Supplementary Material

Table S1. Metabolites information, MRM parameters and quantification performance.

Metabolites	**CAS NO.**	**Formula**	**MS polarity**	**Q1**	**Q3**	**DP**	**CE**	**LLOQ (ng mL^{-1})**	**Dynamic range**	***r***
Choline	62-49-7	$C5H14NO^{+}$	Positive	104.1	60	90	40	2	20-1000	0.9953
Niacinamide	98-92-0	C6H6N2O	Positive	123.1	80	70	30	1	20-2000	0.9949
1,3-Diaminopropane	109-76-2	C3H10N2	Positive	75	58	112	15	2	20-1000	0.9964
Glycerol	56-81-5	C3H8O3	Positive	93	66	207	21	100	500-5000	0.9971
L-Glutamine	56-85-9	C5H10N2O3	Positive	147	84	140	35	10	20-1000	0.9994
L-Histidine	71-00-1	C6H9N3O2	Positive	156.1	110	70	20	1	2-1000	0.9945
L-Proline	147-85-3	C5H9NO2	Positive	116	70	100	40	0.5	20-2000	0.9918
L-Phenylalanine	63-91-2	C9H11NO2	Positive	166	120	90	18	0.2	2-2000	0.9961
L-Glutamic acid monohydrate	56-86-0	C5H9NO4	Positive	148.1	84	60	38	10	20-2000	0.9972
L-isoleucine	73-32-5	C6H13NO2	Positive	132	86	50	14	0.1	20-2000	0.9946
L-Tyrosine	60-18-4	C9H11NO3	Positive	182	136	120	19	2	20-5000	0.9992
L-Cystine	56-89-3	C6H12N2O4S2	Positive	241	152	80	19	100	200-5000	0.9946
L-Alanine	56-41-7	C3H7NO2	Positive	90	44	104	20	10	50-5000	0.9943

Metabolites	CAS NO.	Formula	MS polarity	Q1	Q3	DP	CE	LLOQ (ng mL^{-1})	Dynamic range	*r*
HEPES	7365-45-9	C8H18N2O4S	Positive	239.2	131	200	30	2	20-2000	0.9960
Thiamine pyrophosphate	154-87-0	C12H19ClN4O7P2S	Positive	425.2	122	120	40	100	500-5000	0.9968
5'-Methylthioadenosine	2457-80-9	C11H15N5O3S	Positive	298.1	136	90	27	0.05	0.2-500	0.9969
S-Adenosyl-L-methionine	86867-01-8	C15H25Cl3N6O5S	Positive	399.4	298	100	12	20	200-5000	0.9944
AMP	61-19-8	C10H14N5O7P	Positive	348.1	136	80	70	1	20-5000	0.9993
GMP	7665-99-8	C10H12N5O7P	Positive	346.1	152	90	30	0.1	2-2000	0.9968
dAMP	653-63-4	C10H14N5O6P	Positive	332.1	136	60	22	0.5	50-5000	0.9984
L-Carnosine	305-84-0	C9H14N4O3	Positive	227.3	122	100	19	20	100-5000	0.9973
Homocysteine	454-29-5	C4H9NO2S	Positive	136.1	90	60	15	2	20-5000	0.9948
Guanosine	118-00-3	C10H13N5O5	Positive	284.2	152	60	20	0.2	0.5-2000	0.9969
CMP	63-37-6	C9H14N3O8P	Positive	324.1	112	60	25	2	50-5000	0.9961
L-Aspartate	56-84-8	C4H7NO4	Positive	134	74	60	20	50	100-5000	0.9985
DL 2:0	3040-38-8	C9H17NO4	Positive	204.2	85	100	69	10	50-5000	0.9978
L-Asparagine	70-47-3	C4H8N2O3	Positive	133.1	87	50	12	10	50-2000	0.9932
L-Valine	72-18-4	C5H11NO2	Positive	118	72	115	14	1	100-5000	0.9964
Histamine	51-45-6	C5H9N3	Positive	112	95	60	10	1	2-500	0.9944

Metabolites	CAS NO.	Formula	MS polarity	Q1	Q3	DP	CE	LLOQ (ng mL^{-1})	Dynamic range	*r*
L-Lysine	56-87-1	C6H14N2O2	Positive	147.1	84	65	35	2	50-5000	0.9941
Glycine	56-40-6	C2H5NO2	Positive	76	30	30	20	20	200-5000	0.9940
L-Leucine	61-90-5	C6H13NO2	Positive	132.1	86	100	20	0.1	20-5000	0.9989
trans-4-Hydroxy-L-proline	51-35-4	C5H9NO3	Positive	132.1	86	100	19	1	20-5000	0.9985
Thymidine	50-89-5	C10H14N2O5	Positive	243.1	127	80	20	1	5-5000	0.9975
L-Serine	56-45-1	C3H7NO3	Positive	106	60	55	15	2	20-2000	0.9956
Nicotinate	59-67-6	C6H5NO2	Positive	124.1	80	120	30	10	20-2000	0.9946
Ornithine	3184-13-2	C5H12N2O2	Positive	133.1	70	100	22	1	5-2000	0.9972
L-Tryptophan	73-22-3	C11H12N2O2	Positive	205.2	188	100	14	0.1	0.5-2000	0.9984
sn-Glycero-3-phosphocholine	28319-77-9	C8H20NO6P	Positive	258.2	104	100	22	1	20-5000	0.9964
GMP	85-32-5	C10H14N5O8P	Positive	364.1	152.1	60	28	20	100-5000	0.9962
Trimethylamine-N-oxide	1184-78-7	C3H9NO	Positive	76.1	42	160	34	10	50-2000	0.9925
NG,NG-Dimethylarginine	30315-93-6	C8H18N4O2	Positive	203.2	158	120	20	2	20-2000	0.9963
L-Kynurenine	2922-83-0	C10H12N2O3	Positive	209.2	94	40	20	0.5	2-5000	0.9989
N-Acetyl-L-Glutamine	2490-97-3	C7H12N2O4	Positive	189.2	130	35	23	1	5-2000	0.9965
Adenine	73-24-5	C5H5N5	Positive	135.8	118.8	60	20	10	50-2000	0.9960

