Additional file 2: Quality control of metabolites quantified with targeted metabolomics

Name	Abbreviation	Occurrence [a] (%)	CV_{QC} [b] (%)	CV_{tot} [c] (%)	Included [d]
Metabolites measured with MS					
Carnitine (free)	C0	100	7.3	19.7	Yes
Acetylcarnitine	C2	100	7.7	35.1	Yes
Propionylcarnitine	C3	100	12.3	28.7	Yes
Hydroxybutyrylcarnitine	C3-DC	75.7	19.8	64.2	No
Hydroxypropionylcarnitine	C3-OH	0.1	NA	NA	No
Propenoylcarnitine	C3:1	0.3	NA	31.7	No
Butyrylcarnitine	C4	100	10.4	41.1	Yes
Butenoylcarnitine	C4:1	3.6	13.6	30.3	No
Isovalerylcarnitine	C5	97.4	13.0	25.6	Yes
Glutarylcarnitine	C5-DC	21.2	10.8	28.1	No
Methylglutarylcarnitine	C5-M-DC	0.1	NA	NA	No
Hydroxyisovalerylcarnitine	C5-OH	14.8	31.0	30.6	No
Tiglylcarnitine	C5:1	0.3	NA	11.3	No
Glutaconylcarnitine	C5:1-DC	4.9	NA	112.8	No
Hexanoylcarnitine	C6	20.9	NA	31.0	No
Hexenoylcarnitine	C6:1	0.1	NA	NA	No
Pimelylcarnitine	C7-DC	70.1	20.4	33.6	No
Octanoylcarnitine	C8	33.7	59.3	41.7	No
Nonanoylcarnitine	C9	77.4	30.8	34.4	No
Decanoylcarnitine	C10	89.3	11.2	43.9	Yes
Decenoylcarnitine	C10:1	2.2	NA	27.6	No
Decadienoylcarnitine	C10:2	39.2	2.8	22.1	No
Dodecanoylcarnitine	C12	65.6	20.6	32.7	No
Dodecanedioylcarnitine	C12-DC	0.0	NA	NA	No
Dodecenoylcarnitine	C12:1	2.5	NA	14.5	No
Tetradecanoylcarnitine	C14	78.4	32.9	29.0	No
Tetradecenoylcarnitine	C14:1	100	15.6	31.0	No
Hydroxytetradecenoylcarnitine	C14:1-OH	21.3	NA	29.7	No
Tetradecadienoylcarnitine	C14:2	64	18.7	35.0	No
Hydroxytetradecadienoylcarnitine	C14:2-OH	12.7	9.8	54.1	No
Hexadecanoylcarnitine	C16	100	11.1	22.5	Yes
Hydroxyhexadecanolycarnitine	C16-OH	8.2	NA	32.0	No
Hexadecenoylcarnitine	C16:1	7.6	NA	21.1	No
Hydroxyhexadecanolycarnitine	C16:1-OH	11.9	NA	56.5	No
Hexadecadienoylcarnitine	C16:2	22.7	18.7	29.3	No
Hydroxyhexadecadienoylcarnitine	C16:2-OH	0.1	NA	NA	No
Octadecanoylcarnitine	C18	100	17.4	25.5	No
Octadecenoylcarnitine	C18:1	99.4	8.9	25.6	Yes
Hydroxyoctadecenoylcarnitine	C18:1-OH	0.3	NA	72.6	No
Octadecadienoylcarnitine	C18:2	100	11.7	31.0	Yes
Alanine	Ala	100	10.7	24.9	Yes
Arginine	Arg	100	11.8	25.4	Yes
Asparagine	Asn	100	21.2	21.3	No
Aspartate	Asp	99.2	16.8	38.2	No
Citrulline	Cit	100	23.5	28.8	No
Glutamine	Gln	100	18.6	22.5	No
Glutamate	Glu	100	22.6	57.7	No
Glycine	Gly	100	16.0	27.1	No
Histidine	His	100	11.4	15.4	Yes
Isoleucine	Ile	100	13.1	19.6	Yes
Leucine	Leu	100	10.2	18.2	Yes
Lysine	Lys	100	14.0	19.4	Yes
Methionine	Met	100	16.0	22.7	No
Ornithine	Orn	100	13.6	27.5	Yes
Phenylalanine	Phe	100	10.5	15.3	Yes

