

## Supplemental Material

### Integrative analysis of metabolome and gut microbiota in Patients with pancreatic ductal adenocarcinoma

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Supplemental Material, Table S1. Identified significantly changed metabolites (fold change >1.5  $p < 0.05$  compared to resectable PDAC) in serum samples.

VIP	mz	RT	HMDB_ID	Adduct	Name	P	FC(UN/RES)
1.63	520.3396	8.92	HMDB0010386	M+H	LysoPC(18:2(9Z,12Z)/0:0)	1.44E-07	1.74E-14
1.37	522.3554	9.48	HMDB0002815	M+H	LysoPC(18:1(9Z)/0:0)	2.18E-05	3.51E-14
1.63	518.3218	9.24	HMDB0240262	M+Na	LysoPC(0:0/16:0)	1.15E-07	5.05E-13
1.15	546.3532	10.19	HMDB0010384	M+Na	LysoPC(18:0/0:0)	4.39E-04	9.57E-13
1.49	193.0346	1.09	HMDB0000094	M+H	Citric acid	2.13E-06	1.05E-12
1.11	464.3350	5.68	HMDB0013339	M+Na	3-Hydroxy-11Z-octadecenoylcarnitine	1.31E-03	1.90E-12
1.14	302.3054	8.33	HMDB0000269	M+H	Sphinganine	6.06E-04	2.39E-12
1.07	566.4282	5.81	HMDB0011497	M+H	LysoPE(0:0/24:0)	1.90E-03	2.84E-12
1.83	205.0972	4.01	HMDB0000929	M+H	L-Tryptophan	6.85E-10	3.06E-12
1.11	546.3554	9.26	HMDB0010393	M+H	LysoPC(20:3(5Z,8Z,11Z)/0:0)	6.56E-04	5.08E-12
1.32	494.3242	8.64	HMDB0010383	M+H	LysoPC(16:1(9Z)/0:0)	3.67E-05	7.42E-12
1.22	116.0708	0.79	HMDB0000162	M+H	L-Proline	1.65E-04	1.06E-11
1.19	688.5205	10.30	HMDB0007928	M+H	PC(14:1(9Z)/P-16:0)	2.61E-04	1.07E-11
1.77	480.3362	9.50	HMDB0010407	M+H	LysoPC(P-16:0/0:0)	4.28E-09	1.21E-11
1.38	426.3577	9.59	HMDB0005065	M+H	Oleoylcarnitine	1.55E-05	1.25E-11
1.47	746.5639	10.73	HMDB0007938	M+H	PC(15:0/18:1(11Z))	2.82E-06	1.34E-11
1.57	802.5373	10.09	HMDB0008182	M+H	PC(18:3(6Z,9Z,12Z)/20:5(5Z,8Z,11Z,14Z,17Z))	4.31E-07	1.43E-11
1.12	702.5439	10.75	HMDB0008951	M+H	PE(16:0/P-18:1(11Z))	6.32E-04	1.72E-11
1.91	834.6049	10.67	HMDB0113305	M+H	PE-NMe(20:0/22:6(4Z,7Z,10Z,13Z,16Z,19Z))	5.77E-11	1.75E-11
1.79	482.3242	10.11	HMDB0010381	M+H	LysoPC(15:0/0:0)	2.40E-09	1.77E-11
1.44	764.5565	11.66	HMDB0008029	M+Na	PC(16:1(9Z)/P-18:1(11Z))	4.91E-06	2.04E-11
1.12	407.3017	8.26	HMDB0011543	M+Na	MG(0:0/20:1(11Z)/0:0)	6.14E-04	2.16E-11
1.08	159.0277	1.07	HMDB0000157	M+Na	Hypoxanthine	1.23E-03	2.69E-11
2.11	796.5260	11.09	HMDB0009710	M+Na	PE(22:6(4Z,7Z,10Z,13Z,16Z,19Z)/P-18:1(11Z))	2.37E-14	2.73E-11
1.16	757.5617	9.54	HMDB0114872	M+H	PA(16:1(9Z)/24:1(15Z))	3.48E-04	2.73E-11
1.53	820.5269	11.66	HMDB0112336	M+Na	PS(15:0/22:4(7Z,10Z,13Z,16Z))	1.00E-06	2.83E-11
1.95	188.0706	4.02	HMDB0000734	M+H	Indoleacrylic acid	1.69E-11	3.18E-11
2.04	424.3422	9.14	HMDB0006461	M+H	Linoelaidyl carnitine	4.76E-13	3.23E-11
1.72	548.3709	9.72	HMDB0010392	M+H	LysoPC(20:2(11Z,14Z)/0:0)	1.42E-08	5.02E-11
1.50	776.5732	10.24	HMDB0009644	M+H	PE(22:5(4Z,7Z,10Z,13Z,16Z)/P-18:1(11Z))	1.65E-06	5.25E-11

