

Table S1. Overview of the 237 integration numbers (variables) and their corresponding integration regions and contributing metabolites. All integration regions and corresponding metabolites are defined by spiking experiments. FAC: fatty acid chain; NAG: N-acetylated glycoproteins; NI: non-identified; PC: phosphatidylcholine; PL: phospholipids; SM: sphingomyelin; TG: triglycerides; VAR: variable (assigned integration number).

Assigned integration number (variable)	Integration region (ppm)	Corresponding metabolite(s)
VAR 001	8.460 - 8.484	Formate
VAR 002	8.190 - 8.240	Hypoxanthine
VAR 003	7.945 - 8.170	NI 1
VAR 004	7.905 - 7.945	1-methylhistidine
VAR 005	7.875 - 7.905	Uridine
VAR 006	7.845 - 7.875	Histidine
VAR 007	7.820 - 7.845	NI 2
VAR 008	7.720 - 7.780	Tryptophan NI 3
VAR 009	7.650 - 7.700	3-methylhistidine
VAR 010	7.530 - 7.580	Tryptophan
VAR 011	7.350 - 7.480	Phenylalanine
VAR 012	7.330 - 7.350	Phenylalanine Tryptophan
VAR 013	7.260 - 7.320	Tryptophan NI 4
VAR 014	7.240 - 7.260	NI 5
VAR 015	7.180 - 7.240	Tryptophan Tyrosine
VAR 016	7.080 - 7.140	Histidine
VAR 017	6.998 - 7.071	1-methylhistidine 3-methylhistidine NI 6
VAR 018	6.954 - 6.986	NI 7
VAR 019	6.890 - 6.950	Tyrosine
VAR 020	6.730 - 6.775	NI 8
VAR 021	6.533 - 6.547	Fumarate
VAR 022	5.907 - 5.946	Uridine
VAR 023	5.720 - 5.865	NI 9
VAR 024	5.405 - 5.415	Allantoin
VAR 025	5.238 - 5.267	Glucose
VAR 026	5.196 - 5.210	Mannose
VAR 027	4.919 - 4.928	Mannose
VAR 028	4.633 - 4.703	Glucose Hydroxyproline NI 10
VAR 029	4.560 - 4.614	Carnitine
VAR 030	4.528 - 4.540	NI 11
VAR 031	4.521 - 4.527	NI 12
VAR 032	4.450 - 4.490	NI 13

VAR 033	4.347 - 4.430	Hydroxyproline N-acetylcysteine Uridine Lipids: C ₁ H and C ₃ H in glycerol backbone of PL and TG
VAR 034	4.299 - 4.347	Lipids: (O-CH ₂ -CH ₂ -N ⁺ (CH ₃) ₃) of PC and SM; C ₁ H and C ₃ H in glycerol backbone of PL and TG
VAR 035	4.269 - 4.299	Threonine Lipids: (O-CH ₂ -CH ₂ -N ⁺ (CH ₃) ₃) of PC and SM
VAR 036	4.237 - 4.269	Threonine Uridine
VAR 037	4.172 - 4.216	Pyroglutamate β-Hydroxybutyrate
VAR 038	4.153 - 4.172	Proline Uridine β-Hydroxybutyrate
VAR 039	4.147 - 4.153	Lactate Proline Uridine
VAR 040	4.133 - 4.147	Lactate Proline Uridine β-Hydroxybutyrate Cystine
VAR 041	4.110 - 4.133	Lactate Cystine
VAR 042	4.054 - 4.102	Choline Creatinine Myoinositol Tryptophan Isopropanol NI 14
VAR 043	4.043 - 4.054	Isopropanol NI 14
VAR 044	4.034 - 4.043	Isopropanol
VAR 045	4.021 - 4.034	2-hydroxybutyrate Asparagine Phenylalanine Serine Isopropanol
VAR 046	4.006 - 4.021	2-hydroxybutyrate Asparagine Histidine Phenylalanine Serine Isopropanol
VAR 047	4.001 - 4.006	Histidine Phenylalanine

		Serine
VAR 048	3.993 - 4.001	3-methylhistidine Histidine Serine
VAR 049	3.985 - 3.992	3-methylhistidine Cysteine
VAR 050	3.979 - 3.985	3-methylhistidine Cysteine Serine
VAR 051	3.968 - 3.979	1-methylhistidine 3-methylhistidine Cysteine Mannose Serine Tyrosine
VAR 052	3.960 - 3.968	1-methylhistidine Mannose Serine Tyrosine
VAR 053	3.954 - 3.960	1-methylhistidine Mannose Tyrosine
VAR 054	3.946 - 3.954	1-methylhistidine Creatine Mannose Serine
VAR 055	3.934 - 3.946	Mannose Uridine
VAR 056	3.930 - 3.934	Aspartate Glucose
VAR 057	3.914 - 3.930	Aspartate Betaine Glucose Mannose Uridine
VAR 058	3.909 - 3.914	Aspartate Glucose
VAR 059	3.900 - 3.909	Glucose Mannose NI 15
VAR 060	3.893 - 3.900	NI 15
VAR 061	3.885 - 3.893	Mannose Methionine
VAR 062	3.873 - 3.885	Glucose Mannose Methionine NI 15

