

**Supplementary Table S1.** Salivary metabolites showing significant difference between PRE and POST samples

Metabolites	PRE		POST		F.C. (POST/PRE)	P-value	FDR	VIP score
	Mean	S.D.	Mean	S.D.				
<i>o</i> -Acetylcarnitine	0.187	0.110	0.0488	0.0455	0.26	$1.53 \times 10^{-5}$	$1.55 \times 10^{-4}$	1.7
Citrulline	7.99	9.11	2.49	2.63	0.31	$1.53 \times 10^{-5}$	$1.55 \times 10^{-4}$	1.2
Glutamine	15.5	8.93	5.31	3.87	0.34	$1.53 \times 10^{-5}$	$1.55 \times 10^{-4}$	1.5
Trimethylamine <i>N</i> -oxide	0.0684	0.0363	0.0234	0.00962	0.34	$1.53 \times 10^{-5}$	$1.55 \times 10^{-4}$	1.1
<i>N</i> -Acetylglucosamine	1.65	1.82	0.601	0.555	0.36	$1.53 \times 10^{-5}$	$1.55 \times 10^{-4}$	1.2
<i>N</i> <sup>6</sup> , <i>N</i> <sup>6</sup> , <i>N</i> <sup>6</sup> -Trimethyllysine	0.0182	0.00913	0.00748	0.00386	0.41	$1.53 \times 10^{-5}$	$1.55 \times 10^{-4}$	1.9
Creatine	5.16	2.02	2.15	0.95	0.42	$1.53 \times 10^{-5}$	$1.55 \times 10^{-4}$	1.8
GABA	0.594	0.328	0.257	0.128	0.43	$3.05 \times 10^{-5}$	$2.71 \times 10^{-4}$	1.8
Guanosine	0.337	0.364	0.146	0.139	0.43	$7.62 \times 10^{-5}$	$6.02 \times 10^{-4}$	0.77
2-Oxoglutarate	0.894	0.406	0.396	0.232	0.44	$1.07 \times 10^{-4}$	$6.32 \times 10^{-4}$	1.8
Arginine	9.80	5.56	4.64	2.54	0.47	$1.07 \times 10^{-4}$	$6.32 \times 10^{-4}$	1.5
Glutamate	13.4	4.13	6.47	4.05	0.48	$1.07 \times 10^{-4}$	$6.32 \times 10^{-4}$	1.5
Creatinine	4.89	1.55	2.37	0.750	0.48	$1.52 \times 10^{-4}$	$8.33 \times 10^{-4}$	1.2
Indoleacetate	0.348	0.414	0.172	0.177	0.50	$2.14 \times 10^{-4}$	0.0010	0.70
Alanine	12.5	10.1	6.35	3.56	0.51	$2.14 \times 10^{-4}$	0.0010	0.56
Gluconate	0.639	0.359	0.327	0.191	0.51	$2.90 \times 10^{-4}$	0.0012	1.1
Asparagine	1.18	1.07	0.604	0.282	0.51	$2.90 \times 10^{-4}$	0.0012	0.63
Nicotinamide	0.181	0.116	0.0982	0.0558	0.54	$3.81 \times 10^{-4}$	0.0015	0.67
Guanine	0.497	0.344	0.273	0.248	0.55	$5.48 \times 10^{-4}$	0.0020	1.2
<i>N</i> -Acetylputrescine	0.431	0.475	0.240	0.162	0.56	$6.56 \times 10^{-4}$	0.0022	0.59
Serine	5.49	2.99	3.09	1.18	0.56	$6.56 \times 10^{-4}$	0.0022	0.44
<i>b</i> -Alanine	2.40	1.03	1.39	0.597	0.58	$8.39 \times 10^{-4}$	0.0026	1.42
7-Methylguanine	0.0466	0.0189	0.0277	0.00893	0.59	$8.39 \times 10^{-4}$	0.0026	0.62
Adenine	0.402	0.313	0.243	0.216	0.60	0.0011	0.0030	0.75

