacteria		
<i>Bergeyella zoohelcum</i> ATCC 43767	<i>Flavobacteriaceae</i>	oral cavity
<i>Capnocytophaga canimorsus</i> Cc5	<i>Flavobacteriaceae</i>	dog and cat oral cavity/zoonotic infections
<i>Capnocytophaga gingivalis</i> ATCC 33624	<i>Flavobacteriaceae</i>	oral cavity
<i>Capnocytophaga ochracea</i> DSM 7271	<i>Flavobacteriaceae</i>	oral cavity
<i>Capnocytophaga</i> sp. CM59	<i>Flavobacteriaceae</i>	oral cavity
<i>Capnocytophaga</i> sp. oral taxon 324 str. F0483	<i>Flavobacteriaceae</i>	oral cavity
<i>Capnocytophaga</i> sp. oral taxon 326 str. F0382	<i>Flavobacteriaceae</i>	oral cavity
<i>Capnocytophaga</i> sp. oral taxon 329 str. F0087	<i>Flavobacteriaceae</i>	oral cavity
<i>Capnocytophaga</i> sp. oral taxon 335 str. F0486	<i>Flavobacteriaceae</i>	oral cavity
<i>Capnocytophaga</i> sp. oral taxon 380 str. F0488	<i>Flavobacteriaceae</i>	oral cavity
<i>Capnocytophaga</i> sp. oral taxon 412 str. F0487	<i>Flavobacteriaceae</i>	oral cavity
<i>Capnocytophaga sputigena</i> ATCC 33612	<i>Flavobacteriaceae</i>	oral cavity
<i>Chryseobacterium</i> sp. CF314	<i>Flavobacteriaceae</i>	vegetation
<i>Flavobacteriaceae</i> bacterium S85	<i>Flavobacteriaceae</i>	environmental sample (seawater)
<i>Flavobacterium branchiophilum</i> FL-15	<i>Flavobacteriaceae</i>	fish pathogen
<i>Flavobacterium columnare</i> ATCC 49512	<i>Flavobacteriaceae</i>	fish pathogen
<i>Flavobacterium psychrophilum</i> JIP02/86	<i>Flavobacteriaceae</i>	fish pathogen
<i>Fluviicola taffensis</i> DSM 16823	<i>Cryomorphaceae</i>	environmental sample (fresh water)
<i>Galbibacter</i> sp. ck-12-15	<i>Flavobacteriaceae</i>	extremophile (deep sea sediment)
<i>Joostella marina</i> DSM 19592	<i>Flavobacteriaceae</i>	environmental sample (seawater)
<i>Kordia algicida</i> OT-1	<i>Flavobacteriaceae</i>	environmental sample (seawater)
<i>Myroides injenensis</i> M09-0166	<i>Flavobacteriaceae</i>	human clinical specimens
<i>Myroides odoratus</i> DSM 2801	<i>Flavobacteriaceae</i>	fish

