

TABLE S2 Gene mutations conferring decreased fitness after 12, 24 and 48 hour incubation with human saliva.
 Columns i, j, k: Comparing with other related genome-wide studies.
 (a) Highlighted gene are found to be expressed in vivo in the monkey oropharynx. (Virtaneva et al., 2005)
 (b) Homologous of highlighted genes are found to be required for *Pneumococcus* fitness in saliva. (Verhagen et al., 2014)
 (c) Highlighted genes are found to be required for GAS fitness in human blood. (Le Breton, et al., 2013)

No.	locus_tag	gene_name	function	Fitness in saliva, 12h	Fitness in saliva, 24h	Fitness in saliva, 48h	Expressed in NHP (a)	Pneumo fitness gene in saliva (b)	GAS fitness gene in blood (c)
				Fold-change	Fold-change	Fold-change			
1	M5005_Spy0004	M5005_Spy0004	GTP-binding protein	-1.578970785	-1.58557353	-1.742569733	YES	YES	
2	M5005_Spy0019	recO	DNA repair protein			-1.754292769	YES		
3	M5005_Spy0085	M5005_Spy0085	putative DNA binding protein			-2.299023255	YES		
4	M5005_Spy0104	M5005_Spy0104	tRNA-dihydrodrouidine synthase			-3.304617837	YES	YES	
5	M5005_Spy0105	M5005_Spy0105	33 kDa chaperone			-2.072901471	YES	YES	
6	M5005_Spy0122	M5005_Spy0122	putative DNA-binding protein			-2.341099429	YES		
7	M5005_Spy0249	oppA	oligopeptide-binding protein			-1.737837023	YES		
8	M5005_Spy0251	oppC	oligopeptide transport system permease protein			-2.004743036	YES	YES	
9	M5005_Spy0253	oppF	oligopeptide transport ATP-binding protein			-1.626716488		YES	
10	M5005_Spy0301	M5005_Spy0301	integral membrane protein			-1.557764268			
11	M5005_Spy0327	upp	uracil phosphoribosyltransferase		-1.742587365	-1.55537654	YES		
12	M5005_Spy0382	msrA2	peptide methionine sulfoxide reductase		-1.695205174		YES		
13	M5005_Spy0401	M5005_Spy0401	putative cytosolic protein		-1.614876005	-1.676926824			
14	M5005_Spy0436	vicK	two-component sensor histidine kinase	-1.700538087	-1.684383807		YES		
15	M5005_Spy0448	M5005_Spy0448	hypothetical protein			-1.821002051	YES		
16	M5005_Spy0485	igt	prolipoprotein diacylglycerol transferase			-2.856429687	YES	YES	
17	M5005_Spy0486	M5005_Spy0486	hypothetical protein		-1.611614426	-2.522773501			
18	M5005_Spy0566	sagE	streptolysin S putative self-immunity protein			-1.848273909			
19	M5005_Spy0567	sagF	streptolysin S biosynthesis protein			-1.564898859	YES		
20	M5005_Spy0568	sagG	streptolysin S export ATP-binding protein	-13.89049981	-7.982236796	-12.05706834	YES		
21	M5005_Spy0569	sagH	streptolysin S export transmembrane protein	-11.5309895	-13.50127029	-750.0033792	YES		
22	M5005_Spy0570	sagI	streptolysin S export transmembrane protein	-10.44822569	-28.60167119	-11.59878722	YES		
23	M5005_Spy0611	M5005_Spy0611	hypothetical protein			-1.671569461	YES		
24	M5005_Spy0630	nfsI	cysteine desulfhydrase		-1.723983908	-22.42314591	YES		
25	M5005_Spy0631	thil	thiamine biosynthesis protein		-1.855500353	-24.08627611	YES		