5-Aminopentanoate	82.0	62.4	49.6	40.8	0.61	0.0011	0.0030	0.15
Histidine	7.53	4.80	4.58	3.03	0.61	0.0013	0.0037	0.22
Hydroxyproline	0.859	0.468	0.523	0.455	0.61	0.0026	0.0068	0.95
Proline	15.8	17.7	9.66	13.9	0.61	0.0032	0.0080	0.59
Adenosine	0.236	0.100	0.145	0.0627	0.61	0.0045	0.011	0.67
Choline	1.70	0.779	1.10	0.527	0.65	0.0046	0.011	1.2
Aspartate	7.03	3.16	4.58	2.19	0.65	0.0046	0.011	0.02
Tryptophan	0.223	0.138	0.146	0.0896	0.65	0.0056	0.012	0.34
Tyrosine	10.3	5.58	6.76	4.68	0.66	0.0079	0.017	0.22
Taurine	15.6	7.93	10.4	4.48	0.67	0.0093	0.020	0.40
3-Methylguanine	0.0335	0.0143	0.0255	0.0117	0.76	0.011	0.022	0.13
Carnitine	0.753	0.356	0.579	0.193	0.77	0.011	0.022	0.37
Phenylalanine	4.87	3.08	3.79	3.22	0.78	0.015	0.029	0.30
Glycolate	3.11	1.76	4.51	2.20	1.5	0.017	0.031	1.5
<i>N</i> <sup>1</sup> -Acetylspermine	0.0169	0.00507	0.0272	0.00560	1.6	0.023	0.040	1.6
Succinate	2.85	1.86	4.69	3.13	1.6	0.023	0.040	1.6
2-Hydroxyglutarate	0.512	0.305	1.42	2.03	2.8	0.023	0.040	1.3
Citrate	1.58	1.13	5.78	4.03	3.7	0.031	0.0504	1.8
Hexylamine	0.139	0.0184	0.913	0.228	6.6	0.031	0.0504	1.9

S.D. and F.C. indicate standard deviation and fold change, respectively.

FDR indicate false dscovery rate-corrected P-value.

VIP score indicates variable importance in projection that was obtained from PLS-DA model.

**Supplementary Table S2.** The linearity range of standard mixture samples

Metabolites	Regression equation	slope	intercept	Linariity(R <sup>2</sup> )	Linear range (μmol/L)
<b>Positive</b>					
GABA	Y = 0.4151x +0.0103	0.415	0.01026	0.9971	0.01-1
Adenine	Y = 1.6055x +0.1929	1.605	0.19293	0.9967	0.01-10
Adenosine	Y = 2.4149x +0.3217	2.415	0.32173	0.9960	0.001-10
Anthranilate	Y = 0.7222x -0.0187	0.722	-0.01866	0.9978	0.01-10
Arginine	Y = 1.0084x +0.1042	1.008	0.10418	0.9970	0.003-10
N-Acetylputrescine	Y = 1.7444x +0.1922	1.744	0.19223	0.9985	0.001-30
6-Aminohexanoate	Y = 1.1233x +0.0166	1.123	0.01658	0.9983	0.01-30
N-Acetylhistidine	Y = 1.0135x +0.0803	1.013	0.08032	0.9977	0.003-10
N-Acetylhistamine	Y = 3.6034x +0.3633	3.603	0.36329	0.9958	0.001-10
Agmatine	Y = 4.3211x +0.0151	4.321	0.01509	0.9994	0.001-1
2-Aminoadipate	Y = 0.6272x +0.0248	0.627	0.02476	0.9981	0.001-1
N1-Acetylspermine	Y = 0.6755x +0.0109	0.676	0.01089	0.9987	0.001-10
N8-Acetylspermidine	Y = 0.535x +0.1189	0.535	0.11891	0.9965	0.001-30
N-Acetylglucosamine	Y = 0.7161x +0.0207	0.716	0.02068	0.9991	0.003-3
5-Aminopentanoate	Y = 0.5277x +0.2157	0.528	0.21570	0.9983	0.1-30
O-Acetylcarnitine	Y = 6.0668x +0.1962	6.067	0.19620	0.9995	0.001-10
N-Epsilon-Acetyllysine	Y = 0.9048x -0.2267	0.905	-0.22668	0.9964	0.003-30
ADMA	Y = 1.0699x +0.0826	1.070	0.08261	0.9958	0.003-30
3-Aminoisobutanoate	Y = 0.4525x +0.0179	0.453	0.01795	0.9980	0.01-3
N1-Acetylspermidine	Y = 0.8946x -0.0188	0.895	-0.01884	0.9969	0.001-10
Choline	Y = 5.7929x +0.0395	5.793	0.03950	0.9995	0.003-3
Creatine	Y = 1.3479x +0.0351	1.348	0.03508	0.9951	0.003-1
Cytidine	Y = 0.2799x -0.0123	0.280	-0.01229	0.9984	0.03-3
Cadaverine	Y = 0.768x +0.0066	0.768	0.00665	0.9986	0.01-0.3