VAR 063	3.857 - 3.873	2-hydroxy-3-methylbutyrate Glucose Mannose Methionine Serine
VAR 064	3.851 - 3.857	Glucose Mannose Serine
VAR 065	3.846 - 3.851	Glucose Mannose
VAR 066	3.829 - 3.844	Glucose Mannose Uridine
VAR 067	3.818 - 3.829	Alanine Mannose Uridine Glycerol
VAR 068	3.808 - 3.818	Alanine Ornithine Uridine Glycerol
VAR 069	3.796 - 3.808	Alanine Arginine Glucose Glutamine Mannose Ornithine Glycerol
VAR 070	3.785 - 3.796	Alanine Arginine Glucose Glutamate Glutamine Lysine Mannose Ornithine Glycerol
VAR 071	3.770 - 3.785	Arginine Glucose Glutamate Glutamine Lysine Mannose
VAR 072	3.765 - 3.770	Glutamate Leucine Lysine
VAR 073	3.748 - 3.765	Glucose

		Leucine Mannose
VAR 074	3.739 - 3.748	Glucose Leucine Mannose 2-aminobutyrate
VAR 075	3.728 - 3.739	Glucose 2-aminobutyrate
VAR 076	3.715 - 3.728	1-methylhistidine Glucose 2-aminobutyrate NI 16
VAR 077	3.709 - 3.713	3-methylhistidine
VAR 078	3.704 - 3.709	NI 16
VAR 079	3.685 - 3.704	Isoleucine Mannose Glycerol NI 16 NI 17 Lipids: (O-CH ₂ -CH ₂ -N ⁺ (CH ₃) ₃ of PC and SM
VAR 080	3.678 - 3.685	Mannose Glycerol NI 17 Lipids: (O-CH ₂ -CH ₂ -N ⁺ (CH ₃) ₃ of PC and SM
VAR 081	3.673 - 3.678	Mannose Lipids: (O-CH ₂ -CH ₂ -N ⁺ (CH ₃) ₃ of PC and SM
VAR 082	3.664 - 3.673	Mannose Glycerol NI 17 Lipids: (O-CH ₂ -CH ₂ -N ⁺ (CH ₃) ₃ of PC and SM
VAR 083	3.654 - 3.664	Myoinositol Glycerol NI 17 Lipids: (O-CH ₂ -CH ₂ -N ⁺ (CH ₃) ₃ of PC and SM
VAR 084	3.649 - 3.654	Lipids: (O-CH ₂ -CH ₂ -N ⁺ (CH ₃) ₃ of PC and SM
VAR 085	3.642 - 3.647	Myoinositol
VAR 086	3.633 - 3.641	Valine
VAR 087	3.623 - 3.633	Myoinositol Sarcosine Valine
VAR 088	3.608 - 3.616	Mannose Threonine
VAR 089	3.600 - 3.606	Threonine
VAR 090	3.594 - 3.600	Mannose Glycerol
VAR 091	3.584 - 3.589	Glycerol
VAR 092	3.576 - 3.584	Glycine

		Mannose Glycerol
VAR 093	3.559 - 3.572	Glucose Myoinositol Glycerol
VAR 094	3.541 - 3.555	Choline Glucose Myoinositol
VAR 095	3.534 - 3.541	Choline
VAR 096	3.524 - 3.534	Choline Glucose
VAR 097	3.507 - 3.522	Glucose Hydroxyproline Tryptophan
VAR 098	3.500 - 3.504	Glucose Tryptophan
VAR 099	3.490 - 3.500	Glucose Hydroxyproline Tryptophan
VAR 100	3.467 - 3.490	Glucose Tryptophan
VAR 101	3.460 - 3.467	Proline Acetoacetate
VAR 102	3.455 - 3.460	Carnitine
VAR 103	3.437 - 3.455	Carnitine Glucose Proline Taurine
VAR 104	3.433 - 3.437	Glucose
VAR 105	3.429 - 3.433	Proline Taurine
VAR 106	3.413 - 3.429	Mannose Glucose Proline Cystine
VAR 107	3.401 - 3.413	Glucose Mannose
VAR 108	3.387 - 3.401	Hydroxyproline Mannose Cystine
VAR 109	3.383 - 3.387	Hydroxyproline
VAR 110	3.375 - 3.383	Hydroxyproline Proline
VAR 111	3.354 - 3.373	Proline
VAR 112	3.346 - 3.352	Proline Tryptophan
VAR 113	3.332 - 3.340	1-methylhistidine