1.37	542.3240	8.51	HMDB0010397	M+H	LysoPC(20:5(5Z,8Z,11Z,14Z,17Z)/0:0)	1.61E-05	8.86E-11
1.31	468.3085	8.37	HMDB0010379	M+H	LysoPC(14:0/0:0)	4.79E-05	9.23E-11
1.59	550.3866	10.36	HMDB0010391	M+H	LysoPC(20:1(11Z)/0:0)	5.11E-07	1.11E-10
1.19	808.5815	10.38	HMDB0000593	M+Na	PC(18:1(9Z)/18:1(9Z))	3.29E-04	1.18E-10
1.29	269.0879	1.28	HMDB0000195	M+H	Inosine	1.03E-04	1.23E-10
1.34	111.0078	1.09	HMDB0000243	M+Na	Pyruvic acid	2.89E-05	1.28E-10
1.14	248.1493	1.16	HMDB0013127	M+H	3-Hydroxybutyrylcarnitine	4.85E-04	1.47E-10
1.99	144.0115	1.80	HMDB0003417	M+Na	D-Cysteine	3.13E-12	1.74E-10
1.10	537.3620	5.75	HMDB0115487	M+H	PA(8:0/16:0)	2.35E-03	1.90E-10
1.08	572.3713	9.59	HMDB0010401	M+H	LysoPC(22:4(7Z,10Z,13Z,16Z)/0:0)	1.00E-03	2.07E-10
1.29	733.5537	10.27	HMDB0114793	M+H	PA(14:0/24:0)	5.92E-05	2.10E-10
1.28	814.5718	11.09	HMDB0008457	M+Na	PC(20:4(5Z,8Z,11Z,14Z)/P-18:1(11Z))	7.26E-05	2.40E-10
1.61	506.3603	10.19	HMDB0010408	M+H	LysoPC(P-18:1(9Z)/0:0)	1.66E-07	2.53E-10
1.48	232.1544	3.60	HMDB0000736	M+H	Isobutyryl-L-carnitine	2.87E-06	2.55E-10
1.27	848.5942	11.10	HMDB0009113	M+Na	PE(18:2(9Z,12Z)/24:1(15Z))	8.51E-05	2.56E-10
1.16	391.3427	11.32	HMDB0240583	M+H	Arachidonoylcholine	3.87E-04	2.73E-10
1.26	590.3212	8.90	HMDB0010404	M+Na	LysoPC(22:6(4Z,7Z,10Z,13Z,16Z,19Z)/0:0)	1.06E-04	2.97E-10
1.53	621.3101	12.52	HMDB0061690	M+H	LysoPI(20:4(5Z,8Z,11Z,14Z)/0:0)	8.90E-07	4.49E-10
1.20	792.5886	11.05	HMDB0008095	M+Na	PC(18:1(11Z)/P-18:1(11Z))	2.19E-04	5.37E-10
1.22	527.4351	11.30	HMDB0071469	M+H	TG(8:0/8:0/i-12:0)	1.72E-04	5.44E-10
1.92	380.2562	8.29	HMDB0000277	M+H	Sphingosine 1-phosphate	4.06E-11	5.58E-10
1.16	882.5904	13.15	HMDB0008321	M+Na	PC(20:1(11Z)/22:6(4Z,7Z,10Z,13Z,16Z,19Z))	3.64E-04	7.06E-10
1.54	300.2896	11.65	HMDB0000252	M+H	Sphingosine	9.76E-07	7.92E-10
1.04	500.2748	8.88	HMDB0011477	M+Na	LysoPE(0:0/18:2(9Z,12Z))	2.00E-03	8.66E-10
1.56	532.3438	9.68	HMDB0011481	M+Na	LysoPE(0:0/20:0)	5.30E-07	8.80E-10
1.33	508.3395	9.05	HMDB0011482	M+H	LysoPE(0:0/20:1(11Z))	4.55E-05	1.01E-09
1.52	398.3265	8.96	HMDB0006317	M+H	trans-Hexadec-2-enoyl carnitine	1.23E-06	1.02E-09
1.96	438.2982	9.46	HMDB0011152	M+H	LysoPE(P-16:0/0:0)	1.10E-11	1.03E-09
1.28	833.6449	11.65	HMDB0042117	M+Na	TG(14:0/15:0/20:5(5Z,8Z,11Z,14Z,17Z))	7.15E-05	1.09E-09
2.06	163.1328	5.70	HMDB0033625	M+H	(3R,7R)-1,3,7-Octanetriol	4.21E-13	1.22E-09
1.02	530.3580	9.72	HMDB0013122	M+Na	LysoPC(P-18:0/0:0)	1.97E-03	1.25E-09
1.24	480.3037	5.67	HMDB0011475	M+H	LysoPE(0:0/18:1(11Z))	1.82E-04	1.34E-09
1.67	1109.6534	8.92	HMDB0116822	M+Na	CL(8:0/8:0/8:0/21:0)	4.88E-08	1.74E-09
1.18	396.3108	8.51	HMDB0013334	M+H	9,12-Hexadecadienoylcarnitine	3.24E-04	2.00E-09

