

Fig S1

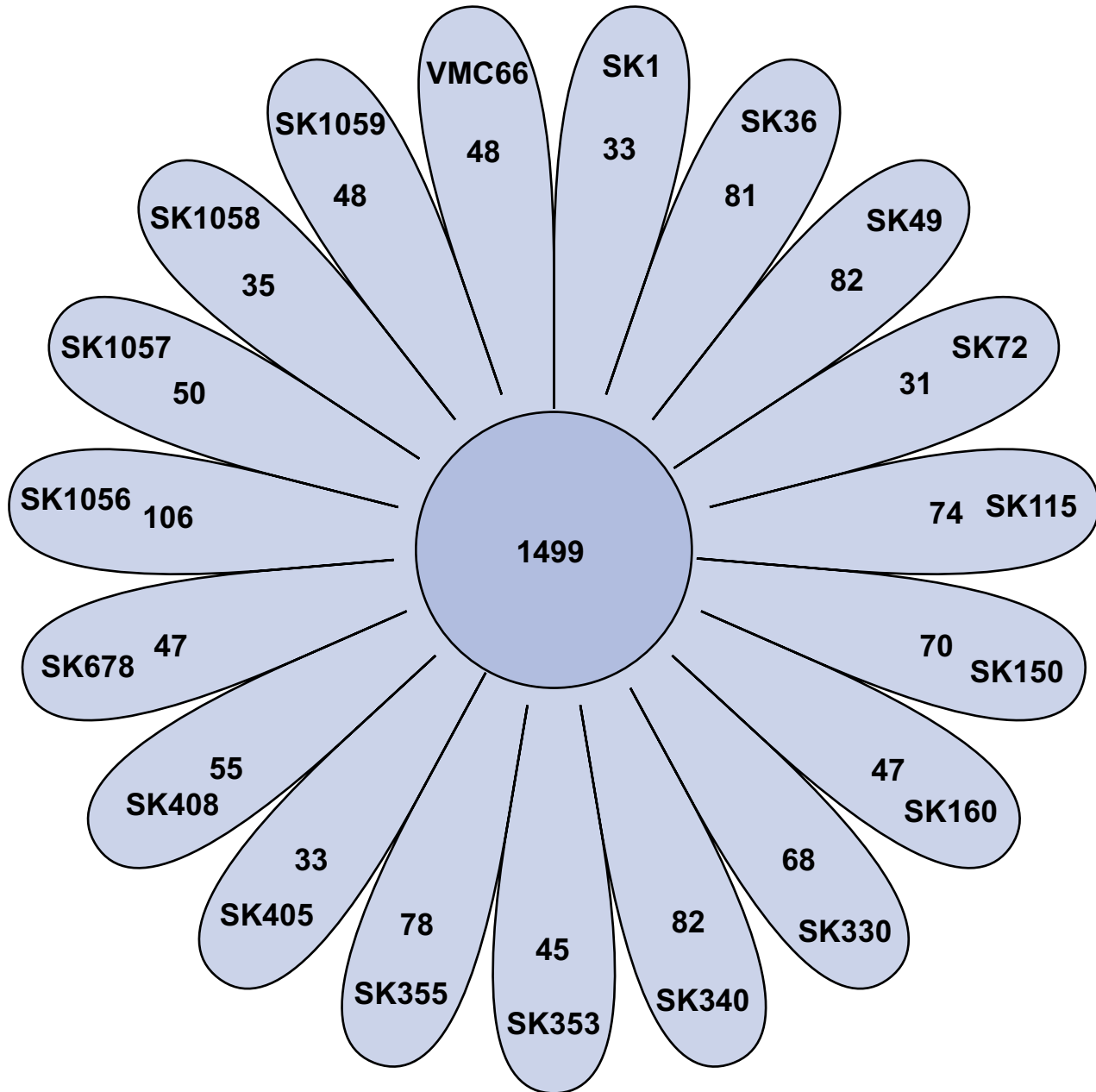


Fig S1 Graphical representation of core genome (center) and unique genes (petals).

