

Table S1. List of primers used for multiplex qPCR.

Target virus, Gene	Primer and probe sequences	Fluorescent and quenched signal
Influenza A virus, M1	F: GACCRATCCTGTCACCTCTGAC R: AGGGCATTYTGGACAAAKCGTCTA P: TGCAGTCCTCGCTCACTGGGCACG	5'-FAM, 3'-BHQ1
Influenza B virus, HA	F: AAATACGGTGGATTAAATAAAAAGCAA R: CCAGCAATAGCTCCGAAGAAA P: CACCCATATTGGGCAATTTCCTAT	5'-HEX, 3'-BHQ1
RSV, matrix protein	F: GCAAATATGGAAACATACGTGAACA R: GCACCCATATTGTWAGTGATGCA P: CTTCACGAAGGCTCCACATACACAGCWG	5'-TexasRed, 3'-BHQ2
Rhinovirus, 5' UTR	F1: GGTGTGAAGAGCCSRTGTGCT F2: GGTGTGAAGACTCGCATGTGCT F3: GGGTGYGAAGAGYCTANTGTGCT R3: GGACACCCAAAGTAGTYGGTYC P: CGGGCCCCCTGAATGYGGCTAACYC	5'-CY5, 3'-MGB

Table S2. The differential genera between virus-positive and negative groups.

Difference genera in LEfSe analysis	Enriched groups	LDA value	P value	Comparison between groups
<i>Aequorivita</i>	FluA	3.192	0.035	FluA vs Health
<i>Truepera</i>	FluA	3.372	0.035	FluA vs Health
<i>Staphylococcus</i>	FluA	2.600	0.029	FluA vs Health
<i>uncultured Desulfocaldu ssp.</i>	FluA	3.148	0.035	FluA vs Health
<i>Cardiobacterium</i>	FluA	2.399	0.046	FluA vs Health
<i>Planktosalinus</i>	FluA	3.164	0.035	FluA vs Health
<i>Tyzzerella 3</i>	FluA	2.518	0.003	FluA vs Health
<i>Faecalibaculum</i>	FluA	2.948	0.035	FluA vs Health
<i>Allorhizobium-Neorhizobium-Pararhizobium-Rhizobium</i>	FluA	2.715	0.035	FluA vs Health
<i>Ralstonia</i>	FluA	3.324	0.024	FluA vs Health
<i>Arenimonas</i>	FluA	3.299	0.035	FluA vs Health
<i>Actinomadura</i>	FluA	3.046	0.035	FluA vs Health
<i>Lactobacillus</i>	FluA	2.333	0.002	FluA vs Health
<i>Petrimonas</i>	FluA	2.296	0.031	FluA vs Health
<i>Geobacter</i>	FluA	3.085	0.035	FluA vs Health
<i>Veillonella</i>	FluA	4.287	0.013	FluA vs Health
<i>Dietzia</i>	FluA	3.460	0.035	FluA vs Health
<i>Bosea</i>	FluA	3.330	0.035	FluA vs Health
<i>Pseudoramibacter</i>	FluA	2.291	0.003	FluA vs Health
<i>Lachnospiraceae NK4A136</i>	FluA	2.330	0.029	FluA vs Health
<i>Lachnoanaero baculum</i>	FluA	3.130	0.014	FluA vs Health
<i>Solobacterium</i>	FluA	3.083	0.018	FluA vs Health
<i>Luteimonas</i>	FluA	3.116	0.035	FluA vs Health
<i>Ornithobacterium</i>	FluA	3.161	0.035	FluA vs Health
<i>Uncultured Sphingobacteriia</i>	FluA	2.982	0.035	FluA vs Health
<i>Mogibacterium</i>	FluA	2.244	0.003	FluA vs Health
<i>Phycicoccus</i>	FluA	3.016	0.035	FluA vs Health
<i>Atopobium</i>	FluA	3.623	<0.001	FluA vs Health
<i>Phascolarcto bacterium</i>	FluA	2.530	0.027	FluA vs Health
<i>Pantoea</i>	FluA	2.314	0.029	FluA vs Health
<i>Macrococcus</i>	FluA	3.150	0.035	FluA vs Health
<i>Gracilibacteria bacterium oral taxon 873</i>	Health	2.282	0.022	FluA vs Health
<i>Filifactor</i>	Health	2.722	0.048	FluA vs Health
<i>Actinobacillus</i>	Health	3.801	<0.001	FluA vs Health
<i>Streptococcus</i>	Health	4.551	0.043	FluA vs Health
<i>Corynebacterium 1</i>	Health	2.048	0.043	FluA vs Health
<i>Granulicatella</i>	Health	3.669	0.050	FluA vs Health
<i>Abiotrophia</i>	FluB	2.791	<0.001	FluB vs Health

<i>Streptobacillus</i>	FluB	2.544	0.045	FluB vs Health
<i>Veillonella</i>	FluB	4.312	<0.001	FluB vs Health
<i>Fusobacterium</i>	FluB	4.218	0.014	FluB vs Health
<i>F0058</i>	FluB	2.250	0.030	FluB vs Health
<i>Pseudoramibacter</i>	FluB	2.627	0.004	FluB vs Health
<i>Eubacterium nodatum</i> group	FluB	2.836	0.022	FluB vs Health
<i>Prevotella</i>	FluB	3.929	0.014	FluB vs Health
<i>Lachnoanaerobaculum</i>	FluB	2.874	0.013	FluB vs Health
<i>F0332</i>	FluB	2.237	0.037	FluB vs Health
<i>Atopobium</i>	FluB	3.038	0.001	FluB vs Health
<i>Arcobacter</i>	FluB	2.812	0.037	FluB vs Health
<i>Leptotrichia</i>	Health	3.964	<0.001	FluB vs Health
<i>Sphingomonas</i>	Health	3.544	0.017	FluB vs Health
<i>Brevundimonas</i>	Health	3.439	0.039	FluB vs Health
<i>Campylobacter</i>	Health	2.574	0.005	FluB vs Health
<i>Gracilibacteria bacterium oral taxon 873</i>	Health	2.258	0.004	FluB vs Health
<i>Ruminococcaceae UCG_014</i>	Health	3.203	0.010	FluB vs Health
<i>Prevotella 1</i>	Health	2.861	0.033	FluB vs Health
<i>Prevotella 2</i>	Health	3.050	0.025	FluB vs Health
<i>Alteromonas</i>	Health	3.139	0.017	FluB vs Health
<i>Ralstonia</i>	Health	2.530	0.001	FluB vs Health
<i>Sediminispirochaeta</i>	Health	3.145	0.039	FluB vs Health
<i>Mobiluncus</i>	Health	2.252	0.017	FluB vs Health
<i>Mesorhizobium</i>	Health	3.180	0.017	FluB vs Health
<i>Catonella</i>	Health	2.828	<0.001	FluB vs Health
<i>Peptostreptococcus</i>	Health	2.681	0.002	FluB vs Health
<i>Aggregatibacter</i>	Health	3.166	0.008	FluB vs Health
<i>Filifactor</i>	Health	2.610	0.008	FluB vs Health
<i>Bergeyella</i>	Health	2.589	0.022	FluB vs Health
<i>Synechococcus CC9902</i>	Health	3.251	0.039	FluB vs Health
<i>Treponema 2</i>	Health	2.556	0.010	FluB vs Health
<i>Actinobacillus</i>	Health	3.313	<0.001	FluB vs Health
<i>Pseudomonas</i>	Health	2.250	<0.001	FluB vs Health
<i>Acinetobacter</i>	Health	2.447	0.040	FluB vs Health
<i>Streptococcus</i>	Health	4.334	0.014	FluB vs Health
<i>Uruburuella</i>	Health	2.831	<0.001	FluB vs Health
<i>Granulicatella</i>	Health	3.582	<0.001	FluB vs Health
<i>Eubacterium yurii</i> group	Health	2.308	0.009	FluB vs Health
<i>Leptotrichia</i>	Health	3.901	0.013	HRV vs Health
<i>Gracilibacteria bacterium oral taxon 873</i>	Health	2.382	0.005	HRV vs Health
<i>Bacteroidia bacterium feline oral taxon 312</i>	Health	2.917	0.050	HRV vs Health

