

**Supplementary Table 2.** List of the differentially represented viral biomarkers found by LefSe, ranked accordingly to their effect size, associated with the group with the highest median. Viral biomarkers appear with their corresponding taxonomic level, before reads assembly (A), and after assembly (B).

(A)

Viral biomarker	Group	LDA Score (log10)	p-value
<i>Viruses</i>	Volunteer	5.03	0.0030
<i>Prophages</i>	Crohn	5.03	0.0030
<i>o__Clostridiales_phage</i>	Crohn	4.85	0.0318
<i>o__Caudovirales</i>	Volunteer	4.81	0.0082
<i>f__Myoviridae</i>	Volunteer	4.63	0.0318
<i>g__T4_like_viruses</i>	Volunteer	4.50	0.0208
<i>s__Enterobacteria_phage_T4_sensu_lato</i>	Volunteer	4.47	0.0475
<i>s__Salmonella_phage_MB78</i>	Volunteer	4.43	0.0082
<i>o__n_n_n_Bartonella_henselae_phage_60457</i>	Volunteer	4.42	0.0128
<i>f__n_n_Bartonella_henselae_phage_60457</i>	Volunteer	4.42	0.0128
<i>s__Bartonella_henselae_phage_60457</i>	Volunteer	4.42	0.0128
<i>g__n_Bartonella_henselae_phage_60457</i>	Volunteer	4.42	0.0128
<i>s__Streptomyces_phage_phiBT1</i>	Volunteer	4.33	0.0062
<i>g__PhiC31_like_viruses</i>	Volunteer	4.33	0.0062
<i>f__Podoviridae</i>	Volunteer	4.30	0.0030
<i>g__T7_like_viruses</i>	Volunteer	4.06	0.0048
<i>s__Phage_PhiI</i>	Volunteer	4.00	0.0098
<i>f__Microviridae</i>	Volunteer	3.85	0.0202
<i>o__n_Microviridae</i>	Volunteer	3.85	0.0202
<i>s__Clostridium_acetobutylicum_phage</i>	Crohn	3.82	0.0447
<i>g__Epsilon15_like_viruses</i>	Volunteer	3.66	0.0194
<i>s__Escherichia_phage_phiV10</i>	Volunteer	3.66	0.0194
<i>s__Mycobacterium_phage_U2</i>	Volunteer	3.60	0.0194
<i>s__Synechococcus_phage_S_CBS1</i>	Crohn	3.53	0.0022
<i>s__Alphapapillomavirus_10</i>	Volunteer	3.50	0.0331
<i>o__Alteromonadales_phage</i>	Crohn	3.48	0.0344

Viral biomarker	Group	LDA Score (log10)	p-value
<i>g_Levivirus</i>	Volunteer	3.43	0.0362
<i>o_n_Adenoviridae</i>	Volunteer	3.42	0.0395
<i>f_Adenoviridae</i>	Volunteer	3.42	0.0395
<i>s_Enterobacteria_phage_MS2</i>	Volunteer	3.42	0.0447
<i>o_n_n_n_Klebsiella_phage_KPP95</i>	Volunteer	3.40	0.0403
<i>f_n_n_Klebsiella_phage_KPP95</i>	Volunteer	3.40	0.0403
<i>g_n_Klebsiella_phage_KPP95</i>	Volunteer	3.39	0.0403
<i>s_Klebsiella_phage_KPP95</i>	Volunteer	3.38	0.0403
<i>s_Bacillus_phage_SPO1</i>	Volunteer	3.35	0.0331
<i>s_Enterobacteria_phage_lambda</i>	Volunteer	3.33	0.0159
<i>g_Aviadenovirus</i>	Volunteer	3.31	0.0034
<i>s_Bacillus_phage_0305phi8_36</i>	Volunteer	3.30	0.0213
<i>g_Varicellovirus</i>	Volunteer	3.30	0.0257
<i>s_Enterococcus_phage_phiFL4A</i>	Volunteer	3.29	0.0101
<i>s_Fowl_adenovirus_A</i>	Volunteer	3.29	0.0109
<i>s_Suid_herpesvirus_1</i>	Volunteer	3.29	0.0205
<i>s_Lettuce_mosaic_virus</i>	Volunteer	3.28	0.0109
<i>g_P22_like_viruses</i>	Volunteer	3.28	0.0320
<i>s_Staphylococcus_epidermidis_phage</i>	Volunteer	3.28	0.0362
<i>f_Oxalobacteraceae_phage</i>	Volunteer	3.27	0.0331
<i>s_Bacillus_clausii_phage</i>	Volunteer	3.26	0.0031
<i>g_Potyvirus</i>	Volunteer	3.25	0.0163
<i>s_Enterobacteria_phage_CP_1639</i>	Volunteer	3.24	0.0109
<i>s_Lactobacillus_brevis_phage</i>	Volunteer	3.24	0.0163
<i>o_n_n_n_Enterobacteria_phage_CP_1639</i>	Volunteer	3.24	0.0109
<i>f_n_n_Enterobacteria_phage_CP_1639</i>	Volunteer	3.24	0.0109
<i>s_Janthinobacterium_sp_Marseille_phage</i>	Volunteer	3.23	0.0331
<i>g_n_Enterobacteria_phage_CP_1639</i>	Volunteer	3.22	0.0109
<i>g_Janthinobacterium_phage</i>	Volunteer	3.22	0.0331
<i>s_Vibrio_phage_RRE_2008</i>	Volunteer	3.21	0.0077
<i>g_c2_like_viruses</i>	Volunteer	3.20	0.0169
<i>s_Yersinia_phage_phiYeO3_12</i>	Volunteer	3.19	0.0023
<i>s_Listeria_phage_A511</i>	Volunteer	3.19	0.0403