Table S1 Blood vs. oral gene comparison

SK405 Locus_Tag	Predicted Function	Oral¹	Blood²
HMPREF9390_RS07860	hypothetical lipoprotein	2	8
HMPREF9390_RS08320	Phosphoribosyl transferase (PRT)-type I domain protein	2	6
HMPREF9390_RS08325	Phosphoribosyl transferase (PRT)	2	6
HMPREF9390_RS08330	YceG family protein	2	6
HMPREF9390_RS08335	TelA	2	6
HMPREF9390_RS08340	TerD3 family protein	2	6
HMPREF9390_RS08345	TerD2 family protein	2	6
HMPREF9390_RS08350	TerD family protein	2	6
HMPREF9390_RS08355	calcium-translocating P-type ATPase, PMCA-type	2	6
HMPREF9390_RS08360	haloacid dehalogenase-like hydrolase	2	6
HMPREF9390_RS08365	ATP/GTP-binding protein	2	6

¹Number of genomes of oral isolates containing the designated gene.

²Number of genomes of blood isolates containing the designated gene.

Table S2 Candidate virulence genes

SK405 Locus_Tag	Predicted Function	Less Virulent ¹	More Virulent ²
HMPREF9390_RS00505	hypothetical protein	0	3
HMPREF9390_RS01040 ³	zinc-binding dehydrogenase family oxidoreductase	0	3
HMPREF9390_RS01045	TetR family transcriptional regulator	0	3
HMPREF9390_RS01515	molecular chaperone HscC	0	3
HMPREF9390_RS01520	hypothetical protein	0	3
HMPREF9390_RS03570	ABC transporter ATP-binding protein	0	3
HMPREF9390_RS03575	ABC transporter permease	0	3
HMPREF9390_RS03635	membrane protein	0	3
HMPREF9390_RS06090	hypothetical protein	0	3
HMPREF9390_RS06105	N-acetyltransferase	0	3
HMPREF9390_RS06115	alpha/beta hydrolase	0	3
HMPREF9390_RS06500	glycosyl transferase family 1	0	3
HMPREF9390_RS06505	von Willebrand factor A	0	3
HMPREF9390_RS07665	hypothetical protein	0	3
HMPREF9390_RS07670	alpha/beta hydrolase	0	3
HMPREF9390_RS07780	hypothetical protein	0	3
HMPREF9390_RS08320	Phosphoribosyl transferase (PRT)-type I domain protein	0	3
HMPREF9390_RS08325	Phosphoribosyl transferase (PRT)	0	3
HMPREF9390_RS08330	YceG family protein	0	3
HMPREF9390_RS08335	TelA	0	3
HMPREF9390_RS08340	TerD3 family protein	0	3
HMPREF9390_RS08345	TerD2 family protein	0	3
HMPREF9390_RS08350	TerD family protein	0	3
HMPREF9390_RS08355	calcium-translocating P-type ATPase, PMCA-type	0	3
HMPREF9390_RS08360	haloacid dehalogenase-like hydrolase	0	3
HMPREF9390_RS08365	ATP/GTP-binding protein	0	3
HMPREF9390_RS09105	hypothetical protein	0	3
HMPREF9390_RS09160	hypothetical protein	0	3
HMPREF9390_RS09535	TIGR01741 family protein	0	3
HMPREF9390_RS11625	hypothetical protein	0	3

¹Less virulent strains include SK330, SK115, SK49 and SK355.²More virulent strains include SK405, SK678 and SK 160.³Highlighting indicates contiguous genes.

Table S3 Phage prediction.