Additional file 2: (Continued)

Name	Abbreviation	Occurrence [a] (%)	CV_{QC} [b] (%)	CV_{tot} [c] (%)	Included [d]
Proline	Pro	100	11.4	25.2	Yes
Serine	Ser	100	19.8	28.0	No
Threonine	Thr	100	15.6	23.0	No
Tryptophan	Trp	100	14.5	19.5	Yes
Tyrosine	Tyr	100	13.3	22.8	Yes
Valine	Val	100	20.2	22.7	No
Acetylornithine	Ac-Orn	0.4	25.2	53.5	No
Asymmetric dimethylarginine	ADMA	89.4	23.3	33.8	No
Alpha-aminoadipic acid	Alpha-AAA	99.2	20.6	45.4	No
Carnosine	-	14.2	52.0	137.1	No
Creatinine	-	100	5.4	14.3	Yes
Dihydroxyphenylalanine	DOPA	19.1	55.5	49.4	No
Dopamine	-	2.1	NA	122.1	No
Histamine	-	0.7	NA	77.0	No
Kynurenine	-	100	16.8	25.5	No
Methionine-sulfoxide	Met-SO	100	19.5	76.4	No
Nitrotyrosine	Nitro-Tyr	2.7	NA	116.4	No
Hydroxyproline	OH-Pro	70.6	72.3	58.9	No
Phenylethylamine	PEA	0.2	NA	17.5	No
Putrescine	-	0.0	NA	NA	No
Sarcosine	-	100	15.1	30.4	No
Symmetric dimethylarginine	SDMA	99.7	46.1	52.4	No
Serotonin	-	100	40.1	129.2	No
Spermidine	-	99.0	12.6	48.6	Yes
Spermine	-	18.1	0.4	240.5	No
Taurine	-	100	11.4	26.1	Yes
Phosphatidylcholine (diacyl) Cx:y	PC aa C24:0	31.2	14.4	62.0	No
Phosphatidylcholine (diacyl) Cx:y	PC aa C26:0	0.8	NA	31.1	No
Phosphatidylcholine (diacyl) Cx:y	PC aa C28:1	100	7.9	22.4	Yes
Phosphatidylcholine (diacyl) Cx:y	PC aa C30:0	100	9.9	29.3	Yes
Phosphatidylcholine (diacyl) Cx:y	PC aa C30:2	0.1	NA	NA	No
Phosphatidylcholine (diacyl) Cx:y	PC aa C32:0	100	9.5	20.1	Yes
Phosphatidylcholine (diacyl) Cx:y	PC aa C32:1	100	9.9	46.7	Yes
Phosphatidylcholine (diacyl) Cx:y	PC aa C32:2	100	12.1	37.0	Yes
Phosphatidylcholine (diacyl) Cx:y	PC aa C32:3	100	15.1	27.2	No
Phosphatidylcholine (diacyl) Cx:y	PC aa C34:1	100	9.1	22.0	Yes
Phosphatidylcholine (diacyl) Cx:y	PC aa C34:2	100	12.3	19.3	Yes
Phosphatidylcholine (diacyl) Cx:y	PC aa C34:3	100	12.2	25.1	Yes
Phosphatidylcholine (diacyl) Cx:y	PC aa C34:4	100	12.5	31.4	Yes
Phosphatidylcholine (diacyl) Cx:y	PC aa C36:0	100	14.2	34.9	Yes
Phosphatidylcholine (diacyl) Cx:y	PC aa C36:1	100	11.7	22.9	Yes
Phosphatidylcholine (diacyl) Cx:y	PC aa C36:2	100	10.0	18.7	Yes
Phosphatidylcholine (diacyl) Cx:y	PC aa C36:3	100	8.8	19.6	Yes
Phosphatidylcholine (diacyl) Cx:y	PC aa C36:4	100	9.7	21.3	Yes
Phosphatidylcholine (diacyl) Cx:y	PC aa C36:5	100	10.4	46.6	Yes
Phosphatidylcholine (diacyl) Cx:y	PC aa C36:6	100	11.8	36.4	Yes
Phosphatidylcholine (diacyl) Cx:y	PC aa C38:0	100	12.7	28.5	Yes
Phosphatidylcholine (diacyl) Cx:y	PC aa C38:1	96.8	22.4	42.5	No
Phosphatidylcholine (diacyl) Cx:y	PC aa C38:3	100	9.0	22.1	Yes
Phosphatidylcholine (diacyl) Cx:y	PC aa C38:4	100	10.1	23.1	Yes
Phosphatidylcholine (diacyl) Cx:y	PC aa C38:5	100	8.6	24.7	Yes
Phosphatidylcholine (diacyl) Cx:y	PC aa C38:6	100	8.6	29.2	Yes
Phosphatidylcholine (diacyl) Cx:y	PC aa C40:1	72.8	13.9	24.0	Yes
Phosphatidylcholine (diacyl) Cx:y	PC aa C40:2	100	16.0	38.3	No
Phosphatidylcholine (diacyl) Cx:y	PC aa C40:3	100	12.6	25.7	Yes
Phosphatidylcholine (diacyl) Cx:y	PC aa C40:4	100	11.3	28.4	Yes