Cytosine	$Y = 0.6343x + 0.0242$	0.634	0.02424	0.9977	0.01-3
Creatinine	$Y = 1.0966x + 0.0327$	1.097	0.03272	0.9978	0.003-3
Carnitine	$Y = 4.8275x + 0.0449$	4.828	0.04493	0.9967	0.003-1
gamma-Butyrobetaine	$Y = 4.5884x + 0.064$	4.588	0.06400	0.9981	0.001-3
Diethanolamine	$Y = 2.4829x + 0.0247$	2.483	0.02474	0.9989	0.01-0.3
Deoxycytidine	$Y = 0.0148x - 0.0021$	0.015	-0.00213	0.9965	0.1-10
5'-Methylthioadenosine	$Y = 3.1492x + 0.2799$	3.149	0.27989	0.9962	0.001-10
Deoxyinosine	$Y = 1.2253x + 0.0217$	1.225	0.02175	0.9968	0.003-1
N1,N8-Diacetylspermidine	$Y = 1.1824x - 0.0328$	1.182	-0.03278	0.9978	0.001-3
N1,N12-Diacetylspermine	$Y = 0.9334x - 0.0343$	0.933	-0.03432	0.9964	0.001-3
Oxiglutatione	$Y = 0.0999x - 0.0008$	0.100	-0.00083	0.9983	0.03-1
Guanine	$Y = 0.7003x + 0.1135$	0.700	0.11349	0.9975	0.01-30
Guanosine	$Y = 0.3866x - 0.0112$	0.387	-0.01120	0.9978	0.01-10
4-Guanidinobutanoate	$Y = 1.7643x + 0.2271$	1.764	0.22711	0.9970	0.001-10
Glucosamine	$Y = 0.2479x + 0.0019$	0.248	0.00189	0.9969	0.01-0.3
Histidine	$Y = 0.3459x + 0.0204$	0.346	0.02036	0.9968	0.01-3
Hypoxanthine	$Y = 3.8119x - 0.0501$	3.812	-0.05006	0.9995	0.003-10
Hexylamine	$Y = 2.2422x + 0.2284$	2.242	0.22843	0.9958	0.003-10
Histamine	$Y = 1.9954x + 0.0051$	1.995	0.00510	0.9995	0.003-0.3
Hydroxylysine	$Y = 0.4358x + 0.0246$	0.436	0.02457	0.9960	0.01-3
Inosine	$Y = 0.1477x - 0.056$	0.148	-0.05598	0.9953	0.03-30
Indoleacetate	$Y = 0.5212x + 0.0271$	0.521	0.02713	0.9963	0.01-3
Imidazoleacetate	$Y = 0.8581x + 0.0394$	0.858	0.03936	0.9978	0.01-3
Leucine	$Y = 1.2707x - 0.0711$	1.271	-0.07105	0.9996	0.01-10
Lysine	$Y = 0.3681x + 0.02$	0.368	0.02004	0.9953	0.003-3
Methionine	$Y = 0.6653x - 0.019$	0.665	-0.01901	0.9977	0.01-30
1-Methylhistamine	$Y = 1.6756x + 0.4213$	1.676	0.42135	0.9979	0.003-30
Metformin	$Y = 4.6789x + 0.0979$	4.679	0.09791	0.9974	0.003-3
3-Methylguanine	$Y = 0.8233x + 0.0992$	0.823	0.09917	0.9985	0.01-30

7-Methylguanine	$Y = 1.2501x + 0.0318$	1.250	0.03183	0.9986	0.001-3
1-Methyladenosine	$Y = 3.2986x + 0.0935$	3.299	0.09355	0.9962	0.001-3
1-Methylnicotinamide	$Y = 5.187x + 0.0597$	5.187	0.05967	0.9962	0.001-1
N-Methylaniline	$Y = 4.2528x - 0.0517$	4.253	-0.05167	0.9999	0.003-3
3-Methylhistidine	$Y = 0.7127x + 0.0214$	0.713	0.02144	0.9975	0.003-3
Nicotinamide	$Y = 0.6158x + 0.029$	0.616	0.02898	0.9968	0.003-3
Nicotine	$Y = 3.1544x + 0.1142$	3.154	0.11416	0.9968	0.003-3
N6,N6,N6-Trimethyllysine	$Y = 1.4937x + 0.0893$	1.494	0.08929	0.9983	0.001-10
Ornithine	$Y = 0.2275x + 0.0072$	0.228	0.00723	0.9968	0.01-1
Ophthalmate	$Y = 0.8365x - 0.3259$	0.836	-0.32594	0.9955	0.01-30
Phenylalanine	$Y = 1.6136x - 0.068$	1.614	-0.06798	0.9996	0.003-10
Proline	$Y = 1.2221x + 0.0273$	1.222	0.02727	0.9996	0.01-10
Pipecolate	$Y = 1.7392x - 0.0637$	1.739	-0.06373	0.9998	0.003-10
Pyridoxamine	$Y = 2.3173x + 0.0035$	2.317	0.00348	0.9985	0.003-0.1
Spermidine	$Y = 1.064x + 0.2046$	1.064	0.20465	0.9964	0.003-30
Spermine	$Y = 0.8628x + 0.0088$	0.863	0.00877	0.9959	0.01-10
SDMA	$Y = 1.1824x - 0.0328$	1.182	-0.03278	0.9978	0.001-3
Tyrosine	$Y = 0.5199x - 0.0775$	0.520	-0.07752	0.9977	0.01-30
Tryptophan	$Y = 1.089x - 0.2607$	1.089	-0.26070	0.9976	0.01-30
Tyramine	$Y = 0.6267x - 0.0278$	0.627	-0.02780	0.9975	0.003-30
Thymine	$Y = 0.8581x + 0.0394$	0.858	0.03936	0.9978	0.01-3
Thiamine	$Y = 5.215x + 0.0719$	5.215	0.07189	0.9970	0.003-1
Uracil	$Y = 0.038x + 0.0023$	0.038	0.00231	0.9979	0.1-3
Urocanate	$Y = 0.5332x + 0.1991$	0.533	0.19909	0.9950	0.01-30
Valine	$Y = 0.9887x - 0.1574$	0.989	-0.15742	0.9980	0.3-30
Xanthine	$Y = 0.1307x + 0.0042$	0.131	0.00421	0.9961	0.1-1
Alanine	$Y = 0.2367x + 0.0062$	0.237	0.00620	0.9989	0.01-3
Asparagine	$Y = 0.2605x + 0.0099$	0.260	0.00994	0.9994	0.01-10
Aspartate	$Y = 0.2064x + 0.0294$	0.206	0.02936	0.9965	0.01-10