		Proline Tryptophan
VAR 114	3.313 - 3.325	1-methylhistidine Myoinositol Phenylalanine Tryptophan
VAR 115	3.304 - 3.313	1-methylhistidine Phenylalanine Tryptophan
VAR 116	3.300 - 3.304	Myoinositol
VAR 117	3.291 - 3.300	1-methylhistidine Phenylalanine Taurine Lipids: (O-CH ₂ -CH ₂ -N ⁺ (CH ₃) ₃ of PC and SM
VAR 118	3.284 - 3.289	Betaine Myoinositol Phenylalanine Lipids: (O-CH ₂ -CH ₂ -N ⁺ (CH ₃) ₃ of PC and SM
VAR 119	3.278 - 3.284	Glucose Histidine Taurine Lipids: (O-CH ₂ -CH ₂ -N ⁺ (CH ₃) ₃ of PC and SM
VAR 120	3.270 - 3.278	Arginine Histidine Taurine Lipids: (O-CH ₂ -CH ₂ -N ⁺ (CH ₃) ₃ of PC and SM
VAR 121	3.263 - 3.270	Arginine Glucose Lipids: (O-CH ₂ -CH ₂ -N ⁺ (CH ₃) ₃ of PC and SM
VAR 122	3.250 - 3.263	Arginine Glucose Histidine Lipids: (O-CH ₂ -CH ₂ -N ⁺ (CH ₃) ₃ of PC and SM
VAR 123	3.244 - 3.250	1-methylhistidine Carnitine Histidine Lipids: (O-CH ₂ -CH ₂ -N ⁺ (CH ₃) ₃ of PC and SM
VAR 124	3.236 - 3.244	Lipids: (O-CH ₂ -CH ₂ -N ⁺ (CH ₃) ₃ of PC and SM
VAR 125	3.231 - 3.236	1-methylhistidine Tyrosine Lipids: (O-CH ₂ -CH ₂ -N ⁺ (CH ₃) ₃ of PC and SM
VAR 126	3.227 - 3.231	Cystine Lipids: (O-CH ₂ -CH ₂ -N ⁺ (CH ₃) ₃ of PC and SM
VAR 127	3.224 - 3.227	Tyrosine Lipids: (O-CH ₂ -CH ₂ -N ⁺ (CH ₃) ₃ of PC and SM
VAR 128	3.217 - 3.222	1-methylhistidine Choline

		Tyrosine Lipids: (O-CH ₂ -CH ₂ -N ⁺ (CH ₃) ₃ of PC and SM
VAR 129	3.211 - 3.217	β-alanine Tyrosine Cystine Lipids: (O-CH ₂ -CH ₂ -N ⁺ (CH ₃) ₃ of PC and SM
VAR 130	3.195 - 3.211	1-methylhistidine 3-methylhistidine β-alanine Tyrosine Cystine Lipids: (O-CH ₂ -CH ₂ -N ⁺ (CH ₃) ₃ of PC and SM
VAR 131	3.187 - 3.193	β-alanine Cystine
VAR 132	3.177 - 3.183	3-methylhistidine Histidine
VAR 133	3.169 - 3.175	3-methylhistidine
VAR 134	3.135 - 3.169	Histidine Phenylalanine
VAR 135	3.122 - 3.134	Cysteine Phenylalanine
VAR 136	3.100 - 3.122	3-methylhistidine Cysteine
VAR 137	3.090 - 3.100	3-methylhistidine Cysteine Tyrosine
VAR 138	3.077 - 3.090	3-methyl-2-oxobutyrate 3-methylhistidine Ornithine Tyrosine
VAR 139	3.066 - 3.077	3-methyl-2-oxobutyrate 3-methylhistidine Cysteine Ornithine Tyrosine
VAR 140	3.060 - 3.066	3-methyl-2-oxobutyrate Creatinine Cysteine Ornithine
VAR 141	3.053 - 3.060	3-methyl-2-oxobutyrate Creatine Lysine Tyrosine
VAR 142	3.040 - 3.053	3-methyl-2-oxobutyrate 4-aminobutyrate Cysteine Lysine

