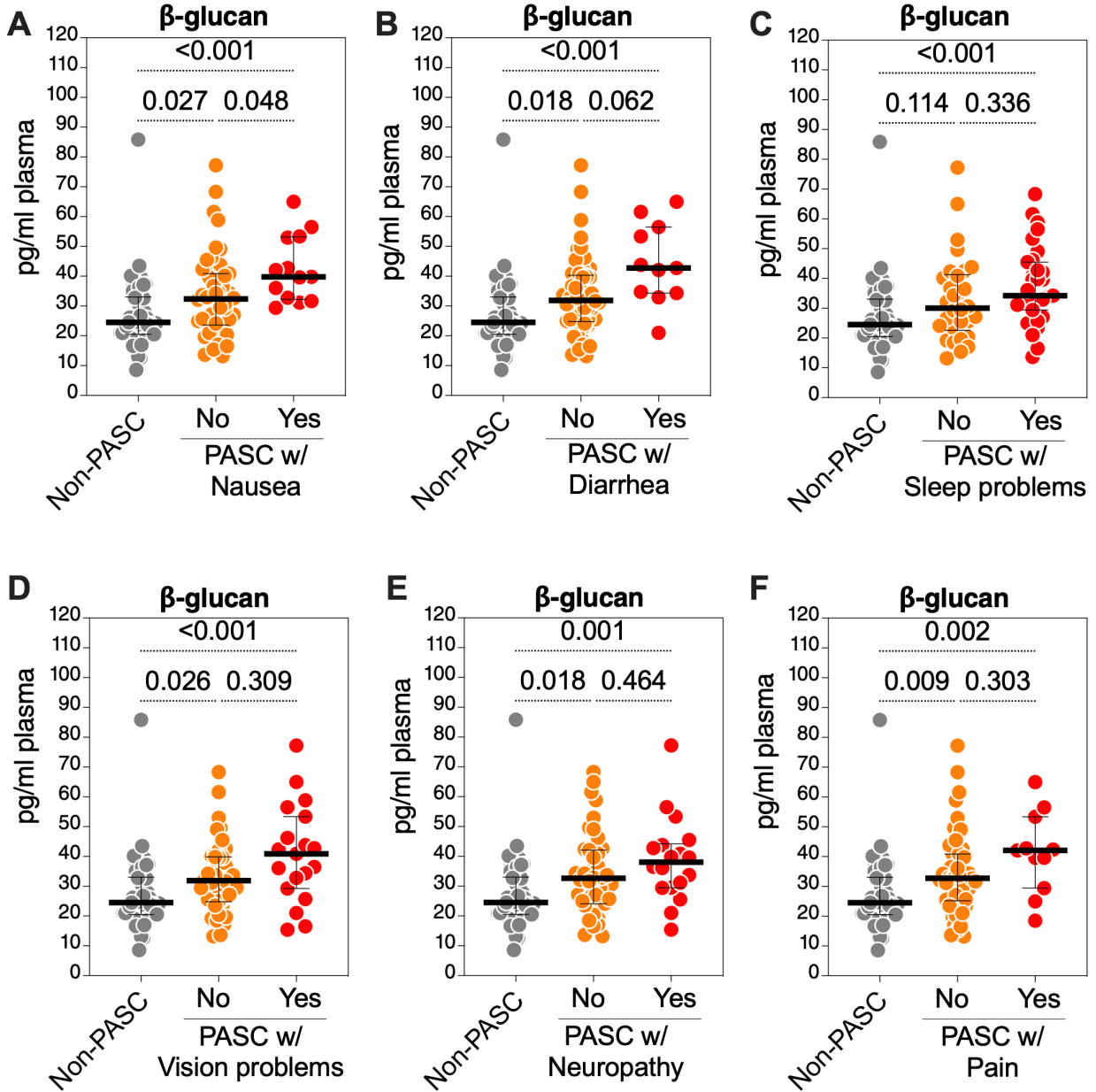
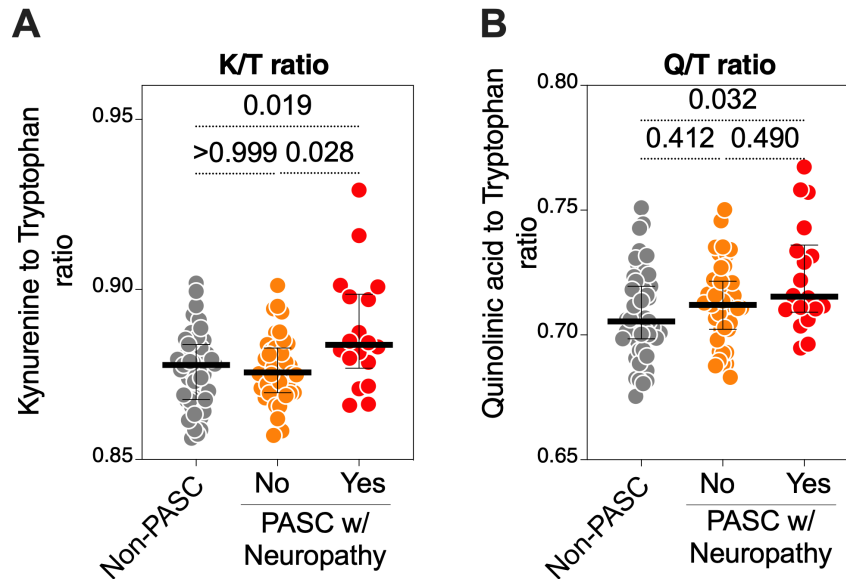