Strain	Len (kb)	Score ¹	Annotation	Number of Proteins	Coordinates	GC%	Phage ²
SK1 ^{3,4}	7.5	10	incomplete	8	28468-35983	45.22	1
SK1056	7.5	10	incomplete	8	2334967-2342481	45.51	1
SK1059	7.5	10	incomplete	8	1830314-1837829	45.02	1
SK330 ⁵	7.5	10	incomplete	8	28488-35993	45.3	1
SK340	7.5	10	incomplete	8	533992-541507	45.29	1
SK353	7.5	10	incomplete	9	62142-69658	45.44	1
SK355	7.5	10	incomplete	10	28477-36003	45.3	1
SK405	7.5	10	incomplete	8	28452-35966	45.15	1
SK408	7.5	10	incomplete	9	28463-35978	45.33	1
SK678	7.5	10	incomplete	8	28471-35986	45.21	1
VMC66	7.5	10	incomplete	9	28440-35955	45.17	1
SK72	7.7	40	incomplete	7	1343249-1351022	43.67	2
SK49	8.4	50	incomplete	8	978694-987180	43.25	2
SK1058	9.3	60	incomplete	10	1592356-1601754	42.93	2
SK115	12	70	questionable	11	324086-336155	43.84	2
SK1	7.9	20	incomplete	8	604244-612221	44.5	3
SK678	7.9	20	incomplete	8	1194559-1202536	44.5	3
SK1059	8	20	incomplete	9	1762979-1770988	40.01	4
SK340	8	20	incomplete	9	32320-40327	39.86	4
SK353	8	20	incomplete	9	2256434-2264443	39.79	4
SK408	9.7	10	incomplete	11	323822-333574	33.98	5
SK678	21.8	20	incomplete	16	315436-337313	36.35	5
SK408	10.2	10	incomplete	10	212919-223191	45.33	6
SK1056	11.6	50	incomplete	13	675056-686659	39.23	7
SK353	12.3	10	incomplete	9	1000348-1012646	44.62	8
SK355	12.3	10	incomplete	8	1424349-1436685	45.02	8
SK1059	13	30	incomplete	16	951986-965067	40.25	9
SK150	26.4	30	incomplete	23	522736-549138	36.15	10
SK160	31.7	40	incomplete	24	2138865-2170652	42.22	11
SK72	35.5	80	questionable	34	1274314-1309911	39.79	12
SK405	40	40	incomplete	16	607936-648000	41.91	13
SK115	44.9	90	questionable	42	357854-402792	41.06	14
SK1057	51.6	100	complete	53	928157-1033829	39.46	15
SK36	7	40	incomplete	7	1376694-1383753	44.66	16
SK355	7	30	incomplete	10	432225-439243	42.48	17

¹PHASTER score. Range is from 10-100. Phage regions scoring 100 are considered complete.

²Like numbers indicate a shared phage as determined by manual BLAST analysis.

³Black text = oral strains

⁴Red text = IE isolates

⁵Blue highlight = strains not included in the Bar-seq experiment

Table S4 Sequence alterations made to nucleotide files that were required to run PGAP.

Sequence ID	Strain and file	Alteration
HMPREF9398_RS11715	VMC66.nuc	removed last C and added a stop codon
HMPREF9398_RS03620	VMC66.nuc	added an AG to complete stop codon
HMPREF9398_RS03630	VMC66.nuc	removed last A and added a stop codon (TAG)
HMPREF9398_RS03625	VMC66.nuc	removed last A and added a stop codon (TAG)
HMPREF9388_RS04845	SK353.nuc	added an AG to complete stop codon
HMPREF9392_RS10655	SK1058.nuc	added TAG stop codon
HMPREF9392_RS00005	SK1058.nuc	removed last A and added a stop codon (TAG)
HMPREF9381_RS00940	SK72.nuc	removed last T and added a stop codon
HMPREF9381_RS00045	SK72.nuc	removed the last G and added a stop codon
HMPREF9382_RS09320	SK115.nuc	added an AG to complete stop codon
HMPREF9383_RS06900	SK150.nuc	removed last two A's
HMPREF9383_RS00045	SK150.nuc	added TAG stop codon
HMPREF9378_RS00040	SK1.nuc	removed last two A's
HMPREF9378_RS11090	SK1.nuc	added a G (aa file had additional Ala, nucleotide file was one nuc short of coding for an A. CG-. A final G was added.
HMPREF9391_RS11795	SK408.nuc	added TAG stop codon
HMPREF9395_RS00040	SK678.nuc	added a G (aa file had additional Ala, nucleotide file was one nuc short of coding for an A. GC-. A final G was added.
HMPREF9395_RS05400	SK678.nuc	removed the last T
HMPREF9397_RS00095	SK1059.nuc	removed last C
HMPREF9397_RS04240	SK1059.nuc	removed last A
HMPREF9380_RS07690	SK49.nuc	added TAG stop codon
HMPREF9389_RS00055	SK355.nuc	added TAG stop codon
HMPREF9389_RS10220	SK355.nuc	added TAG stop codon
HMPREF9381_RS00945	SK72.nuc	added TAG stop codon

Table S5 Primers used in strain construction.