VAR 143	3.035 - 3.040	3-methyl-2-oxobutyrate Cysteine α -ketoglutarate
VAR 144	3.029 - 3.035	4-aminobutyrate Lysine
VAR 145	3.023 - 3.029	3-methyl-2-oxobutyrate α -ketoglutarate
VAR 146	3.017 - 3.023	4-aminobutyrate
VAR 147	3.010 - 3.017	α -ketoglutarate
VAR 148	2.979 - 2.991	Asparagine
VAR 149	2.966 - 2.979	3-methyl-2-oxopentanoate N-acetylcysteine
VAR 150	2.958 - 2.966	3-methyl-2-oxopentanoate Asparagine
VAR 151	2.950 - 2.958	Asparagine N-acetylcysteine
VAR 152	2.911 - 2.950	3-methyl-2-oxopentanoate N-acetylcysteine
VAR 153	2.875 - 2.904	Asparagine
VAR 154	2.854 - 2.875	Asparagine Lipids: $=CH-CH_2-CH=$ in FAC
VAR 155	2.812 - 2.854	Aspartate Lipids: $=CH-CH_2-CH=$ in FAC
VAR 156	2.762 - 2.812	Lipids: $=CH-CH_2-CH=$ in FAC
VAR 157	2.757 - 2.762	Sarcosine Lipids: $=CH-CH_2-CH=$ in FAC
VAR 158	2.741 - 2.757	Lipids: $=CH-CH_2-CH=$ in FAC
VAR 159	2.724 - 2.741	NI 18 Lipids: $=CH-CH_2-CH=$ in FAC
VAR 160	2.718 - 2.724	Aspartate Lipids: $=CH-CH_2-CH=$ in FAC
VAR 161	2.712 - 2.718	Lipids: $=CH-CH_2-CH=$ in FAC
VAR 162	2.702 - 2.712	Aspartate Citrate
VAR 163	2.690 - 2.694	Aspartate
VAR 164	2.673 - 2.685	Aspartate Citrate Methionine
VAR 165	2.647 - 2.668	Methionine
VAR 166	2.615 - 2.634	4-methyl-2-oxovalerate
VAR 167	2.571 - 2.592	β -alanine
VAR 168	2.533 - 2.571	β -alanine Citrate Pyroglutamate
VAR 169	2.501 - 2.533	Glutamine Pyroglutamate

VAR 170	2.484 - 2.501	Carnitine Glutamine Pyroglutamate
VAR 171	2.476 - 2.484	Glutamine
VAR 172	2.450 - 2.476	Carnitine Glutamine Hydroxyproline α -ketoglutarate
VAR 173	2.439 - 2.450	Carnitine Glutamine Hydroxyproline α -ketoglutarate β -Hydroxybutyrate
VAR 174	2.427 - 2.439	Carnitine Glutamine Hydroxyproline Pyroglutamate β -Hydroxybutyrate
VAR 175	2.418 - 2.427	Carnitine Pyroglutamate Succinate β -Hydroxybutyrate
VAR 176	2.405 - 2.418	Glutamate Pyroglutamate β -Hydroxybutyrate
VAR 177	2.380 - 2.405	3-hydroxy-3-methylbutyrate Glutamate Oxaloacetate Proline Pyruvate
VAR 178	2.349 - 2.380	Glutamate Proline
VAR 179	2.337 - 2.349	Glutamate Proline β -Hydroxybutyrate
VAR 180	2.324 - 2.337	4-aminobutyrate Glutamate Valine β -Hydroxybutyrate
VAR 181	2.312 - 2.324	4-aminobutyrate Valine β -Hydroxybutyrate
VAR 182	2.305 - 2.312	Valine β -Hydroxybutyrate
VAR 183	2.294 - 2.305	4-aminobutyrate Valine Acetoacetate

VAR 184	2.282 - 2.294	Valine
VAR 185	2.264 - 2.282	Valine Lipids: -CH ₂ -C=O or -CH ₂ -CH=CH- in FAC
VAR 186	2.254 - 2.264	Lipids: -CH ₂ -C=O or -CH ₂ -CH=CH- in FAC
VAR 187	2.221 - 2.254	Methionine Lipids: -CH ₂ -C=O or -CH ₂ -CH=CH- in FAC
VAR 188	2.208 - 2.221	Methionine
VAR 189	2.151 - 2.208	Glutamate Glutamine Hydroxyproline Methionine
VAR 190	2.128 - 2.151	4-methyl-2-oxovalerate Glutamate Glutamine Methionine
VAR 191	2.114 - 2.128	4-methyl-2-oxovalerate Glutamate Glutamine Methionine Proline
VAR 192	2.102 - 2.114	4-methyl-2-oxovalerate Glutamate Glutamine Methionine Proline Lipids: -CH ₂ -CH=CH- in FAC; CH ₃ of NAG
VAR 193	2.078 - 2.102	Glutamate N-acetylcysteine Proline Pyroglutamate Lipids: -CH ₂ -CH=CH- in FAC; CH ₃ of NAG
VAR 194	2.042 - 2.078	2-hydroxy-3-methylbutyrate Glutamate Proline Pyroglutamate Lipids: -CH ₂ -CH=CH- in FAC; CH ₃ of NAG
VAR 195	2.013 - 2.042	2-hydroxy-3-methylbutyrate Isoleucine Proline Pyroglutamate Lipids: -CH ₂ -CH=CH- in FAC; CH ₃ of NAG
VAR 196	2.001 - 2.013	Isoleucine Ornithine Proline Lipids: -CH ₂ -CH=CH- in FAC; CH ₃ of NAG