S-Adenosylmethionine	$Y = 0.4795x + 0.0279$	0.479	0.02788	0.9995	0.003-10
beta-Alanine	$Y = 0.249x + 0.0164$	0.249	0.01643	0.9960	0.01-3
S-Adenosylhomocysteine	$Y = 0.2561x - 0.0124$	0.256	-0.01238	0.9966	0.01-3
alpha-Aminobutyrate	$Y = 0.2552x + 0.0096$	0.255	0.00959	0.9961	0.03-3
Putrescine	$Y = 0.4779x + 0.0113$	0.478	0.01134	0.9973	0.01-1
Carnosine	$Y = 0.6388x - 0.1042$	0.639	-0.10420	0.9951	0.01-10
Citrulline	$Y = 0.3771x - 0.0192$	0.377	-0.01921	0.9987	0.01-30
Cysteine	$Y = 0.2783x + 0.0018$	0.278	0.00175	0.9996	0.01-3
Cystathionine	$Y = 0.2281x + 0.0688$	0.228	0.06879	0.9955	0.01-30
Levodopa	$Y = 0.5322x + 0.0146$	0.532	0.01457	0.9970	0.003-3
Glutathione	$Y = 0.4707x + 0.0073$	0.471	0.00727	0.9984	0.01-30
Glycine	$Y = 0.1275x + 0.0083$	0.127	0.00834	0.9966	0.03-3
Glutamine	$Y = 0.5233x + 0.0107$	0.523	0.01072	0.9984	0.003-30
Glutamate	$Y = 0.4496x + 0.0062$	0.450	0.00624	0.9997	0.003-3
Homoserine	$Y = 1.0702x - 0.0051$	1.070	-0.00512	0.9999	0.003-3
Hydroxyproline	$Y = 0.765x + 0.161$	0.765	0.16101	0.9960	0.01-30
Homocysteine	$Y = 0.4931x + 0.0281$	0.493	0.02806	0.9954	0.01-3
Hypotaurine	$Y = 0.3471x - 0.0253$	0.347	-0.02530	0.9984	0.1-30
Isoleucine	$Y = 1.2159x - 0.0448$	1.216	-0.04483	0.9999	0.03-10
Serine	$Y = 0.1994x + 0.0086$	0.199	0.00860	0.9958	0.01-3
Taurine	$Y = 0.0739x + 0.0347$	0.074	0.03473	0.9956	0.1-30
Threonine	$Y = 1.0702x - 0.0051$	1.070	-0.00512	0.9999	0.003-3
Uridine	$Y = 0.0195x + 0.0309$	0.019	0.03092	0.9809	0.03-30
Trimethylamine N-oxide	$Y = 2.505x + 0.0126$	2.505	0.01255	0.9978	0.003-3
<b>Negative</b>					
AMP	$Y = 0.0848x + 0.0027$	0.085	0.00266	0.9971	0.003-3
ADP	$Y = 0.0894x - 0.007$	0.089	-0.00698	0.9917	1-10
cis-Aconitate	$Y = 0.103x - 0.0168$	0.103	-0.01683	0.9852	0.1-30