<i>Ruminococcaceae UCG_014</i>	Health	3.351	<0.001	HRV vs Health
<i>Prevotella 2</i>	Health	3.121	0.001	HRV vs Health
<i>Ralstonia</i>	Health	2.666	0.012	HRV vs Health
<i>Peptostreptococcus</i>	Health	2.829	<0.001	HRV vs Health
<i>Aggregatibacter</i>	Health	2.993	0.010	HRV vs Health
<i>Pseudomonas</i>	Health	2.472	0.001	HRV vs Health
<i>F0332</i>	Health	2.362	0.005	HRV vs Health
<i>Acinetobacter</i>	Health	2.579	0.011	HRV vs Health
<i>Haemophilus</i>	Health	4.126	0.025	HRV vs Health
<i>Granulicatella</i>	Health	3.832	0.001	HRV vs Health
<i>Abiotrophia</i>	HRV	2.785	<0.001	HRV vs Health
<i>Veillonella</i>	HRV	4.206	0.002	HRV vs Health
<i>F0058</i>	HRV	2.589	0.039	HRV vs Health
<i>Actinobacillus</i>	HRV	3.400	0.036	HRV vs Health
<i>Pseudoramibacter</i>	HRV	3.281	0.001	HRV vs Health
<i>Scardovia</i>	HRV	2.681	0.013	HRV vs Health
<i>Eubacterium nodatum group</i>	HRV	2.662	0.033	HRV vs Health
<i>Prevotella</i>	HRV	3.876	0.021	HRV vs Health
<i>Atopobium</i>	HRV	2.935	0.018	HRV vs Health
<i>Gracilibacteria bacterium oral taxon 873</i>	Health	2.522	0.015	RSV vs Health
<i>Ruminococcaceae UCG_014</i>	Health	3.268	0.031	RSV vs Health
<i>Prevotella 2</i>	Health	3.243	0.005	RSV vs Health
<i>Oribacterium</i>	Health	3.041	0.009	RSV vs Health
<i>Catonella</i>	Health	2.823	0.003	RSV vs Health
<i>Peptostreptococcus</i>	Health	2.960	<0.001	RSV vs Health
<i>Aggregatibacter</i>	Health	3.295	0.003	RSV vs Health
<i>Pseudomonas</i>	Health	2.580	0.001	RSV vs Health
<i>Solobacterium</i>	Health	2.875	0.003	RSV vs Health
<i>Acinetobacter</i>	Health	2.678	0.039	RSV vs Health
<i>Uruburuella</i>	Health	3.015	0.033	RSV vs Health
<i>Haemophilus</i>	Health	4.178	0.010	RSV vs Health
<i>Granulicatella</i>	Health	3.897	0.002	RSV vs Health
<i>Eubacterium yurii group</i>	Health	2.495	0.009	RSV vs Health
<i>Prevotella 6</i>	RSV	2.574	0.038	RSV vs Health
<i>Clostridiales bacterium canine oral taxon 260</i>	RSV	3.318	0.004	RSV vs Health
<i>Abiotrophia</i>	RSV	2.843	<0.001	RSV vs Health
<i>Anaeroglobus</i>	RSV	2.805	<0.001	RSV vs Health
<i>Veillonella</i>	RSV	4.338	0.034	RSV vs Health
<i>F0332</i>	RSV	2.469	0.001	RSV vs Health

Table S3, In the random forest model with 100 resamplings, the Mean Decrease Accuracy from group 1 and group 2 was used for the Wilcoxon test.

Taxon	group1	group2	p	p.adj	p.signif	method
<i>p_Firmicutes;c_Bacilli;o_Lactobacillales;f_Carnobacteriaceae;g_Granulicatella</i>	FluA	FluB	3.14E-17	2.80E-16	****	Wilcoxon
<i>p_Firmicutes;c_Bacilli;o_Lactobacillales;f_Carnobacteriaceae;g_Granulicatella</i>	FluA	RSV	0.002479	0.0074	**	Wilcoxon
<i>p_Firmicutes;c_Bacilli;o_Lactobacillales;f_Carnobacteriaceae;g_Granulicatella</i>	FluA	HRV	0.013809	0.028	*	Wilcoxon
<i>p_Firmicutes;c_Bacilli;o_Lactobacillales;f_Carnobacteriaceae;g_Granulicatella</i>	FluA	Infection	4.25E-09	3.00E-08	****	Wilcoxon
<i>p_Firmicutes;c_Bacilli;o_Lactobacillales;f_Carnobacteriaceae;g_Granulicatella</i>	FluB	RSV	2.01E-11	1.60E-10	****	Wilcoxon
<i>p_Firmicutes;c_Bacilli;o_Lactobacillales;f_Carnobacteriaceae;g_Granulicatella</i>	FluB	HRV	2.15E-18	2.20E-17	****	Wilcoxon
<i>p_Firmicutes;c_Bacilli;o_Lactobacillales;f_Carnobacteriaceae;g_Granulicatella</i>	FluB	Infection	0.000187	0.00093	***	Wilcoxon
<i>p_Firmicutes;c_Bacilli;o_Lactobacillales;f_Carnobacteriaceae;g_Granulicatella</i>	RSV	HRV	0.138501	0.14	ns	Wilcoxon
<i>p_Firmicutes;c_Bacilli;o_Lactobacillales;f_Carnobacteriaceae;g_Granulicatella</i>	RSV	Infection	0.001067	0.0043	**	Wilcoxon
<i>p_Firmicutes;c_Bacilli;o_Lactobacillales;f_Carnobacteriaceae;g_Granulicatella</i>	HRV	Infection	3.64E-07	2.20E-06	****	Wilcoxon
<i>p_Bacteroidetes;c_Bacteroidia;o_Bacteroidales;f_Prevotellaceae;g_Prevotella 7;s_Prevotella sp. oral clone P4PB_83 P2</i>	FluA	FluB	1.11E-26	1.00E-25	****	Wilcoxon
<i>p_Bacteroidetes;c_Bacteroidia;o_Bacteroidales;f_Prevotellaceae;g_Prevotella 7;s_Prevotella sp. oral clone P4PB_83 P2</i>	FluA	RSV	8.13E-09	2.40E-08	****	Wilcoxon
<i>p_Bacteroidetes;c_Bacteroidia;o_Bacteroidales;f_Prevotellaceae;g_Prevotella 7;s_Prevotella sp. oral clone P4PB_83 P2</i>	FluA	HRV	0.261253	0.26	ns	Wilcoxon
<i>p_Bacteroidetes;c_Bacteroidia;o_Bacteroidales;f_Prevotellaceae;g_Prevotella 7;s_Prevotella sp. oral clone P4PB_83 P2</i>	FluA	Infection	2.63E-18	1.80E-17	****	Wilcoxon
<i>p_Bacteroidetes;c_Bacteroidia;o_Bacteroidales;f_Prevotellaceae;g_Prevotella 7;s_Prevotella sp. oral clone P4PB_83 P2</i>	FluB	RSV	1.18E-14	7.10E-14	****	Wilcoxon
<i>p_Bacteroidetes;c_Bacteroidia;o_Bacteroidales;f_Prevotellaceae;g_Prevotella 7;s_Prevotella sp. oral clone P4PB_83 P2</i>	FluB	HRV	1.70E-31	1.70E-30	****	Wilcoxon
<i>p_Bacteroidetes;c_Bacteroidia;o_Bacteroidales;f_Prevotellaceae;g_Prevotella 7;s_Prevotella sp. oral clone P4PB_83 P2</i>	FluB	Infection	3.87E-11	1.50E-10	****	Wilcoxon
<i>p_Bacteroidetes;c_Bacteroidia;o_Bacteroidales;f_Prevotellaceae;g_Prevotella 7;s_Prevotella sp. oral clone P4PB_83 P2</i>	RSV	HRV	1.78E-08	3.60E-08	****	Wilcoxon
<i>p_Bacteroidetes;c_Bacteroidia;o_Bacteroidales;f_Prevotellaceae;g_Prevotella 7;s_Prevotella sp. oral clone P4PB_83 P2</i>	RSV	Infection	3.47E-14	1.70E-13	****	Wilcoxon
<i>p_Bacteroidetes;c_Bacteroidia;o_Bacteroidales;f_Prevotellaceae;g_Prevotella 7;s_Prevotella sp. oral clone P4PB_83 P2</i>	HRV	Infection	2.73E-23	2.20E-22	****	Wilcoxon
<i>p_Proteobacteria;c_Gammaproteobacteria;o_Pasteurellales;f_Pasteurellaceae;g_Haemophilus</i>	FluA	FluB	0.066916	0.33	ns	Wilcoxon
<i>p_Proteobacteria;c_Gammaproteobacteria;o_Pasteurellales;f_Pasteurellaceae;g_Haemophilus</i>	FluA	RSV	0.002375	0.024	**	Wilcoxon
<i>p_Proteobacteria;c_Gammaproteobacteria;o_Pasteurellales;f_Pasteurellaceae;g_Haemophilus</i>	FluA	HRV	0.008529	0.06	**	Wilcoxon
<i>p_Proteobacteria;c_Gammaproteobacteria;o_Pasteurellales;f_Pasteurellaceae;g_Haemophilus</i>	FluA	Infection	0.203285	0.81	ns	Wilcoxon
<i>p_Proteobacteria;c_Gammaproteobacteria;o_Pasteurellales;f_Pasteurellaceae;g_Haemophilus</i>	FluB	RSV	0.003885	0.031	**	Wilcoxon
<i>p_Proteobacteria;c_Gammaproteobacteria;o_Pasteurellales;f_Pasteurellaceae;g_Haemophilus</i>	FluB	HRV	0.002361	0.024	**	Wilcoxon
<i>p_Proteobacteria;c_Gammaproteobacteria;o_Pasteurellales;f_Pasteurellaceae;g_Haemophilus</i>	FluB	Infection	0.312946	0.94	ns	Wilcoxon
<i>p_Proteobacteria;c_Gammaproteobacteria;o_Pasteurellales;f_Pasteurellaceae;g_Haemophilus</i>	RSV	HRV	0.626976	1	ns	Wilcoxon
<i>p_Proteobacteria;c_Gammaproteobacteria;o_Pasteurellales;f_Pasteurellaceae;g_Haemophilus</i>	RSV	Infection	0.021042	0.13	*	Wilcoxon
<i>p_Proteobacteria;c_Gammaproteobacteria;o_Pasteurellales;f_Pasteurellaceae;g_Haemophilus</i>	HRV	Infection	0.792703	1	ns	Wilcoxon
<i>p_Proteobacteria;c_Gammaproteobacteria;o_Pasteurellales;f_Pasteurellaceae;g_Actinobacillus</i>	FluA	FluB	5.23E-08	2.60E-07	****	Wilcoxon
<i>p_Proteobacteria;c_Gammaproteobacteria;o_Pasteurellales;f_Pasteurellaceae;g_Actinobacillus</i>	FluA	RSV	3.17E-07	1.30E-06	****	Wilcoxon
<i>p_Proteobacteria;c_Gammaproteobacteria;o_Pasteurellales;f_Pasteurellaceae;g_Actinobacillus</i>	FluA	HRV	7.28E-12	5.80E-11	****	Wilcoxon