Primer Name	Sequence ¹	Purpose
1 spcUP	CCGCTCTAGAACTAGTGGATCC	Generate SK36 Sc^f by overlap extension PCR <i>aad9</i> with native promoter <i>aad9</i> with native promoter left fragment left fragment right fragment right fragment
2 spcDO	CAATTTTTTATAATTTTTTAAATCTG	
3 MJY1	CCAGACGATCACTTCATCC	
4 MJY5-R	GGATCCACTAGTTCAGAGCGGGAATAGAGGTTTTTAAAGAATATTGACAAC	
5 MYJ6-F	CAGATTAATAAAAAATTATAAAAAAATTGCTAGATAAACTTCTGTTCTAC	
6 MYJ2-R	TGTATAGCATTTCATTCCAAG	
7 Tet-F2	ATGAAAATTATAATATTGGAGT	Generate SK36 ΔssaACB Tc^f by overlap extension PCR <i>tetM</i> <i>tetM</i> left fragment left fragment right fragment right fragment
8 Tet-R2	TCACTAAGTTATTTTTATTGAACAT	
9 0262-F1	GCACGATGATAAGCTCCTG	
10 0262-R1	CCAATATTAATAATTTTCAITCTCATACACCTCTATAGT	
11 0260T-F3	CAATAAAATAACTTAGTGATAATAAAAGGTTAGGAAGACA	right fragment
12 0260-R3	CGTTTTCTCAATATTATCAATCCA	
13 Kan-F2	ATGGCTAAAATGAGAATATCACC	Generate SK36 ΔssaACB Km^f by overlap extension PCR <i>apha-3</i> <i>apha-3</i> left fragment left fragment right fragment right fragment
14 Kan-R2	CTAAACAATTCATCCAGTA	
15 0262-F1	GCACGATGATAAGCTCCTG	
16 0262-R1S	TCTCATTTTAGCCATCTCATACACCTCTATAGT	
17 0260-F3	GATGAATTGTTTTAGTAATAAAAGGTTAGGAAGACA	
18 0260-R3	CGTTTTCTCAATATTATCAATCCA	
19 spcUP-short	CCGCTCTAGAACTAGTGGATCC	Generate SK405 Sc^f by overlap extension PCR <i>aad9</i> with native promoter <i>aad9</i> with native promoter left fragment left fragment right fragment right fragment
20 spcDO-long	GAAGTTTATCTAGCAATTTTTTATAATTTTTTAAATCTG	
21 MJY1	CCAGACGATCACTTCATCC	
22 MJY5-R	GGATCCACTAGTTCAGAGCGGGAATAGAGGTTTTTAAAGAATATTGACAAC	
23 MYJ6-F	CAGATTAATAAAAAATTATAAAAAAATTGCTAGATAAACTTCTGTTCTAC	
24 MYJ2-R	TGTATAGCATTTCATTCCAAG	
25 TetProm	CTAGGTTGATTTTCGTTCTG	Generate SK405 Δlipo by overlap extension PCR <i>tetM</i> with native promoter <i>tetM</i> with native promoter SK405Δlipo SK405Δlipo SK405Δlipo SK405Δlipo
26 Tet_R1	GAGTAAAAATTTTTAGACACTAAGTTATTTTATTGAACATATATC	
27 SK405_lipo_Lflank_L1	ACGCTGCTGGATTTTGATAC	
28 SK405_lipo_Lflank_R1	TATTCACGAACGAAAATCAACCTAGTTGCAGTCTCCTTATGGAAC	
29 SK405_lipo_Rflank_L1	AAATAACTTAGTGTCTAAAAAATTTTAACTCTGTCAAG	
30 SK405_lipo_Rflank_R1	GAAAAAACGGGACATAC	
31 kan F2p	GATAAACCCAGCGAACCATTGTA	Generate SK405 Δtel by overlap extension PCR <i>apha3</i> with native promoter <i>apha3</i> with native promoter SK405Δtel SK405Δtel SK405Δtel SK405Δtel
32 Kan-R2Med	AGGTACTAAAACAATTCATCCAGT	
33 SK405-F1	TGGCCAGTTCGATAGCTTCA	
34 SK405-R1	GCTCAACTGTCACTTTAATACTTCA	
35 SK405-F3	ACACACGCATTAATACTGAAC	
36 SK405-R3	CTCCTTATCGGGACATCGCT	
37 Spec_Bseq_L1	CCGCTCTAGAACTAGTGG	Generate BC strains by overlap extension PCR <i>aad9</i> with native promoter <i>aad9</i> with native promoter
38 Spec_Bseq_R1	CGGCGGCCTTATAATTTTTTAAATCT	
39 Lflank_36Bseq_L1	ATTAACACTCTATGAGTAAAC TCCACTAGTTCTAGAGCGGG GACTGACTAC AGTTGCTATCACAGGTGGACGAATAGAGGTTTTTA	BC strains: SK36, BC strains: SK36, SK353, SK150, SK160, SK330, SK405, SK408, SK1056, SK1057, SK1058, SK1059
40 Lflank_36Bseq_R1	AAGAAT	
41 Rflank_36Bseq_L1	GATTAATAAAAAATTATAAGGCCGCCGCTAGATAAACTTCTGTTCTACAC	
42 Rflank_36Bseq_R1	AAAATTTCACTCCAAAGGTTAG GATCCACTAGTTCTAGAGCGGG TAAACCACT AGTTGCTATCACAGGTGGACGAATAGAGGCTTT	
43 Lflank_49Bseq_R1	TAAAGAA	
		BC strains: SK49