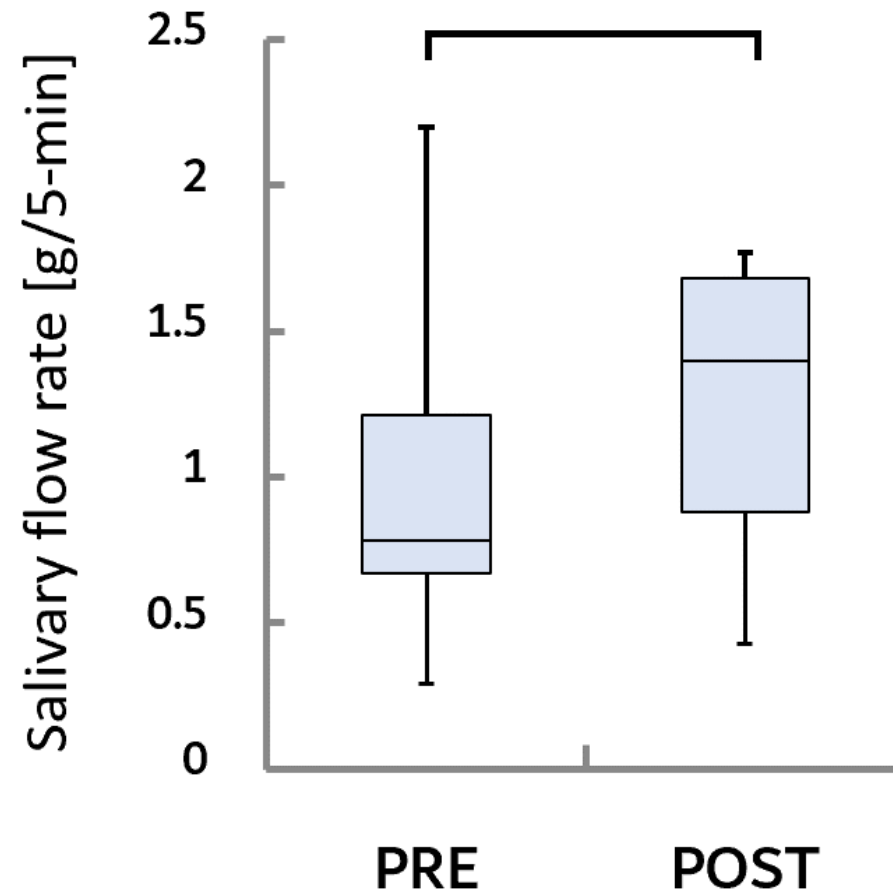
cAMP	$Y = 0.1279x + 0.0071$	0.128	0.00708	0.9985	0.003-10
Citrate	$Y = 0.0619x + 0.0026$	0.062	0.00258	0.9963	0.01-3
CMP	$Y = 0.0584x + 0.0009$	0.058	0.00090	0.9972	0.01-1
3-Sulfinioalanine	$Y = 0.0059x + 0.001$	0.006	0.00098	0.9658	0.03-3
CDP	$Y = 0.0745x + 0.002$	0.075	0.00202	0.9954	0.03-3
NADH	$Y = 0.0133x - 0.00003$	0.013	-0.00003	0.9940	0.3-10
NAD+	$Y = 0.0105x + 0.0017$	0.010	0.00171	0.9980	0.3-3
Dihydroxyacetone phosphate	$Y = 0.0218x + 0.0044$	0.022	0.00442	0.9852	0.3-3
Fructose 6-phosphate	$Y = 0.2452x + 0.0038$	0.245	0.00384	0.9958	0.01-1
FAD	$Y = 0.0949x + 0.0007$	0.095	0.00071	0.9989	0.03-10
Fumarate	$Y = 0.0092x + 0.0001$	0.009	0.00009	0.9937	0.1-1
Fructose 1,6-bisphosphate	$Y = 0.0483x + 0.0112$	0.048	0.01125	0.9691	0.3-10
Glucose 6-phosphate	$Y = 0.2452x + 0.0038$	0.245	0.00384	0.9958	0.01-1
Glycolate	$Y = 0.0235x - 0.0077$	0.024	-0.00775	0.9953	0.3-10
Glyoxylate	$Y = 0.0115x - 0.0011$	0.011	-0.00110	0.9954	0.1-10
GMP	$Y = 0.0817x + 0.0024$	0.082	0.00240	0.9961	0.003-3
Glucose 1-phosphate	$Y = 0.2452x + 0.0038$	0.245	0.00384	0.9958	0.01-1
GDP	$Y = 0.0535x + 0.1552$	0.053	0.15524	0.9048	3-30
Glyceraldehyde 3-phosphate	$Y = 0.0218x + 0.0044$	0.022	0.00442	0.9852	0.3-3
Glycerol 3-phosphate	$Y = 0.0533x + 0.002$	0.053	0.00197	0.9982	0.01-1
Gluconate	$Y = 0.0728x + 0.0021$	0.073	0.00214	0.9968	0.01-1
cGMP	$Y = 0.1045x + 0.0148$	0.105	0.01482	0.9955	0.01-10
2-Hydroxyglutarate	$Y = 0.0507x + 0.004$	0.051	0.00403	0.9952	0.01-10
Isocitrate	$Y = 0.0479x + 0.0039$	0.048	0.00389	0.9950	0.03-1
IMP	$Y = 0.1x + 0.0033$	0.100	0.00335	0.9967	0.01-3
Lactate	$Y = 0.0214x + 0.0031$	0.021	0.00313	0.9959	0.1-3
Malate	$Y = 0.0372x + 0.0004$	0.037	0.00038	0.9955	0.03-1
3-Methyl-2-oxobutanoate	$Y = 0.0323x + 0.0054$	0.032	0.00540	0.9966	0.1-10
NADP+	$Y = 0.0453x - 0.0014$	0.045	-0.00140	0.9983	0.1-3