FluA	Infection	0.014253	0.029	*	Wilcoxon
FluB	RSV	1.74E-09	1.20E-08	****	Wilcoxon
FluB	HRV	6.18E-23	6.20E-22	****	Wilcoxon
FluB	Infection	0.002755	0.0083	**	Wilcoxon
RSV	HRV	0.159414	0.16	ns	Wilcoxon
RSV	Infection	2.46E-08	1.50E-07	****	Wilcoxon
HRV	Infection	1.53E-16	1.40E-15	****	Wilcoxon
FluA	FluB	4.40E-06	3.50E-05	****	Wilcoxon
FluA	RSV	0.016368	0.082	*	Wilcoxon
FluA	HRV	2.97E-07	2.70E-06	****	Wilcoxon
FluA	Infection	4.77E-08	4.80E-07	****	Wilcoxon
FluB	RSV	0.097467	0.29	ns	Wilcoxon
FluB	HRV	0.000125	0.00075	***	Wilcoxon
FluB	Infection	0.435704	0.87	ns	Wilcoxon
RSV	HRV	0.481102	0.87	ns	Wilcoxon
RSV	Infection	0.073494	0.29	ns	Wilcoxon
HRV	Infection	3.13E-05	0.00022	****	Wilcoxon
FluA	FluB	7.78E-07	5.40E-06	****	Wilcoxon
FluA	RSV	3.05E-09	2.40E-08	****	Wilcoxon
FluA	HRV	1.63E-11	1.60E-10	****	Wilcoxon
FluA	Infection	1.42E-10	1.30E-09	****	Wilcoxon
FluB	RSV	0.383294	1	ns	Wilcoxon
FluB	HRV	0.004697	0.028	**	Wilcoxon
FluB	Infection	0.083102	0.42	ns	Wilcoxon
RSV	HRV	0.300664	1	ns	Wilcoxon
RSV	Infection	0.909065	1	ns	Wilcoxon
HRV	Infection	0.532642	1	ns	Wilcoxon
FluA	FluB	2.06E-13	1.20E-12	****	Wilcoxon
FluA	RSV	0.946434	0.95	ns	Wilcoxon
FluA	HRV	0.014827	0.03	*	Wilcoxon
FluA	Infection	2.51E-13	1.30E-12	****	Wilcoxon
FluB	RSV	8.02E-29	8.00E-28	****	Wilcoxon
FluB	HRV	2.85E-21	2.30E-20	****	Wilcoxon
FluB	Infection	0.008898	0.027	**	Wilcoxon
RSV	HRV	6.19E-06	2.50E-05	****	Wilcoxon
RSV	Infection	3.92E-28	3.50E-27	****	Wilcoxon
HRV	Infection	7.68E-19	5.40E-18	****	Wilcoxon

FluA	FluB	0.546816	1	ns	Wilcoxon
FluA	RSV	0.097101	0.58	ns	Wilcoxon
FluA	Infection	0.57982	1	ns	Wilcoxon
FluB	RSV	0.198837	0.95	ns	Wilcoxon
FluB	Infection	0.883474	1	ns	Wilcoxon
RSV	Infection	0.190396	0.95	ns	Wilcoxon
FluA	FluB	1.63E-11	9.80E-11	****	Wilcoxon
FluA	RSV	1.72E-09	6.90E-09	****	Wilcoxon
FluA	HRV	1.24E-08	3.70E-08	****	Wilcoxon
FluA	Infection	1.66E-11	9.80E-11	****	Wilcoxon
FluB	RSV	5.24E-19	3.70E-18	****	Wilcoxon
FluB	HRV	2.77E-25	2.50E-24	****	Wilcoxon
FluB	Infection	0.049593	0.099	*	Wilcoxon
RSV	HRV	0.345558	0.35	ns	Wilcoxon
RSV	Infection	9.34E-24	7.50E-23	****	Wilcoxon
HRV	Infection	5.56E-29	5.60E-28	****	Wilcoxon
FluA	FluB	1.11E-26	1.00E-25	****	Wilcoxon
FluA	RSV	8.13E-09	2.40E-08	****	Wilcoxon
FluA	HRV	0.261253	0.26	ns	Wilcoxon
FluA	Infection	2.63E-18	1.80E-17	****	Wilcoxon
FluB	RSV	1.18E-14	7.10E-14	****	Wilcoxon
FluB	HRV	1.70E-31	1.70E-30	****	Wilcoxon
FluB	Infection	3.87E-11	1.50E-10	****	Wilcoxon
RSV	HRV	1.78E-08	3.60E-08	****	Wilcoxon
RSV	Infection	3.47E-14	1.70E-13	****	Wilcoxon
HRV	Infection	2.73E-23	2.20E-22	****	Wilcoxon
FluA	FluB	4.40E-06	3.50E-05	****	Wilcoxon
FluA	RSV	0.016368	0.082	*	Wilcoxon
FluA	HRV	2.97E-07	2.70E-06	****	Wilcoxon
FluA	Infection	4.77E-08	4.80E-07	****	Wilcoxon
FluB	RSV	0.097467	0.29	ns	Wilcoxon
FluB	HRV	0.000125	0.00075	***	Wilcoxon
FluB	Infection	0.435704	0.87	ns	Wilcoxon
RSV	HRV	0.481102	0.87	ns	Wilcoxon
RSV	Infection	0.073494	0.29	ns	Wilcoxon
HRV	Infection	3.13E-05	0.00022	****	Wilcoxon
FluA	FluB	7.78E-07	5.40E-06	****	Wilcoxon

p_Firmicutes;c_Erysipelotrichia;o_Erysipelotrichales;f_Erysipelotrichaceae;g_Solobacterium
 p_Firmicutes;c_Gammaproteobacteria;o_Enterobacterales;f_Enterobacteriaceae
 p_Proteobacteria;c_Gammaproteobacteria;o_Enterobacterales;f_Enterobacteriaceae
 p_Bacteroidetes;c_Bacteroidia;o_Bacteroidales;f_Tannerellaceae;g_Tannerella;s_uncultured bacterium
 p_Bacteroidetes;c_Bacteroidia;o_Bacteroidales;f_Tannerellaceae;g_Tannerella;sPrevotella shahii DSM 15611 = JCM 12083
 p_Bacteroidetes;c_Bacteroidia;o_Bacteroidales;f_Tannerellaceae;g_Tannerella;sPrevotella shahii DSM 15611 = JCM 12083

FluA	RSV	3.05E-09	2.40E-08	****	Wilcoxon
FluA	HRV	1.63E-11	1.60E-10	****	Wilcoxon
FluA	Infection	1.42E-10	1.30E-09	****	Wilcoxon
FluB	RSV	0.383294	1	ns	Wilcoxon
FluB	HRV	0.004697	0.028	**	Wilcoxon
FluB	Infection	0.083102	0.42	ns	Wilcoxon
RSV	HRV	0.300664	1	ns	Wilcoxon
RSV	Infection	0.909065	1	ns	Wilcoxon
HRV	Infection	0.532642	1	ns	Wilcoxon
FluA	FluB	0.066916	0.33	ns	Wilcoxon
FluA	RSV	0.002375	0.024	**	Wilcoxon
FluA	HRV	0.008529	0.06	**	Wilcoxon
FluA	Infection	0.203285	0.81	ns	Wilcoxon
FluB	RSV	0.003885	0.031	**	Wilcoxon
FluB	HRV	0.002361	0.024	**	Wilcoxon
FluB	Infection	0.312946	0.94	ns	Wilcoxon
RSV	HRV	0.626976	1	ns	Wilcoxon
RSV	Infection	0.021042	0.13	*	Wilcoxon
HRV	Infection	0.792703	1	ns	Wilcoxon
FluA	FluB	1.11E-26	1.00E-25	****	Wilcoxon
FluA	RSV	8.13E-09	2.40E-08	****	Wilcoxon
FluA	HRV	0.261253	0.26	ns	Wilcoxon
FluA	Infection	2.63E-18	1.80E-17	****	Wilcoxon
FluB	RSV	1.18E-14	7.10E-14	****	Wilcoxon
FluB	HRV	1.70E-31	1.70E-30	****	Wilcoxon
FluB	Infection	3.87E-11	1.50E-10	****	Wilcoxon
RSV	HRV	1.78E-08	3.60E-08	****	Wilcoxon
RSV	Infection	3.47E-14	1.70E-13	****	Wilcoxon
HRV	Infection	2.73E-23	2.20E-22	****	Wilcoxon
FluA	FluB	4.40E-06	3.50E-05	****	Wilcoxon
FluA	RSV	0.016368	0.082	*	Wilcoxon
FluA	HRV	2.97E-07	2.70E-06	****	Wilcoxon
FluA	Infection	4.77E-08	4.80E-07	****	Wilcoxon
FluB	RSV	0.097467	0.29	ns	Wilcoxon
FluB	HRV	0.000125	0.00075	***	Wilcoxon
FluB	Infection	0.435704	0.87	ns	Wilcoxon
RSV	HRV	0.481102	0.87	ns	Wilcoxon