44 Rflank_49Bseq_L1	GATTAATAAAATTATAAGGCCGCCGCTAGATAAACTTCTGTTCTACTC GATCCACTAGTTCTAGAGCGGG CCAAATCCGT AGTTGCTATCACAGGTGGACGAATAGAAGCTTT	BC strains: SK49, VMC66
45 Lflank_66Bseq_R1	TAAAGAA	BC strains: VMC66
46 Rflank_72Bseq_R1	AAAAAATTCACCTCAAAGG GATCCACTAGTTCTAGAGCGGG CCCATATGTC AGTTGCTATCACAGGTGGACGAACAGAGGTATT	BC strains: SK160, SK405, SK408, SK1056, SK1057
47 Lflank_115Bseq_R1	AAAGGCT	BC strains: SK115,
48 Rflank_115Bseq_L1	GATTAATAAAATTATAAGGCCGCCGATAGATAAACTTCTGTTCTACTC	BC strains: SK115,
49 Lflank_150Bseq_L1	ATTGAACACTCAATGAGTAAAC GATCCACTAGTTCTAGAGCGGG TGCTAGTTA AGTTGCTATCACAGGTGGACGAATAGAGGCTTT	BC strains: SK150, SK355
50 Lflank_150Bseq_R1	TAAAGAA	BC strains: SK150,
51 Rflank_150Bseq_R1	CTTTTGGAGTGTTTTTTATCTAAAATTTG GATCCACTAGTTCTAGAGCGGG CGACACATCC AGTTGCTATCACAGGTGGACGAATAGAAGCTTT	BC strains: SK49, VMC66, SK150, SK355, SK1056
52 Lflank_160Bseq_R1	TAAAGAA GATCCACTAGTTCTAGAGCGGG CTATAACTGA AGTTGCTATCACAGGTGGACGAATAGAGGCTTC	BC strains: SK160,
53 Lflank_330Bseq_R1	TAAAGAA	BC strains: SK330,
54 Rflank_330Bseq_R1	AAAAATTCACCTCAAAGG GATCCACTAGTTCTAGAGCGGG TACCCATAT AGTTGCTATCACAGGTGGACGAGTAGAGGTTTT	BC strains: SK330,
55 Lflank_340Bseq_R1	TAAAGAA	BC strains: SK340, SK678
56 Rflank_340Bseq_L1	GATTAATAAAATTATAAGGCCGCCGCTAGATAAACTTCTTTTCAACACG	BC strains: SK340, SK1058
57 Rflank_340Bseq_R1	CTTTTGGAGTTTTTTTTATCTAAAATTTG	BC strains: SK340
58 Lflank_353Bseq_L1	ATTAACAATCTATGGGTAACCC GATCCACTAGTTCTAGAGCGGG GTGTTTGT AGTTGCTATCACAGGTGGACGAATAGAGGCTTC	BC strains: SK353,
59 Lflank_353Bseq_R1	TAAAGAA GATCCACTAGTTCTAGAGCGGG CCCACAAGAG AGTTGCTATCACAGGTGGACGAATAGAGGCTTC	BC strains: SK353,
60 Lflank_355Bseq_R1	TTAAAGAA	BC strains: SK355,
61 Rflank_355Bseq_L1	GATTAATAAAATTATAAGGCCGCCGCTAGATAAACTTCTGTTCTACAAG GATCCACTAGTTCTAGAGCGGG GCAACTTTGG AGTTGCTATCACAGGTGGACGAATAGAGGTTTT	BC strains: SK355,
62 Lflank_405Bseq_R1	TAAAGAA GATCCACTAGTTCTAGAGCGGG CATTGACTAC AGTTGCTATCACAGGTGGACGAATAGAAGCTTT	BC strains: SK405