Metabolites	CAS NO.	Formula	MS polarity	Q1	Q3	DP	CE	LLOQ (ng mL^{-1})	Dynamic range	*r*
Allantoin	97-59-6	C4H6N4O3	Positive	159.1	116	60	11	2	20-2000	0.9962
Aminoisobutyrate	62-57-7	C4H9NO2	Positive	104.1	58	100	17	1	5-2000	0.9954
Glycylglycine	556-50-3	C4H8N2O3	Positive	133.1	76	70	13	0.5	5-2000	0.9973
γ-Aminobutanoate	56-12-2	C4H9NO2	Positive	104.1	58	100	17	0.5	5-2000	0.9942
Betaine	107-43-7	C5H11NO2	Positive	118.1	43	100	55	20	100-5000	0.9940
Hypoxanthine	68-94-0	C5H4N4O	Positive	137.1	110	160	28	1	20-2000	0.8843
Creatine	57-00-1	C4H9N3O2	Positive	132.1	90	135	27	2	20-1000	0.9954
Cysteine	52-90-4	C3H7NO2S	Positive	122.2	59	45	30	2	20-2000	0.9923
DL-Pyroglutamic acid	149-87-1	C5H7NO3	Positive	130.1	84	70	18	1	200-5000	0.9980
Hippurate	495-69-2	C9H9NO3	Positive	180.1	105	60	20	0.5	0.5-2000	0.9978
Cystamine	51-85-4	C4H12N2S2	Positive	153.2	108	90	25	10	100-2000	0.9915
DOPA	59-92-7	C9H11NO4	Positive	198.2	152	100	20	1	20-5000	0.9984
Citrulline	372-75-8	C6H13N3O3	Positive	176.1	70	70	31	2	5-2000	0.9978
cAMP	60-92-4	C10H12N5O6P	Positive	330.1	136	110	33	0.1	0.5-2000	0.9966
Inositol	87-89-8	C6H12O6	Positive	181.1	139	145	15	10	100-5000	0.9969
Uracil	66-22-8	C4H4N2O2	Positive	113	70	140	20	2	50-2000	0.9958

Metabolites	CAS NO.	Formula	MS polarity	Q1	Q3	DP	CE	LLOQ (ng mL^{-1})	Dynamic range	*r*
Pantothenate	137-08-6	C18H32CaN2O10	Positive	220.1	90	80	20	0.5	2-5000	0.9967
7-Methylxanthine	552-62-5	C6H6N4O2	Positive	167.1	124	100	28	0.5	2-2000	0.9977
2'-Deoxyadenosine	16373-93-6	C10H15N5O4	Positive	252.3	94	80	61	2	5-500	0.9952
Pyridoxal 5'-phosphate monohydrate	41468-25-1	C8H12NO7P	Positive	248.2	150	100	27	0.2	20-2000	0.9963
5-Methyluridine	1463-10-1	C10H14N2O6	Positive	259.1	127	60	16	1	5-5000	0.9966
2'-Deoxycytidine	951-77-9	C9H13N3O4	Positive	228.1	112	50	20	0.2	5-2000	0.9951
Deoxyuridine	951-78-0	C9H12N2O5	Positive	229.2	113	60	20	2	50-5000	0.9933
Inosine	58-63-9	C10H12N4O5	Positive	269.1	137	60	23	0.2	5-1000	0.9990
Carnitine	541-15-1	C7H15NO3	Positive	162.1	103	60	35	2	5-500	0.9909
4-Aminobenzoate	150-13-0	C7H7NO2	Positive	138.1	94	80	18	2	5-5000	0.9984
Hydroxyproline	51-35-4	C5H9NO3	Positive	132.1	86	60	17	1	5-2000	0.9964
Pyridoxine	65-23-6	C8H11NO3	Positive	170	134.2	60	20	0.2	2-1000	0.9918
Cytosine	71-30-7	C4H5N3O	Positive	112	95	60	20	1	2-1000	0.9976
Dopamine	51-61-6	C8H11NO2	Positive	154.1	119	105	29	1	20-5000	0.9963
Creatinine	60-27-5	C4H7N3O	Positive	114.1	86	140	22	10	50-2000	0.9920
Cytidine	65-46-3	C9H13N3O5	Positive	244.1	112	70	24	0.2	20-5000	0.9986

Metabolites	CAS NO.	Formula	MS polarity	Q1	Q3	DP	CE	LLOQ (ng mL^{-1})	Dynamic range	*r*
N-Acetyl-D-glucosamine	7512-17-6	C8H15NO6	Positive	222.1	138	50	21	10	50-2000	0.9962
5-Methylcytidine	2140-61-6	C10H15N3O5	Positive	258.1	126	65	24	0.2	2-5000	0.9976
N,N-Dimethylglycine	1118-68-9	C4H9NO2	Positive	104.1	58	50	21	0.5	5-500	0.9924
Cysteamine	60-23-1	C2H7NS	Positive	78.1	61	88	17	2	50-2000	0.9955
Melatonin	73-31-4	C13H16N2O2	Positive	233.3	174	130	21	0.05	0.2-500	0.9960
Uridine	58-96-8	C9H12N2O6	Positive	245.1	113	60	20	1	20-5000	0.9953
1,7-Dimethylxanthine;Paraxanthine	611-59-6	C7H8N4O2	Positive	181.1	124	90	27	0.1	0.5-2000	0.9957
Homocystine	626-72-2	C8H16N2O4S2	Positive	269.3	136	90	14	1	20-5000	0.9941
(±)-Epinephrine	51-43-4	C9H13NO3	Positive	184.2	107	100	30	10	100-5000	0.9903
N-Acetylornithine	6205-08-9	C7H14N2O3	Positive	175	69.8	60	30	1	5-2000	0.9968
Cobalamin	68-19-9	C63H88CoN14O14P	Positive	678.8	147	230	65	0.5	2-5000	0.9975
3-Methylxanthine	1076-22-8	C6H6N4O2	Positive	167.1	124	100	24	0.5	0.5-5000	0.9960
L-Arginine	74-79-3	C6H14N4O2	Positive	175	69.8	60	30	2	5-2000	0.9968
L-Threonine	72-19-5	C4H9NO3	Positive	120.1	74	31	15	2	5-2000	0.9936
Oxidized glutathione	27025-41-8	C20H32N6O12S2	Positive	613.1	230.8	180	48	20	100-5000	0.9940
L-homoserine	16504-56-6	C4H9NO3	Positive	120	60	100	23	20	50-2000	0.9944