26	M5005_Spy0642	carA	carbamoyl-phosphate synthase small chain			-1.549580679	YES		YES
27	M5005_Spy0643	carB	carbamoyl-phosphate synthase large chain			-1.631651082	YES		YES
28	M5005_Spy0644	M5005_Spy0644	periplasmic component of efflux system	-2.252987968	-2.29658991	-2.910849618			
29	M5005_Spy0645	M5005_Spy0645	ABC transporter ATP-binding protein	-1.87635273	-2.005171629	-2.721826223	YES		
30	M5005_Spy0646	M5005_Spy0646	ABC transporter permease protein	-2.16470395	-2.115199827	-2.999056121	YES		
31	M5005_Spy0665	M5005_Spy0665	transposase			-1.57793436			
32	M5005_Spy0693	M5005_Spy0693	hypothetical protein			-1.605451025	YES		
33	M5005_Spy0718	M5005_Spy0718	hypothetical protein			-1.588522263	YES		
34	M5005_Spy0722	miaA	tRNA delta(2)-isopentenylpyrophosphate transferase			-1.862764877	YES		
35	M5005_Spy0805	srtK	nisin biosynthesis sensor protein			-1.508429525	YES		
36	M5005_Spy0810	srtG	lantibiotic transport permease protein			-1.661863515			
37	M5005_Spy0817	dacA1	D-alanyl-D-alanine carboxypeptidase			-1.565288324	YES		
38	M5005_Spy0826	poIA	spermidine/putrescine transport system ATP-binding protein	-1.521799626		-3.088251227	YES		
39	M5005_Spy0829	M5005_Spy0829	spermidine/putrescine-binding protein			-1.946753612			YES
40	M5005_Spy0841	M5005_Spy0841	glutamine amidotransferase			-1.633038038	YES		
41	M5005_Spy0847	M5005_Spy0847	GTP pyrophosphokinase	-1.697639654	-1.566951387		YES		
42	M5005_Spy0860	apbE	thiamine biosynthesis lipoprotein	-1.535387549	-2.002338933		YES		
43	M5005_Spy0864	hemK	peptide release factor-glutamine N5-methyltransferase	-1.725261326			YES		
44	M5005_Spy0872	nox	NADH oxidase H2O-forming			-1.514291312	YES		
45	M5005_Spy0926	M5005_Spy0926	cardiolipin synthetase	-3.061011447	-5.999314076	-22.92056556	YES	YES	
46	M5005_Spy0944	M5005_Spy0944	16S rRNA m(2)G 1207 methyltransferase			-1.537389119	YES		
47	M5005_Spy0951	psIB	phosphate transport ATP-binding protein		-3.030859923	-7.879985046		YES	
48	M5005_Spy0952	psIB2	phosphate transport ATP-binding protein	-1.636657929	-3.627287832	-8.2199908713	YES	YES	
49	M5005_Spy0953	psIA	phosphate transport system permease protein	-1.64675359	-3.71529891	-12.6715751	YES	YES	
50	M5005_Spy0954	psIC	phosphate transport system permease protein	-1.702665738	-3.822470575	-13.28351681	YES	YES	
51	M5005_Spy0955	psIS	phosphate-binding protein	-1.609345238	-4.081100056	-10.69078939	YES	YES	
52	M5005_Spy0971	M5005_Spy0971	general stress protein, Glx24 family		-1.658159678	-2.48787223	YES		
53	M5005_Spy0973	M5005_Spy0973	general stress protein, Glx24 family		-1.736815972	-1.903457746	YES		
54	M5005_Spy0975	M5005_Spy0975	hypothetical protein	-1.770147517	-1.904237938	-3.605469009	YES		
55	M5005_Spy0987	sipC	signal peptidase I		-1.669798494	-3.583806216	YES		
56	M5005_Spy0992	M5005_Spy0992	ABC transporter ATP-binding protein	-2.35058252	-2.001534524	-2.847001093			
