Supplementary Table 1. Parameters selected for the MS-DIAL pre-processing of raw metabolomics data obtained in positive or negative ionization mode.

Data collection parameters	Positive ion mode	Negative ion mode
Retention time		
start	0	0
end	100	100
Mass range		
start	0	0
end	5000	5000
Centroid parameters		
MS1 tolerance	0.01	0.005
MS2 tolerance	0.025	0.025
Isotope recognition		
Maximum charged number	2	2
Peak detection parameters		
Smoothing method	LinearWeightedMovingAverage	LinearWeightedMovingAverage
Smoothing level	3	3
Minimum peak width	5	5
Minimum peak height	50000	50000
Peak spotting parameters		
Mass slice width	0.1	0.1
Deconvolution parameters		
Sigma window value	0.5	0.5
MS2Dec amplitude cut-off	30	30
Exclude after precursor	TRUE	TRUE
Keep isotope until	0.5	0.5
Keep original precursor isotpes	FALSE	FALSE
Exclude after precursor	TRUE	TRUE
Retention time tolerance	0.1	0.01
Accurate mass tolerance	0.01	0.05
Identification score cut-off	85	90
Adduct ion setting		
	$[M+H]^+$	$[M+H]^-$
	$[M+NH_4]^+$	$[M+NH_4]^-$
	$[M+Na]^+$	$[M+Na]^-$
	$[M+CH_3OH+H]^+$	$[M+CH_3OH+H]^-$
	$[M+ACN+H]^+$	$[M+ACN+H]^-$
	$[M+H-H_2O]^+$	$[M+H-H_2O]^-$
	$[M+H-2H_2O]^+$	$[M+H-2H_2O]^-$
	$[M+ACN+Na]^+$	$[M+ACN+Na]^-$
	$[2M+H]^+$	$[2M+H]^-$
	$[2M+NH_4]^+$	$[2M+NH_4]^-$
	$[2M+Na]^+$	$[2M+Na]^-$
	$[2M+ACN+H]^+$	$[2M+ACN+H]^-$
	$[2M+ACN+Na]^+$	$[2M+ACN+Na]^-$
Alignment parameters setting		
Retention time tolerance	0.1	0.1

MS1 tolerance	0.01	0.015
Retention time factor	0.5	0.5
MS1 factor	0.7	0.7
Peak count filter	80	80
QC at least filter	FALSE	FALSE
Remove feature based on peak height fold-change	TRUE	TRUE
Sample max / blank average	5	5
Sample average / blank average	5	5
Keep identified and annotated metabolites	TRUE	TRUE
Keep removable features and assign the tag for checking	TRUE	TRUE
Replace true zero values with 1/2 of minimum peak height over all samples	FALSE	FALSE

Supplementary Table 2. List of proteins included in the statistical analyses.

Accession number*	No#	Protein name	MW [kDa]
ACTB	1	Actin, cytoplasmic 1	42
ALBU1	2	Serum albumin 1	67
B5X1B5	3	Alpha-enolase	47
B5XFE6	4	Deoxyribonuclease	32
B5X3U6	5	Heat shock cognate 70 kDa protein	72
B5X4R7	6	Transketolase	68
C0PU67	7	Gelsolin (Fragment)	59
B5X2B3	8	Serotransferrin	75
B5X4K4	9	L-lactate dehydrogenase	36
B9EM17	10	Transaldolase	37
B5X1Z0	11	WD repeat-containing protein 1-like	66
B5X3K2	12	Glyceraldehyde-3-phosphate dehydrogenase	36
B5DGE0	13	Adenosylhomocysteinase	48
B5XD42	14	Hemoglobin subunit beta	16
B5DGL3	15	Triosephosphate isomerase	27
C0H9I1	16	Fructose-bisphosphate aldolase	40
B5XBZ2	17	Glutathione S-transferase P	23
C0H9M4	18	Glucose-6-phosphate isomerase	62
B5X6G0	19	SH3 domain-binding glutamic acid-rich-like protein 3	10
B5XDT6	20	Glutathione S-transferase P	24
C0PUL2	21	Lysine-tRNA ligase (Fragment)	65
B5X2C6	22	Alanyl-tRNA synthetase, cytoplasmic	107
Q91471	23	Beta-globin OS=Salmo salar	16
B5X1S6	24	Rab GDP-dissociation inhibitor	51
B9ELX6	25	Cofilin-2	19
B5XGV3	26	Deoxyribonuclease	31
C0PUK9	27	Pyruvate kinase (Fragment)	57
C0H9C0	28	Tropomyosin alpha-3 chain	28
C0H9U3	29	6-phosphogluconate dehydrogenase, decarboxylating	53
B9ENX5	30	Glutathione transferase omega-1	28
B5X9C6	31	Aldose reductase	35
B5XFF2	32	Apolipoprotein A-I-	28
B5XF08	33	14-3-3 protein beta/alpha-1-like	28
B5X4T6	34	Aminopeptidase B	71
B5XC25	35	Cofilin-2	19
B5XE59	36	GDP-mannose 4,6 dehydratase	42
B5X5I8	37	Profilin	15
C0PU58	38	Protein disulfide-isomerase (Fragment)	47
C0H820	39	Malate dehydrogenase	36