Metabolites	CAS NO.	Formula	MS polarity	Q1	Q3	DP	CE	LLOQ (ng mL^{-1})	Dynamic range	*r*
DL 8:0	25243-95-2	C15H29NO4	Positive	288.2	85	60	20	0.05	0.2-500	0.9951
L-Cystathionine	56-88-2	C7H14N2O4S	Positive	223.2	134	100	21	0.5	20-5000	0.9918
normetanephrine	1011-74-1	C9H14ClNO3	Positive	184.2	134	80	24	10	100-2000	0.9959
Ala-Gly	3695-73-6	C5H10N2O3	Positive	147.1	90	100	19	10	20-2000	0.9968
Adenosine	131-99-7	C10H13N5O4	Positive	268.1	136	70	30	0.5	0.2-500	0.9928
DCTP	2056-98-6	C9H16N3O13P3	Positive	468.1	395	60	15	100	500-5000	0.9998
Putrescine	110-60-1	C4H12N2	Positive	89.1	72	100	23	100	200-5000	0.9933
Spermidine	124-20-9	C7H19N3	Positive	146.2	112	100	13	10	50-2000	0.9906
Spermine	71-44-3	C10H26N4	Positive	203.2	112.1	60	29	10	50-5000	0.9976
Thiamine Hydrochloride (B1)	70-16-6	$C12H17N4OS^{+}$	Positive	265.3	122	100	52	2	2-200	0.9946
Aldosterone	52-39-1	C21 H28 O5	Positive	361.2	343	170	26	2	2-5000	0.9937
11-Deoxycortisol	152-58-9	C21 H30 O4	Positive	347.2	97	170	33	0.2	0.5-2000	0.9964
11-Deoxycorticosterone	64-85-7	C21 H30 O3	Positive	331.2	97	170	27	0.5	0.5-2000	0.9961
Corticosterone	50-22-6	C21 H30 O4	Positive	347.2	121.1	100	33	0.5	2-2000	0.9954
Dehydroepiandrosterone (DHEA)	53-43-0	C19 H28 O2	Positive	289.2	85	100	27	0.2	0.2-500	0.9953
Cortisol	50-23-7	C21 H30 O5	Positive	363.2	121	180	32	0.2	0.5-2000	0.9975

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Dihydrotestosterone	521-18-6	C19H30O2	Positive	291.2	145	70	23	10	20-5000	0.9975
Androstenedione	63-05-8	C19H26O2	Positive	287.2	97	170	30	0.2	0.2-1000	0.9923
Testosterone	58-22-0	C19H28O2	Positive	289.2	109	100	32	0.2	0.5-1000	0.9964
4-Pyridoxic acid	82-82-6	C8H9NO4	Positive	184	148	60	40	0.1	2-1000	0.9959
Reduced glutathione	70-18-8	C10H17N3O6S	Positive	308	179	150	18	2	50-5000	0.9976
Lactose	63-42-3	C12H22O11	Negative	341	89	-120	-25	10	50-2000	0.9951
D-Gluconic acid	133-42-6	C6H12O7	Negative	195	129	-80	-27	2	20-5000	0.9949
Taurine	107-35-7	C2H7NO3S	Negative	124	80	-100	-32	0.1	2-2000	0.9967
Fructose	57-48-7	C6H12O6	Negative	179.1	89	-90	-13	2	20-1000	0.9960
Ascorbic acid	50-81-7	C6H8O6	Negative	174.9	86.8	-60	-20	10	500-5000	0.9974
Oxoacetic Acid	298-12-4	C2H2O3	Negative	73	45	-120	-11	20	200-5000	0.9971
Glucose	50-99-7	C6H12O6	Negative	179.1	89	-90	-13	2	20-1000	0.9944
MOPS	1132-61-2	C7H15NO4S	Negative	207.8	79.9	-60	-30	0.05	0.5-2000	0.9982
Xylitol	87-99-0	C5H12O5	Negative	151	89	-100	-16	2	20-1000	0.9974
Succinate	150-90-3	C4H4Na2O4	Negative	117	73	-70	-15	2	20-5000	0.9977
DCMP 钠盐	13085-50-2	C9H12N3Na2O7P	Negative	306	79	-120	-50	0.2	20-5000	0.9970