Strain ^a	Class	Isolation/habitat ^b
Flavobacteria (continued)		
<i>Ornithobacterium rhinotracheale</i> DSM 15997	Flavobacteriaceae	bird respiratory tract
<i>Psychroflexus torquis</i> ATCC 700755	Flavobacteriaceae	extremophile (antarctic ice)
<i>Riemerella anatipestifer</i> ATCC 11845 = DSM 15868	Flavobacteriaceae	bird
<i>Weeksella virosa</i> DSM 16922	Flavobacteriaceae	genital tract/urine
<i>Zunongwangia profunda</i> SM-A87	Flavobacteriaceae	extremophile (deep sea sediment)
Sphingobacteria		
<i>Mucilaginibacter paludis</i> DSM 18603	Sphingobacteriaceae	food (fermented)
<i>Niabella soli</i> DSM 19437	Chitinophagaceae	environmental sample (soil)
<i>Sphingobacterium spiritivorum</i> ATCC 33861	Sphingobacteriaceae	human clinical specimens
Firmicutes		
Bacilli		
<i>Alicyclophilus denitrificans</i> K601	Alicyclobacillaceae	environmental sample (sewage)
<i>Alicyclobacillus hesperidum</i> URH17-3-68	Alicyclobacillaceae	extremophile (hot water spring)
<i>Bacillus cereus</i> Rock1-15	Bacillaceae	environmental sample (soil)
<i>Bacillus smithii</i> 7 3 47FAA	Bacillaceae	human clinical specimens
<i>Bacillus thuringiensis</i> serovar <i>finitimus</i> YBT-020	Bacillaceae	environmental sample (soil)
<i>Brevibacillus laterosporus</i> GI-9	Paenibacillaceae	environmental sample (soil)
<i>Catelicoccus marimammalium</i> M35/04/3	Enterococcaceae	grey seal gastrointestinal tract
<i>Dolosigranulum pigrum</i> ATCC 51524	Carnobacteriaceae	human clinical specimens
<i>Enterococcus faecalis</i> TX0012	Enterococcaceae	gastrointestinal tract/feces
<i>Enterococcus faecium</i> 1231408	Enterococcaceae	gastrointestinal tract/feces
<i>Enterococcus hirae</i> ATCC 9790	Enterococcaceae	gastrointestinal tract/feces
<i>Enterococcus italicus</i> DSM 15952	Enterococcaceae	food (fermented)
<i>Enterococcus</i> sp. 7L76	Enterococcaceae	gastrointestinal tract/feces
<i>Facklamia hominis</i> CCUG 36813	Aerococcaceae	buruncle (human)
<i>Fructobacillus fructosus</i> KCTC 3544	Leuconostocaceae	vegetation
<i>Gemella haemolysans</i> ATCC 10379	Streptococcaceae	oral cavity
<i>Gemella moribillum</i> M424	Streptococcaceae	gastrointestinal tract/feces
<i>Lactobacillus animalis</i> KCTC 3501	Lactobacillaceae	food (fermented)
<i>Lactobacillus brevis</i> subsp. <i>gravesensis</i> ATCC 27305	Lactobacillaceae	food (fermented)
<i>Lactobacillus buchneri</i> ATCC 11577	Lactobacillaceae	food (fermented)
<i>Lactobacillus casei</i> str. Zhang	Lactobacillaceae	gastrointestinal tract/feces
<i>Lactobacillus coryniformis</i> subsp. <i>coryniformis</i> KCTC 3167	Lactobacillaceae	food (fermented)
<i>Lactobacillus coryniformis</i> subsp. <i>torquens</i> KCTC 3535	Lactobacillaceae	food (fermented)
<i>Lactobacillus crispatus</i> FB049-03	Lactobacillaceae	genital tract
<i>Lactobacillus curvatus</i> CRL 705	Lactobacillaceae	food (fermented)
<i>Lactobacillus delbrueckii</i> subsp. <i>bulgaricus</i> 2038	Lactobacillaceae	food (fermented)
<i>Lactobacillus farciminis</i> KCTC 3681	Lactobacillaceae	food (fermented)
<i>Lactobacillus fermentum</i> ATCC 14931	Lactobacillaceae	food (fermented)
<i>Lactobacillus florum</i> 2F	Lactobacillaceae	vegetation
<i>Lactobacillus gasseri</i> JV-V03	Lactobacillaceae	oral cavity
<i>Lactobacillus hominis</i> CRBIP 24.179	Lactobacillaceae	gastrointestinal tract/feces
<i>Lactobacillus iners</i> LactinV 11V1-d	Lactobacillaceae	genital tract/urine
<i>Lactobacillus jensenii</i> 269-3	Lactobacillaceae	genital tract/blood
<i>Lactobacillus johnsonii</i> DPC 6026	Lactobacillaceae	pig gastrointestinal tract
<i>Lactobacillus mucosae</i> LM1	Lactobacillaceae	wild pig gastrointestinal tract
<i>Lactobacillus paracasei</i> subsp. <i>paracasei</i> 8700:2	Lactobacillaceae	food (fermented)
<i>Lactobacillus pentosus</i> IG1	Lactobacillaceae	food (fermented)
<i>Lactobacillus plantarum</i> ZJ316	Lactobacillaceae	gastrointestinal tract/feces
<i>Lactobacillus rhamnosus</i> GG	Lactobacillaceae	gastrointestinal tract/feces
<i>Lactobacillus ruminis</i> ATCC 25644	Lactobacillaceae	rumen
<i>Lactobacillus salivarius</i> UCC118	Lactobacillaceae	oral cavity
<i>Lactobacillus sanfranciscensis</i> TMW 1-1304	Lactobacillaceae	food (fermented)
<i>Lactobacillus</i> sp. 66c	Lactobacillaceae	ND
<i>Lactobacillus versmoldensis</i> KCTC 3814	Lactobacillaceae	food (fermented)
<i>Leuconostoc gelidum</i> KCTC 3527	Leuconostocaceae	food (fermented)
<i>Leuconostoc pseudomesenteroides</i> 4882	Leuconostocaceae	food (fermented)