Viral biomarker	Group	LDA Score (log10)	p-value
<i>s__Lactococcus_phage_CHL92</i>	Volunteer	3.18	0.0042
<i>o__Vibrionales_phage</i>	Volunteer	3.17	0.0184
<i>f__Vibrionaceae_phage</i>	Volunteer	3.16	0.0184
<i>s__Rhodococcus_phage_ReqiPoco6</i>	Volunteer	3.16	0.0057
<i>s__Avian_leukosis_virus</i>	Volunteer	3.15	0.0331
<i>s__Mycobacterium_phage_Angelica</i>	Volunteer	3.15	0.0034
<i>s__Lactobacillus_casei_phage</i>	Volunteer	3.15	0.0123
<i>s__Burkholderia_phage_phiE255</i>	Volunteer	3.15	0.0250
<i>s__Streptococcus_phage_YMC_2011</i>	Volunteer	3.14	0.0331
<i>s__Burkholderia_vietnamiensis_phage</i>	Volunteer	3.13	0.0114
<i>f__Neisseriaceae_phage</i>	Volunteer	3.13	0.0331
<i>o__Neisseriales_phage</i>	Volunteer	3.12	0.0331
<i>s__Rhizobium_phage_16_3</i>	Volunteer	3.12	0.0109
<i>s__Salmonella_phage_A10a</i>	Volunteer	3.11	0.0010
<i>s__Bacillus_cytotoxicus_phage</i>	Volunteer	3.11	0.0109
<i>s__Stygiolobus_rod_shaped_virus</i>	Volunteer	3.11	0.0430
<i>g__n__Streptococcus_phage_YMC_2011</i>	Volunteer	3.11	0.0331
<i>s__Stenotrophomonas_phage_phiSHP2</i>	Volunteer	3.10	0.0430
<i>s__Mycobacterium_phage_SirDuracell</i>	Volunteer	3.10	0.0331
<i>s__Pseudomonas_phage_Pf3</i>	Volunteer	3.10	0.0023
<i>f__n__n__Streptococcus_phage_YMC_2011</i>	Volunteer	3.09	0.0331
<i>s__Propionibacterium_phage_PAS2</i>	Volunteer	3.08	0.0034
<i>s__Enterobacteria_phage_Mu</i>	Volunteer	3.08	0.0109
<i>o__n__n__n__Mycobacterium_phage_SirDuracell</i>	Volunteer	3.07	0.0331
<i>s__Haemophilus_influenzae_phage</i>	Volunteer	3.07	0.0430
<i>o__n__n__n__Mycobacterium_phage_Oosterbaan</i>	Volunteer	3.07	0.0109
<i>s__Shigella_phage_Sf6</i>	Volunteer	3.07	0.0058
<i>s__Mycobacterium_phage_Oosterbaan</i>	Volunteer	3.06	0.0109
<i>g__Acholeplasma_phage</i>	Volunteer	3.06	0.0291
<i>s__Listeria_phage_B025</i>	Volunteer	3.06	0.0109
<i>g__n__Mycobacterium_phage_SirDuracell</i>	Volunteer	3.05	0.0331
<i>o__Acholeplasmatales_phage</i>	Volunteer	3.05	0.0291
<i>s__Acholeplasma_laidlawii_phage</i>	Volunteer	3.05	0.0291