2-Oxoglutarate	$Y = 0.0239x - 0.0009$	0.024	-0.00093	0.9994	0.1-10
Phosphoenolpyruvate	$Y = 0.0283x - 0.0033$	0.028	-0.00325	0.9947	0.3-30
Pyruvate	$Y = 0.0096x + 0.0014$	0.010	0.00143	0.9618	1-3
3-Phosphoglycerate	$Y = 0.0671x + 0.0007$	0.067	0.00066	0.9951	0.1-3
2-Phosphoglycerate	$Y = 0.0671x + 0.0007$	0.067	0.00066	0.9951	0.1-3
6-Phosphogluconate	$Y = 0.0721x + 0.0001$	0.072	0.00013	0.9960	0.01-1
Ribose 5-phosphate	$Y = 0.1391x - 0.0011$	0.139	-0.00114	0.9965	0.03-0.3
Ribulose 5-phosphate	$Y = 0.1391x - 0.0011$	0.139	-0.00114	0.9965	0.03-0.3
Succinate	$Y = 0.0394x + 0.0017$	0.039	0.00167	0.9964	0.03-1
Sedoheptulose 7-phosphate	$Y = 0.0932x - 0.00001$	0.093	-0.00001	0.9975	0.01-0.3
dTDP	$Y = 0.0407x + 0.4928$	0.041	0.49285	0.9613	10-100
dTMP	$Y = 0.1522x + 0.003$	0.152	0.00302	0.9989	0.01-3
Erythrose 4-phosphate	$Y = 0.0214x + 0.0007$	0.021	0.00070	0.9910	0.01-1