Supplementary Figure 1



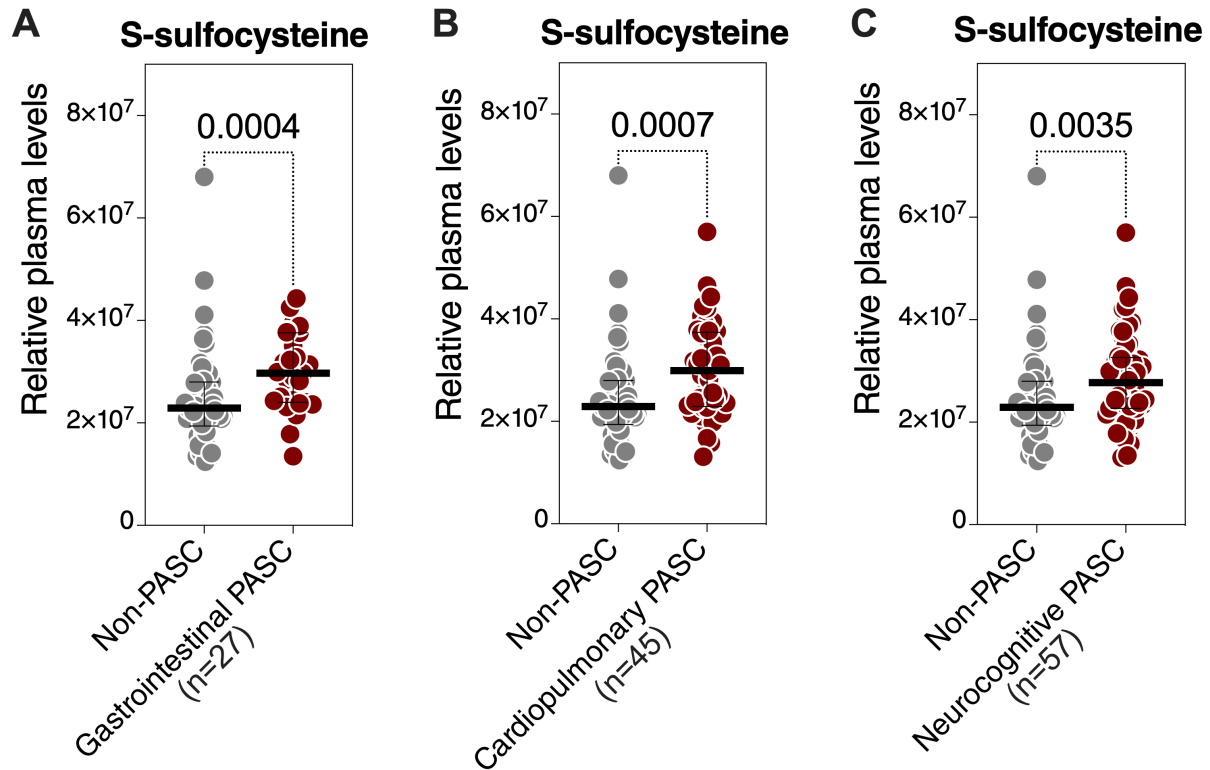
Supplementary Figure 1. β -glucan levels in plasma correlate with certain PASC symptoms. Kruskal-Wallis tests comparing β -glucan levels in non-PASC and PASC groups (from the UCSF LIINC cohort) with or without (A) nausea, (B) diarrhea, (C) vision problems, (D) sleep problems, (E) neuropathy, or (F) pain. Median and IQR are displayed.