Metabolites	CAS NO.	Formula	MS polarity	Q1	Q3	DP	CE	LLOQ (ng mL^{-1})	Dynamic range	*r*
Pyridoxal phosphate	853645-22-4	C8H10NO6P	Negative	246	79	-120	-60	2	5-5000	0.9961
Thymidine 5′-monophosphate (DTMP)disodium salt hydrate	33430-62-5	C10H13N2Na2O8P	Negative	321.1	79	-70	-60	2	2-5000	0.9969
Phosphoethanolamine	1071-23-4	C2H8NO4P	Negative	140	79	-80	-30	0.5	5-1000	0.9996
D-Glucosamine 6-phosphate	3616-42-0	C6H14NO8P	Negative	258.1	79	-120	-120	1	5-1000	0.9982
DL-Glyceraldehyde 3-phosphate solution	591-59-3	C3H7O6P	Negative	169	79	-110	-45	10	100-5000	0.9957
Urate	69-93-2	C5H4N4O3	Negative	167	124	-190	-20	0.5	50-2000	0.9937
Pyruvate	127-17-3	C3H4O3	Negative	87	32	-40	-13	20	200-5000	0.9948
α-Keto-glutarate	328-50-7	C5H6O5	Negative	145	101	-100	-18	100	500-5000	0.9900
Thymine	65-71-4	C5H6N2O2	Negative	125	42	-100	-32	1	2-5000	0.9984
Fumarate	110-17-8	C4H4O4	Negative	115	71	-40	-11	10	100-5000	0.9980
L-Gulono-1,4-lactone	1128-23-0	C6H10O6	Negative	177	89	-120	-17	10	20-2000	0.9968
Xanthine	69-89-6	C5H4N4O2	Negative	151.1	108	-140	-22	10	20-5000	0.9957
Biotin	58-85-5	C10H16N2O3S	Negative	243.2	200	-120	-21	0.2	0.5-5000	0.9978
Benzoate	65-85-0	C7H6O2	Negative	120.9	77.1	-60	-10	100	100-2000	0.9936
Mevalonate	150-97-0	C6H12O4	Negative	147.1	59	-110	-37	100	500-5000	0.9965
Orotate	65-86-1	C5H4N2O4	Negative	155	111	-50	-17	10	100-5000	0.9975

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N-acetyl-L-glutamate	1188-37-0	C7H11NO5	Negative	188	102	-40	-24	1	5-5000	0.9976
2-Oxoglutarate	328-50-7	C5H6O5	Negative	145.1	101	-90	-17	100	200-5000	0.9976
L-(-)-Malic acid	97-67-6	C4H6O5	Negative	133	115	-70	-16	10	20-2000	0.9923
Phenylacetylglycine	500-98-1	C10H11NO3	Negative	192	74	-60	-10	0.1	0.5-5000	0.9978
L-Cysteic acid monohydrate	23537-25-9	C3H9NO6S	Negative	168.1	81	-100	-56	2	20-2000	0.9968
OH-Phenylpyruvate	156-39-8	C9H8O4	Negative	179.2	107	-45	-12	10	50-5000	0.9941
D-glucose 6-phosphate	56-73-5	C6H13O9P	Negative	258.8	96.8	-60	-10	10	100-2000	0.9992
3',5'-Cyclic AMP	60-92-4	C10H12N5O6P	Negative	328	134	-60	-30	0.02	0.2-2000	0.9964
N-Acetylneuraminate	131-48-6	C11H19NO9	Negative	308.2	170	-70	-19	2	20-5000	0.9967
NADH	58-68-4	C21H29N7O14P2	Negative	663.2	79	-120	-128	10	100-5000	0.9968
Folate	59-30-3	C19H19N7O6	Negative	440.1	311	-120	-33	1	2-2000	0.9979
Sucrose	57-50-1	C12H22O11	Negative	341	89	-120	-25	10	100-2000	0.9967
D-Fructose 6-phosphate	643-13-0	C6H13O9P	Negative	259	79	-80	-60	2	20-5000	0.9970
L-Lactic Acid	79-33-4	C3H6O3	Negative	89	43	-100	-25	20	200-5000	0.9990
Xanthosine Dihydrate	146-80-5	C10H12N4O6	Negative	283.1	108	-100	-50	0.1	0.5-5000	0.9993
Lipoate	1200-22-2	C8H14O2S2	Negative	205	170.8	-60	-10	0.1	0.5-5000	0.9951

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UDP-glucose	133-89-1	C15H24N2O17P2	Negative	565	79	-150	-120	50	50-5000	0.9946
D-Glucose 1-phosphate	59-56-3	C6H13O9P	Negative	259	79	-120	-120	2	20-5000	0.9989
D-Ribose	50-69-1	C5H10O5	Negative	149	89	-110	-10	10	100-2000	0.9917
Maleate	110-16-7	C4H4O4	Negative	115	71	-100	-26	20	20-5000	0.9980
N-Acetyl-Asp-Glu(N-Acetylaspartate)	3106-85-2	C11H16N2O8	Negative	303.2	96	-80	-54	2	20-5000	0.9959
1-Methyluric acid	708-79-2	C6H6N4O3	Negative	181	138	-80	-20	0.2	20-5000	0.9941
IMP	352195-40-5	C10H13N4O8P	Negative	347	79	-120	-80	2	20-5000	0.9953
D-Erythrose 4-phosphate	585-18-2	C4H9O7P	Negative	199	97	-55	-15	10	100-5000	0.9981
Dihydrofolate	4033-27-6	C19H21N7O6	Negative	442.1	176	-110	-35	0.5	5-5000	0.9982
ESTRIOL E3	50-27-1	C18 H24 O3	Negative	287	143	-190	-70	100	500-5000	0.9983
17-hydroxypregnenolone	387-79-1	C21 H32 O3	Negative	331	287	-150	-26	100	100-5000	0.9986
ESTRONE E1	53-16-7	C18 H22 O2	Negative	269	145	-180	-48	100	500-5000	0.9957
Pregnenolone	145-13-1	C21 H32 O2	Negative	315.2	282.2	-230	-30	2	5-5000	0.9959
UMP	3387-36-8	C9H13N2O9P	Negative	323	79	-100	-80	100	100-5000	0.9973
FA 12:0	143-07-7	C12H24O2	Negative	199.2	199.2	-100	-10	2	200-5000	0.9948
FA 14:0	544-63-8	C14H28O2	Negative	227.2	227.2	-100	-10	2	200-5000	0.9940