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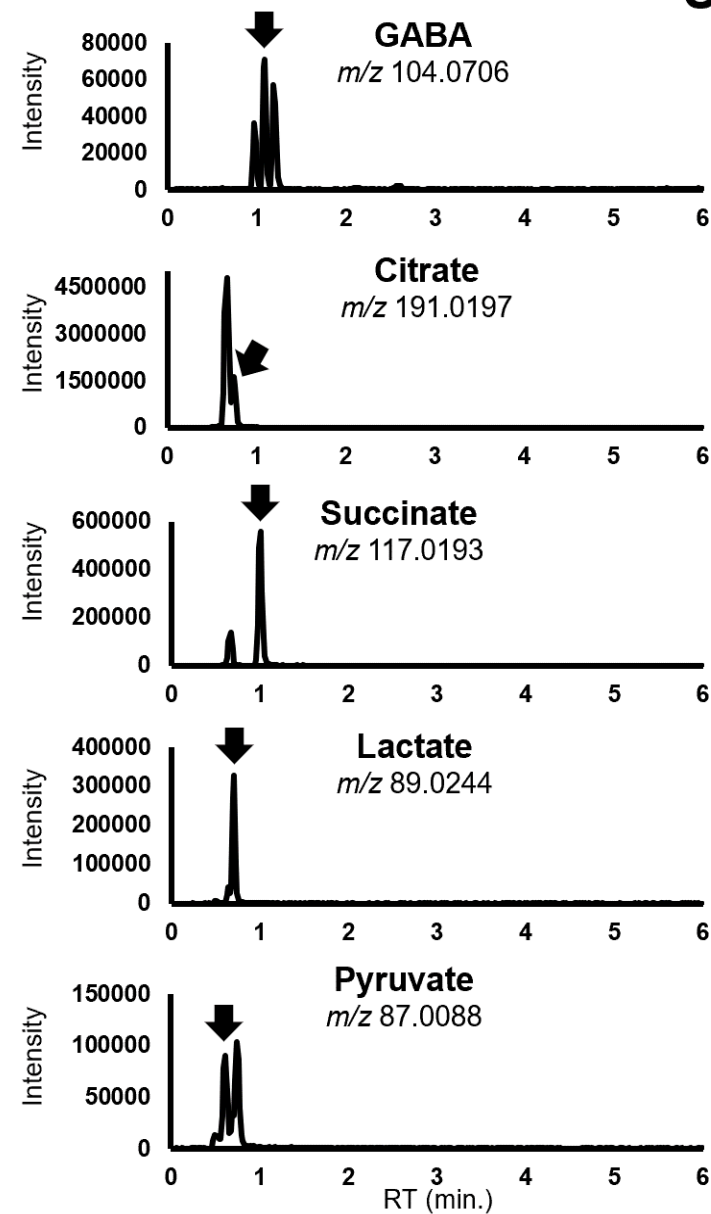
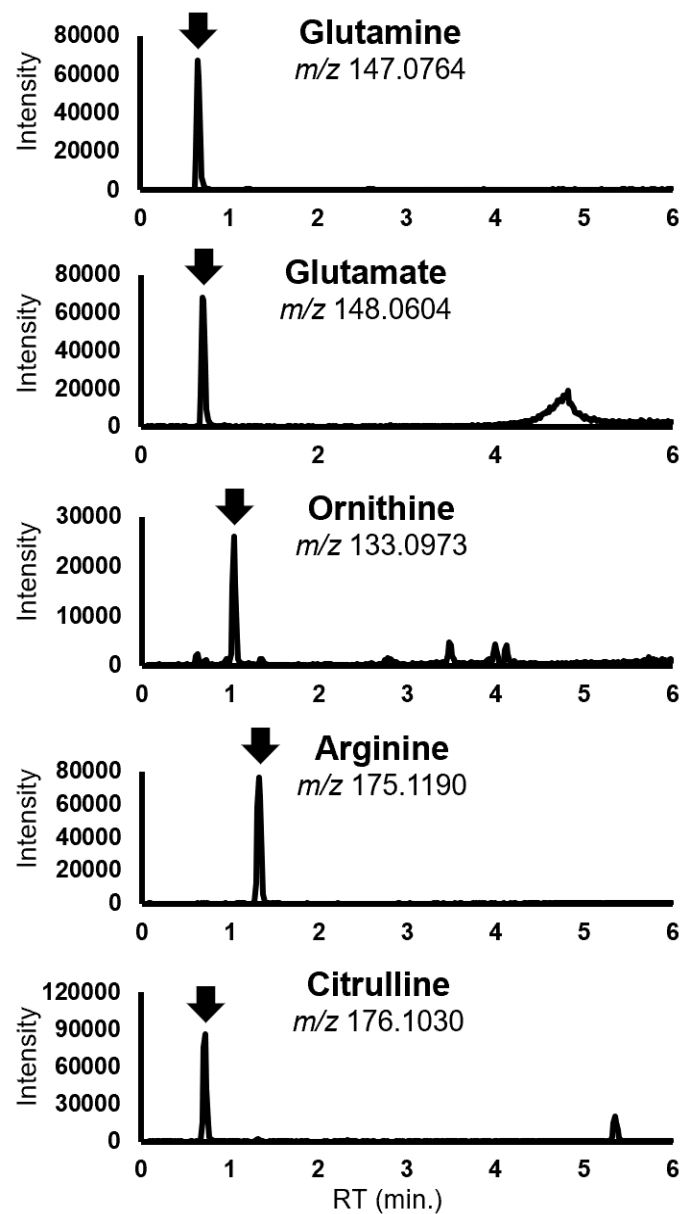
Substances that could not be separated are shown with the same color.