Strain ^a	Class	Isolation/habitat ^b
Bacilli (continued)		
<i>Listeria innocua</i> Clip11262	Listeriaceae	environmental sample (soil)
<i>Listeria ivanovii</i> FSL F6-596	Listeriaceae	animal and human/environmental samples
<i>Listeria monocytogenes</i> str. 1/2a F6854	Listeriaceae	animal and human/environmental samples
<i>Listeria seeligeri</i> FSL N1-067	Listeriaceae	animal and human/environmental samples
Listeriaceae bacterium TTU M1-001	Listeriaceae	environmental sample (soil)
<i>Oenococcus kitaharae</i> DSM 17330	Leuconostocaceae	food (fermented)
<i>Pediococcus acidilactici</i> DSM 20284	Lactobacillaceae	vegetation
<i>Pediococcus lolii</i> NGRI 0510Q	Lactobacillaceae	vegetation (fermented)
<i>Planococcus antarcticus</i> DSM 14505	Planococcaceae	extremophile (antarctic)
<i>Sporolactobacillus vineae</i> DSM 21990 = SL153	Sporolactobacillaceae	environmental sample (soil)
<i>Staphylococcus aureus</i> subsp. <i>aureus</i>	Staphylococcaceae	human clinical specimens
<i>Staphylococcus lugdunensis</i> M23590	Staphylococcaceae	human clinical specimens
<i>Staphylococcus massiliensis</i> S46	Staphylococcaceae	skin
<i>Staphylococcus pseudintermedius</i> ED99	Staphylococcaceae	dog skin
<i>Staphylococcus simulans</i> ACS-120-V-Sch1	Staphylococcaceae	genital tract
<i>Streptococcus agalactiae</i> 2603V/R	Streptococcaceae	gastrointestinal tract/feces
<i>Streptococcus anginosus</i> F0211	Streptococcaceae	oral cavity
<i>Streptococcus bovis</i> ATCC 700338	Streptococcaceae	rumen/zoonotic infections
<i>Streptococcus canis</i> FSL Z3-227	Streptococcaceae	food (fermented)
<i>Streptococcus constellatus</i> subsp. <i>constellatus</i> SK53	Streptococcaceae	human clinical specimens
<i>Streptococcus downei</i> F0415	Streptococcaceae	monkey oral cavity
<i>Streptococcus dysgalactiae</i> DSM 12112	Streptococcaceae	various animals/zoonotic infections
<i>Streptococcus equi</i> subsp. <i>zoepidemicus</i> MGCS10565	Streptococcaceae	horse respiratory tract
<i>Streptococcus equinus</i> ATCC 9812	Streptococcaceae	ruminants alimentary tract
<i>Streptococcus gallolyticus</i> UCN34	Streptococcaceae	ruminants alimentary tract
<i>Streptococcus gordonii</i> str. Challis substr. CH1	Streptococcaceae	oral cavity
<i>Streptococcus infantarius</i> ATCC BAA-102	Streptococcaceae	gastrointestinal tract/feces
<i>Streptococcus iniae</i> 9117	Streptococcaceae	fish/human pathogen
<i>Streptococcus macacae</i> NCTC 11558	Streptococcaceae	monkey oral cavity
<i>Streptococcus macedonicus</i> ACA-DC 198	Streptococcaceae	food (fermented)
<i>Streptococcus mitis</i> ATCC 6249	Streptococcaceae	oral cavity
<i>Streptococcus mutans</i> UA159	Streptococcaceae	oral cavity
<i>Streptococcus oralis</i> SK1074	Streptococcaceae	oral cavity
<i>Streptococcus parasanguinis</i> F0449	Streptococcaceae	oral cavity
<i>Streptococcus pasteurianus</i> ATCC 43144	Streptococcaceae	oral cavity
<i>Streptococcus pseudoporcinus</i> SPIN 20026	Streptococcaceae	blood
<i>Streptococcus pyogenes</i> SF370	Streptococcaceae	genital tract
<i>Streptococcus rattus</i> FA-1 = DSM 20564	Streptococcaceae	oral cavity/wounds
<i>Streptococcus salivarius</i> JIM8777	Streptococcaceae	rat oral cavity
<i>Streptococcus sanguinis</i> VMC66	Streptococcaceae	oral cavity
<i>Streptococcus</i> sp. BS35b	Streptococcaceae	oral cavity
<i>Streptococcus</i> sp. C150	Streptococcaceae	oral cavity
<i>Streptococcus</i> sp. C300	Streptococcaceae	oral cavity (expectorated sputum)
<i>Streptococcus</i> sp. F0441	Streptococcaceae	oral cavity (expectorated sputum)
<i>Streptococcus</i> sp. F0441	Streptococcaceae	oral cavity
<i>Streptococcus</i> sp. GMD4S	Streptococcaceae	oral cavity
<i>Streptococcus</i> sp. GMD6S	Streptococcaceae	oral cavity
<i>Streptococcus</i> sp. M334	Streptococcaceae	oral cavity
<i>Streptococcus</i> sp. oral taxon 056 str. F0418	Streptococcaceae	oral cavity (expectorated sputum)
<i>Streptococcus</i> sp. oral taxon 071 str. 73H25AP	Streptococcaceae	oral cavity
<i>Streptococcus suis</i> 89/1591	Streptococcaceae	oral cavity
<i>Streptococcus thermophilus</i> LMD-9	Streptococcaceae	pig
<i>Streptococcus vestibularis</i> ATCC 49124	Streptococcaceae	food (fermented)
	Streptococcaceae	oral cavity
Clostridia		
<i>Acidaminococcus intestini</i> RyC-MR95	Acidaminococcaceae	wound/abscess
<i>Acidaminococcus</i> sp. D21	Acidaminococcaceae	gastrointestinal tract/feces
<i>Aminomonas paucivorans</i> DSM 12260	Syntrophomonadaceae	environmental sample (sewage)
<i>Anaerococcus tetradius</i> ATCC 35098	Peptostreptococcaceae	human clinical specimens
<i>Butyrivibrio fibrisolvens</i> 16/4	Lachnospiraceae	rumen
<i>Catenibacterium mitsuokai</i> DSM 15897	Lachnospiraceae	gastrointestinal tract/feces
<i>Clostridium cellulolyticum</i> H10	Clostridiaceae	vegetation (composted)