Metabolites	CAS NO.	Formula	MS polarity	Q1	Q3	DP	CE	LLOQ (ng mL^{-1})	Dynamic range	*r*
FA 16:4	29259-52-7	C16H24O2	Negative	247.2	247.2	-100	-10	1	200-5000	0.9983
FA 16:1	373-49-9	C16H30O2	Negative	253.2	253.2	-100	-10	1	200-5000	0.9981
FA 16:0	57-10-3	C16H32O2	Negative	255.2	255.2	-100	-30	1	10-2000	0.9930
FA 17:1	29743-97-3	C17H32O2	Negative	267.2	267.2	-100	-10	1	10-2000	0.9912
FA 17:0	506-12-7	C17H34O2	Negative	269.2	269.2	-100	-10	1	10-2000	0.9998
FA 18:4	20290-75-9	C18H28O2	Negative	275.2	275.2	-100	-10	1	10-2000	0.9907
FA 18:3-α	463-40-1	C18H30O2	Negative	277.2	277.2	-100	-30	1	10-2000	0.9956
FA 18:3-γ	506-26-3	C18H30O2	Negative	277.2	277.2	-100	-10	1	10-2000	0.9945
FA 18:2	60-33-3	C18H32O2	Negative	279.2	279.2	-100	-30	1	10-2000	0.9989
FA 18:1	112-80-1	C18H34O2	Negative	281.2	281.2	-100	-30	1	10-2000	0.9912
FA 18:0	57-11-4	C18H36O2	Negative	283.2	283.2	-100	-30	1	10-2000	0.9934
FA 20:5	10417-94-4	C20H30O2	Negative	301.2	301.2	-100	-10	1	10-2000	0.9923
FA 20:4	506-32-1	C20H32O2	Negative	303.2	303.2	-100	-30	1	10-2000	0.9967
FA 20:3	1783-84-2	C20H34O2	Negative	305.2	305.2	-100	-10	1	10-2000	0.9978
FA 20:2	135498-07-6	C20H36O2	Negative	307.2	307.2	-100	-10	1	10-2000	0.9932
FA 20:1	62322-84-3	C20H38O2	Negative	309.2	309.2	-100	-10	1	10-2000	0.9954

Metabolites	CAS NO.	Formula	MS polarity	Q1	Q3	DP	CE	LLOQ (ng mL^{-1})	Dynamic range	*r*
FA 20:0	506-30-9	C20H40O2	Negative	311.2	311.2	-100	-10	1	10-2000	0.9962
FA 22:6	6217-54-5	C22H32O2	Negative	327.2	327.2	-100	-30	1	10-2000	0.9981
FA 22:5- n3	24880-45-3	C22H34O2	Negative	329.2	329.2	-100	-10	1	10-2000	0.9916
FA 22:5- n6	25182-74-5	C22H34O2	Negative	329.2	329.2	-100	-10	1	10-2000	0.9930
FA 22:4	-	C22H36O2	Negative	331.2	331.2	-100	-10	1	10-2000	0.9985
FA 22:3-iso1	28845-86-5	C22H38O2	Negative	333.2	333.2	-100	-10	1	10-2000	0.9980
FA 22:2	17735-98-7	C22H40O2	Negative	335.2	335.2	-100	-10	1	10-2000	0.9970
FA 22:1	112-86-7	C22H42O2	Negative	337.2	337.2	-100	-10	1	10-2000	0.9932
FA 22:0	112-85-6	C22H44O2	Negative	339.2	339.2	-100	-10	1	10-2000	0.9940
Dehydrolithocholic acid	1553-56-6	C24H38O3	Negative	373.3	373.3	-150	-20	0.05	20-500	0.9995
Lithocholic acid	434-13-9	C24H40O3	Negative	375.3	375.3	-150	-15	0.05	2-2000	0.9986
Alloisolithocholic acid	2276-93-9	C24H40O3	Negative	375.3	375.3	-150	-20	0.1	5-5000	0.9965
Isolithocholic acid	1534-35-6	C24H40O3	Negative	375.3	375.3	-150	-20	0.1	5-5000	0.9959
Nordeoxycholic acid	53608-86-9	C23H38O4	Negative	377.3	377.3	-150	-20	0.1	0.5-2000	0.9978
5α-cholanic acid-3,6-dione	6929-22-2	C24 H36 O4	Negative	387.3	387.3	-150	-15	0.1	5-2000	0.9958
3,7-Diketocholanic acid	859-97-2	C24 H36 O4	Negative	387.3	387.3	-150	-20	0.2	2-2000	0.9973

Metabolites	CAS NO.	Formula	MS polarity	Q1	Q3	DP	CE	LLOQ (ng mL^{-1})	Dynamic range	*r*
Apocholic acid	641-81-6	C24H38O4	Negative	389.3	389.3	-150	-20	0.1	20-5000	0.9950
5α-cholanic acid-3α-ol-6-one	10573-17-8	C24 H38 O4	Negative	389.3	389.3	-150	-20	0.1	0.5-2000	0.9946
7-Ketolithocholic acid	4651-67-6	C24 H38 O4	Negative	389.3	389.3	-150	-20	0.1	2-2000	0.9981
12-Ketolithocholic acid	5130-29-0	C24 H38 O4	Negative	389.3	389.3	-150	-20	0.1	0.2-2000	0.9973
Isodeoxycholic acid	566-17-6	C24H40O4	Negative	391.3	391.3	-150	-15	0.05	0.5-2000	0.9950
Deoxycholic acid	83-44-3	C24H40O4	Negative	391.3	391.3	-150	-20	0.05	2-1000	0.9959
Ursodeoxycholic acid	128-13-2	C24H40O4	Negative	391.3	391.3	-150	-20	0.05	0.5-2000	0.9950
Hyodeoxycholic acid	83-49-8	C24H40O4	Negative	391.3	391.3	-150	-20	0.05	0.5-5000	0.9971
Dehydrocholic acid	81-23-2	C24H34O5	Negative	401.3	401.3	-150	-20	0.05	2-5000	0.9984
Dioxolithocholic acid	517-33-9	C24H36O5	Negative	403.3	403.3	-150	-20	0.1	5-5000	0.9985
6,7-Diketolithocholic acid	-	C24H36O5	Negative	403.3	403.3	-150	-20	0.1	2-2000	0.9954
12-Ketochenodeoxycholic acid	2458-08-4	C24H38O5	Negative	405.3	405.3	-260	-20	0.05	2-2000	0.9965
Cholic acid	81-25-4	C24H40O5	Negative	407.3	407.3	-150	-20	0.1	0.5-2000	0.9980
Glycoursocholanic acid	-	C26H43NO3	Negative	416.3	416.3	-150	-20	0.1	20-500	0.9970
Glycodeoxycholic acid	360-65-6	C26H43NO5	Negative	448.3	448.3	-150	-15	0.05	2-2000	0.9963
Glycoursodeoxycholic acid	64480-66-6	C26H43NO5	Negative	448.3	448.3	-150	-15	0.05	0.5-2000	0.9976