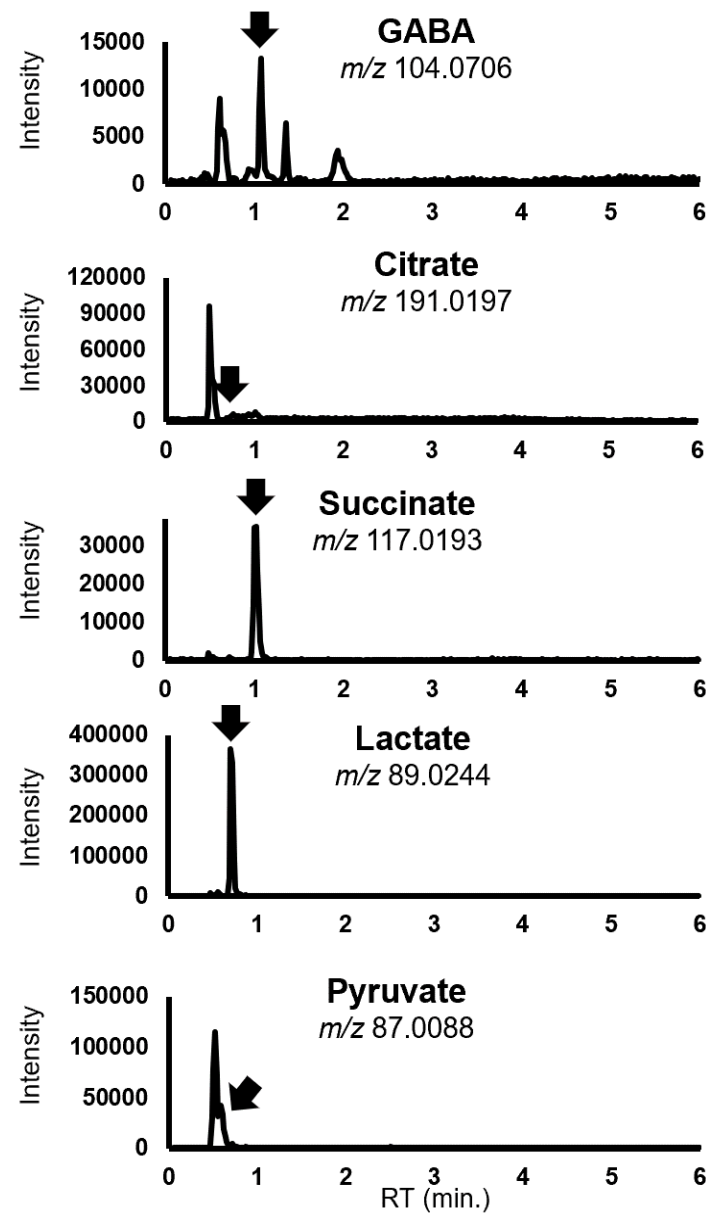
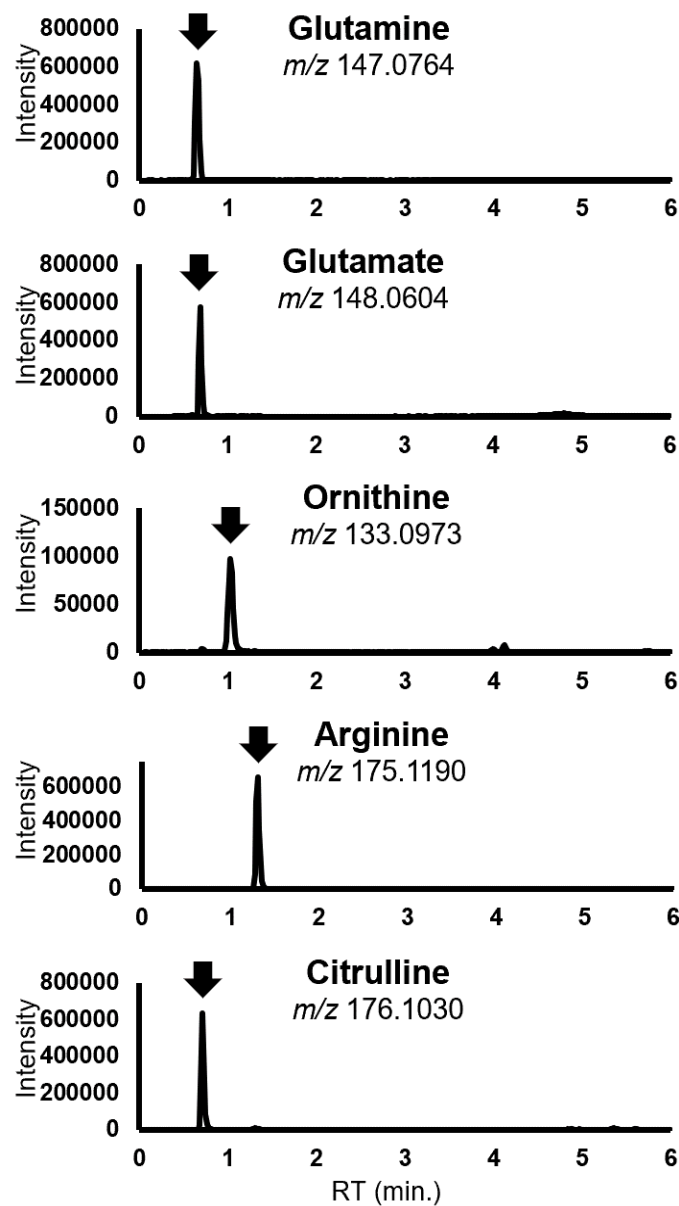
**Supplementary Figure S1.** Change in unstimulated salivary flow rate  
The unstimulated salivary flow rate was evaluated using a 5-min spitting procedure.  $P < 0.05$ , Wilcoxon signed-rank test.

# STD



**Supplementary Figures S2-1.** Representative LCMS chromatogram of 10 metabolites ( in standard mixture samples)

QC



**Supplementary Figures S2-2.** Representative LCMS chromatogram of 10 metabolites (in quality control samples)