B5X0W2	40	Rho GDP-dissociation inhibitor 1	23
B5DGE7	41	Betaine-homocysteine methyltransferase	44
C0HBI8	42	Prolyl endopeptidase	80
C0H808	43	Tubulin beta chain	50
B5XGZ2	44	Glutathione S-transferase P	23
B9EN93	45	Cold-inducible RNA-binding protein	16
Q9W6K6	46	Heat shock protein 90-beta 1	83
C0HAA7	47	Alpha-galactosidase	48
B5X2U4	48	Asparagine synthetase	64
C0H9I5	49	Alpha-actinin-1	103
B5XAP9	50	Argininosuccinate synthase	47
B9ENS1	51	Glutathione S-transferase A	26
B5X1B9	52	Thimet oligopeptidase	78
B5DGF0	53	Adenosine kinase A	43
B5X1V6	54	Cystathionine gamma-lyase	44
B5XCJ8	55	Nucleoside diphosphate kinase	17
B5X2Q1	56	Malate dehydrogenase	36
B5X4C0	57	Tropomyosin alpha-3 chain	29
C0H868	58	S-(hydroxymethyl)glutathione dehydrogenase	40
B5X2G1	59	Sialic acid synthase	40
B5DGC6	60	Nucleoside diphosphate kinase	17
B9EPZ9	61	Thioredoxin	16
C0HA95	62	Calpastatin	97
B5DGE8	63	Tubulin alpha chain	50
ALBU2	64	Serum albumin 2	67
B5X348	65	Iron-responsive element-binding protein 1	100
C0H9N2	66	Elongation factor 2	96
C0H7I8	67	Hemoglobin subunit alpha	15
B5X746	68	Hemoglobin subunit alpha-4	16
B9EPT4	69	Peptidyl-prolyl cis-trans isomerase	18
B5X2H6	70	Aldehyde dehydrogenase family 9 member A1-A	55
B5X0S9	71	aldehyde dehydrogenase family 7 member A1 homolog	59
B5DGB9	72	14-3-3 protein beta/alpha-2	28
B5X397	73	78 kDa glucose-regulated protein precursor	72
C0PU59	74	Echinoderm microtubule-associated protein-like 1 (Fragment)	68
C0H939	75	Actin-related protein 2-A	45
C0HA52	76	Major vault protein	98
B5X7X7	77	Peroxiredoxin-1	22
B5DFX8	78	Phosphoglycerate kinase	45
B5XGN3	79	Carbonyl reductase 1	30
K4LAG6	80	Calpastatin 2	32
B5X1H7	81	Protein disulfide-isomerase	55
C0HAL2	82	Elongation factor 1-alpha	50