p_Bacteroidetes;c_Bacteroidia;o_Bacteroidales;f_Prevotellaceae;g_Prevotella shahii DSM 15611 = JCM 12083
 p_Bacteroidetes;c_Bacteroidia;o_Bacteroidales;f_Prevotellaceae;g_Prevotella shahii DSM 15611 = JCM 12083
 p_Firmicutes;c_Bacilli;o_Lactobacillales;f_Aerococcaceae;g_Abiotrophia;s_uncultured bacterium
 p_Firmicutes;c_Clostridia;o_Clostridiales;f_Peptostreptococcaceae;g_Peptostreptococcus;s_uncultured organism
 p_Firmicutes;c_Fusobacteria;c_Fusobacteriia;o_Fusobacteriales;f_Fusobacteriaceae;g_Fusobacterium
 p_Firmicutes;c_Fusobacteria;c_Fusobacteriia;o_Fusobacteriales;f_Fusobacteriaceae;g_Fusobacterium
 p_Firmicutes;c_Fusobacteria;c_Fusobacteriia;o_Fusobacteriales;f_Fusobacteriaceae;g_Fusobacterium
 p_Firmicutes;c_Fusobacteria;c_Fusobacteriia;o_Fusobacteriales;f_Fusobacteriaceae;g_Fusobacterium
 p_Firmicutes;c_Fusobacteria;c_Fusobacteriia;o_Fusobacteriales;f_Fusobacteriaceae;g_Fusobacterium
 p_Bacteroidetes;c_Bacteroidia;o_Bacteroidales;f_Prevotellaceae;g_Alloprevotella;s_uncultured Prevotellaceae bacterium
 p_Bacteroidetes;c_Bacteroidia;o_Bacteroidales;f_Prevotellaceae;g_Alloprevotella;s_uncultured Prevotellaceae bacterium

RSV	Infection	0.073494	0.29	ns	Wilcoxon
HRV	Infection	3.13E-05	0.00022	****	Wilcoxon
FluA	FluB	1.11E-26	1.00E-25	****	Wilcoxon
FluA	RSV	8.13E-09	2.40E-08	****	Wilcoxon
FluA	HRV	0.261253	0.26	ns	Wilcoxon
FluA	Infection	2.63E-18	1.80E-17	****	Wilcoxon
FluB	RSV	1.18E-14	7.10E-14	****	Wilcoxon
FluB	HRV	1.70E-31	1.70E-30	****	Wilcoxon
FluB	Infection	3.87E-11	1.50E-10	****	Wilcoxon
RSV	HRV	1.78E-08	3.60E-08	****	Wilcoxon
RSV	Infection	3.47E-14	1.70E-13	****	Wilcoxon
HRV	Infection	2.73E-23	2.20E-22	****	Wilcoxon
FluA	FluB	7.78E-07	5.40E-06	****	Wilcoxon
FluA	RSV	3.05E-09	2.40E-08	****	Wilcoxon
FluA	HRV	1.63E-11	1.60E-10	****	Wilcoxon
FluA	Infection	1.42E-10	1.30E-09	****	Wilcoxon
FluB	RSV	0.383294	1	ns	Wilcoxon
FluB	HRV	0.004697	0.028	**	Wilcoxon
FluB	Infection	0.083102	0.42	ns	Wilcoxon
RSV	HRV	0.300664	1	ns	Wilcoxon
RSV	Infection	0.909065	1	ns	Wilcoxon
HRV	Infection	0.532642	1	ns	Wilcoxon
FluA	FluB	0.00175	0.0088	**	Wilcoxon
FluA	HRV	0.021263	0.044	*	Wilcoxon
FluA	Infection	7.23E-05	0.00043	****	Wilcoxon
FluB	HRV	0.266667	0.27	ns	Wilcoxon
FluB	Infection	0.003612	0.014	**	Wilcoxon
HRV	Infection	0.014706	0.044	*	Wilcoxon
FluA	FluB	5.23E-08	2.60E-07	****	Wilcoxon
FluA	RSV	3.17E-07	1.30E-06	****	Wilcoxon
FluA	HRV	7.28E-12	5.80E-11	****	Wilcoxon
FluA	Infection	0.014253	0.029	*	Wilcoxon
FluB	RSV	1.74E-09	1.20E-08	****	Wilcoxon
FluB	HRV	6.18E-23	6.20E-22	****	Wilcoxon
FluB	Infection	0.002755	0.0083	**	Wilcoxon
RSV	HRV	0.159414	0.16	ns	Wilcoxon
RSV	Infection	2.46E-08	1.50E-07	****	Wilcoxon