Metabolites	CAS NO.	Formula	MS polarity	Q1	Q3	DP	CE	LLOQ (ng mL^{-1})	Dynamic range	*r*
Glycochenodeoxycholic acid	640-79-9	C26H43NO5	Negative	448.3	448.3	-150	-20	0.1	0.2-5000	0.9959
Glycohyodeoxycholic acid	13042-33-6	C26H43NO5	Negative	448.3	448.3	-150	-20	0.05	0.5-2000	0.9970
Glycodehydrocholic acid	-	C26H37NO6	Negative	458.3	458.3	-150	-15	0.05	2-5000	0.9968
Glycocholic acid	475-31-0	C26H43NO6	Negative	464.3	464.3	-150	-15	0.05	0.5-2000	0.9966
Taurolithocholic acid	-	C26H45NO5S	Negative	482.5	80	-150	-110	0.02	0.2-5000	0.9968
Tauroursodeoxycholic acid/Taurohyodeoxycholic acid	14605-22-2	C26H45NO6S	Negative	498.3	80	-150	-120	0.02	0.2-2000	0.9967
Taurodeoxycholic acid	516-50-7	C26H45NO6S	Negative	498.3	80	-150	-120	0.02	0.2-2000	0.9980
Taurochenodeoxycholic acid	516-35-8	C26H45NO6S	Negative	498.5	80	-150	-120	0.02	0.2-2000	0.9976
Taurodehydrocholic acid	517-37-3	C26H39NO7S	Negative	508.5	80	-150	-120	0.02	0.2-5000	0.9987
Taurocholic acid	81-24-3	C26H45NO7S	Negative	514.5	80	-150	-140	0.02	0.2-5000	0.9982

Table S2. Information of the 67 significantly changed metabolites between pre- and post-dose.

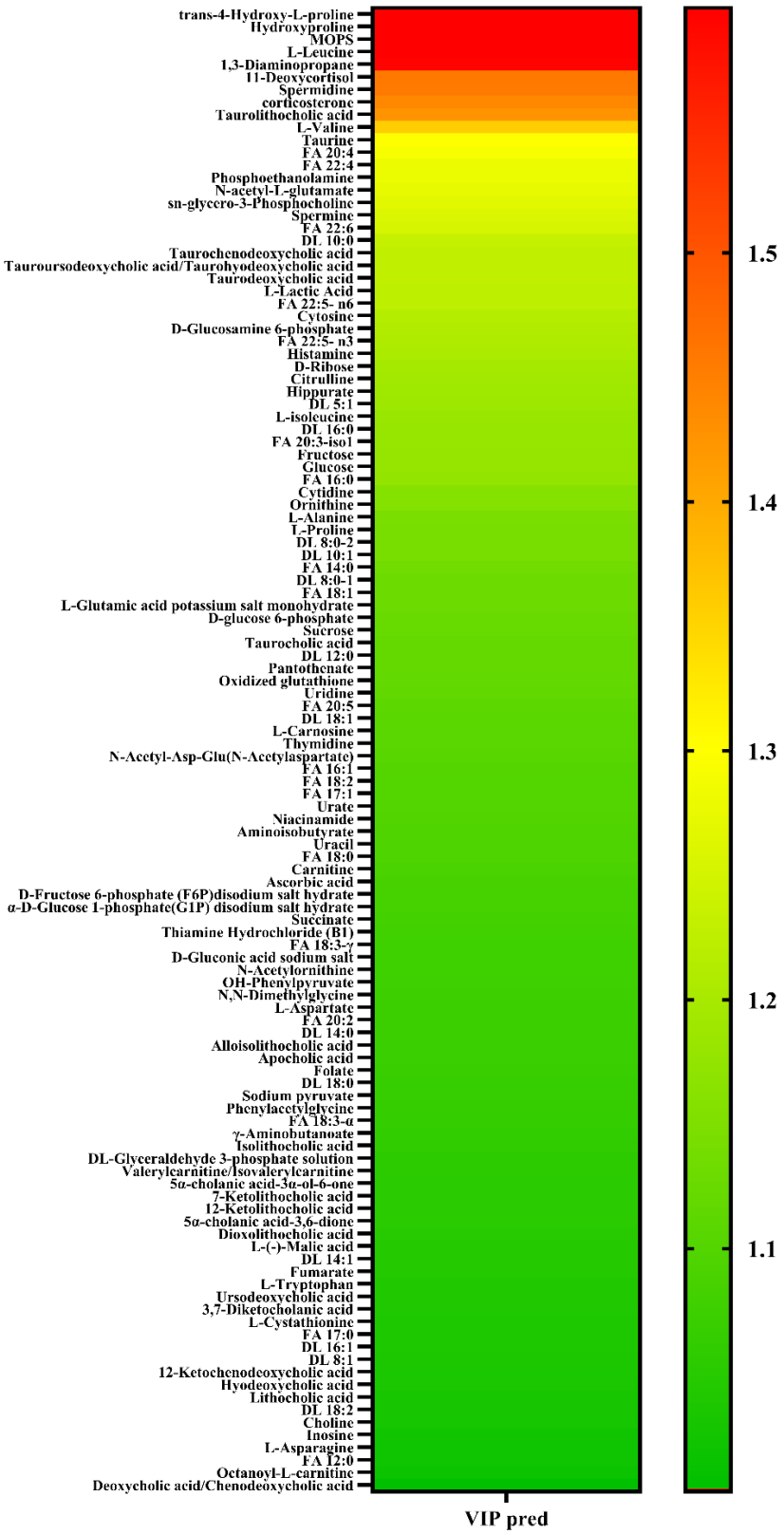
Compound name	Category	Formula	P-value
Taurine	Amino acids	C2H7NO3S	6.85E-13
Phosphoethanolamine	Organic phosphoric acids and derivatives	C2H8NO4P	1.02E-11
Cytosine	Pyrimidines	C4H5N3O	7.23E-11
sn-glycero-3-Phosphocholine	phosphatidylcholine	C8H20NO6P	8.76E-12
Histamine	Biogenic amines	C5H9N3	1.29E-10
DL 10:0	Carnitine	/	4.59E-10
L-Valine	Amino acids	C5H11NO2	1.21E-08
Hydroxyproline	Amino acids	C5H9NO3	5.23E-08
L-Leucine	Amino acids	C6H13NO2	5.41E-08
MOPS	Free Acid	C7H15NO4S	5.78E-08
trans-4-Hydroxy-L-proline	Amino acids and derivatives	C5H9NO3	5.94E-08
DL 8:0-2	Carnitine	C7H15NO3	2.45E-08
Sodium pyruvate	Carboxylic acids	C3H3NaO3	3.46E-09
DL 8:0-1	Carnitine	/	4.33E-08
Citrulline	Amino acids and derivatives	C6H13N3O3	2.24E-07
L-Carnosine	Amino acids	C9H14N4O3	1.40E-07
L-isoleucine	Amino acids	C6H13NO2	3.29E-06
D-glucose 6-phosphate	Phosphoric acid	C6H13O9P	2.47E-06
DL-Glyceraldehyde 3-phosphate	Phosphoric acid	C3H7O6P	2.66E-05
L-Tryptophan	Amino acids and derivatives	C11H12N2O2	5.83E-05
Octanoyl-L-carnitine	Carnitine	/	2.05E-05
L-Aspartate	Amino acids	C4H7NO4	6.11E-05
D-Glucosamine 6-phosphate	Phosphoric acid	C6H14NO8P	2.39E-04
DL 18:0	Carnitine	/	1.13E-04
Alloisolithocholic acid	Cholic Acids	C24H40O3	2.58E-05
Apocholic acid	Bile acids	C24H38O4	6.25E-06
D-Ribose	Carbohydrates	C5H10O5	4.69E-04
DL 12:0	Carnitine	/	2.54E-04
DL 10:1	Carnitine	/	7.36E-05
L-(-)-Malic acid	Malic acid	C4H6O5	1.54E-04