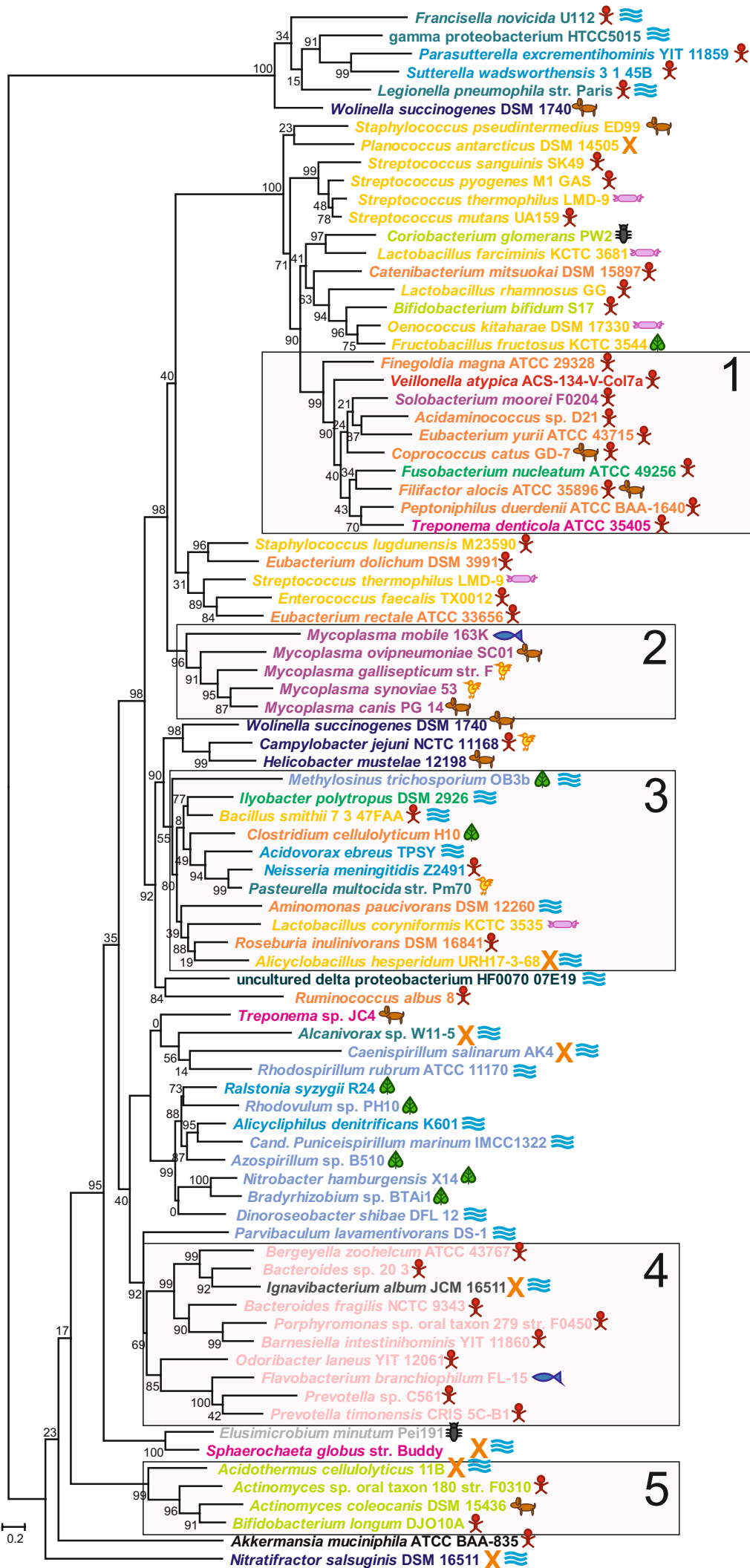
Strain ^a	Class	Isolation/habitat ^b
Clostridia (continued)		
<i>Clostridium perfringens</i> D str. JGS1721	<i>Clostridiaceae</i>	environmental sample (vegetation/marine sediment)
<i>Clostridium spiroforme</i> DSM 1552	<i>Clostridiaceae</i>	gastrointestinal tract/feces
<i>Coprococcus catus</i> GD/7	<i>Lachnospiraceae</i>	gastrointestinal tract/feces
<i>Coprococcus comes</i> ATCC 27758	<i>Lachnospiraceae</i>	gastrointestinal tract/feces
<i>Dorea longicatena</i> DSM 13814	<i>Clostridiaceae</i>	gastrointestinal tract/feces
<i>Eubacterium dolichum</i> DSM 3991	<i>Eubacteriaceae</i>	gastrointestinal tract/feces
<i>Eubacterium rectale</i> ATCC 33656	<i>Eubacteriaceae</i>	gastrointestinal tract/feces
<i>Eubacterium</i> sp. AS15	<i>Eubacteriaceae</i>	oral cavity
<i>Eubacterium ventriosum</i> ATCC 27560	<i>Eubacteriaceae</i>	gastrointestinal tract/feces
<i>Eubacterium yurii</i> subsp. <i>margaretiae</i> ATCC 43715	<i>Peptostreptococcaceae</i>	oral cavity
<i>Filifactor alocis</i> ATCC 35896	<i>Peptostreptococcaceae</i>	cat and human oral cavity
<i>Finegoldia magna</i> ATCC 29328	<i>Peptostreptococcaceae</i>	oral cavity
<i>Helcococcus kunzii</i> ATCC 51366	<i>Clostridiales Family XI</i>	wound
<i>Oribacterium sinus</i> F0268	<i>Lachnospiraceae</i>	human clinical specimens
<i>Peptoniphilus duerdenii</i> ATCC BAA-1640	<i>Peptostreptococcaceae</i>	wound
<i>Peptoniphilus</i> sp. oral taxon 386 str. F0131	<i>Peptostreptococcaceae</i>	oral cavity
<i>Phascolarctobacterium</i> sp. YIT 12067	<i>Acidaminococcaceae</i>	gastrointestinal tract/feces
<i>Phascolarctobacterium succinatutens</i> YIT 12067	<i>Acidaminococcaceae</i>	gastrointestinal tract/feces
<i>Pseudoramibacter alactolyticus</i> ATCC 23263	<i>Clostridiaceae</i>	oral cavity
<i>Roseburia intestinalis</i> L1-82	<i>Lachnospiraceae</i>	gastrointestinal tract/feces
<i>Roseburia inulinivorans</i> DSM 16841	<i>Lachnospiraceae</i>	gastrointestinal tract/feces
<i>Ruminococcus albus</i> 8	<i>Ruminococcaceae</i>	gastrointestinal tract/feces
<i>Ruminococcus lactaris</i> ATCC 29176	<i>Ruminococcaceae</i>	gastrointestinal tract/feces
<i>Subdoligranulum</i> sp. 4_3_54A2FAA	<i>Ruminococcaceae</i>	gastrointestinal tract/feces
Negativicutes		
<i>Megasphaera</i> sp. UPII 135-E	<i>Veillonellaceae</i>	rumen