1.14	872.6079	11.65	HMDB0009410	M+Na	PE(20:4(5Z,8Z,11Z,14Z)/24:1(15Z))	4.48E-04	2.01E-09
1.26	923.6897	5.26	HMDB0053013	M+Na	TG(18:3(6Z,9Z,12Z)/20:3(5Z,8Z,11Z)/18:3(6Z,9Z,12Z))	1.06E-04	2.10E-09
1.12	188.0686	2.30	HMDB0000159	M+Na	L-Phenylalanine	5.81E-04	2.15E-09
1.90	476.2749	9.18	HMDB0011473	M+Na	LysoPE(0:0/16:0)	1.21E-10	2.34E-09
1.67	837.6191	10.67	HMDB0115089	M+Na	PA(20:0/24:1(15Z))	4.79E-08	2.40E-09
1.26	689.4934	6.03	HMDB0007208	M+Na	DG(18:1(11Z)/22:6(4Z,7Z,10Z,13Z,16Z,19Z)/0:0)	4.09E-04	2.56E-09
1.02	262.1284	1.11	HMDB0061717	M+H	Succinylcarnitine	1.99E-03	2.75E-09
1.43	436.3057	8.60	HMDB0013333	M+Na	3-Hydroxy-9-hexadecenoylcarnitine	9.50E-06	2.89E-09
1.64	538.3877	10.74	HMDB0011490	M+H	LysoPE(0:0/22:0)	8.91E-08	3.17E-09
1.46	<sup>1091.598</sup> <sub>8</sub>	5.67	HMDB0116851	M+Na	CL(8:0/8:0/10:0/18:2(9Z,11Z))	6.92E-06	3.21E-09
1.11	902.4752	11.38	HMDB0012450	M+Na	PS(22:6(4Z,7Z,10Z,13Z,16Z,19Z)/22:6(4Z,7Z,10Z,13Z,16Z,19Z))	9.45E-04	3.38E-09
1.27	778.4470	0.77	HMDB0012339	M+Na	PS(14:0/20:4(5Z,8Z,11Z,14Z))	7.43E-05	3.52E-09
1.07	908.6505	10.16	HMDB0113770	M+H	PE-NMe(11D5/13M5)	1.09E-03	3.84E-09
1.68	536.3716	9.91	HMDB0011491	M+H	LysoPE(0:0/22:1(13Z))	5.70E-08	4.38E-09
1.70	127.0366	1.33	HMDB0000008	M+Na	2-Hydroxybutyric acid	2.24E-08	4.39E-09
1.30	718.4910	5.26	HMDB0009213	M+Na	PE(18:4(6Z,9Z,12Z,15Z)/P-16:0)	7.20E-05	4.65E-09
1.22	470.3206	5.41	HMDB0006455	M+Na	Arachidonoylcarnitine	4.17E-04	5.16E-09
1.04	<sup>1571.967</sup> <sub>5</sub>	9.24	HMDB0058282	M+Na	CL(18:1(11Z)/22:6(4Z,7Z,10Z,13Z,16Z,19Z)/18:1(11Z)/22:6(4Z,7Z,10Z,13Z,16Z,19Z))	2.30E-03	5.48E-09
1.59	422.3250	8.76	HMDB0000222	M+Na	L-Palmitoylcarnitine	2.54E-07	5.53E-09
1.03	522.2852	7.05	HMDB0000874	M+Na	Tauroursodeoxycholic acid	2.10E-03	5.87E-09
1.20	<sup>1005.793</sup> <sub>5</sub>	0.68	HMDB0050849	M+H	TG(20:1(11Z)/22:6(4Z,7Z,10Z,13Z,16Z,19Z)/22:6(4Z,7Z,10Z,13Z,16Z,19Z))	2.95E-04	9.80E-09
1.06	711.5243	5.35	HMDB0013462	M+Na	SM(d18:0/14:1(9Z)(OH))	1.78E-03	1.04E-08
1.35	556.3371	5.76	HMDB0011492	M+Na	LysoPE(0:0/22:2(13Z,16Z))	4.12E-05	1.05E-08
1.24	733.4881	5.31	HMDB0114827	M+Na	PA(15:0/22:4(7Z,10Z,13Z,16Z))	1.67E-04	1.24E-08
1.84	<sup>1001.692</sup> <sub>3</sub>	9.49	HMDB0061410	M+Na	PC(DiMe(13,5)/DiMe(13,5))	6.46E-10	1.54E-08
1.21	450.3575	9.38	HMDB0000848	M+Na	Stearoylcarnitine	1.87E-04	1.60E-08
1.91	382.2725	8.47	HMDB0001383	M+H	Sphinganine 1-phosphate	6.87E-11	1.63E-08
1.54	368.2398	5.03	HMDB0061637	M+Na	3-hydroxyundecanoyl carnitine	1.19E-06	1.95E-08
1.26	372.3110	10.72	HMDB0005066	M+H	Tetradecanoylcarnitine	9.10E-05	2.60E-08