Supplementary Figure 2



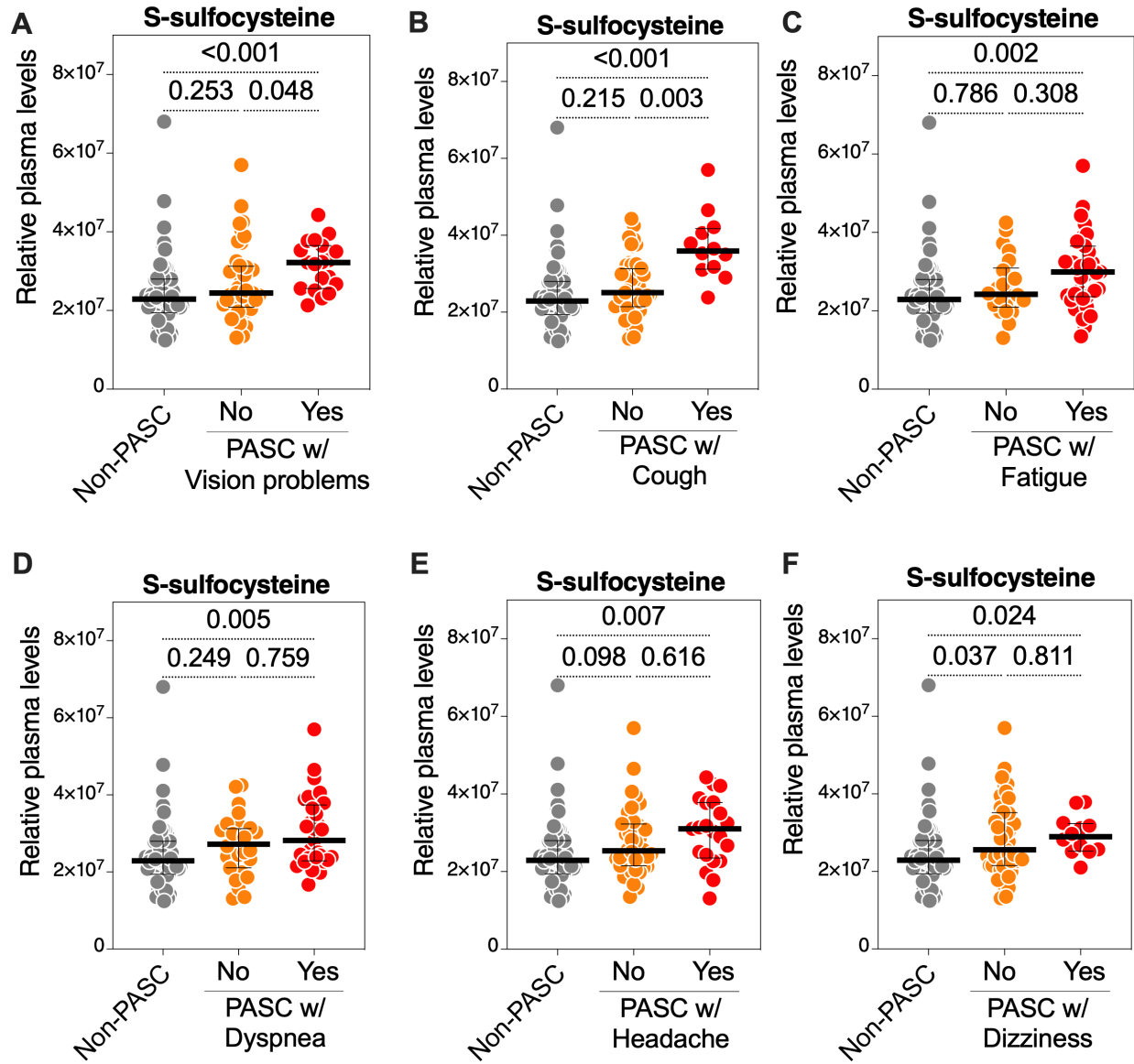
Supplementary Figure 2. K/T and Q/T ratios correlate with neuropathy during PASC. Kruskal-Wallis tests comparing **(A)** K/T ratio and **(B)** Q/T ratio between non-PASC and PASC groups (from the UCSF LIINC cohort) with or without neuropathy symptoms. Median and IQR are displayed.