<i>p_Bacteroidetes;c_Bacteroidia;o_Bacteroidales;f_Prevotellaceae;g_Alloprevotella;s_uncultured Prevotellaceae bacterium</i>	HRV	Infection	1.53E-16	1.40E-15	****	Wilcoxon
<i>p_Firmicutes;c_Clostridia;o_Clostridiales;f_Peptostreptococcaceae;g_[Eubacterium] yuri group;s_uncultured bacterium</i>	FluA	FluB	3.14E-17	2.80E-16	****	Wilcoxon
<i>p_Firmicutes;c_Clostridia;o_Clostridiales;f_Peptostreptococcaceae;g_[Eubacterium] yuri group;s_uncultured bacterium</i>	FluA	RSV	0.002479	0.0074	**	Wilcoxon
<i>p_Firmicutes;c_Clostridia;o_Clostridiales;f_Peptostreptococcaceae;g_[Eubacterium] yuri group;s_uncultured bacterium</i>	FluA	HRV	0.013809	0.028	*	Wilcoxon
<i>p_Firmicutes;c_Clostridia;o_Clostridiales;f_Peptostreptococcaceae;g_[Eubacterium] yuri group;s_uncultured bacterium</i>	FluA	Infection	4.25E-09	3.00E-08	****	Wilcoxon
<i>p_Firmicutes;c_Clostridia;o_Clostridiales;f_Peptostreptococcaceae;g_[Eubacterium] yuri group;s_uncultured bacterium</i>	FluB	RSV	2.01E-11	1.60E-10	****	Wilcoxon
<i>p_Firmicutes;c_Clostridia;o_Clostridiales;f_Peptostreptococcaceae;g_[Eubacterium] yuri group;s_uncultured bacterium</i>	FluB	HRV	2.15E-18	2.20E-17	****	Wilcoxon
<i>p_Firmicutes;c_Clostridia;o_Clostridiales;f_Peptostreptococcaceae;g_[Eubacterium] yuri group;s_uncultured bacterium</i>	FluB	Infection	0.000187	0.00093	***	Wilcoxon
<i>p_Firmicutes;c_Clostridia;o_Clostridiales;f_Peptostreptococcaceae;g_[Eubacterium] yuri group;s_uncultured bacterium</i>	RSV	HRV	0.138501	0.14	ns	Wilcoxon
<i>p_Firmicutes;c_Clostridia;o_Clostridiales;f_Peptostreptococcaceae;g_[Eubacterium] yuri group;s_uncultured bacterium</i>	RSV	Infection	0.001067	0.0043	**	Wilcoxon
<i>p_Firmicutes;c_Clostridia;o_Clostridiales;f_Peptostreptococcaceae;g_[Eubacterium] yuri group;s_uncultured bacterium</i>	HRV	Infection	3.64E-07	2.20E-06	****	Wilcoxon
<i>p_Patescibacteria;c_Gracilibacteria;o_Absconditabacterales(SRI);f_SRI bacterium oral taxon 875;g_SRI bacterium oral taxon 875;s_SRI bacterium oral taxon 875</i>	FluA	FluB	1.40E-05	9.80E-05	****	Wilcoxon
<i>p_Patescibacteria;c_Gracilibacteria;o_Absconditabacterales(SRI);f_SRI bacterium oral taxon 875;g_SRI bacterium oral taxon 875;s_SRI bacterium oral taxon 875</i>	FluA	RSV	9.85E-06	7.90E-05	****	Wilcoxon
<i>p_Patescibacteria;c_Gracilibacteria;o_Absconditabacterales(SRI);f_SRI bacterium oral taxon 875;g_SRI bacterium oral taxon 875;s_SRI bacterium oral taxon 875</i>	FluA	HRV	1.53E-05	9.80E-05	****	Wilcoxon
<i>p_Patescibacteria;c_Gracilibacteria;o_Absconditabacterales(SRI);f_SRI bacterium oral taxon 875;g_SRI bacterium oral taxon 875;s_SRI bacterium oral taxon 875</i>	FluA	Infection	1.59E-05	9.80E-05	****	Wilcoxon
<i>p_Patescibacteria;c_Gracilibacteria;o_Absconditabacterales(SRI);f_SRI bacterium oral taxon 875;g_SRI bacterium oral taxon 875;s_SRI bacterium oral taxon 875</i>	FluB	RSV	0.098959	0.3	ns	Wilcoxon
<i>p_Patescibacteria;c_Gracilibacteria;o_Absconditabacterales(SRI);f_SRI bacterium oral taxon 875;g_SRI bacterium oral taxon 875;s_SRI bacterium oral taxon 875</i>	FluB	HRV	0.653747	0.65	ns	Wilcoxon
<i>p_Patescibacteria;c_Gracilibacteria;o_Absconditabacterales(SRI);f_SRI bacterium oral taxon 875;g_SRI bacterium oral taxon 875;s_SRI bacterium oral taxon 875</i>	FluB	Infection	5.45E-08	5.50E-07	****	Wilcoxon
<i>p_Patescibacteria;c_Gracilibacteria;o_Absconditabacterales(SRI);f_SRI bacterium oral taxon 875;g_SRI bacterium oral taxon 875;s_SRI bacterium oral taxon 875</i>	RSV	HRV	0.219807	0.44	ns	Wilcoxon
<i>p_Patescibacteria;c_Gracilibacteria;o_Absconditabacterales(SRI);f_SRI bacterium oral taxon 875;g_SRI bacterium oral taxon 875;s_SRI bacterium oral taxon 875</i>	RSV	Infection	2.03E-05	9.80E-05	****	Wilcoxon
<i>p_Patescibacteria;c_Gracilibacteria;o_Absconditabacterales(SRI);f_SRI bacterium oral taxon 875;g_SRI bacterium oral taxon 875;s_SRI bacterium oral taxon 875</i>	HRV	Infection	6.27E-07	5.60E-06	****	Wilcoxon
<i>p_Fusobacteria;c_Fusobacteriia;o_Fusobacteriales;f_Leptotrichiaceae;g_Leptotrichia;s_Leptotrichia sp. oral clone FP036</i>	FluA	FluB	5.23E-08	2.60E-07	****	Wilcoxon
<i>p_Fusobacteria;c_Fusobacteriia;o_Fusobacteriales;f_Leptotrichiaceae;g_Leptotrichia;s_Leptotrichia sp. oral clone FP036</i>	FluA	RSV	3.17E-07	1.30E-06	****	Wilcoxon
<i>p_Fusobacteria;c_Fusobacteriia;o_Fusobacteriales;f_Leptotrichiaceae;g_Leptotrichia;s_Leptotrichia sp. oral clone FP036</i>	FluA	HRV	7.28E-12	5.80E-11	****	Wilcoxon
<i>p_Fusobacteria;c_Fusobacteriia;o_Fusobacteriales;f_Leptotrichiaceae;g_Leptotrichia;s_Leptotrichia sp. oral clone FP036</i>	FluA	Infection	0.014253	0.029	*	Wilcoxon
<i>p_Fusobacteria;c_Fusobacteriia;o_Fusobacteriales;f_Leptotrichiaceae;g_Leptotrichia;s_Leptotrichia sp. oral clone FP036</i>	FluB	RSV	1.74E-09	1.20E-08	****	Wilcoxon
<i>p_Fusobacteria;c_Fusobacteriia;o_Fusobacteriales;f_Leptotrichiaceae;g_Leptotrichia;s_Leptotrichia sp. oral clone FP036</i>	FluB	HRV	6.18E-23	6.20E-22	****	Wilcoxon
<i>p_Fusobacteria;c_Fusobacteriia;o_Fusobacteriales;f_Leptotrichiaceae;g_Leptotrichia;s_Leptotrichia sp. oral clone FP036</i>	FluB	Infection	0.002755	0.0083	**	Wilcoxon
<i>p_Fusobacteria;c_Fusobacteriia;o_Fusobacteriales;f_Leptotrichiaceae;g_Leptotrichia;s_Leptotrichia sp. oral clone FP036</i>	RSV	HRV	0.159414	0.16	ns	Wilcoxon
<i>p_Fusobacteria;c_Fusobacteriia;o_Fusobacteriales;f_Leptotrichiaceae;g_Leptotrichia;s_Leptotrichia sp. oral clone FP036</i>	RSV	Infection	2.46E-08	1.50E-07	****	Wilcoxon
<i>p_Fusobacteria;c_Fusobacteriia;o_Fusobacteriales;f_Leptotrichiaceae;g_Leptotrichia;s_Leptotrichia sp. oral clone FP036</i>	HRV	Infection	1.53E-16	1.40E-15	****	Wilcoxon
<i>p_Firmicutes;c_Clostridia;o_Clostridiales;f_Lachnospiraceae;g_Oribacterium;s_Oribacterium sinus</i>	FluA	FluB	7.78E-07	5.40E-06	****	Wilcoxon
<i>p_Firmicutes;c_Clostridia;o_Clostridiales;f_Lachnospiraceae;g_Oribacterium;s_Oribacterium sinus</i>	FluA	RSV	3.05E-09	2.40E-08	****	Wilcoxon
<i>p_Firmicutes;c_Clostridia;o_Clostridiales;f_Lachnospiraceae;g_Oribacterium;s_Oribacterium sinus</i>	FluA	HRV	1.63E-11	1.60E-10	****	Wilcoxon
<i>p_Firmicutes;c_Clostridia;o_Clostridiales;f_Lachnospiraceae;g_Oribacterium;s_Oribacterium sinus</i>	FluA	Infection	1.42E-10	1.30E-09	****	Wilcoxon
<i>p_Firmicutes;c_Clostridia;o_Clostridiales;f_Lachnospiraceae;g_Oribacterium;s_Oribacterium sinus</i>	FluB	RSV	0.383294	1	ns	Wilcoxon
<i>p_Firmicutes;c_Clostridia;o_Clostridiales;f_Lachnospiraceae;g_Oribacterium;s_Oribacterium sinus</i>	FluB	HRV	0.004697	0.028	**	Wilcoxon

FluB	Infection	0.083102	0.42	ns	Wilcoxon
RSV	HRV	0.300664	1	ns	Wilcoxon
RSV	Infection	0.909065	1	ns	Wilcoxon
HRV	Infection	0.532642	1	ns	Wilcoxon
FluA	FluB	0.066916	0.33	ns	Wilcoxon
FluA	RSV	0.002375	0.024	**	Wilcoxon
FluA	HRV	0.008529	0.06	**	Wilcoxon
FluA	Infection	0.203285	0.81	ns	Wilcoxon
FluB	RSV	0.003885	0.031	**	Wilcoxon
FluB	HRV	0.002361	0.024	**	Wilcoxon
FluB	Infection	0.312946	0.94	ns	Wilcoxon
RSV	HRV	0.626976	1	ns	Wilcoxon
RSV	Infection	0.021042	0.13	*	Wilcoxon
HRV	Infection	0.792703	1	ns	Wilcoxon

Table S4. The Spearman interaction of differential pathways, differential ARGs, ARGs count, and differential species in the FluA group and healthy controls.

Objects (A & B means A interacts with B)	R value
<i>Veillonella unclassified</i> & PWY-5840: superpathway of menaquinol-7 biosynthesis	0.775
<i>Veillonella unclassified</i> & PWY-5899: superpathway of menaquinol-13 biosynthesis	0.771
<i>Veillonella unclassified</i> & PWY-5898: superpathway of menaquinol-12 biosynthesis	0.771
<i>Veillonella unclassified</i> & PWY-5897: superpathway of menaquinol-11 biosynthesis	0.771
<i>Veillonella unclassified</i> & PWY-5837: 1,4-dihydroxy-2-naphthoate biosynthesis I	0.782
<i>Veillonella unclassified</i> & PWY-5791: 1,4-dihydroxy-2-naphthoate biosynthesis II (plants)	0.782
<i>Veillonella unclassified</i> & PWY-5005: biotin biosynthesis II	0.833
<i>Veillonella parvula</i> & PWY-5005: biotin biosynthesis II	0.773
PWY-6897: thiamin salvage II & <i>Streptococcus constellatus</i>	0.660
PWY-6897: thiamin salvage II & <i>Rothia mucilaginosa</i>	-0.502
COA-PWY: coenzyme A biosynthesis I & <i>Veillonella parvula</i>	0.504
COA-PWY: coenzyme A biosynthesis I & <i>Rothia mucilaginosa</i>	-0.555
ARO_3003479 <i>tetR</i> & PWY-5840: superpathway of menaquinol-7 biosynthesis	-0.776
ARO_3003479 <i>tetR</i> & ARG+POLYAMINE-SYN: superpathway of arginine and polyamine biosynthesis	-0.760
ARO_3003479 <i>tetR</i> & ARGs count	0.714
ARO_3003479 <i>tetR</i> & <i>Veillonella unclassified</i>	-0.723
ARO_3003479 <i>tetR</i> & <i>Rothia mucilaginosa</i>	0.613
ARO_3000165 <i>tet(A)</i> & ARG+POLYAMINE-SYN: superpathway of arginine and polyamine biosynthesis	-0.776
ARO_3000165 <i>tet(A)</i> & ARGs count	0.703
ARO_3000165 <i>tet(A)</i> & <i>Veillonella unclassified</i>	-0.738
ARO_3000165 <i>tet(A)</i> & <i>Rothia mucilaginosa</i>	0.576
PWY-6147: 6-hydroxymethyl-dihydropterin diphosphate biosynthesis I & <i>Streptococcus constellatus</i>	0.589
PWY-6147: 6-hydroxymethyl-dihydropterin diphosphate biosynthesis I & <i>Rothia mucilaginosa</i>	-0.629
PWY-6147: 6-hydroxymethyl-dihydropterin diphosphate biosynthesis I & <i>Lachnospiraceae oral taxon 107</i>	0.508
SULFATE-CYS-PWY: superpathway of sulfate assimilation and cysteine biosynthesis & <i>Lachnospiraceae oral taxon 107</i>	0.659
PWY-7282: 4-amino-2-methyl-5-phosphomethylpyrimidine biosynthesis (yeast) & <i>Rothia mucilaginosa</i>	-0.544