VAR 197	1.967 - 2.001	Arginine Isoleucine Ornithine Proline 2-aminobutyrate Lipids: -CH ₂ -CH=CH- in FAC; CH ₃ of NAG
VAR 198	1.949 - 1.967	Arginine Lysine Ornithine 2-aminobutyrate
VAR 199	1.906 - 1.949	4-aminobutyrate Acetate Arginine Lysine Ornithine 2-aminobutyrate
VAR 200	1.823 - 1.906	4-aminobutyrate Arginine Lysine Ornithine 2-aminobutyrate
VAR 201	1.800 - 1.823	Ornithine
VAR 202	1.729 - 1.800	2-hydroxybutyrate 3-methyl-2-oxopentanoate Arginine Leucine Lysine Ornithine
VAR 203	1.717 - 1.729	2-hydroxybutyrate 3-methyl-2-oxopentanoate Arginine Leucine Lysine
VAR 204	1.678 - 1.717	2-hydroxybutyrate 3-methyl-2-oxopentanoate Arginine Leucine
VAR 205	1.655 - 1.678	2-hydroxybutyrate Arginine
VAR 206	1.650 - 1.655	Arginine
VAR 207	1.630 - 1.650	2-hydroxybutyrate Arginine Lipids: -CH ₂ -CH ₂ -C=O or -CH ₂ -CH ₂ -CH=CH- in FAC
VAR 208	1.572 - 1.630	Lipids: -CH ₂ -CH ₂ -C=O or -CH ₂ -CH ₂ -CH=CH- in FAC
VAR 209	1.535 - 1.572	Lysine Lipids: -CH ₂ -CH ₂ -C=O or -CH ₂ -CH ₂ -CH=CH- in FAC

VAR 210	1.509 - 1.535	Isoleucine Lysine
VAR 211	1.489 - 1.509	Alanine Isoleucine Lysine
VAR 212	1.446 - 1.489	3-methyl-2-oxopentanoate Isoleucine Lysine
VAR 213	1.408 - 1.446	3-methyl-2-oxopentanoate Lysine NI 19
VAR 214	1.358 - 1.405	Lipids: CH ₃ -(CH ₂) _n - in FAC
VAR 215	1.338 - 1.358	Lactate Threonine Lipids: CH ₃ -(CH ₂) _n - in FAC
VAR 216	1.296 - 1.338	Lipids: CH ₃ -(CH ₂) _n - in FAC
VAR 217	1.289 - 1.296	Isoleucine Lipids: CH ₃ -(CH ₂) _n - in FAC
VAR 218	1.285 - 1.289	3-hydroxy-3-methylbutyrate Isoleucine Lipids: CH ₃ -(CH ₂) _n - in FAC
VAR 219	1.226 - 1.285	Isoleucine Lipids: CH ₃ -(CH ₂) _n - in FAC
VAR 220	1.211 - 1.226	Isoleucine β-Hydroxybutyrate Lipids: CH ₃ -(CH ₂) _n - in FAC
VAR 221	1.200 - 1.211	Lipids: CH ₃ -(CH ₂) _n - in FAC
VAR 222	1.182 - 1.198	Isopropanol
VAR 223	1.128 - 1.151	3-methyl-2-oxobutyrate
VAR 224	1.103 - 1.123	3-methyl-2-oxopentanoate
VAR 225	1.078 - 1.101	NI 20
VAR 226	1.052 - 1.072	Valine
VAR 227	1.020 - 1.039	Isoleucine
VAR 228	1.008 - 1.020	Valine 2-aminobutyrate
VAR 229	1.001 - 1.008	Valine
VAR 230	0.996 - 1.001	2-aminobutyrate
VAR 231	0.984 - 0.996	2-hydroxy-3-methylbutyrate Leucine 2-aminobutyrate
VAR 232	0.976 - 0.984	2-hydroxy-3-methylbutyrate Leucine
VAR 233	0.964 - 0.976	Isoleucine Leucine
VAR 234	0.938 - 0.964	4-methyl-2-oxovalerate Isoleucine

VAR 235	0.929 - 0.938	2-hydroxybutyrate
VAR 236	0.882 - 0.929	2-hydroxybutyrate 3-methyl-2-oxopentanoate Lipids: $\text{CH}_3\text{-(CH}_2)_n\text{-}$ in FAC
VAR 237	0.800 - 0.882	2-hydroxy-3-methylbutyrate Lipids: $\text{CH}_3\text{-(CH}_2)_n\text{-}$ in FAC

Table S2: Overview of the intrasample variability of the 237 integration regions. Shown is the small relative standard deviation (%RSD) of each variable based on the analysis of 12 identical plasma samples from a plasma pool. The signal of maleic acid was used to normalize all integration regions. Integration regions having an %RSD >10% are colored in red and were excluded from further statistical analysis. RSD: Relative standard deviation; VAR: variable.