Supplementary Figure 3



Supplementary Figure 3. Levels of plasma S-sulfocysteine are higher in individuals experiencing three PASC phenotypes, based on clinical symptom clusters, compared to those without PASC. PASC was divided to three phenotypes based on clinical symptom clusters defined as having at least one symptom in the cluster – gastrointestinal (nausea, diarrhea, loss of appetite, abdominal pain, vomiting), cardiopulmonary (cough, dyspnea, chest pain, palpitations), and neurocognitive (headache, concentration problems, dizziness, balance problems, neuropathy, vision problems). S-sulfocysteine levels were higher in individuals experiencing each of the three PASC symptom clusters compared to individuals who are not experiencing PASC. Mann–Whitney U tests. Median and IQR are displayed.

Supplementary Figure 4



Supplementary Figure 4. S-sulfocysteine levels in plasma correlate with certain PASC symptoms. Kruskal-Wallis tests comparing S-sulfocysteine levels in non-PASC and PASC groups (from the UCSF LIINC cohort) with or without (A) vision problems, (B) fatigue, (C) headache, (D) dizziness, (E) cough, or (F) dyspnea. Median and IQR are displayed.

Supplementary Table 1. Plasma metabolites differ between PASC and non-PASC participants in the LIINC cohort.

Marker		PASC	n	mean*	SD	SEM	min	25%	median	75%	max	Wilcoxon rank-sum P value
Higher in PASC than no-PASC	S-sulfocysteine	No	55	24.48	0.47	0.06	23.56	24.21	24.45	24.74	26.02	0.0025
		Yes	61	24.71	0.44	0.06	23.64	24.44	24.72	24.97	25.76	
	L-Cystine	No	55	27.35	0.52	0.07	25.93	26.99	27.35	27.69	28.58	0.0046
		Yes	61	27.63	0.51	0.06	26.34	27.31	27.66	28.01	28.49	
	L-Glutamine	No	55	32.88	0.19	0.03	32.35	32.77	32.87	33.01	33.36	0.0333
		Yes	61	32.97	0.24	0.03	32.45	32.85	32.95	33.15	33.49	
	Quinolinic acid	No	55	21.78	0.52	0.07	20.73	21.42	21.71	22.14	23.41	0.0352
		Yes	61	21.98	0.50	0.06	21.01	21.61	21.90	22.28	23.39	
	Ornithine	No	55	29.78	0.26	0.03	29.32	29.56	29.81	29.99	30.37	0.0387
		Yes	61	29.89	0.27	0.03	29.26	29.73	29.86	30.08	30.38	
	2-Phenylphenol	No	55	20.29	1.56	0.21	18.66	19.43	20.27	20.65	30.47	0.0392
		Yes	61	20.76	2.27	0.29	18.49	19.74	20.64	20.83	30.96	
Lower in PASC than no-PASC	Sarcosine	No	55	26.48	0.27	0.04	25.67	26.30	26.47	26.67	27.09	0.0058
		Yes	61	26.36	0.26	0.03	25.71	26.18	26.34	26.54	27.26	
	1-Methylnicotinamide	No	55	24.02	1.08	0.15	21.35	23.40	23.91	24.72	27.46	0.0174
		Yes	61	23.66	0.94	0.12	22.04	23.13	23.59	24.10	27.95	
	3,5-Dihydroxybenzoic acid	No	55	23.19	1.24	0.17	19.93	22.25	23.16	24.19	25.88	0.0376
		Yes	61	22.72	1.23	0.16	20.09	21.66	22.79	23.45	25.59	
	Indole-3-lactic acid	No	55	25.32	0.48	0.06	24.25	25.03	25.28	25.55	26.89	0.0436
		Yes	61	25.11	0.51	0.07	23.07	24.75	25.16	25.40	26.10	
	L-Methionine	No	55	30.18	0.31	0.04	28.94	29.98	30.22	30.38	30.76	0.0408
		Yes	61	30.07	0.33	0.04	29.06	29.90	30.09	30.26	30.93	
	Pipicolinic acid	No	55	27.66	0.99	0.13	26.17	26.98	27.45	28.27	30.91	0.0430
		Yes	61	27.38	1.16	0.15	25.43	26.64	27.07	27.93	31.43	

* Log₂transformed data

SD = Standard deviation

SEM= Standard Error of the Mean

Supplementary Table 2. Correlations between metabolites and clinical and inflammatory markers in the LIINC cohort.