B5X8M6	83	Transgelin	22
C0HB84	84	Moesin	68
B5X1B2	85	Phosphoacetylglucosamine mutase	60
B5X931	86	Carbonyl reductase 1	30
B5DG40	87	actin, alpha cardiac-like	42
O73866	88	Fructose-bisphosphate aldolase	39
B5X340	89	Asparaginyl-tRNA synthetase, cytoplasmic	64
B5DFX7	90	Heat shock cognate 70 kDa protein	71
B5XAM0	91	Thymosin beta-12	5
B5XA95	92	Protein S100	11
B5X764	93	Inorganic pyrophosphatase	33
B5X5Q6	94	Peroxiredoxin-5, mitochondrial	20
B9ELZ6	95	Fatty acid-binding protein 7	15
B5XGM0	96	protein S100-A5-like	12
B5X2E1	97	Adenylyl cyclase-associated protein	50
B5DG94	98	Peptidyl-prolyl cis-trans isomerase	18
B5XB10	99	Triosephosphate isomerase	27
B5X3R3	100	F-actin-capping protein subunit beta isoform X2	31
B5XCY4	101	14-3-3 protein beta/alpha-1	28
C0H9G2	102	Bifunctional purine biosynthesis protein PURH	64
B9EMD4	103	Elongation factor 1-gamma	51
B5XB38	104	Beta-microseminoprotein precursor	13
C0H878	105	Alpha-enolase	47
B5X779	106	Glutathione S-transferase 3	24
B5X5D9	107	Thymosin beta-a	5
C0PUI9	108	Fructose-1,6-bisphosphatase 1 (Fragment)	36
B5XGX4	109	Protein S100	10
B5X320	110	Keratin, type II cytoskeletal 8	59
B5DGD5	111	Arp2/3 complex 34 kDa subunit	34
B9EPW1	112	Proteasome activator complex subunit 1	29
C0HBE5	113	Actin-related protein 3	47
B5X1T5	114	Beta-hexosaminidase	62
B5X0S0	115	Creatine kinase B-type	43
B5XF13	116	Anterior gradient protein 2 homolog	19
B5X2E5	117	Rho GDP-dissociation inhibitor 1	23
B5X435	118	Dipeptidyl peptidase 3	82
RAN	119	GTP-binding nuclear protein Ran	24
B5DFX5	120	14-3-3 protein epsilon-like isoform X2	29
Q70SU8	121	Cathepsin M precursor	39
B5XBQ0	122	Lactoylglutathione lyase	20
C0H826	123	Alcohol dehydrogenase	37
B5X4A7	124	Angiotensinogen precursor	52
C0PUM7	125	Serine/threonine-prot. phosphatase 2A 65 kDa reg. sub. A β (frag.)	65

B5X344	126	Transforming protein RhoA	22
B5X4T2	127	Profilin	15
B5DG32	128	Rab GDP-dissociation inhibitor	50
B5XDI6	129	Plastin-2	25
B5X6W1	130	Calpain small subunit 1	25
B5XDS7	131	GDP-L-fucose synthetase	37
B5X0W7	132	N(G),N(G)-dimethylarginine dimethylaminohydrolase 2 isoform X1	32
B5X1H6	133	N-acylneuraminate cytidylyltransferase 1	48
B5XAW0	134	Nucleoside diphosphate kinase	17
B5X374	135	Xaa-Pro aminopeptidase 1	70
B5X4K2	136	Cytosolic non-specific dipeptidase	31
B5XDV8	137	Cystatin-B	11
B5XBX3	138	Hemoglobin subunit beta	16
C0H8U7	139	Cold-inducible RNA-binding protein	19
B5X2M8	140	T-complex protein 1 subunit beta	58
B5X0R8	141	Phosphoglycerate mutase	29
B5DFW8	142	Phosphomannomutase	28
B5X3Q1	143	ADP-ribosylation factor 1	21
B9EM68	144	Superoxide dismutase [Cu-Zn]	16
C0H8N3	145	Heterogeneous nuclear ribonucleoprotein A1	38
B5X1I3	146	Glucose-6-phosphate 1-dehydrogenase	59
B5X6E1	147	Proteasome activator complex subunit 2	28
B5XD07	148	Ubiquitin-conjugating enzyme E2 L3	18
B5XDR4	149	Myosin light polypeptide 6	17
C0H9A4	150	Myotrophin	13
B9EPN0	151	6-phosphogluconolactonase isoform X1	27
C0H9H1	152	Alpha-1,4 glucan phosphorylase	98
B5X4M2	153	T-complex protein 1 subunit theta	59
B5X2H9	154	F-actin-capping protein subunit alpha-1 isoform X1	33
C0HAI2	155	L-lactate dehydrogenase	36
B5X5V9	156	C type lectin receptor B isoform X1	28
C0H958	157	Epithelial cadherin	97
B5XFG4	158	17-beta-hydroxysteroid dehydrogenase 14-like	28
C0HBJ4	159	Ras-related protein Rab-1A	22
C0PU50	160	Myosin-9 (Fragment)	60
B5X7N9	161	PDZ and LIM domain protein 1	34
C0H959	162	Coronin	51
C0PUU5	163	Calreticulin (Fragment)	45
B8YBH8	164	Non-specific Cytotoxic Cell receptor protein-1	27
B5X431	165	Ras-related protein Rab-7a	23
Q6R758	166	muscle Fatty acid-binding protein	15
B5DFV4	167	DJ-1 protein	20
C0HA30	168	T-complex protein 1 subunit alpha	60