Assigned integration number (variable)	RSD(%)	Assigned integration number (variable)	RSD(%)
VAR 001	11.75	VAR 042	1.62
VAR 002	6.10	VAR 043	2.76
VAR 003	6.79	VAR 044	4.38
VAR 004	5.72	VAR 045	1.60
VAR 005	5.76	VAR 046	2.27
VAR 006	6.21	VAR 047	3.07
VAR 007	5.57	VAR 048	1.69
VAR 008	5.07	VAR 049	3.61
VAR 009	13.59	VAR 050	2.52
VAR 010	7.13	VAR 051	1.59
VAR 011	2.70	VAR 052	2.41
VAR 012	2.93	VAR 053	4.07
VAR 013	4.75	VAR 054	2.43
VAR 014	6.38	VAR 055	2.27
VAR 015	2.82	VAR 056	4.15
VAR 016	3.73	VAR 057	1.24
VAR 017	4.20	VAR 058	3.36
VAR 018	7.42	VAR 059	2.25
VAR 019	1.95	VAR 060	2.96
VAR 020	5.22	VAR 061	2.74
VAR 021	336.77	VAR 062	0.99
VAR 022	18.02	VAR 063	0.94
VAR 023	5.03	VAR 064	0.87
VAR 024	13.9	VAR 065	2.31
VAR 025	1.41	VAR 066	0.97
VAR 026	6.94	VAR 067	3.87
VAR 027	55.22	VAR 068	2.24
VAR 028	4.56	VAR 069	2.43
VAR 029	18.82	VAR 070	1.00
VAR 030	9.83	VAR 071	1.52
VAR 031	13.26	VAR 072	1.55
VAR 032	8.08	VAR 073	1.15
VAR 033	5.38	VAR 074	2.48
VAR 034	3.25	VAR 075	1.10
VAR 035	3.07	VAR 076	1.04
VAR 036	3.71	VAR 077	6.73
VAR 037	3.45	VAR 078	1.84
VAR 038	2.68	VAR 079	1.78
VAR 039	1.49	VAR 080	2.01

VAR 040	1.93	VAR 081	1.63
VAR 041	1.27	VAR 082	3.00
VAR 083	2.78	VAR 129	3.13
VAR 084	3.19	VAR 130	5.33
VAR 085	3.14	VAR 131	7.77
VAR 086	2.39	VAR 132	6.94
VAR 087	2.45	VAR 133	4.42
VAR 088	1.54	VAR 134	7.16
VAR 089	3.39	VAR 135	6.93
VAR 090	2.87	VAR 136	6.56
VAR 091	1.93	VAR 137	4.51
VAR 092	2.23	VAR 138	5.14
VAR 093	0.90	VAR 139	3.39
VAR 094	1.32	VAR 140	2.12
VAR 095	6.14	VAR 141	2.63
VAR 096	1.54	VAR 142	2.77
VAR 097	1.46	VAR 143	3.05
VAR 098	4.70	VAR 144	3.26
VAR 099	1.71	VAR 145	4.51
VAR 100	1.27	VAR 146	4.10
VAR 101	3.80	VAR 147	3.88
VAR 102	2.15	VAR 148	4.66
VAR 103	1.74	VAR 149	2.33
VAR 104	3.24	VAR 150	5.06
VAR 105	5.54	VAR 151	3.61
VAR 106	1.21	VAR 152	4.00
VAR 107	1.83	VAR 153	6.54
VAR 108	5.20	VAR 154	4.29
VAR 109	3.57	VAR 155	1.87
VAR 110	3.85	VAR 156	2.60
VAR 111	3.85	VAR 157	3.75
VAR 112	4.67	VAR 158	1.85
VAR 113	7.07	VAR 159	2.74
VAR 114	4.07	VAR 160	4.81
VAR 115	6.26	VAR 161	2.19
VAR 116	7.01	VAR 162	2.41
VAR 117	3.12	VAR 163	8.03
VAR 118	4.67	VAR 164	2.05
VAR 119	1.15	VAR 165	5.74
VAR 120	2.74	VAR 166	9.20
VAR 121	1.46	VAR 167	7.22
VAR 122	2.95	VAR 168	3.70
VAR 123	2.47	VAR 169	6.31
VAR 124	2.05	VAR 170	3.42
VAR 125	2.63	VAR 171	1.39
VAR 126	1.82	VAR 172	2.05

VAR 127	7.30	VAR 173	3.41
VAR 128	2.76	VAR 174	4.11
VAR 175	3.33	VAR 207	3.57
VAR 176	3.41	VAR 208	3.88
VAR 177	3.94	VAR 209	2.37
VAR 178	2.56	VAR 210	3.28
VAR 179	3.27	VAR 211	1.33
VAR 180	2.27	VAR 212	2.72
VAR 181	2.84	VAR 213	2.25
VAR 182	3.97	VAR 214	2.33
VAR 183	2.02	VAR 215	3.11
VAR 184	4.94	VAR 216	1.72
VAR 185	4.80	VAR 217	3.85
VAR 186	3.61	VAR 218	3.51
VAR 187	2.31	VAR 219	3.97
VAR 188	1.88	VAR 220	1.22
VAR 189	1.83	VAR 221	2.49
VAR 190	3.22	VAR 222	2.76
VAR 191	2.28	VAR 223	2.93
VAR 192	2.57	VAR 224	4.45
VAR 193	1.97	VAR 225	4.24
VAR 194	2.72	VAR 226	1.52
VAR 195	1.72	VAR 227	2.39
VAR 196	1.87	VAR 228	1.61
VAR 197	1.94	VAR 229	1.18
VAR 198	1.80	VAR 230	2.06
VAR 199	4.64	VAR 231	1.50
VAR 200	5.93	VAR 232	2.68
VAR 201	2.50	VAR 233	2.05
VAR 202	3.37	VAR 234	2.25
VAR 203	2.67	VAR 235	3.66
VAR 204	3.34	VAR 236	1.87
VAR 205	3.45	VAR 237	2.50
VAR 206	4.63		

Table S3: Overview of the 30 variables with the highest total VIP-value based on the OPLS-DA model constructed with 78 variables. The variables are shown with decreasing VIP-value. Red and green arrows indicate respectively a decrease or increase in integration values of these variables in lung cancer patients compared to healthy controls. VAR: variable (assigned integration number); VIP: variable importance in projection.