Viral biomarker	Group	LDA Score (log10)	p-value
<i>f__Acholeplasmataceae_phage</i>	Volunteer	3.05	0.0291
<i>g__n_Mycobacterium_phage_Oosterbaan</i>	Volunteer	3.05	0.0109
<i>s__Clostridium_phage_c_st</i>	Volunteer	3.04	0.0430
<i>f__n_n_Mycobacterium_phage_SirDuracell</i>	Volunteer	3.04	0.0331
<i>f__n_n_Mycobacterium_phage_Oosterbaan</i>	Volunteer	3.04	0.0109
<i>s__Clostridium_phage_phiCP340</i>	Volunteer	3.03	0.0331
<i>o__n_n_n_Streptococcus_phage_YMC_2011</i>	Volunteer	3.03	0.0331
<i>s__Mycobacterium_phage_Giles</i>	Volunteer	3.03	0.0331
<i>g__Haemophilus_phage</i>	Volunteer	3.02	0.0430
<i>s__Vibrio_phage_SIO_2</i>	Volunteer	3.01	0.0250
<i>s__Vibrio_phage_VHML</i>	Volunteer	3.01	0.0109
<i>s__Rhodococcus_phage_ReqiPine5</i>	Volunteer	3.01	0.0274
<i>s__Mosquito_VEM_virus_SDRBAJ</i>	Volunteer	2.99	0.0109
<i>s__Xanthomonas_phage_OP2</i>	Volunteer	2.98	0.0447
<i>g__Betapapillomavirus</i>	Volunteer	2.98	0.0034
<i>o__n_n_n_Mosquito_VEM_virus_SDRBAJ</i>	Volunteer	2.98	0.0109
<i>s__Escherichia_phage_phiEB49</i>	Volunteer	2.98	0.0321
<i>f__n_n_Escherichia_phage_phiEB49</i>	Volunteer	2.97	0.0321
<i>g__n_Escherichia_phage_phiEB49</i>	Volunteer	2.97	0.0321
<i>o__n_n_n_Escherichia_phage_phiEB49</i>	Volunteer	2.97	0.0321
<i>s__Salmonella_phage_ST64T</i>	Volunteer	2.95	0.0109
<i>f__n_n_Mosquito_VEM_virus_SDRBAJ</i>	Volunteer	2.95	0.0109
<i>g__n_Mosquito_VEM_virus_SDRBAJ</i>	Volunteer	2.93	0.0109
<i>s__Streptococcus_phage_Sfi21</i>	Volunteer	2.93	0.0034
<i>s__Streptococcus_pyogenes_phage_T12</i>	Volunteer	2.92	0.0109
<i>f__n_n_Streptococcus_pyogenes_phage_T12</i>	Volunteer	2.92	0.0109
<i>s__Herminiimonas_arsenicoydans_phage</i>	Volunteer	2.92	0.0109
<i>g__n_Streptococcus_pyogenes_phage_T12</i>	Volunteer	2.91	0.0109
<i>s__Betapapillomavirus_2</i>	Volunteer	2.91	0.0109
<i>o__n_n_n_Streptococcus_pyogenes_phage_T12</i>	Volunteer	2.90	0.0109
<i>g__Herminiimonas_phage</i>	Volunteer	2.89	0.0109
<i>s__Bacillus_subtilis_phage</i>	Volunteer	2.86	0.0109
<i>s__Geobacillus_kaustophilus_phage</i>	Volunteer	2.83	0.0034

(B)