Markers	Parameter	Spearman correlations among all patients											Spearman correlations among no-PASC patients											Spearman correlations among PASC patients										
		# of symptoms	QoL score	GFAP	NFL	MCP1	IFN α	IFN γ	IL-6	IL-10	TNF α	IP-10	# of symptoms	QoL score	GFAP	NFL	MCP1	IFN α	IFN γ	IL-6	IL-10	TNF α	IP-10	# of symptoms	QoL score	GFAP	NFL	MCP1	IFN α	IFN γ	IL-6	IL-10	TNF α	IP-10
Higher in PASC than no-PASC	S-sulfocysteine	<i>rho</i>	0.3474	-0.0975	-0.1653	-0.1215	0.0594	-0.1517	-0.1287	-0.1154	0.1906	0.0980	-0.1051	-0.1909	0.0320	0.3566	0.1019	0.1053	0.0178	0.0716	0.1245	0.3072	-0.1592	-0.0975	-0.1992	0.0021	-0.3727	-0.0862	0.0607	-0.1841	0.1556	0.0677		
		<i>P value</i>	0.0001	0.3925	0.1377	0.2770	0.5960	0.6048	0.8495	0.2493	0.3020	0.0863	0.3842	0.5543	0.2579	0.8508	0.0303	0.5724	0.5352	0.9168	0.6737	0.4630	0.0160	0.2963	0.5240	0.1895	0.9890	0.2589	0.5824	0.6819	0.2262	0.3074	0.6626	
		<i>n</i>	116	79	82	82	82	14	76	82	82	82	81	34	37	37	37	33	37	37	37	37	61	45	45	45	45	11	43	45	45	45	44	
	L-Cystine	<i>rho</i>	0.3145	-0.2378	-0.0607	0.0521	0.1829	-0.3451	-0.0887	0.5489	0.1334	0.4746	0.1469	-0.0484	-0.0756	0.2354	0.2909	-0.0572	0.7110	-0.0121	0.4772	0.2776	0.2431	-0.0994	-0.0302	-0.0501	0.1943	-0.4636	-0.0807	0.4224	0.2148	0.4605	-0.0065	
		<i>P value</i>	0.0006	0.0348	0.5882	0.6418	0.1001	0.2269	0.4462	<0.0001	0.2320	<0.0001	0.1907	0.7859	0.6564	0.1607	0.0807	0.7521	<0.0001	0.9434	0.0028	0.0962	0.0590	0.5161	0.8440	0.7440	0.2008	0.1509	0.6069	0.0038	0.1566	0.0015	0.9667	
		<i>n</i>	116	79	82	82	82	14	76	82	82	82	81	34	37	37	37	33	37	37	37	37	61	45	45	45	45	11	43	45	45	45	44	
	L-Glutamine	<i>rho</i>	0.1950	0.0173	0.1811	-0.0923	-0.1799	0.1912	0.0394	0.0245	0.1196	-0.0188	-0.0792	-0.0069	0.1560	0.0624	-0.1313	-0.2386	-0.0218	0.2385	-0.0007	-0.2224	0.0521	0.1797	0.2551	-0.1751	-0.2115	-0.0273	0.1701	-0.0229	0.0285	-0.1073	-0.0795	