63 Lflank_408Bseq_R1	TAAAGAA GATCCACTAGTTCTAGAGCGGG CGCACCAATG AGTTGCTATCACAGGTGGACGAATAGAGGCTTC	BC strains: SK408
64 Lflank_678Bseq_R1	CTAAAGAA	BC strains: SK678
65 Rflank_678Bseq_L1	GATTAATAAAATTATAAGGCCGCCGCTAGATAAACTTCTGTTCTACAC GATCCACTAGTTCTAGAGCGGG GTATAAAGCG AGTTGCTATCACAGGTGGACGAATAGAGGCTTC	BC strains: SK678
66 Lflank_1056Bseq_R1	TTAAAGAA GATCCACTAGTTCTAGAGCGGG GTGAGCCCAA AGTTGCTATCACAGGTGGACGAATAGAGGTTTT	BC strains: SK1056
67 Lflank_1057Bseq_R1	TTAAAGAA GATCCACTAGTTCTAGAGCGGG GTATCCTGGC AGTTGCTATCACAGGTGGACGAGTAGAGGTTTT	BC strains: SK1057
68 Lflank_1058Bseq_R1	TTAAAGAA GATCCACTAGTTCTAGAGCGGG CTTAGTCGCC AGTTGCTATCACAGGTGGACGAATAGAGGATTT	BC strains: SK1058
69 Lflank_1087Bseq_R1	TAAAGAA	BC strains: SK1059
70 Rflank_1087Bseq_L1	GATTAATAAAATTATAAGGCCGCCGCTAGATAAACTTCTGTTCTACAC	BC strains: SK1059
Amplification of BC strains for Illumina Sequencing Using Staggered Primers		
71 Bseq-quant1L	5' TCGTCGGCAGCGTCAGATGTGTATAAGAGACAGCCACCTGTGATAGCAACT	Total DNA: inocula and homogenized rabbit tissue
72 Bseq-quant2L	5' TCGTCGGCAGCGTCAGATGTGTATAAGAGACAGTCCACCTGTGATAGCAACT	Total DNA: inocula and homogenized rabbit tissue
73 Bseq-quant3L	5' TCGTCGGCAGCGTCAGATGTGTATAAGAGACAGGTCCACCTGTGATAGCAACT	Total DNA: inocula and homogenized rabbit tissue
74 Bseq-quant4L	5' TCGTCGGCAGCGTCAGATGTGTATAAGAGACAGCGACCACCTGTGATAGCAACT	Total DNA: inocula and homogenized rabbit tissue
75 Bseq-quant1R	5' GTCTCGTGGGCTCGGAGATGTGTATAAGAGACAGTATTCAAATATATCCTCCTCAC	Total DNA: inocula and homogenized rabbit tissue
76 Bseq-quant2R	5' GTCTCGTGGGCTCGGAGATGTGTATAAGAGACAGATATTCAAATATATCCTCCTCAC	Total DNA: inocula and homogenized rabbit tissue
77 Bseq-quant3R	5' GTCTCGTGGGCTCGGAGATGTGTATAAGAGACAGTCTATTCAAATATATCCTCCTCAC	Total DNA: inocula and homogenized rabbit tissue
78 Bseq-quant4R	5' GTCTCGTGGGCTCGGAGATGTGTATAAGAGACAGCTATATTCAAATATATCCTCCTCAC	Total DNA: inocula and homogenized rabbit tissue

¹Red letters indicate unique barcodes