Assigned integration number (variable)	Total VIP-value	Assigned integration number (variable)	Total VIP-value
VAR 195	3.61 ↓	VAR 061	1.19 ↑
VAR 218	2.28 ↓	VAR 034	1.18 ↓
VAR 186	2.19 ↓	VAR 080	1.10 ↑
VAR 185	2.13 ↓	VAR 126	1.10 ↓
VAR 187	2.03 ↓	VAR 062	1.10 ↑
VAR 156	1.88 ↓	VAR 082	1.03 ↑
VAR 057	1.83 ↑	VAR 067	1.03 ↑
VAR 222	1.83 ↑	VAR 127	0.95 ↓
VAR 042	1.57 ↓	VAR 081	0.95 ↑
VAR 059	1.54 ↑	VAR 055	0.87 ↑
VAR 066	1.31 ↑	VAR 207	0.86 ↓
VAR 035	1.27 ↓	VAR 202	0.85 ↑
VAR 060	1.25 ↑	VAR 090	0.85 ↑
VAR 227	1.25 ↑	VAR 083	0.84 ↑
VAR 209	1.22 ↓	VAR 078	0.82 ↑

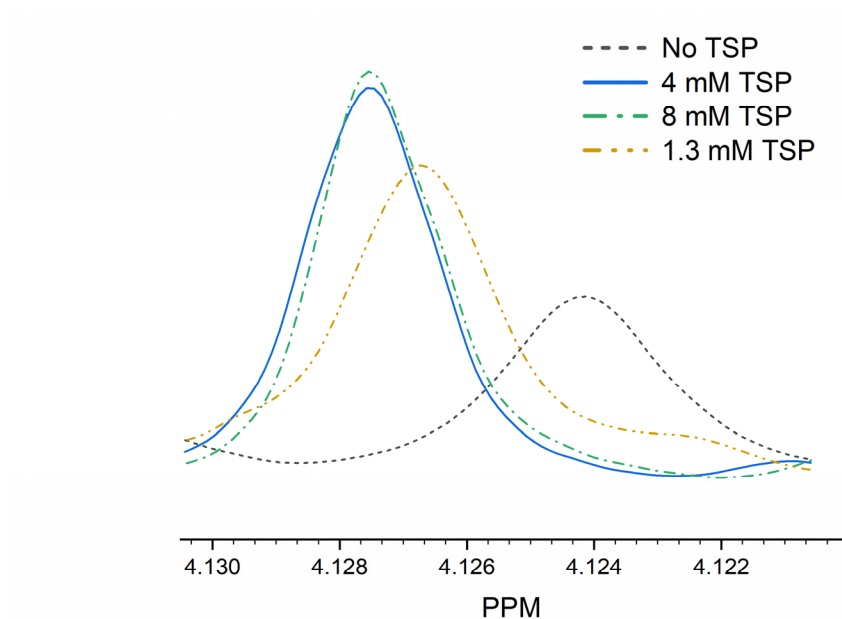


Figure S1: Zoom-in of a lactate signal (of the αCH quadruplet) upon the addition of different amounts of TSP. After addition of 4 mM TSP, stable chemical shifts and signal intensities are reached. Higher TSP concentrations do not influence the spectrum further. TSP: trimethylsilyl-2,2,3,3-tetradeteropropionic acid.