		<i>P value</i>	0.0360	0.8795	0.1035	0.4094	0.1057	0.5126	0.7352	0.8269	0.2845	0.8667	0.4823	0.9691	0.3565	0.7139	0.4384	0.1811	0.8980	0.1552	0.9967	0.1859	0.8902	0.2375	0.0908	0.2500	0.1632	0.9366	0.2756	0.8812	0.8528	0.4832	0.6080	
		<i>n</i>	116	79	82	82	82	14	76	82	82	82	81	34	37	37	37	33	37	37	37	37	61	45	45	45	45	11	43	45	45	45	44	
	Quinolinic acid	<i>rho</i>	0.2091	-0.2667	-0.1205	0.1882	0.2445	-0.2615	0.0439	0.4423	0.1934	0.5146	0.2732	0.0847	-0.0299	0.3092	0.3075	0.0488	0.4829	0.0413	0.4054	0.3376	0.0951	-0.2555	-0.0862	0.1748	0.2849	-0.5818	0.0745	0.3391	0.3229	0.5725	0.1821	
		<i>P value</i>	0.0243	0.0175	0.2809	0.0904	0.0268	0.3664	0.7067	<0.0001	0.0817	<0.0001	0.0136	0.6341	0.8607	0.0626	0.0641	0.7874	0.0025	0.8085	0.0128	0.0410	0.4662	0.0902	0.5736	0.2507	0.0579	0.0604	0.6351	0.0227	0.0305	<0.0001	0.2368	
		<i>n</i>	116	79	82	82	82	14	76	82	82	82	81	34	37	37	37	33	37	37	37	37	61	45	45	45	45	11	43	45	45	45	44	
Ornithine	<i>rho</i>	0.1815	0.0064	-0.1242	0.0941	0.1028	0.0593	0.0809	-0.0201	0.2537	0.0267	0.0309	-0.0961	-0.0704	-0.2184	0.2053	0.2253	0.0773	-0.1859	0.1577	0.1055	0.0065	0.1758	-0.1294	0.3322	0.0603	-0.0182	0.0360	-0.1322	0.3183	-0.1170	-0.0665		
	<i>P value</i>	0.0512	0.9557	0.2661	0.4007	0.3582	0.8403	0.4871	0.8579	0.0215	0.8120	0.7839	0.5887	0.6788	0.1942	0.2228	0.2075	0.6493	0.2707	0.3514	0.5343	0.9604	0.2481	0.3970	0.0258	0.6938	0.9577	0.8186	0.3869	0.0331	0.4440	0.6679		
	<i>n</i>	116	79	82	82	82	14	76	82	82	82	81	34	37	37	37	33	37	37	37	37	61	45	45	45	45	11	43	45	45	45	44		
2-Phenylphenol	<i>rho</i>	0.1608	0.0604	-0.0130	-0.0589	-0.0221	-0.0506	-0.0198	0.0013	-0.0080	0.0000	-0.0226	0.1387	0.1719	-0.0505	0.0688	-0.1043	-0.0213	0.1098	-0.2079	0.0775	-0.0436	0.0994	-0.0730	-0.0999	-0.0623	0.0818	0.0527	-0.0600	-0.0974	0.0307	-0.1915		
	<i>P value</i>	0.0847	0.5969	0.9077	0.5991	0.8436	0.8637	0.8654	0.9909	0.9433	0.9998	0.8472	0.4341	0.3090	0.7666	0.6860	0.5636	0.9002	0.5178	0.2169	0.6483	0.7387	0.5158	0.6337	0.5139	0.6842	0.8110	0.7371	0.6957	0.5246	0.8413	0.2129		