PWY-7282: 4-amino-2-methyl-5-phosphomethylpyrimidine biosynthesis (yeast) & <i>Lachnospiraceae oral taxon 107</i>	0.682
PWY-5154: L-arginine biosynthesis III (via N-acetyl-L-citrulline) & ARO_3000194 <i>tetW</i>	0.473
PWY-5154: L-arginine biosynthesis III (via N-acetyl-L-citrulline) & <i>Veillonella unclassified</i>	0.626
PWY-5154: L-arginine biosynthesis III (via N-acetyl-L-citrulline) & <i>Veillonella parvula</i>	0.523
PWY-5154: L-arginine biosynthesis III (via N-acetyl-L-citrulline) & <i>Rothia mucilaginosa</i>	-0.594
PWY-5154: L-arginine biosynthesis III (via N-acetyl-L-citrulline) & <i>Lachnospiraceae oral taxon 107</i>	0.464
PANTOSYN-PWY: pantothenate and coenzyme A biosynthesis I & <i>Veillonella unclassified</i>	0.574
PANTOSYN-PWY: pantothenate and coenzyme A biosynthesis I & <i>Rothia mucilaginosa</i>	-0.630
PANTOSYN-PWY: pantothenate and coenzyme A biosynthesis I & <i>Lachnospiraceae oral taxon 107</i>	0.598
PANTOSYN-PWY: pantothenate and coenzyme A biosynthesis I & <i>Atopobium rimate</i>	0.648
P42-PWY: incomplete reductive TCA cycle & <i>Veillonella unclassified</i>	0.447
P42-PWY: incomplete reductive TCA cycle & <i>Lachnospiraceae oral taxon 107</i>	0.585
P42-PWY: incomplete reductive TCA cycle & <i>Atopobium rimate</i>	0.600
POLYAMSYN-PWY: superpathway of polyamine biosynthesis I & ARO_3003479 <i>tetR</i>	-0.729
POLYAMSYN-PWY: superpathway of polyamine biosynthesis I & ARO_3000165 <i>tet(A)</i>	-0.738
POLYAMSYN-PWY: superpathway of polyamine biosynthesis I & ARO_3000194 <i>tetW</i>	0.458
POLYAMSYN-PWY: superpathway of polyamine biosynthesis I & ARGs count	-0.615
POLYAMSYN-PWY: superpathway of polyamine biosynthesis I & <i>Veillonella unclassified</i>	0.651
POLYAMSYN-PWY: superpathway of polyamine biosynthesis I & <i>Rothia mucilaginosa</i>	-0.528
POLYAMSYN-PWY: superpathway of polyamine biosynthesis I & <i>Atopobium rimate</i>	0.471
PWY-5840: superpathway of menaquinol-7 biosynthesis & ARO_3003479 <i>tetR</i>	-0.776
PWY-5840: superpathway of menaquinol-7 biosynthesis & ARO_3000165 <i>tet(A)</i>	-0.756
PWY-5840: superpathway of menaquinol-7 biosynthesis & ARGs count	-0.747
PWY-5840: superpathway of menaquinol-7 biosynthesis & <i>Veillonella unclassified</i>	0.775
PWY-5840: superpathway of menaquinol-7 biosynthesis & <i>Veillonella parvula</i>	0.588

PWY-5840: superpathway of menaquinol-7 biosynthesis & <i>Rothia mucilaginosa</i>	-0.669
PWY-5840: superpathway of menaquinol-7 biosynthesis & <i>Atopobium rimate</i>	0.644
PWY-4242: pantothenate and coenzyme A biosynthesis III & <i>Veillonella unclassified</i>	0.534
PWY-4242: pantothenate and coenzyme A biosynthesis III & <i>Veillonella parvula</i>	0.568
PWY-4242: pantothenate and coenzyme A biosynthesis III & <i>Rothia mucilaginosa</i>	-0.711
PWY-4242: pantothenate and coenzyme A biosynthesis III & <i>Lachnospiraceae oral taxon 107</i>	0.514
PWY-4242: pantothenate and coenzyme A biosynthesis III & <i>Atopobium rimate</i>	0.616
PWY-5899: superpathway of menaquinol-13 biosynthesis & ARO_3003479 tetR	-0.510
PWY-5899: superpathway of menaquinol-13 biosynthesis & ARO_3000165 tet(A)	-0.543
PWY-5899: superpathway of menaquinol-13 biosynthesis & <i>Veillonella unclassified</i>	0.771
PWY-5899: superpathway of menaquinol-13 biosynthesis & <i>Veillonella parvula</i>	0.665
PWY-5899: superpathway of menaquinol-13 biosynthesis & <i>Rothia mucilaginosa</i>	-0.710
PWY-5899: superpathway of menaquinol-13 biosynthesis & <i>Lachnospiraceae oral taxon 107</i>	0.559
PWY-5899: superpathway of menaquinol-13 biosynthesis & <i>Atopobium rimate</i>	0.681
PWY-5898: superpathway of menaquinol-12 biosynthesis & ARO_3003479 tetR	-0.510
PWY-5898: superpathway of menaquinol-12 biosynthesis & ARO_3000165 tet(A)	-0.543
PWY-5898: superpathway of menaquinol-12 biosynthesis & <i>Veillonella unclassified</i>	0.771
PWY-5898: superpathway of menaquinol-12 biosynthesis & <i>Veillonella parvula</i>	0.665
PWY-5898: superpathway of menaquinol-12 biosynthesis & <i>Rothia mucilaginosa</i>	-0.710
PWY-5898: superpathway of menaquinol-12 biosynthesis & <i>Lachnospiraceae oral taxon 107</i>	0.559
PWY-5898: superpathway of menaquinol-12 biosynthesis & <i>Atopobium rimate</i>	0.681
PWY-5897: superpathway of menaquinol-11 biosynthesis & ARO_3003479 tetR	-0.510
PWY-5897: superpathway of menaquinol-11 biosynthesis & ARO_3000165 tet(A)	-0.543
PWY-5897: superpathway of menaquinol-11 biosynthesis & <i>Veillonella unclassified</i>	0.771
PWY-5897: superpathway of menaquinol-11 biosynthesis & <i>Veillonella parvula</i>	0.665
PWY-5897: superpathway of menaquinol-11 biosynthesis & <i>Rothia mucilaginosa</i>	-0.710
PWY-5897: superpathway of menaquinol-11 biosynthesis & <i>Lachnospiraceae oral taxon 107</i>	0.559
PWY-5897: superpathway of menaquinol-11 biosynthesis & <i>Atopobium rimate</i>	0.681
ARG+POLYAMINE-SYN: superpathway of arginine and polyamine biosynthesis & ARO_3003479 tetR	-0.760
ARG+POLYAMINE-SYN: superpathway of arginine and polyamine biosynthesis & ARO_3000165 tet(A)	-0.776
ARG+POLYAMINE-SYN: superpathway of arginine and polyamine biosynthesis & ARO_3000194 tetW	0.507

ARG+POLYAMINE-SYN: superpathway of arginine and polyamine biosynthesis & ARGs count	-0.611
ARG+POLYAMINE-SYN: superpathway of arginine and polyamine biosynthesis & <i>Veillonella unclassified</i>	0.720
ARG+POLYAMINE-SYN: superpathway of arginine and polyamine biosynthesis & <i>Rothia mucilaginosa</i>	-0.553
ARG+POLYAMINE-SYN: superpathway of arginine and polyamine biosynthesis & <i>Atopobium rimate</i>	0.513
PWY0-1586: peptidoglycan maturation (meso-diaminopimelate containing) & ARO_3003479 <i>tetR</i>	-0.556
PWY0-1586: peptidoglycan maturation (meso-diaminopimelate containing) & ARO_3000165 <i>tet(A)</i>	-0.559
PWY0-1586: peptidoglycan maturation (meso-diaminopimelate containing) & <i>Veillonella unclassified</i>	0.661
PWY0-1586: peptidoglycan maturation (meso-diaminopimelate containing) & <i>Veillonella parvula</i>	0.660
PWY0-1586: peptidoglycan maturation (meso-diaminopimelate containing) & <i>Rothia mucilaginosa</i>	-0.701
PWY0-1586: peptidoglycan maturation (meso-diaminopimelate containing) & <i>Lachnospiraceae oral taxon 107</i>	0.518
PWY0-1586: peptidoglycan maturation (meso-diaminopimelate containing) & <i>Atopobium rimate</i>	0.648
PWY-5837: 1,4-dihydroxy-2-naphthoate biosynthesis I & ARO_3003479 <i>tetR</i>	-0.504
PWY-5837: 1,4-dihydroxy-2-naphthoate biosynthesis I & ARO_3000165 <i>tet(A)</i>	-0.547
PWY-5837: 1,4-dihydroxy-2-naphthoate biosynthesis I & ARO_3000194 <i>tetW</i>	0.506
PWY-5837: 1,4-dihydroxy-2-naphthoate biosynthesis I & ARGs count	-0.474
PWY-5837: 1,4-dihydroxy-2-naphthoate biosynthesis I & <i>Veillonella unclassified</i>	0.782
PWY-5837: 1,4-dihydroxy-2-naphthoate biosynthesis I & <i>Veillonella parvula</i>	0.727
PWY-5837: 1,4-dihydroxy-2-naphthoate biosynthesis I & <i>Rothia mucilaginosa</i>	-0.703
PWY-5837: 1,4-dihydroxy-2-naphthoate biosynthesis I & <i>Atopobium rimate</i>	0.582
PWY-5791: 1,4-dihydroxy-2-naphthoate biosynthesis II (plants) & ARO_3003479 <i>tetR</i>	-0.504
PWY-5791: 1,4-dihydroxy-2-naphthoate biosynthesis II (plants) & ARO_3000165 <i>tet(A)</i>	-0.547
PWY-5791: 1,4-dihydroxy-2-naphthoate biosynthesis II (plants) & ARO_3000194 <i>tetW</i>	0.506
PWY-5791: 1,4-dihydroxy-2-naphthoate biosynthesis II (plants) & ARGs count	-0.474
PWY-5791: 1,4-dihydroxy-2-naphthoate biosynthesis II (plants) & <i>Veillonella unclassified</i>	0.782
PWY-5791: 1,4-dihydroxy-2-naphthoate biosynthesis II (plants) & <i>Veillonella parvula</i>	0.727
PWY-5791: 1,4-dihydroxy-2-naphthoate biosynthesis II (plants) & <i>Rothia mucilaginosa</i>	-0.703