B5XCL8	169	Lipocalin	20
B5X8H5	170	Peroxiredoxin	22
B5DG90	171	RAB2A, member RAS oncogene family	24
C0HBT4	172	EF-hand domain-containing protein D2	26
B5X7L6	173	Flavin reductase	23
B5X688	174	Gastrotropin	14
B5X1Z2	175	T-complex protein 1 subunit delta	57
B5XCZ5	176	Actin-related protein 2/3 complex subunit 5	17
B5XBH3	177	Apolipoprotein A-I precursor	30
B5XB84	178	Cofilin-2	19
C0PUR6	179	Carboxylic ester hydrolase (Fragment)	61
B5DH01	180	Tubulin alpha chain	50
B5RI17	181	T-complex protein 1 subunit gamma (Fragment)	60
Q4ZHV1	182	Caspase 6A (Fragment)	33
B5XCM2	183	Calmodulin	15
C0HAB4	184	N-acetylglucosamine-6-sulfatase	58
B9ELE8	185	Ubiquitin	18
B5X9N1	186	Heterogeneous nuclear ribonucleoprotein A0	29
C0H850	187	Cathepsin B	36
B5X189	188	Eukaryotic translation initiation factor 4H	27
B5XAC1	189	Translationally-controlled tumor like protein	19
B5X3D1	190	Glucosamine--fructose-6-phosphate aminotransferase 1	77
C0HAU4	191	Acidic leucine-rich nuclear phosphoprotein 32 family member E	28
C0H8S8	192	F-actin-capping protein subunit alpha-1-like	33
C0H7R0	193	Peptidyl-prolyl isomerase	12
B5X8L7	194	Cellular retinoic acid-binding protein	16
B5X3F7	195	Thymidine phosphorylase	48
B5X9U3	196	Actin-related protein 2/3 complex subunit 4	20
C0H9N7	197	Serine/threonine-protein phosphatase	35
B5XE81	198	Cell division control protein 42 homolog	21
C0H9F4	199	2,3-cyclic-nucleotide 3-phosphodiesterase	75
C0PUF6	200	FAM139A (Fragment)	81
PTER	201	Phosphotriesterase-related protein	39
B5XF51	202	Aldose reductase	36
C0HAA0	203	ATP-dependent 6-phosphofructokinase	86
B5DFV7	204	SET translocation	31
B5XDU3	205	14-3-3 protein zeta	28
B5XGW7	206	Actin-related protein 2/3 complex subunit 3	20
B5X1Z3	207	N-acetylgalactosamine kinase	50
A6PZ97	208	Lysozyme g	22
Q9PTA8	209	Antithrombin	51
B5X304	210	Probable aminopeptidase NPEPL1	55
B5X265	211	Ran-specific GTPase-activating protein	24