1.07	190.0858	6.41	HMDB0002302	M+H	Indole-3-propionic acid	1.82E-03	3.85E-08
1.61	434.2856	5.21	HMDB0013335	M+Na	3-Hydroxyhexadecadienoylcar nitine	2.33E-07	3.94E-08
1.28	952.6765	10.26	HMDB0112735	M+Na	PS(22:0/24:1(15Z))	6.29E-05	4.42E-08
1.21	769.5552	6.56	HMDB0114831	M+Na	PA(15:0/24:0)	7.81E-04	4.84E-08
1.17	945.6708	5.26	HMDB0010536	M+Na	TG(20:5(5Z,8Z,11Z,14Z,17Z)/ 18:2(9Z,12Z)/20:5(5Z,8Z,11Z, 14Z,17Z))	3.42E-04	6.10E-08
1.54	1019.703 8	10.18	HMDB0010560	M+Na	TG(22:6(4Z,7Z,10Z,13Z,16Z,1 9Z)/20:5(5Z,8Z,11Z,14Z,17Z)/ 22:6(4Z,7Z,10Z,13Z,16Z,19Z))	7.42E-07	1.85E-07
1.02	632.4416	7.62	HMDB0008855	M+H	PE(14:1(9Z)/14:1(9Z))	2.41E-03	3.96E-07
1.04	535.0370	5.30	HMDB0001018	M-H	UDP-D-Xylose	5.51E-08	3.91E-04
1.33	757.4882	5.30	HMDB0010570	M+Cl	PG(16:0/16:0)	1.27E-07	4.65E-02
1.30	682.4041	5.41	HMDB0008856	M+Cl	PE(14:1(9Z)/15:0)	1.21E-13	6.19E-02
1.11	768.4937	5.49	HMDB0112331	M-H	PS(15:0/20:4(5Z,8Z,11Z,14Z))	3.45E-08	8.00E-02
1.60	470.3203	5.27	HMDB0006510	M-H	Cervonyl carnitine	1.89E-14	8.78E-02
1.17	732.4722	0.78	HMDB0009147	M+Cl	PE(18:3(6Z,9Z,12Z)/P-16:0)	1.15E-09	9.14E-02
1.05	841.5553	10.46	HMDB0115170	M+Cl	PA(20:4(5Z,8Z,11Z,14Z)/24:1( 15Z))	2.87E-08	1.01E-01
1.03	800.6676	0.72	HMDB0011695	M-H	SM(d17:1/24:0)	2.92E-06	1.07E-01
1.67	756.4861	5.29	HMDB0112297	M-H	PS(14:0/20:3(5Z,8Z,11Z))	3.25E-13	1.38E-01
1.13	285.2064	8.82	HMDB0000672	M-H	Hexadecanedioic acid	5.77E-06	1.44E-01
1.14	674.5108	0.78	HMDB0008851	M-H	PE(14:0/P-18:0)	1.10E-09	1.45E-01
1.06	818.4440	0.77	HMDB0009210	M+Cl	PE(18:4(6Z,9Z,12Z,15Z)/22:6( 4Z,7Z,10Z,13Z,16Z,19Z))	3.20E-07	2.24E-01
1.13	688.5242	0.78	HMDB0007895	M-H	PC(14:0/P-16:0)	1.06E-07	2.27E-01
1.18	751.4957	5.48	HMDB0114825	M+Cl	PA(15:0/22:1(13Z))	7.60E-09	2.37E-01
1.16	1502.054 6	5.92	HMDB0057130	M-H	CL(18:0/18:1(11Z)/20:4(5Z,8Z ,11Z,14Z)/20:4(5Z,8Z,11Z,14Z )	7.42E-09	2.44E-01
1.10	297.2428	9.52	HMDB0010736	M-H	3-Oxoostadecanoic acid	1.29E-07	2.90E-01
1.09	702.5282	0.79	HMDB0007961	M-H	PC(15:0/P-16:0)	8.12E-09	2.92E-01
1.20	781.4604	5.49	HMDB0114918	M+Cl	PA(18:1(11Z)/22:6(4Z,7Z,10Z, 13Z,16Z,19Z))	3.12E-10	2.92E-01
1.22	990.7927	0.67	HMDB0008783	M+Cl	PC(24:0/24:1(15Z))	2.68E-11	2.97E-01
1.33	255.2325	11.53	HMDB0000220	M-H	Palmitic acid	8.90E-15	3.22E-01
1.44	277.2167	10.67	HMDB0001388	M-H	alpha-Linolenic acid	3.67E-16	3.22E-01
1.16	812.4044	0.78	HMDB0012351	M+Cl	PS(14:1(9Z)/22:6(4Z,7Z,10Z,1 3Z,16Z,19Z))	9.28E-10	3.31E-01
1.12	822.5689	5.42	HMDB0007887	M+Cl	PC(14:0/22:1(13Z))	5.17E-09	3.42E-01
1.34	279.2326	11.10	HMDB0000673	M-H	Linoleic acid	4.84E-15	3.44E-01
1.29	188.0170	1.62	HMDB0001476	M+Cl	3-Hydroxyanthranilic acid	2.55E-13	3.49E-01