PWY-5791: 1,4-dihydroxy-2-naphthoate biosynthesis II (plants) & <i>Atopobium rimaе</i>	0.582
PWY-5005: biotin biosynthesis II & ARO_3003479 <i>tetR</i>	-0.555
PWY-5005: biotin biosynthesis II & ARO_3000165 <i>tet(A)</i>	-0.590
PWY-5005: biotin biosynthesis II & ARO_3000194 <i>tetW</i>	0.468
PWY-5005: biotin biosynthesis II & ARGs count	-0.575
PWY-5005: biotin biosynthesis II & <i>Veillonella unclassified</i>	0.833
PWY-5005: biotin biosynthesis II & <i>Veillonella parvula</i>	0.773
PWY-5005: biotin biosynthesis II & <i>Rothia mucilaginosa</i>	-0.594
PWY-5005: biotin biosynthesis II & <i>Atopobium rimaе</i>	0.572
ARO_3000194 <i>tetW</i> & ARGs count	-0.494
ARO_3000194 <i>tetW</i> & <i>Veillonella unclassified</i>	0.644
ARO_3000194 <i>tetW</i> & <i>Aggregatibacter unclassified</i>	-0.517
ARGs count & <i>Veillonella unclassified</i>	-0.703
ARGs count & <i>Gemella morbillorum</i>	0.473
ARGs count & <i>Atopobium rimaе</i>	-0.459
ARGs count & <i>Aggregatibacter unclassified</i>	0.449

Table S5. The growth rate of potential pathogens in situ calculated by GRID algorithm

Potential pathogens	Growth rate	Coverage	Groups
<i>Fusobacterium nucleatum</i>	2.06	3.33	FluB
<i>Fusobacterium nucleatum</i>	2.04	4.28	FluA/FluB
<i>Fusobacterium nucleatum</i>	1.84	20.81	FluB
<i>Fusobacterium nucleatum</i>	1.44	13.78	FluB
<i>Fusobacterium nucleatum</i>	1.75	0.99	FluA
<i>Fusobacterium nucleatum</i>	1.73	10.53	FluA
<i>Fusobacterium nucleatum</i>	1.46	1.49	FluA
<i>Fusobacterium nucleatum</i>	1.7	4.70	FluB
<i>Fusobacterium nucleatum</i>	1.37	0.42	FluA/FluB
<i>Fusobacterium nucleatum</i>	1.54	0.28	FluA
<i>Fusobacterium nucleatum</i>	1.48	0.26	FluA
<i>Fusobacterium nucleatum</i>	1.79	0.24	FluA
<i>Fusobacterium nucleatum</i>	1.86	19.31	FluA/FluB
<i>Fusobacterium nucleatum</i>	1.59	1.60	FluA
<i>Fusobacterium nucleatum</i>	1	0.27	FluB
<i>Fusobacterium nucleatum</i>	1.45	1.18	FluA/FluB
<i>Fusobacterium nucleatum</i>	1.62	2.41	FluA
<i>Fusobacterium nucleatum</i>	1.81	1.36	FluA/FluB
<i>Fusobacterium nucleatum</i>	2.27	1.85	FluA/FluB
<i>Fusobacterium nucleatum</i>	1.98	4.82	FluA/FluB
<i>Fusobacterium nucleatum</i>	2.03	6.65	FluA
<i>Fusobacterium nucleatum</i>	2.01	2.41	FluA/FluB
<i>Fusobacterium nucleatum</i>	2.36	0.90	FluA/FluB
<i>Fusobacterium nucleatum</i>	1.72	1.23	FluA
<i>Fusobacterium nucleatum</i>	1.66	2.65	FluA/FluB
<i>Fusobacterium nucleatum</i>	2.01	6.18	FluB
<i>Fusobacterium nucleatum</i>	1.63	0.28	FluB
<i>Fusobacterium nucleatum</i>	1.63	0.77	FluB
<i>Fusobacterium nucleatum</i>	1.63	20.04	FluB
<i>Fusobacterium nucleatum</i>	1.6	1.17	Health
<i>Fusobacterium nucleatum</i>	2.21	1.44	Health
<i>Fusobacterium nucleatum</i>	1.46	0.24	Health
<i>Fusobacterium nucleatum</i>	2.08	2.17	Health
<i>Fusobacterium nucleatum</i>	1.38	0.57	Health
<i>Fusobacterium nucleatum</i>	1.57	1.16	Health
<i>Fusobacterium nucleatum</i>	1.7	0.70	Health
<i>Fusobacterium nucleatum</i>	1.63	0.28	Health
<i>Fusobacterium nucleatum</i>	1.45	1.09	Health
<i>Fusobacterium nucleatum</i>	1.59	0.61	Health
<i>Haemophilus influenzae</i>	1	0.23	FluA/FluB
<i>Haemophilus influenzae</i>	1.45	1.18	FluB

<i>Haemophilus influenzae</i>	1.31	1.05	FluB
<i>Haemophilus influenzae</i>	1.24	0.24	FluB
<i>Haemophilus influenzae</i>	1.53	0.82	FluA
<i>Haemophilus influenzae</i>	1.47	0.42	FluA
<i>Haemophilus influenzae</i>	1.12	0.91	FluB
<i>Haemophilus influenzae</i>	1.55	0.35	FluA/FluB
<i>Haemophilus influenzae</i>	1.35	1.64	FluA
<i>Haemophilus influenzae</i>	1	0.37	FluB
<i>Haemophilus influenzae</i>	1	0.36	FluA/FluB
<i>Haemophilus influenzae</i>	1.69	5.66	FluA/FluB
<i>Haemophilus influenzae</i>	1	0.42	FluA/FluB
<i>Haemophilus influenzae</i>	1.21	1.64	FluA
<i>Haemophilus influenzae</i>	1.27	3.55	FluA/FluB
<i>Haemophilus influenzae</i>	1.31	0.51	FluA/FluB
<i>Haemophilus influenzae</i>	1.53	0.98	FluA/FluB
<i>Haemophilus influenzae</i>	1.7	0.81	FluB
<i>Haemophilus influenzae</i>	1.19	1.01	FluB
<i>Haemophilus influenzae</i>	1.5	0.29	Health
<i>Haemophilus influenzae</i>	1.22	0.34	Health
<i>Haemophilus influenzae</i>	1.26	0.87	Health
<i>Haemophilus influenzae</i>	1.13	1.09	Health
<i>Haemophilus influenzae</i>	1.2	0.48	Health
<i>Haemophilus influenzae</i>	1	0.21	Health
<i>Haemophilus influenzae</i>	1	0.22	Health
<i>Haemophilus sputorum</i>	1	0.53	FluB
<i>Haemophilus sputorum</i>	2.36	1.19	FluA/FluB
<i>Haemophilus sputorum</i>	8.61	3.33	FluB
<i>Haemophilus sputorum</i>	2.2	6.01	FluB
<i>Haemophilus sputorum</i>	1	0.21	FluB
<i>Haemophilus sputorum</i>	2.32	6.78	FluA
<i>Haemophilus sputorum</i>	2.44	1.89	FluA
<i>Haemophilus sputorum</i>	3.01	2.72	FluB
<i>Haemophilus sputorum</i>	2.09	0.41	FluA/FluB
<i>Haemophilus sputorum</i>	3.82	1.07	FluA
<i>Haemophilus sputorum</i>	2.04	0.38	FluA
<i>Haemophilus sputorum</i>	1	0.54	FluB
<i>Haemophilus sputorum</i>	2.04	1.95	FluA/FluB
<i>Haemophilus sputorum</i>	2.47	0.42	FluA
<i>Haemophilus sputorum</i>	2.31	1.92	FluA/FluB
<i>Haemophilus sputorum</i>	3.04	1.30	FluA/FluB
<i>Haemophilus sputorum</i>	1	1.45	FluA/FluB
<i>Haemophilus sputorum</i>	2.39	4.24	FluA/FluB
<i>Haemophilus sputorum</i>	1	0.29	FluA/FluB
<i>Haemophilus sputorum</i>	3.55	0.46	FluA