<i>Veillonella atypica</i> ACS-134-V-Col7a	<i>Veillonellaceae</i>	oral cavity
<i>Veillonella parvula</i> ATCC17745	<i>Veillonellaceae</i>	gastrointestinal/genital tract
<i>Veillonella</i> sp. 6_1_27	<i>Veillonellaceae</i>	gastrointestinal tract/feces
<i>Veillonella</i> sp. oral taxon 780 str. F0422	<i>Veillonellaceae</i>	oral cavity
Proteobacteria		
Alphaproteobacteria		
<i>Acetobacter aceti</i> NBRC 14818	<i>Acetobacteraceae</i>	environmental sample
<i>Azospirillum</i> sp. B510	<i>Rhodospirillaceae</i>	vegetation
<i>Bradyrhizobium</i> sp. BTai1	<i>Bradyrhizobiaceae</i>	vegetation
<i>Caenispirillum salinarum</i> AK4	<i>Rhodospirillaceae</i>	extremophile (solar saltern)
<i>Dinoroseobacter shibae</i> DFL 12	<i>Rhodobacteraceae</i>	environmental sample (seawater)
<i>Gluconacetobacter diazotrophicus</i> PA15	<i>Acetobacteriaceae</i>	vegetation
<i>Maritimibacter alkaliphilus</i> ATCC2654	<i>Rhodobacteraceae</i>	environmental sample (seawater)
<i>Methylocystis</i> sp. ATCC 49242	<i>Methylocystaceae</i>	environmental sample (sewage, fresh water)
<i>Methylosinus trichosporium</i> OB3b	<i>Methylocystaceae</i>	environmental sample (soil, fresh water)
<i>Nitrobacter hamburgensis</i> X14	<i>Bradyrhizobiaceae</i>	environmental sample (soil)
<i>Parvibaculum lavamentivorans</i> DS-1	<i>Phyllobacteriaceae</i>	environmental sample (sewage)
<i>Puniceispirillum marinum</i> IMCC1322	<i>SAR16 clade</i>	environmental sample (seawater)
<i>Rhodopseudomonas palustris</i> BisB18	<i>Bradyrhizobiaceae</i>	environmental sample (soil)
<i>Rhodospirillum rubrum</i> ATCC 11170	<i>Rhodospirillaceae</i>	environmental sample (sea mud)
<i>Rhodovulum</i> sp. PH10	<i>Rhodobacteraceae</i>	environmental sample (soil)
<i>Sphingobium</i> sp. AP49	<i>Sphingomonadaceae</i>	vegetation
<i>Sphingomonas</i> sp. S17	<i>Sphingomonadaceae</i>	environmental sample (stromatolite)
<i>Tistrella mobilis</i> KA081020-065	<i>Rhodospirillaceae</i>	environmental sample (seawater)
Betaproteobacteria		
<i>Acidovorax avenae</i> subsp. <i>avenae</i> ATCC 19860	<i>Comamonadaceae</i>	environmental sample (soil)
<i>Acidovorax ebreus</i> TPSY	<i>Comamonadaceae</i>	environmental sample (water)
<i>Burkholderiales</i> bacterium 1 1 47	<i>Burkholderiales</i>	gastrointestinal tract/feces
<i>Kingella kingae</i> ATCC 23330	<i>Neisseriaceae</i>	oral cavity