Additional file 2: (Continued)

Name	Abbreviation	Occurrence [a] (%)	CV_{QC} [b] (%)	CV_{tot} [c] (%)	Included [d]
Phosphatidylcholine (diacyl) Cx:y	PC aa C40:5	100	8.9	26.7	Yes
Phosphatidylcholine (diacyl) Cx:y	PC aa C40:6	100	8.7	32.3	Yes
Phosphatidylcholine (diacyl) Cx:y	PC aa C42:0	100	14.1	28.9	Yes
Phosphatidylcholine (diacyl) Cx:y	PC aa C42:1	100	13.2	28.7	Yes
Phosphatidylcholine (diacyl) Cx:y	PC aa C42:2	100	16.0	28.5	No
Phosphatidylcholine (diacyl) Cx:y	PC aa C42:4	100	13.6	34.5	Yes
Phosphatidylcholine (diacyl) Cx:y	PC aa C42:5	100	13.1	29.0	Yes
Phosphatidylcholine (diacyl) Cx:y	PC aa C42:6	100	15.7	31.7	No
Phosphatidylcholine (acyl-alkyl) Cx:y	PC ae C30:0	99.4	34.8	33	No
Phosphatidylcholine (acyl-alkyl) Cx:y	PC ae C30:1	27.8	66.8	62.7	No
Phosphatidylcholine (acyl-alkyl) Cx:y	PC ae C30:2	100	15.0	33.4	Yes
Phosphatidylcholine (acyl-alkyl) Cx:y	PC ae C32:1	100	16.6	25.4	No
Phosphatidylcholine (acyl-alkyl) Cx:y	PC ae C32:2	100	19.7	26.9	No
Phosphatidylcholine (acyl-alkyl) Cx:y	PC ae C34:0	100	11.8	25.5	Yes
Phosphatidylcholine (acyl-alkyl) Cx:y	PC ae C34:1	100	11.4	20.1	Yes
Phosphatidylcholine (acyl-alkyl) Cx:y	PC ae C34:2	100	9.3	25.0	Yes
Phosphatidylcholine (acyl-alkyl) Cx:y	PC ae C34:3	100	12.4	28.6	Yes
Phosphatidylcholine (acyl-alkyl) Cx:y	PC ae C36:0	100	27.9	52.4	No
Phosphatidylcholine (acyl-alkyl) Cx:y	PC ae C36:1	100	11.0	23.0	Yes
Phosphatidylcholine (acyl-alkyl) Cx:y	PC ae C36:2	100	10.7	22.2	Yes
Phosphatidylcholine (acyl-alkyl) Cx:y	PC ae C36:3	100	10.2	22.6	Yes
Phosphatidylcholine (acyl-alkyl) Cx:y	PC ae C36:4	100	9.7	24.5	Yes
Phosphatidylcholine (acyl-alkyl) Cx:y	PC ae C36:5	100	10.4	27.4	Yes
Phosphatidylcholine (acyl-alkyl) Cx:y	PC ae C38:0	100	13.4	29.3	Yes
Phosphatidylcholine (acyl-alkyl) Cx:y	PC ae C38:1	58.9	12.5	80.4	Yes
Phosphatidylcholine (acyl-alkyl) Cx:y	PC ae C38:2	100	13.5	31.4	Yes
Phosphatidylcholine (acyl-alkyl) Cx:y	PC ae C38:3	100	10.0	24.5	Yes