57	M5005_Spy0993	M5005_Spy0993	ABC transporter permease protein	-2.794310569	-2.144272007	-2.784840361	YES		
58	M5005_Spy1021	M5005_Spy1021	phage protein			-1.541202391			
59	M5005_Spy1023	M5005_Spy1023	terminase large subunit			-1.553884241			
60	M5005_Spy1067	malX	maltose/maltodextrin-binding protein			-1.896662761	YES		
61	M5005_Spy1068	M5005_Spy1068	transposase		-1.511512107	-1.886032564			
62	M5005_Spy1075	uvrB	excinuclease ABC subunit B		-1.530782126		YES		
63	M5005_Spy1107	murZ	UDP-N-acetylglucosamine 1-carboxyvinyl transferase	-1.64501845			YES		
64	M5005_Spy1139	nagB	glucosamine-6-phosphate isomerase	-1.845643238	-4.268789759	-18.29865104	YES		
65	M5005_Spy1182	M5005_Spy1182	phage protein			-1.660660452			
66	M5005_Spy1226	M5005_Spy1226	degV family protein			-1.548113507		YES	
67	M5005_Spy1242	M5005_Spy1242	putative cytosolic protein	-2.396844911	-14.18022438	-195.1506992	YES		
68	M5005_Spy1273	arcB	ornithine carbamoyltransferase			-2.494894006	YES		
69	M5005_Spy1325	M5005_Spy1325	ribosome-associated factor Y			-2.14292978			
70	M5005_Spy1375	tkt	transketolase	-3.496674695	-5.730245502	-15.59097809	YES	YES	
71	M5005_Spy1381	glpK	glycerol kinase	-1.535859342			YES		
72	M5005_Spy1388	nagA	N-acetylglucosamine-6-phosphate deacetylase	-1.930321315	-7.819520774	-148.3093522	YES	YES	
73	M5005_Spy1402	lacR1	lactose phosphotransferase system repressor			-2.57840735	YES		
74	M5005_Spy1418	M5005_Spy1418	phage protein		-1.501932821				
75	M5005_Spy1439	M5005_Spy1439	portal protein		-2.064830788		YES		
76	M5005_Spy1468	M5005_Spy1468	tRNA (m(7)G46) methyltransferase	-1.588241472	-23.12331138	-8197.940314	YES		
77	M5005_Spy1472	hit	bis(5'-nucleosyl)tetraphosphatase (asymmetrical)		-1.681582108	-2.315088687	YES		
78	M5005_Spy1473	M5005_Spy1473	hypothetical protein			-1.965495543			
79	M5005_Spy1479	manL	PTS system			-1.627000908	YES		
80	M5005_Spy1480	manM	PTS system			-1.915777282			
81	M5005_Spy1481	manN	PTS system			-1.788676679	YES		YES
82	M5005_Spy1519	recG	ATP-dependent DNA helicase	-2.785545672	-2.291381227	-2.168312974	YES		
83	M5005_Spy1560	M5005_Spy1560	phosphatidylglycerophosphatase B		-1.51728074	-2.310177493	YES		
84	M5005_Spy1719	emm1.0	M protein			-1.523545262	YES		
85	M5005_Spy1737	rgg	transcriptional regulator			-1.524186201			
86	M5005_Spy1753	pbp2A	multimodular transpeptidase-transglycosylase	-2.939159969	-2.808870479	-3.251429026	YES	YES	
87	M5005_Spy1769	ahpF	peroxiredoxin reductase (NAD(P)H)			-3.048317251			
88	M5005_Spy1770	hutI	imidazolonepropionase			-1.578855117	YES		
89	M5005_Spy1783	dexS	trehalose-6-phosphate hydrolase			-2.283622667	YES	YES	
90	M5005_Spy1810	M5005_Spy1810	putative membrane spanning protein			-3.920793404	YES		
91	M5005_Spy1823	M5005_Spy1823	integral membrane protein			-1.887367852	YES		
92	M5005_Spy1837	M5005_Spy1837	phosphoesterase	-3.74576977	-18.70421192	-163.915988			
							Sum = 68	Sum = 18	Sum = 4