Strain ^a	Class	Isolation/habitat ^b
Betaproteobacteria (continued)		
<i>Neisseria bacilliformis</i> ATCC BAA-1200	<i>Neisseriaceae</i>	oral cavity
<i>Neisseria cinerea</i> ATCC 14685	<i>Neisseriaceae</i>	oral cavity
<i>Neisseria flavescens</i> SK114	<i>Neisseriaceae</i>	human clinical specimens
<i>Neisseria lactamica</i> 020-06	<i>Neisseriaceae</i>	oral cavity
<i>Neisseria meningitides</i> Z2491	<i>Neisseriaceae</i>	oral cavity
<i>Neisseria mucosa</i> C102	<i>Neisseriaceae</i>	oral cavity (expectorated sputum)
<i>Neisseria</i> sp. oral taxon 014 str. F0314	<i>Neisseriaceae</i>	oral cavity
<i>Neisseria subflava</i> NJ9703	<i>Neisseriaceae</i>	oral cavity
<i>Neisseria wadsworthii</i> 9715	<i>Neisseriaceae</i>	skin
<i>Nitrosomonas</i> sp. AL212	<i>Nitrosomonadaceae</i>	environmental sample (fresh water)
<i>Parasutterella excrementihominis</i> YIT 11859	<i>Alcaligenaceae</i>	gastrointestinal tract/feces
<i>Ralstonia syzygii</i> R24	<i>Burkholderiaceae</i>	environmental sample (soil)
<i>Simonsiella muelleri</i> ATCC 29453	<i>Neisseriaceae</i>	oral cavity
<i>Sutterella parvirubra</i> YIT 11816	<i>Alcaligenaceae</i>	gastrointestinal tract/feces
<i>Sutterella wadsworthensis</i> 3 1 45B	<i>Alcaligenaceae</i>	gastrointestinal tract/feces
<i>Verminephrobacter aporrectodeae</i> subsp. <i>tuberculatae</i> At4	<i>Comamonadaceae</i>	invertebrate (earthworm)
<i>Verminephrobacter eiseniae</i> EF01-2	<i>Comamonadaceae</i>	invertebrate (earthworm)
Gammaproteobacteria		
<i>Actinobacillus minor</i> NM305	<i>Pasteurellaceae</i>	pig respiratory tract
<i>Actinobacillus pleuropneumoniae</i> serovar 10 D13039	<i>Pasteurellaceae</i>	pig respiratory tract
<i>Actinobacillus succinogenes</i> 130Z	<i>Pasteurellaceae</i>	rumen
<i>Actinobacillus suis</i> H91-0380	<i>Pasteurellaceae</i>	pig pathogen
<i>Actinobacillus ureae</i> ATCC 25976	<i>Pasteurellaceae</i>	respiratory tract
<i>Alcanivorax</i> sp. W11-5	<i>Alcanivoracaceae</i>	extremophile (deep sea sediment)
<i>Francisella tularensis</i> subsp. <i>holarctica</i> LVS	<i>Francisellaceae</i>	engineered live vaccine strain
<i>Francisella tularensis</i> subsp. <i>novicida</i> U112	<i>Francisellaceae</i>	human/environmental sample (water)
<i>Francisella tularensis</i> subsp. <i>tularensis</i> WY96-3418	<i>Francisellaceae</i>	wound
gamma proteobacterium HTCC5015	<i>Unclassified</i>	environmental sample (seawater)
gammaproteobacterium HdN1	<i>Unclassified</i>	environmental sample (sewage)
<i>Haemophilus parainfluenzae</i> T3T1	<i>Pasteurellaceae</i>	oral cavity/genital tract
<i>Haemophilus pittmaniae</i> HK 85	<i>Pasteurellaceae</i>	oral cavity
<i>Haemophilus sputorum</i> HK 2154	<i>Pasteurellaceae</i>	oral cavity
<i>Legionella pneumophila</i> str. Paris	<i>Legionellaceae</i>	human clinical specimens
<i>Pasteurella bettyae</i> CCUG 2042	<i>Pasteurellaceae</i>	genital tract
<i>Pasteurella multocida</i> subsp. <i>gallicida</i> X73	<i>Pasteurellaceae</i>	bird pathogen
<i>Pasteurella multocida</i> Pm70	<i>Pasteurellaceae</i>	bird respiratory tract/zoonotic infections
Deltaproteobacteria		
uncultured delta proteobacterium HF0070_07E19	<i>Unclassified</i>	environmental sample (seawater)
Epsilonproteobacteria		
<i>Campylobacter coli</i> 2962	<i>Campylobacteraceae</i>	animals/human pathogen
<i>Campylobacter jejuni</i> NCTC11168	<i>Campylobacteraceae</i>	bird
<i>Campylobacter jejuni</i> subsp. <i>doylei</i> 269-97	<i>Campylobacteraceae</i>	blood
<i>Campylobacter lari</i>	<i>Campylobacteraceae</i>	gastrointestinal tract/feces
<i>Helicobacter canadensis</i> MIT 98-5491	<i>Helicobacteriaceae</i>	gastrointestinal tract/feces
<i>Helicobacter cinaedi</i> CCUG 18818	<i>Helicobacteriaceae</i>	gastrointestinal tract/feces
<i>Helicobacter hepaticus</i> ATCC 51449	<i>Helicobacteriaceae</i>	mouse liver
<i>Helicobacter mustelae</i> 12198	<i>Helicobacteriaceae</i>	ferret
<i>Helicobacter pullorum</i> MIT 98-5489	<i>Helicobacteriaceae</i>	bird/zoonotic infections
<i>Nitratifractor salsuginis</i> DSM 16511	<i>Unclassified</i>	extremophile (deep sea sediment)
<i>Wolinella succinogenes</i> DSM 1740	<i>Helicobacteraceae</i>	rumen
Fusobacteria		
<i>Fusobacterium nucleatum</i> subsp. <i>vincentii</i> ATCC 49256	<i>Fusobacteriaceae</i>	oral cavity
<i>Fusobacterium</i> sp. 1_1_41FAA	<i>Fusobacteriaceae</i>	gastrointestinal tract/feces
<i>Fusobacterium</i> sp. 3_1_27	<i>Fusobacteriaceae</i>	gastrointestinal tract/feces
<i>Fusobacterium</i> sp. 3_1_36A2	<i>Fusobacteriaceae</i>	gastrointestinal tract/feces
<i>Ilyobacter polytropus</i> DSM 2926	<i>Fusobacteriaceae</i>	environmental sample (sea mud)