Viral biomarker	Group	LDA Score (log10)	p-value
<i>f__n_n_Bartonella_henselae_phage_60457</i>	Volunteer	4.39	0.0087
<i>g__n_Bartonella_henselae_phage_60457</i>	Volunteer	4.38	0.0087
<i>s__Bartonella_henselae_phage_60457</i>	Volunteer	4.38	0.0087
<i>o__n_n_n_Bartonella_henselae_phage_60457</i>	Volunteer	4.38	0.0087
<i>o__n_Retroviridae</i>	Crohn	4.21	0.0315
<i>f__Retroviridae</i>	Crohn	4.21	0.0315
<i>f__Podoviridae</i>	Volunteer	4.06	0.0258
<i>g__PhiC31_like_viruses</i>	Volunteer	4.06	0.0005
<i>s__Streptomyces_phage_phiBT1</i>	Volunteer	4.06	0.0005
<i>s__Salmonella_phage_MB78</i>	Volunteer	4.01	0.0287
<i>s__Streptococcus_phage_TP_J34</i>	Volunteer	3.90	0.0321
<i>f__Sphingomonadaceae_phage</i>	Volunteer	3.77	0.0060
<i>o__Sphingomonadales_phage</i>	Volunteer	3.77	0.0060
<i>g__Caudovirales_n_n</i>	Volunteer	3.76	0.0124
<i>f__Caudovirales_n</i>	Volunteer	3.76	0.0124
<i>s__Phage_PhiI</i>	Volunteer	3.75	0.0343
<i>o__n_n_n_Klebsiella_phage_KPP95</i>	Volunteer	3.71	0.0403
<i>s__Klebsiella_phage_KPP95</i>	Volunteer	3.71	0.0403
<i>f__n_n_Klebsiella_phage_KPP95</i>	Volunteer	3.71	0.0403
<i>g__Sphingopyxis_phage</i>	Volunteer	3.71	0.0245
<i>s__Sphingopyxis_alaskensis_phage</i>	Volunteer	3.71	0.0245
<i>g__n_Klebsiella_phage_KPP95</i>	Volunteer	3.71	0.0403
<i>o__n_Microviridae</i>	Volunteer	3.71	0.0067
<i>f__Microviridae</i>	Volunteer	3.71	0.0067
<i>s__Synechococcus_phage_S_CBS1</i>	Crohn	3.70	0.0022
<i>s__Xanthomonas_phage_OP2</i>	Volunteer	3.69	0.0088
<i>g__P22_like_viruses</i>	Volunteer	3.58	0.0184
<i>s__Burkholderia_vietnamiensis_phage</i>	Volunteer	3.55	0.0015
<i>f__Fuselloviridae</i>	Volunteer	3.53	0.0109
<i>s__Rhodococcus_phage_ReqiPoco6</i>	Volunteer	3.50	0.0057
<i>g__Fusellovirus</i>	Volunteer	3.47	0.0109

Viral biomarker	Group	LDA Score (log10)	p-value
<i>s__Shigella_phage_Sf6</i>	Volunteer	3.44	0.0010
<i>o__n__Fuselloviridae</i>	Volunteer	3.44	0.0109
<i>s__Mycobacterium_phage_Giles</i>	Volunteer	3.43	0.0109
<i>s__Streptococcus_phage_Sfi21</i>	Volunteer	3.43	0.0034
<i>s__Enterobacteria_phage_P1</i>	Volunteer	3.40	0.0345
<i>g__P1_like_viruses</i>	Volunteer	3.40	0.0345
<i>s__Salmonella_phage_A10a</i>	Volunteer	3.34	0.0034
<i>g__Betapapillomavirus</i>	Volunteer	3.33	0.0109
<i>s__Betapapillomavirus_2</i>	Volunteer	3.33	0.0109
<i>s__Rhodococcus_phage_ReqiPine5</i>	Volunteer	3.32	0.0216
<i>g__Microvirus</i>	Volunteer	3.31	0.0430
<i>s__Listeria_phage_A511</i>	Volunteer	3.27	0.0430
<i>s__Propionibacterium_phage_PAS2</i>	Volunteer	3.25	0.0034
<i>f__Oxalobacteraceae_phage</i>	Volunteer	3.25	0.0331
<i>g__Alphavirus</i>	Volunteer	3.24	0.0430
<i>s__Salmon_pancreas_disease_virus</i>	Volunteer	3.24	0.0430
<i>s__Yersinia_phage_phiYeO3_12</i>	Volunteer	3.20	0.0109
<i>s__Burkholderia_phage_phiE255</i>	Volunteer	3.18	0.0250
<i>s__Lactococcus_phage_CHL92</i>	Volunteer	3.18	0.0131
<i>s__Janthinobacterium_sp__Marseille_phage</i>	Volunteer	3.18	0.0331
<i>g__Janthinobacterium_phage</i>	Volunteer	3.18	0.0331
<i>s__Haemophilus_influenzae_phage</i>	Volunteer	3.17	0.0109
<i>s__Lactococcus_phage_TP901_1</i>	Volunteer	3.17	0.0109
<i>s__Lactobacillus_casei_phage</i>	Volunteer	3.15	0.0213
<i>g__Haemophilus_phage</i>	Volunteer	3.14	0.0109
<i>s__Vibrio_phage_VSK</i>	Volunteer	3.14	0.0109

Features are discriminative when values are above a non-negative threshold for the logarithmic LDA score =2.0, and p-value  $\leq \alpha=0.05$ .

Green color: differentially represented towards volunteers; red color: differentially represented towards Crohn's patients.

Taxonomic level: o\_\_: order, f\_\_: family, g\_\_: genus, s\_\_: species.