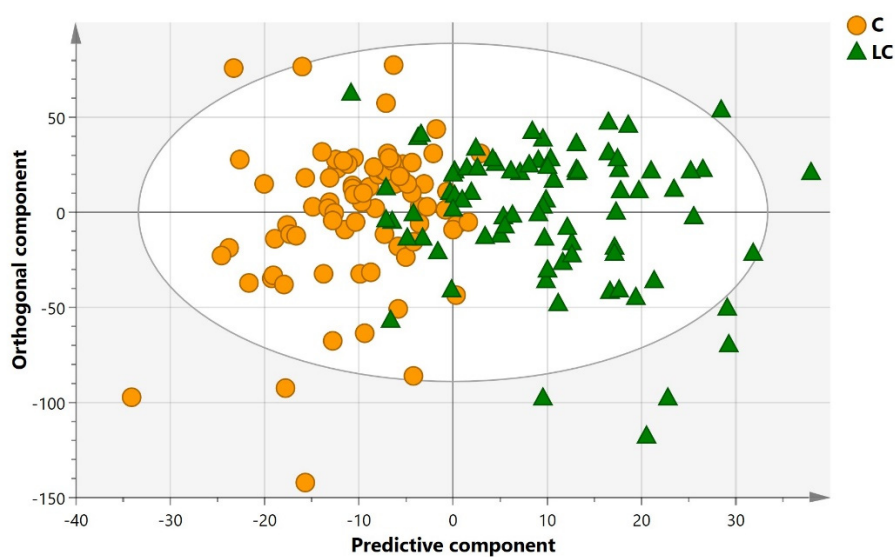


Figure S2: Orthogonal partial least squares discriminant analysis (OPLS-DA) classifier of the training cohort consisting of 80 controls and 80 lung cancer patients, using 221 variables. Model parameter values of $R^2X(\text{cum})$, $R^2Y(\text{cum})$ and $Q^2(\text{cum})$ are 0.833, 0.577 and 0.337 respectively. From this model, values of the loadings and jack knife interval are extracted for each variable in order to perform data reduction. C: controls; LC: lung cancer patients.

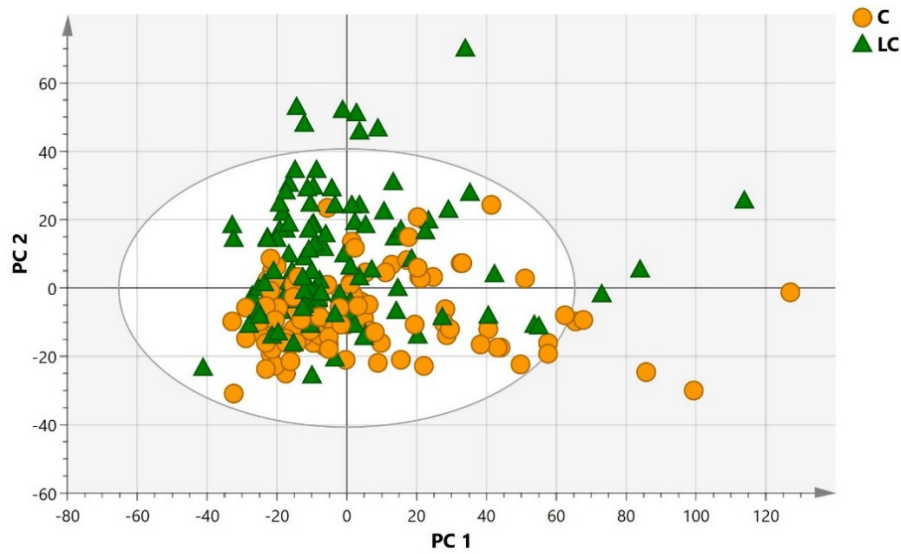


Figure S3: Principal component analysis (PCA) of all 232 subjects (using the reduced dataset of 78 variables) from the training and validation cohort showing a clustering trend for the controls and lung cancer patients. Using only the first two principal components, the PCA model shows a R^2 value of 0.774 and a Q^2 value of 0.749. C: controls; LC: lung cancer patients; PC: principal component.

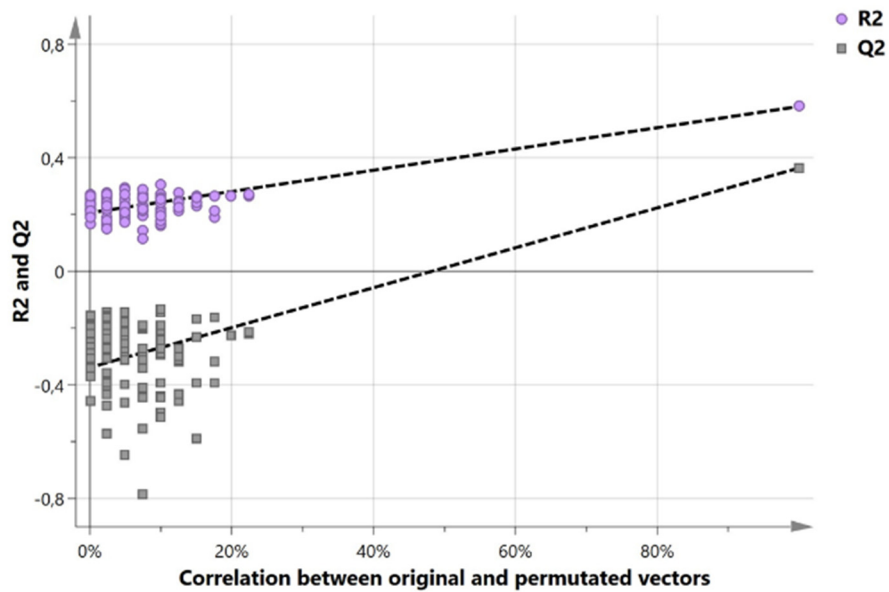


Figure S4: Permutation test of the training model using 100 permutations.