Isolithocholic acid	Cholic acid	C24H40O3	4.81E-05
Ascorbic acid	Vitamin	C6H8O6	3.52E-04
Dioxolithocholic acid	Cholic acid	C24H36O5	3.07E-06
5α-cholanic acid-3,6-dione	Cholic acid	C24 H36 O4	1.86E-05
FA 14:0	Fatty acid	C14H28O2	2.96E-03
5α-cholanic acid-3α-ol-6-one	Cholic acid	C24 H38 O4	2.32E-05
7-Ketolithocholic acid	Cholic acid	C24 H38 O4	2.32E-05
12-Ketolithocholic acid	Cholic acid	C24 H38 O4	2.32E-05
DL 16:0	Carnitine	/	3.07E-03
3,7-Diketocholanic acid	Cholic acid	C24 H36 O4	2.76E-05
Lithocholic acid	Cholic acid	C24H40O3	1.38E-04
Thymidine	Nucleic acids	C10H14N2O5	1.03E-03
Ursodeoxycholic acid	Cholic acid	C24H40O4	5.82E-05
L-Lactic Acid	Carboxylic acids	C3H6O3	6.65E-03
FA 16:1	Fatty acid	C16H30O2	7.22E-03
12-Ketochenodeoxycholic acid	Cholic acid	C24H38O5	6.04E-05
FA 16:0	Fatty acid	C16H32O2	2.78E-02
DL 18:1	Carnitine	/	9.79E-03
Adenine	Purine	C5H5N5	2.35E-03
Hyodeoxycholic acid	Cholic acid	C24H40O4	7.90E-04
L-Glutamine	Amino acids and derivatives	C5H10N2O3	1.69E-03
L-Lysine	Amino acids and derivatives	C6H14N2O2	1.69E-03
Niacinamide	Vitamins	C6H6N2O	3.12E-02
UDP-glucose	Vitamins	C15H24N2O17P	3.59E-03
FA 20:4	Fatty acid	C20H32O2	3.32E-02
Glycine	Amino acids and derivatives	C2H5NO2	8.28E-04
Choline	Vitamins	C5H14NO+	1.39E-02
FA 18:3-γ	Fatty acid	C18H30O2	4.52E-02
Deoxycholic acid/Chenodeoxycholic	Cholic acid	C24H40O4	2.88E-03
Hippurate	Organic acid	C9H9NO3	1.07E-02
5'-Methylthioadenosine	Nucleic acids	C11H15N5O3S	5.62E-03
Corticosterone	Steroids	C21H30O4	1.09E-03
Cholic acid	Cholic acid	C24H40O5	3.21E-03