Strain ^a	Class	Isolation/habitat ^b
Fusobacteria (continued)		
<i>Streptobacillus moniliformis</i> DSM 12112	<i>Leptotrichiaceae</i>	rodent/human pathogen
Spirochaetes		
<i>Leptospira inadai</i> serovar Lyme str. 10	<i>Leptospiraceae</i>	human clinical specimens
<i>Sphaerochaeta globus</i> str. Buddy	<i>Spirochaetaceae</i>	extremophile (marine hot spring)
<i>Treponema denticola</i> ATCC 35405	<i>Spirochaetaceae</i>	oral cavity
<i>Treponema phagedenis</i> F0421	<i>Spirochaetaceae</i>	monkey genital tracts
<i>Treponema</i> sp. JC4	<i>Spirochaetaceae</i>	rumen
<i>Treponema vincentii</i> ATCC 35580	<i>Spirochaetaceae</i>	oral cavity
Tenericutes		
Mollicutes		
<i>Mycoplasma canis</i> PG 14	<i>Mycoplasmataceae</i>	dog oral cavity
<i>Mycoplasma cynos</i> C142	<i>Mycoplasmataceae</i>	dog respiratory tract
<i>Mycoplasma gallisepticum</i> str. F	<i>Mycoplasmataceae</i>	bird pathogen
<i>Mycoplasma iowae</i> 695	<i>Mycoplasmataceae</i>	bird
<i>Mycoplasma mobile</i> 163K	<i>Mycoplasmataceae</i>	fish pathogen
<i>Mycoplasma ovipneumoniae</i> SC01	<i>Mycoplasmataceae</i>	goat respiratory tract
<i>Mycoplasma synoviae</i> 53	<i>Mycoplasmataceae</i>	bird pathogen
<i>Solobacterium moorei</i> F0204	<i>Erysipelotrichaceae</i>	gastrointestinal tract/feces
Elusimicrobia		
<i>Elusimicrobium minutum</i> Pei191	<i>Elusimicrobiaceae</i>	invertebrate (scarab beetle)
Uncultured Termite group 1 bacterium phylotype Rs-D17	<i>Elusimicrobiaceae</i>	invertebrate
Fibrobacteres		
<i>Fibrobacter succinogenes</i> S85	<i>Fibrobacteraceae</i>	rumen
Ignavibacteria		
<i>Ignavibacterium album</i> JCM 16511	<i>Ignavibacteriaceae</i>	extremophile (hot water spring)
Planktomycetes		
<i>Blastopirellula marina</i> DSM 3645	<i>Planctomycetaceae</i>	environmental sample (seawater)
Verrucomicrobia		
<i>Diplosphaera colitermitum</i> TAV2	<i>Opiritaceae</i>	invertebrate (termite)
<i>Akkermansia muciniphila</i> ATCC BAA-835	<i>Verrucomicrobiaceae</i>	gastrointestinal tract/feces
Unclassified		
candidate division TM7 single-cell isolate TM7c	<i>Unclassified</i>	oral cavity
uncultured bacterium	<i>Unclassified</i>	environmental sample (groundwater)
uncultured bacterium	<i>Unclassified</i>	environmental sample (groundwater)
uncultured bacterium T3_7_42578	<i>Unclassified</i>	invertebrate (honeybee)