Phosphatidylcholine (acyl-alkyl) Cx:y	PC ae C38:4	100	8.8	20.7	Yes
Phosphatidylcholine (acyl-alkyl) Cx:y	PC ae C38:5	100	8.7	20.1	Yes
Phosphatidylcholine (acyl-alkyl) Cx:y	PC ae C38:6	100	11.3	26.6	Yes
Phosphatidylcholine (acyl-alkyl) Cx:y	PC ae C40:0	100	12.0	28.7	Yes
Phosphatidylcholine (acyl-alkyl) Cx:y	PC ae C40:1	100	12.4	23.5	Yes
Phosphatidylcholine (acyl-alkyl) Cx:y	PC ae C40:2	100	10.3	23.2	Yes
Phosphatidylcholine (acyl-alkyl) Cx:y	PC ae C40:3	100	10.0	33.3	Yes
Phosphatidylcholine (acyl-alkyl) Cx:y	PC ae C40:4	100	15.1	23.3	No
Phosphatidylcholine (acyl-alkyl) Cx:y	PC ae C40:5	100	10.0	23.1	Yes
Phosphatidylcholine (acyl-alkyl) Cx:y	PC ae C40:6	100	9.5	25.3	Yes
Phosphatidylcholine (acyl-alkyl) Cx:y	PC ae C42:0	11.5	13.2	20.3	No
Phosphatidylcholine (acyl-alkyl) Cx:y	PC ae C42:1	100	14.9	25.5	Yes
Phosphatidylcholine (acyl-alkyl) Cx:y	PC ae C42:2	100	12.0	22.9	Yes
Phosphatidylcholine (acyl-alkyl) Cx:y	PC ae C42:3	100	13.1	22.7	Yes
Phosphatidylcholine (acyl-alkyl) Cx:y	PC ae C42:4	100	10.7	23.7	Yes
Phosphatidylcholine (acyl-alkyl) Cx:y	PC ae C42:5	100	8.3	21.2	Yes
Phosphatidylcholine (acyl-alkyl) Cx:y	PC ae C44:3	98.8	11.7	32.8	Yes
Phosphatidylcholine (acyl-alkyl) Cx:y	PC ae C44:4	99.9	11.3	24.3	Yes
Phosphatidylcholine (acyl-alkyl) Cx:y	PC ae C44:5	100	9.9	25.5	Yes
Phosphatidylcholine (acyl-alkyl) Cx:y	PC ae C44:6	100	10.5	25.5	Yes
Lysophosphatidylcholine Cx:y	LPC C14:0	0.1	NA	NA	No
Lysophosphatidylcholine Cx:y	LPC C16:0	100	13.3	23.1	Yes
Lysophosphatidylcholine Cx:y	LPC C16:1	100	14.3	29.8	Yes
Lysophosphatidylcholine Cx:y	LPC C17:0	100	11.7	28.6	Yes
Lysophosphatidylcholine Cx:y	LPC C18:0	100	9.4	23.4	Yes
Lysophosphatidylcholine Cx:y	LPC C18:1	100	9.7	25.0	Yes
Lysophosphatidylcholine Cx:y	LPC C18:2	100	13.9	32.1	Yes
Lysophosphatidylcholine Cx:y	LPC C20:3	100	9.3	26.6	Yes
Lysophosphatidylcholine Cx:y	LPC C20:4	100	10.5	27.8	Yes

Additional file 2: (Continued)