1.14	734.4723	0.78	HMDB0008847	M-H	PE(14:0/22:6(4Z,7Z,10Z,13Z,16Z,19Z))	5.14E-09	3.50E-01
1.25	810.4076	0.78	HMDB0112496	M+Cl	PS(18:4(6Z,9Z,12Z,15Z)/18:4(6Z,9Z,12Z,15Z))	3.15E-12	3.53E-01
1.35	281.2481	11.66	HMDB0000207	M-H	Oleic acid	6.56E-15	3.60E-01
1.15	916.7056	0.69	HMDB0013449	M+Cl	PC(O-22:0/22:3(10Z,13Z,16Z))	1.76E-09	3.70E-01
1.18	101.0238	1.29	HMDB0000005	M-H	2-Ketobutyric acid	3.58E-08	3.84E-01
1.19	823.5543	5.63	HMDB0116585	M-H	PG(20:4(5Z,8Z,11Z,14Z)/20:1(11Z))	5.21E-10	4.04E-01
1.59	171.0654	5.38	HMDB0000341	M-H	2-Octenedioic acid	1.41E-20	4.04E-01
1.33	307.2635	11.80	HMDB0005060	M-H	Eicosadienoic acid	3.86E-11	4.24E-01
1.08	596.4013	5.18	HMDB0010699	M+Cl	CerP(d18:1/12:0)	8.99E-07	4.48E-01
1.07	750.5247	5.93	HMDB0007897	M+Cl	PC(14:0/P-18:1(11Z))	1.07E-07	4.49E-01
1.24	283.2638	12.53	HMDB0000827	M-H	Stearic acid	9.22E-12	4.49E-01
1.01	119.0342	0.76	HMDB0000337	M-H	(S)-3,4-Dihydroxybutyric acid	2.86E-07	4.50E-01
1.29	124.0096	0.78	HMDB0000251	M-H	Taurine	6.71E-11	4.76E-01
1.14	723.5022	5.48	HMDB0114846	M-H	PA(16:0/22:4(7Z,10Z,13Z,16Z))	3.08E-08	4.82E-01
1.08	720.5002	5.48	HMDB0009215	M-H	PE(18:4(6Z,9Z,12Z,15Z)/P-18:1(11Z))	1.88E-07	4.85E-01
1.16	530.3017	9.24	HMDB0010382	M+Cl	LysoPC(16:0/0:0)	1.03E-09	5.15E-01
1.06	154.0615	0.76	HMDB0000177	M-H	L-Histidine	1.01E-07	5.76E-01
1.12	303.2325	11.00	HMDB0001043	M-H	Arachidonic acid	1.91E-07	5.99E-01
1.05	89.0241	1.06	HMDB0000190	M-H	L-Lactic acid	2.68E-08	6.00E-01
1.05	327.2324	10.85	HMDB0002183	M-H	Docosahexaenoic acid	2.18E-06	6.25E-01
1.06	504.3092	8.92	HMDB0011483	M-H	LysoPE(0:0/20:2(11Z,14Z))	5.83E-05	7.00E-01
1.10	502.2932	9.22	HMDB0011484	M-H	LysoPE(0:0/20:3(11Z,14Z,17Z))	3.81E-04	2.35E+00
1.45	892.6483	6.32	HMDB0009245	M+Cl	PE(20:0/24:1(15Z))	1.75E-09	3.39E+00
1.67	652.4622	6.18	HMDB0010700	M+Cl	CerP(d18:1/16:0)	8.08E-15	4.91E+00