	<i>n</i>	116	79	82	82	82	14	76	82	82	82	81	34	37	37	37	33	37	37	37	37	61	45	45	45	45	11	43	45	45	45	44		
Lower in PASC than no-PASC	Sarcosine	<i>rho</i>	-0.2371	0.1424	0.2452	-0.0982	0.0741	0.0637	0.0435	0.1671	0.2102	0.1017	0.0972	-0.1135	0.1969	0.0673	0.1726	0.0521	0.1916	0.2504	0.0763	0.0481	0.0073	-0.0119	0.2278	-0.2235	-0.0038	0.1546	0.1009	0.2335	0.1867	0.1942	0.1550	
		<i>P value</i>	0.0104	0.2105	0.0264	0.3802	0.5083	0.8286	0.7094	0.1336	0.0581	0.3631	0.3881	0.5226	0.2379	0.6921	0.3070	0.7732	0.2560	0.1350	0.6534	0.7773	0.9556	0.9383	0.1323	0.1401	0.9801	0.6500	0.5198	0.1227	0.2195	0.2011	0.3149	
		<i>n</i>	116	79	82	82	82	14	76	82	82	82	81	34	37	37	37	33	37	37	37	37	61	45	45	45	45	11	43	45	45	45	44	
	1-Methylnicotinamide	<i>rho</i>	-0.1806	0.1084	0.0638	-0.0247	-0.0501	0.0725	0.0543	-0.2808	0.0299	-0.2962	-0.0526	0.0069	-0.1131	-0.0695	-0.0211	0.0371	0.4007	-0.0837	-0.3400	-0.1380	0.0620	-0.0389	0.0490	-0.0119	-0.1702	0.0091	0.0739	-0.1530	0.0735	-0.2111	0.0660	
		<i>P value</i>	0.0524	0.3415	0.5690	0.8255	0.6546	0.8054	0.6414	0.0106	0.7899	0.0069	0.6408	0.9891	0.5051	0.6829	0.9014	0.8376	0.0140	0.6224	0.0395	0.4154	0.6350	0.7998	0.7492	0.9384	0.2636	0.9788	0.6379	0.3158	0.6313	0.1640	0.6705	
		<i>n</i>	116	79	82	82	82	14	76	82	82	82	81	34	37	37	37	33	37	37	37	37	61	45	45	45	45	11	43	45	45	45	44	
	3,5-Dihydroxybenzoic acid	<i>rho</i>	-0.2099	0.1481	0.0416	0.2838	0.2055	0.1121	-0.0101	-0.0774	-0.0548	-0.0526	-0.0222	0.0669	0.1155	0.2814	0.1679	-0.0849	-0.0059	-0.0197	0.0766	0.1375	-0.1318	-0.0185	-0.0386	0.2648	0.1444	-0.1273	0.0337	-0.1228	-0.0842	-0.0949	-0.1834	
		<i>P value</i>	0.0237	0.1927	0.7108	0.0098	0.0640	0.7028	0.9311	0.4895	0.6249	0.6390	0.8439	0.7070	0.4962	0.0915	0.3207	0.6386	0.9722	0.9080	0.6524	0.4170	0.3113	0.9038	0.8012	0.0787	0.3440	0.7092	0.8302	0.4216	0.5824	0.5354	0.2335	
		<i>n</i>	116	79	82	82	82	14	76	82	82	82	81	34	37	37	37	33	37	37	37	37	61	45	45	45	45	11	43	45	45	45	44	