Name	Abbreviation	Occurrence [a] (%)	CV_{QC} [b] (%)	CV_{tot} [c] (%)	Included [d]
Lysophosphatidylcholine Cx:y	LPC C24:0	87.9	12.5	63.7	Yes
Lysophosphatidylcholine Cx:y	LPC C26:0	71.4	17.9	87.8	No
Lysophosphatidylcholine Cx:y	LPC C26:1	95.0	17.6	81.8	No
Lysophosphatidylcholine Cx:y	LPC C28:0	69.0	20.6	67.2	No
Lysophosphatidylcholine Cx:y	LPC C28:1	100	17.1	44.4	No
Hydroxysphingomyelin Cx:y	SM-OH C14:1	100	12.1	23.0	Yes
Hydroxysphingomyelin Cx:y	SM-OH C16:1	100	12.4	23.2	Yes
Hydroxysphingomyelin Cx:y	SM-OH C22:1	100	13.0	23.1	Yes
Hydroxysphingomyelin Cx:y	SM-OH C22:2	100	23.3	22.3	No
Hydroxysphingomyelin Cx:y	SM-OH C24:1	100	26.7	31.0	No
Sphingomyelin Cx:y	SM C16:0	100	12.6	18.7	Yes
Sphingomyelin Cx:y	SM C16:1	100	11.3	18.5	Yes
Sphingomyelin Cx:y	SM C18:0	100	11.3	20.6	Yes
Sphingomyelin Cx:y	SM C18:1	100	11.9	21.9	Yes
Sphingomyelin Cx:y	SM C20:2	99.9	18.3	48.9	No
Sphingomyelin Cx:y	SM C22:3	4.4	85.0	123.3	No
Sphingomyelin Cx:y	SM C24:0	100	20.1	27.1	No
Sphingomyelin Cx:y	SM C24:1	100	12.0	20.6	Yes
Sphingomyelin Cx:y	SM C26:0	99.9	70.2	42.5	No
Sphingomyelin Cx:y	SM C26:1	99.9	54.6	36.8	No
Hexoses	H1	100	10.6	16.7	Yes
Metabolites measured by NMR					
1-Methylguanidine	-	12.9	9.6	43.3	No
1-Methylhistidine	-	0.1	22.2	27.0	No
1, 2-Propanediol	-	35.8	6.3	51.9	No
2-Aminobutyrate	-	100	11.5	23.3	Yes
2-Hydroxybutyrate	-	100	5.5	34.6	Yes
2-Hydroxyisovalerate	-	71.5	7.0	71.0	Yes
2-Ketoglutarate	-	95.0	9.1	19.4	Yes
2-Oxoisocaproate	-	99.5	9.8	24.8	Yes
2-Propanol	-	41.8	18.9	688.9	No
3-Hydroxybutyrate	-	100	6.1	123.3	Yes
3-Hydroxyisovalerate	-	96.5	8.9	23.5	Yes
3-Methyl-2-oxovalerate	-	63.0	30.5	37.6	No
3-Methylhistidine	-	0.7	23.4	78.2	No
Acetate	-	100	8.1	64.1	Yes
Acetoacetate	-	94.9	6.8	105.5	Yes
Acetone	-	100	15.5	57.7	No
Acetylcarnitine	-	100	6.2	30.0	Yes
Acetylglycine	-	37.6	13.4	48.1	No
Alanine	-	100	5.7	22.9	Yes
Arginine	-	94.7	8.7	14.5	Yes
Asparagine	-	97.7	6.9	14.9	Yes
Aspartate	-	0.3	15.8	24.9	No
Betaine	-	100	7.6	17.3	Yes
Carnitine	-	100	5.9	18.8	Yes
Choline	-	100	5.8	20.5	Yes
Citrate	-	100	6.2	21.7	Yes
Creatine	-	100	6.4	52.7	Yes
Creatinine	-	100	6.5	17.3	Yes
Dimethylamine	-	1.5	12.1	44.8	No
Dimethylglycine	-	99.6	6.4	40.7	Yes
Dimethylsulfone	-	100	7.3	45.5	Yes
Ethanol	-	96.2	105.6	506.7	No
Formate	-	99.3	11.3	33.5	Yes
Glucose	-	100	5.8	15.8	Yes