^aSingle strains representing every species found to harbor the *cas9* gene are listed.

^bThe origin of the specific strain and/or typical habitat of the species are given for every strain. ND, no data available. Note that if not specified otherwise, isolates from body sites and feces are human commensals and pathogens.

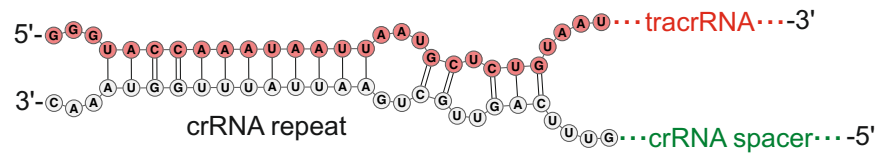


Alphaproteobacteria
 Betaproteobacteria
 Gammaproteobacteria
 Deltaproteobacteria
 Epsilonproteobacteria
 Actinobacteria
 Fusobacteria
 Bacilli
 Clostridia
 Negativicutes
 Spirochaete
 Mollicutes
 Bacteroidetes
 Elusimicrobia
 Ignavibacteria
 Verrucomicrobia

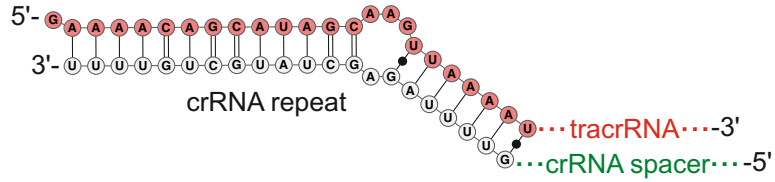
- human
- mammal
- fish
- bird
- invertebrate
- plant/soil
- water
- food
- extreme environment

Supplementary Figure S11. Cas9 tree topology suggests both horizontal and vertical transfer of type II CRISPR-Cas systems. See Figure 1, Supplementary Figure S4 and Supplementary Table S4. The codes for taxonomy (phyla in color) and habitat (symbols) of the bacterial strains harboring representative Cas9 orthologs are indicated (right panel). The clusters grouping evolutionary distant bacteria (1 and 3) but isolated mainly from similar sources (human for cluster 1 and mostly environmental samples for cluster 3) suggest horizontal transfer of type II systems. Clusters 2, 4 and 5 group closely related bacteria isolated from diverse habitats indicating vertical transfer of the systems.

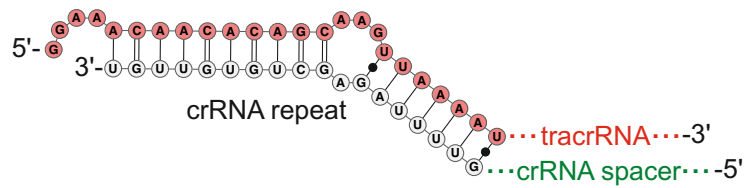
F. novicida



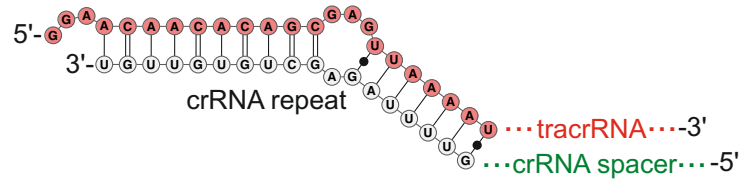
S. pyogenes



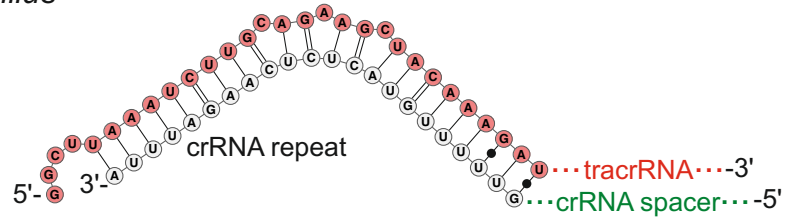
S. mutans



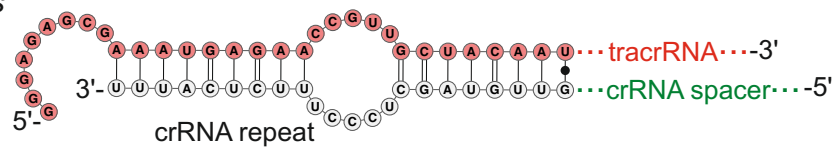
*S. thermophilus**



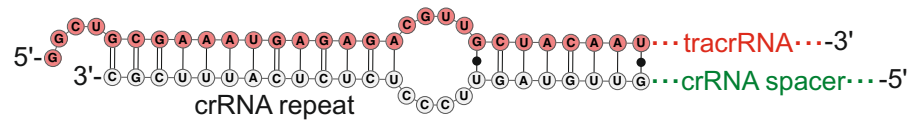
*S. thermophilus***



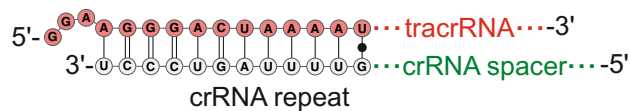
N. meningitidis



P. multocida



C. jejuni



Supplementary Figure S12. tracrRNA:crRNA repeat duplexes form similar secondary structures in loci with closely related Cas9 orthologs. Antirepeat sequence of processed tracrRNA (red) and repeat-derived sequence of mature crRNA (grey) were co-folded for each type II CRISPR-Cas locus studied (see Materials and Methods). Color bars indicated on the left group dual-RNAs from loci with closely related Cas9 (see Figure 1 and Supplementary Figure S4). RNA duplexes belonging to the same groups display structural similarities, suggesting a role of the structure in dual-RNA recognition by Cas9.

Supplementary References

58. Sun, W., Li, G. & Nicholson, A. W. (2004) Mutational analysis of the nuclease domain of *Escherichia coli* ribonuclease III. Identification of conserved acidic residues that are important for catalytic function in vitro. *Biochemistry*, **43**, 13054-13062.
59. Sun, W., Jun, E. & Nicholson, A. W. (2001) Intrinsic double-stranded-RNA processing activity of *Escherichia coli* ribonuclease III lacking the dsRNA-binding domain. *Biochemistry*, **40**, 14976-14984.