<i>Haemophilus sputorum</i>	4.55	1.03	FluA/FluB
<i>Haemophilus sputorum</i>	1	0.95	FluB
<i>Haemophilus sputorum</i>	1	0.26	FluB
<i>Haemophilus sputorum</i>	1	0.20	FluB
<i>Haemophilus sputorum</i>	3.36	0.47	FluB
<i>Haemophilus sputorum</i>	1	0.48	Health
<i>Haemophilus sputorum</i>	1	0.40	Health
<i>Haemophilus sputorum</i>	1.95	2.79	Health
<i>Haemophilus sputorum</i>	2.47	2.22	Health
<i>Haemophilus sputorum</i>	2.19	1.63	Health
<i>Haemophilus sputorum</i>	1.78	0.60	Health
<i>Haemophilus sputorum</i>	2.77	0.32	Health
<i>Haemophilus sputorum</i>	1.86	1.06	Health
<i>Haemophilus sputorum</i>	1	0.61	Health
<i>Porphyromonas gingivalis</i>	1	0.53	FluA/FluB
<i>Porphyromonas gingivalis</i>	1.04	8.68	FluB
<i>Porphyromonas gingivalis</i>	1	0.21	FluA
<i>Porphyromonas gingivalis</i>	1.14	8.29	FluB
<i>Porphyromonas gingivalis</i>	1.06	1.42	FluA/FluB
<i>Porphyromonas gingivalis</i>	1.43	0.66	FluA
<i>Porphyromonas gingivalis</i>	1.37	1.84	FluA
<i>Porphyromonas gingivalis</i>	1.28	0.28	FluA
<i>Porphyromonas gingivalis</i>	1.28	1.93	FluA/FluB
<i>Porphyromonas gingivalis</i>	1.11	4.60	FluA
<i>Porphyromonas gingivalis</i>	1.13	1.09	FluB
<i>Porphyromonas gingivalis</i>	1.17	4.63	FluA
<i>Porphyromonas gingivalis</i>	1.28	1.38	FluA/FluB
<i>Porphyromonas gingivalis</i>	1.18	0.58	FluA
<i>Porphyromonas gingivalis</i>	1.2	4.49	FluA/FluB
<i>Porphyromonas gingivalis</i>	1.15	0.45	FluB
<i>Porphyromonas gingivalis</i>	1.3	1.62	FluB
<i>Porphyromonas gingivalis</i>	1.19	0.94	Health
<i>Porphyromonas gingivalis</i>	1.13	1.31	Health
<i>Porphyromonas gingivalis</i>	1.04	4.97	Health
<i>Porphyromonas gingivalis</i>	1.24	6.23	Health
<i>Porphyromonas gingivalis</i>	1.11	1.69	Health
<i>Porphyromonas gingivalis</i>	1.1	0.73	Health
<i>Porphyromonas gingivalis</i>	1.1	2.41	Health
<i>Treponema denticola</i>	1.27	0.30	FluB
<i>Treponema denticola</i>	1.14	0.44	FluB
<i>Treponema denticola</i>	1.48	0.48	FluA
<i>Treponema denticola</i>	1.15	0.59	FluB
<i>Treponema denticola</i>	1.4	1.23	FluA/FluB
<i>Treponema denticola</i>	1.47	0.31	FluA/FluB

<i>Treponema denticola</i>	1.27	0.72	FluA
<i>Treponema denticola</i>	1.23	0.41	FluB
<i>Treponema denticola</i>	1.41	0.25	FluA/FluB
<i>Treponema denticola</i>	1.28	0.32	FluA
<i>Treponema denticola</i>	1.22	0.28	FluA
<i>Treponema denticola</i>	1.19	0.50	FluA/FluB
<i>Treponema denticola</i>	1.25	0.41	FluB
<i>Treponema denticola</i>	1.13	0.28	Health
<i>Treponema denticola</i>	1.3	0.22	Health
<i>Treponema denticola</i>	1.21	0.39	Health
<i>Treponema denticola</i>	1.21	0.22	Health
<i>Treponema denticola</i>	1.09	0.48	Health
<i>Treponema medium</i>	1.5	0.25	FluA/FluB
<i>Treponema medium</i>	1.64	0.41	FluB
<i>Treponema medium</i>	1.36	0.41	FluB
<i>Treponema medium</i>	1.36	0.54	FluA
<i>Treponema medium</i>	1.37	0.55	FluA
<i>Treponema medium</i>	1.4	1.03	FluB
<i>Treponema medium</i>	1.42	1.00	FluA/FluB
<i>Treponema medium</i>	1.58	0.40	FluA
<i>Treponema medium</i>	1.49	0.73	FluA/FluB
<i>Treponema medium</i>	1.49	0.71	FluA
<i>Treponema medium</i>	1.28	0.44	FluB
<i>Treponema medium</i>	1.27	0.71	FluA/FluB
<i>Treponema medium</i>	1.48	0.33	FluA
<i>Treponema medium</i>	1.72	0.24	FluA/FluB
<i>Treponema medium</i>	1.56	0.53	FluA
<i>Treponema medium</i>	1.57	0.23	FluA/FluB
<i>Treponema medium</i>	1.42	0.70	FluA/FluB
<i>Treponema medium</i>	1.57	0.39	FluB
<i>Treponema medium</i>	1.42	0.31	FluB
<i>Treponema medium</i>	1.46	0.45	FluB
<i>Treponema medium</i>	1.22	0.32	Health
<i>Treponema medium</i>	1.28	0.29	Health
<i>Treponema medium</i>	1.35	1.14	Health
<i>Treponema medium</i>	1.44	0.48	Health
<i>Treponema medium</i>	1.38	0.42	Health
<i>Treponema medium</i>	1.18	0.45	Health

Table S6. The Spearman interaction of all pathways, ARGs, and pathogens.

Objects (A & B means A interacts with B)	R value
<i>Porphyromonas gingivalis</i> & PWY-5088: L-glutamate degradation VIII	-0.583
<i>Haemophilus influenzae</i> & PWY-6305: putrescine biosynthesis IV	-0.656
<i>Haemophilus influenzae</i> & P161-PWY: acetylene degradation	-0.592
<i>Haemophilus influenzae</i> & PWY-7431: aromatic biogenic amine degradation	-0.567
<i>Haemophilus influenzae</i> & PWY0-1298: super-pathway of pyrimidine deoxyribonucleosides degradation	-0.514
<i>Treponema medium</i> & PWY-5005: biotin biosynthesis II	0.509
<i>Treponema medium</i> & PWY-6147: 6-hydroxymethyl-dihydropterin diphosphate biosynthesis I	0.575
<i>Treponema medium</i> & PWY-5897: superpathway of menaquinol-11 biosynthesis	0.611
<i>Treponema medium</i> & PWY-5898: superpathway of menaquinol-12 biosynthesis	0.611
<i>Treponema medium</i> & PWY-5899: superpathway of menaquinol-13 biosynthesis	0.611
<i>Treponema medium</i> & PWY-7282: 4-amino-2-methyl-5-phosphomethylpyrimidine biosynthesis	0.624
<i>Treponema medium</i> & THISYNARA-PWY: superpathway of thiamin diphosphate biosynthesis III	0.649
<i>Treponema denticola</i> & P122-PWY: heterolactic fermentation	-0.613
<i>Treponema denticola</i> & PWY-6269: adenosylcobalamin salvage from cobinamide II	0.537
<i>Treponema medium</i> & PWY-5837: 1,4-dihydroxy-2-naphthoate biosynthesis I	0.658
<i>Treponema medium</i> & PWY-5791: 1,4-dihydroxy-2-naphthoate biosynthesis II	0.658
<i>Treponema denticola</i> & P185-PWY: formaldehyde assimilation III	0.555
<i>Treponema denticola</i> & SALVADEHYPOX-PWY: adenosine nucleotides degradation II	0.580
<i>Treponema denticola</i> & PWY-6353: purine nucleotides degradation II	0.655
<i>Treponema medium</i> & gb AGV10830_1 ARO_3002647 APH(3_-)-IIIa	0.601
<i>Haemophilus sputorum</i> & PWY-7197: pyrimidine deoxyribonucleotide phosphorylation	0.519
<i>Haemophilus sputorum</i> & PWY-5861: superpathway of demethylmenaquinol-8 biosynthesis	0.520
<i>Haemophilus sputorum</i> & PWY-5838: superpathway of menaquinol-8 biosynthesis I	0.528
<i>Haemophilus sputorum</i> & PWY-6168: flavin biosynthesis III	0.531
<i>Haemophilus sputorum</i> & PWY-1269: CMP-3-deoxy-D-manno-octulosonate biosynthesis I	0.542
<i>Haemophilus sputorum</i> & GLYCOL-GLYOXDEG-PWY: superpathway of glycol metabolism and degradation	0.566
<i>Treponema denticola</i> & gb BAE77933_1 ARO_3000518 CRP	-0.565
<i>Treponema denticola</i> & gb YP_007503840_1 ARO_3000165 tet(A)	-0.552