Figure S1. Microbial alpha diversity decreased in Unresectable PDAC and resectable PDAC patients shown by Chao 1 diversity index. (Chao1 index,  $p = 0.81$ ).

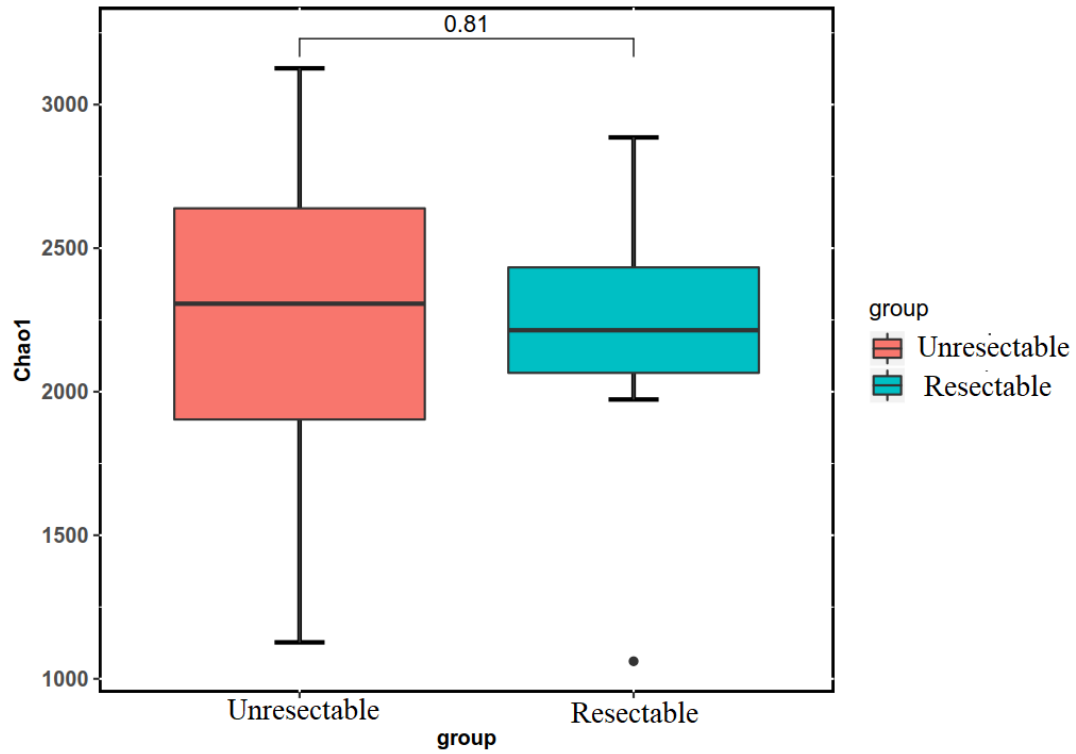


Figure S2. Relative abundance of the bacterial Species.