Additional file 2: (Continued)

Name	Abbreviation	Occurrence [a] (%)	CV_{QC} [b] (%)	CV_{tot} [c] (%)	Included [d]
Glutamate	-	82.6	7.3	51.4	Yes
Glutamine	-	100	5.8	13.0	Yes
Glycerol	-	100	70.7	71.5	No
Glycine	-	100	7.4	20.4	Yes
Hippurate	-	0.1	27.1	38.3	No
Histidine	-	100	5.9	12.9	Yes
Hypoxanthine	-	0.7	20.0	81.4	No
Isobutyrate	-	0.3	25.7	56.8	No
Isocaproate	-	99.1	7.2	8.5	Yes
Isoleucine	-	100	5.8	18.6	Yes
Isovalerate	-	0.3	55.3	123.1	No
Lactate	-	100	5.8	39.6	Yes
Leucine	-	100	5.6	16.3	Yes
Lysine	-	100	5.8	15.4	Yes
Methanol	-	100	45.2	62.0	No
Methionine	-	100	6.6	13.9	Yes
Myo-inositol	-	88.6	11.0	22.4	Yes
O-phosphocholine	-	98.8	13.7	29.8	Yes
Ornithine	-	100	5.8	23.0	Yes
Phenylalanine	-	99.7	6.9	13.8	Yes
Proline	-	100	7.5	25.8	Yes
Propionate	-	42.3	27.5	32.5	No
Pyroglutamate	-	1.5	25.1	29.1	No
Pyruvate	-	99.7	6.2	35.0	Yes
Sarcosine	-	12.5	8.9	23.6	No
Glutamate	-	82.6	7.3	51.4	Yes
Glutamine	-	100	5.8	13.0	Yes
Glycerol	-	100	70.7	71.5	No
Glycine	-	100	7.4	20.4	Yes
Hippurate	-	0.1	27.1	38.3	No
Histidine	-	100	5.9	12.9	Yes
Hypoxanthine	-	0.7	20.0	81.4	No
Isobutyrate	-	0.3	25.7	56.8	No
Isocaproate	-	99.1	7.2	8.5	Yes
Isoleucine	-	100	5.8	18.6	Yes
Isovalerate	-	0.3	55.3	123.1	No
Lactate	-	100	5.8	39.6	Yes
Leucine	-	100	5.6	16.3	Yes
Lysine	-	100	5.8	15.4	Yes
Methanol	-	100	45.2	62.0	No
Methionine	-	100	6.6	13.9	Yes
Myo-inositol	-	88.6	11.0	22.4	Yes
O-phosphocholine	-	98.8	13.7	29.8	Yes
Ornithine	-	100	5.8	23.0	Yes
Phenylalanine	-	99.7	6.9	13.8	Yes
Proline	-	100	7.5	25.8	Yes
Propionate	-	42.3	27.5	32.5	No
Pyroglutamate	-	1.5	25.1	29.1	No
Pyruvate	-	99.7	6.2	35.0	Yes
Sarcosine	-	12.5	8.9	23.6	No
Serine	-	100	6.0	19.5	Yes
Succinate	-	89.4	15.2	43.1	No
Threonine	-	99.7	6.9	16.3	Yes
Trigonelline	-	0.4	55.3	99.2	No
Trimethylamine	-	88.7	7.0	35.2	Yes
Trimethylamine-N-oxide	-	100	11.8	48.2	Yes

Additional file 2: (Continued)

Name	Abbreviation	Occurrence [a] (%)	CV_{QC} [b] (%)	CV_{tot} [c] (%)	Included [d]
Tyrosine	-	100	6.0	18.7	Yes
Valine	-	100	5.8	16.0	Yes

[a] Occurrence (%): Percentage of measurements above the detection limit in the nested cohort.

[b] CV_{QC} (%): Analytical coefficient of variation, calculated based on the measurements in the unspiked quality control (QC) samples.

[c] CV_{tot} (%): Total coefficient of variation, calculated based on the measurements in the nested cohort.

[d] Included (Yes): Occurrence $\geq 50\%$, and $CV_{QC} \leq 15\%$.