	Indole-3-lactic acid	<i>rho</i>	-0.2076	0.0977	0.0622	0.0232	-0.0166	0.4066	-0.0724	0.0259	-0.0029	-0.2940	-0.1782	0.3240	0.0974	-0.2909	-0.0194	-0.1544	-0.2764	0.0026	-0.4524	-0.2755	-0.1110	-0.1940	0.0003	0.2206	-0.0258	0.4364	-0.0253	-0.2294	0.0258	-0.1622	-0.1015	
		<i>P value</i>	0.0253	0.3915	0.5789	0.8360	0.8822	0.1491	0.5343	0.0259	0.9795	0.0073	0.1115	0.0616	0.5662	0.0807	0.9091	0.3909	0.0977	0.9878	0.0049	0.0989	0.3943	0.2017	0.9986	0.1454	0.8663	0.1797	0.8721	0.1296	0.8663	0.2871	0.5122	
		<i>n</i>	116	79	82	82	82	14	76	82	82	82	81	34	37	37	37	33	37	37	37	37	61	45	45	45	45	11	43	45	45	45	44	
L-Methionine	<i>rho</i>	-0.1406	0.1086	0.1052	-0.0750	0.0688	-0.3451	0.0985	0.1044	0.1520	0.0682	0.1501	-0.0302	-0.0832	0.2141	0.2350	0.0050	0.3755	0.1183	0.3523	0.4028	0.1284	0.0320	0.2609	-0.3156	-0.1560	-0.2546	0.1821	0.0460	0.1947	-0.0531	0.0312		
	<i>P value</i>	0.1322	0.3410	0.3467	0.5028	0.5391	0.2269	0.3973	0.3508	0.1727	0.5426	0.1811	0.8656	0.6244	0.2033	0.1616	0.9779	0.0220	0.4856	0.0325	0.0134	0.3243	0.8347	0.0835	0.0347	0.3062	0.4500	0.2424	0.7642	0.1999	0.7290	0.8409		
	<i>n</i>	116	79	82	82	82	14	76	82	82	82	81	34	37	37	37	33	37	37	37	37	61	45	45	45	45	11	43	45	45	45	44		
Pipelicolic acid	<i>rho</i>	-0.1812	0.0697	0.0161	-0.2210	-0.0622	0.2352	-0.0250	-0.2557	0.0239	-0.2046	0.0811	0.0501	-0.1057	-0.1114	-0.1724	-0.0147	-0.2598	-0.0311	-0.2482	0.0804	-0.0095	-0.1221	0.0755	-0.2920	-0.1183	0.4091	-0.0486	-0.2242	0.0066	-0.1571	0.0599		
	<i>P value</i>	0.0516	0.5418	0.8860	0.0460	0.5788	0.4183	0.8300	0.0204	0.8316	0.0652	0.4719	0.7784	0.5334	0.5115	0.3077	0.9353	0.1204	0.8552	0.1385	0.6363	0.9423	0.4243	0.6221	0.0516	0.4389	0.2115	0.7572	0.1386	0.9657	0.3029	0.6993		
	<i>n</i>	116	79	82	82	82	14	76	82	82	82	81	34	37	37	37	33	37	37	37	37	61	45	45	45	45	11	43	45	45	45	44		

Red = significant positive correlation
Blue = significant negative correlation