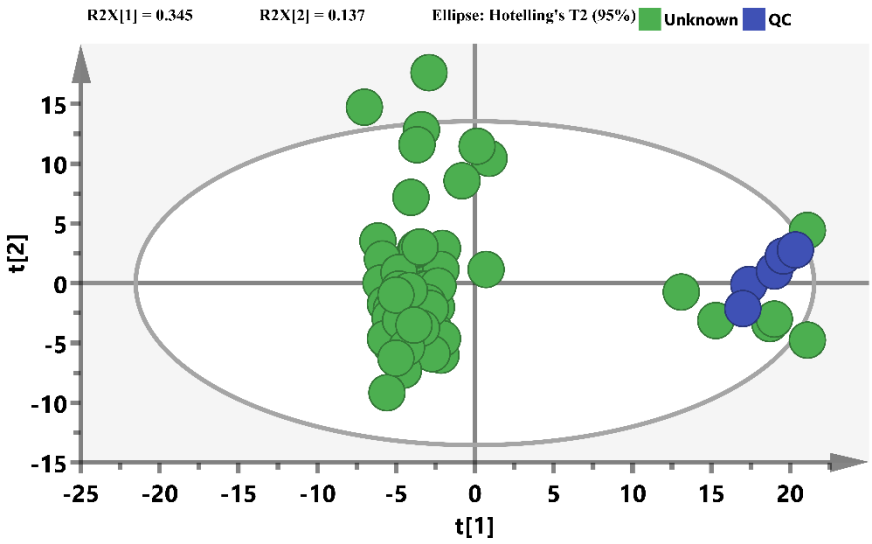
Orotate	Vitamin	C5H4N2O4	9.28E-03
Nordeoxycholic acid	Cholic acid	C23H38O4	2.11E-03
IMP	Glycosides	C10H13N4O8P	1.31E-02
DL 14:1	Carnitine	/	3.35E-02

Table S3. Obviously disturbed metabolic pathways owing to the treatment of Sotorasib.

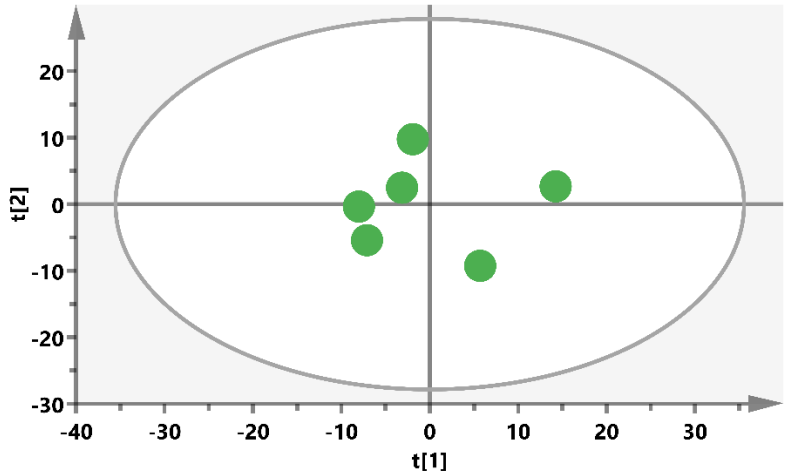
Pathway Name	**Match Status**	**P value**	**Impact**
Taurine and hypotaurine metabolism	2/8	0.002496	0.42857
Primary bile acid biosynthesis	3/46	0.009333	0.06809
Starch and sucrose metabolism	2/18	0.012877	0.14825
Neomycin, kanamycin and gentamicin biosynthesis	1/2	0.019788	0
Glycerophospholipid metabolism	2/36	0.047825	0.07237
One carbon pool by folate	1/9	0.086207	0
Ascorbate and aldarate metabolism	1/10	0.095345	0
Histidine metabolism	1/16	0.14841	0.18852
Pentose and glucuronate interconversions	1/18	0.16544	0.07812
Ether lipid metabolism	1/20	0.18215	0
Sphingolipid metabolism	1/21	0.19039	0.0142
Pyruvate metabolism	1/22	0.19855	0
Glycolysis / Gluconeogenesis	1/26	0.23043	0
Folate biosynthesis	1/27	0.23822	0
Galactose metabolism	1/27	0.23822	0.00228
Inositol phosphate metabolism	1/30	0.26113	0
Amino sugar and nucleotide sugar metabolism	1/37	0.31212	0.06961
Purine metabolism	1/66	0.49036	0.1253
Steroid hormone biosynthesis	1/77	0.54588	0.02572



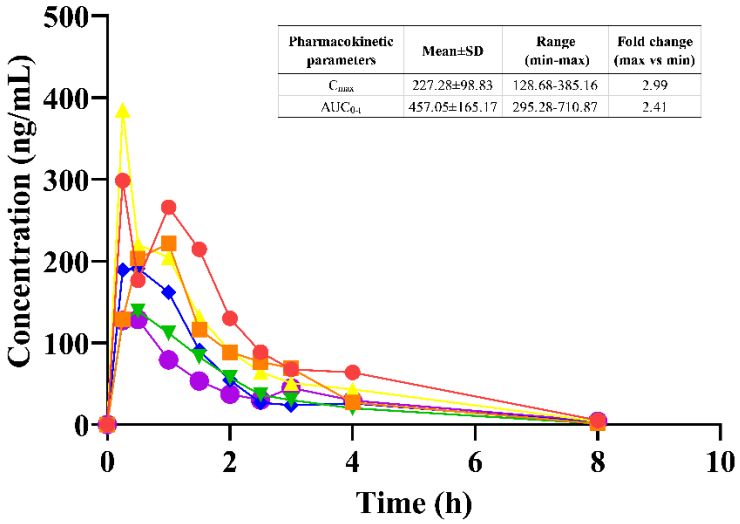
Supplementary Figure S1. The most obviously disturbed metabolites during longitudinal metabonomic fingerprints of Sotorasib.



Supplementary Figure S2. The PCA chart of quality control and unknown samples.



Supplementary Figure S3. Principal component analysis of six rats in PLS model. Each dot represents one rat (95% confidence interval).



Pharmacokinetic parameters	Mean±SD	Range (min-max)	Fold change (max vs min)
C_{max}	227.28±98.83	128.68-385.16	2.99
AUC_{0-t}	457.05±165.17	295.28-710.87	2.41

Supplementary Figure S4. Blood concentration of Sotorasib versus time plot of six rats. Main pharmacokinetic parameters are listed in the table.