B5X0R3	212	Glyoxylate reductase/hydroxypyruvate reductase	35
B5X0Z8	213	Phenylalanyl-tRNA synthetase beta chain	66
B5DG28	214	DNA-(apurinic or apyrimidinic site) lyase	35
B5XAK9	215	ADP-sugar pyrophosphatase isoform X2	24
B5DGU6	216	Proteasome subunit alpha type	28
B5XEM0	217	Delta-aminolevulinic acid dehydratase	36
B5DGJ1	218	Proteasome subunit beta type	23
B5X2G5	219	Plasminogen activator inhibitor 1 RNA-binding	46
B5X2M7	220	Twinfilin-1	40
B5X2K3	221	Leukotriene A(4) hydrolase	71
B5XCH3	222	Peptidyl-prolyl cis-trans isomerase	24
B5XBK0	223	Malate dehydrogenase	35
B5X2W5	224	Carboxypeptidase	53
B5XAL3	225	Proteasome subunit alpha type	29
B5X7H1	226	Glyoxalase domain-containing protein 4	33
B5XDE4	227	14-3-3 protein beta/alpha	28
C0H764	228	Coactosin-like protein	16
B9EL11	229	GDP-L-fucose synthetase	16
B5X3H8	230	Proliferating cell nuclear antigen	29
B5X445	231	Ras-related protein Rab-11B	24
B5XA20	232	Haloacid dehalogenase-like hydrolase domain-contain. protein 1A	26
B5X9E6	233	Elongation factor 1-beta	24
B5X9F8	234	Proteasome subunit alpha type	26
D0QYP1	235	von Willebrand factor A domain-containing 5A	86
C0HBB4	236	T-complex protein 1 subunit epsilon	60
B5X4E3	237	Arginyl-tRNA synthetase, cytoplasmic	75
B5X1B8	238	Glutamate dehydrogenase 1, mitochondrial	60
B5XBP3	239	Histidine triad Nucleotide-binding protein 1	14
B5X815	240	Galectin	29
B5X3E6	241	Sepiapterin reductase	30
B5X4K8	242	UV excision repair protein RAD23 homolog A	41
B5X5R0	243	Chromobox protein homolog 3	22
B5XGI9	244	Proteasome subunit alpha type	28
B5XBT5	245	Homeodomain-only protein	8
B5XAX0	246	Tumor protein D54	19
B5X0V5	247	Calreticulin	48
B5X1Q8	248	Leukocyte elastase inhibitor	43
B5X6A6	249	Cystatin	14
B5X868	250	Thymidylate kinase	14
B5XAP5	251	Protein S100	11
B5X977	252	Glucosamine 6-phosphate N-acetyltransferase	21
A8QKW3	253	Ubiquitin-conjugating enzyme E2 variant 1	17
C0PUT2	254	Filamin-A (Fragment)	54

B9EMT3	256	Ubiquitin-conjugating enzyme E2 N	17
B5XA56	257	Low-molecular-weight phosphotyrosine protein phosphatase	18
H1	258	Histone H1 (Fragment)	5
B5X0U6	259	Phosphoglycerate kinase	45
B5XG47	260	S-formylglutathione hydrolase	31
B5DGS9	261	Myosin regulatory light chain 2, smooth muscle isoform	20
B5X0S5	262	Tubulin alpha chain	51
B5XCG6	263	Tumor protein D52	21
C0H8V2	264	26S proteasome non-ATPase regulatory subunit 2	100
B5RI21	265	Aflatoxin B1 aldehyde reductase member 2	41
C0HAF6	266	Calpain-1 catalytic subunit	80
C0H9X1	267	V-type proton ATPase catalytic subunit A-like	68
B5XAE1	268	Platelet-activating factor acetylhydrolase IB subunit gamma	19
B5DGU3	269	Proteasome subunit alpha type	27
B9ENL7	270	Ras-related protein Rab-5C	23
C0H993	271	SH2/SH3 adaptor crk	34
B5X4M3	272	Ubiquitin carboxyl-terminal hydrolase	94
B5XEA8	273	Dihydropteridine reductase	25
B5X2S2	274	Tropomyosin alpha-4 chain	29
B5X274	275	V-type proton ATPase subunit B, brain isoform	56
B9EPR5	276	Ubiquitin carboxyl-terminal hydrolase	26
B9EPE7	277	SH3 domain-binding glutamic acid-rich-like protein	13
B5X4D6	278	Proactivator polypeptide	58
B5X3B0	279	Ras-related C3 Botulinum toxin substrate 1	21
B5XFZ2	280	Sorbitol dehydrogenase	38
C0HA39	281	Heterogeneous nuclear ribonucleoprotein U-like protein 1	101
B9EMQ5	282	15-hydroxyprostaglandin dehydrogenase [NAD(+)]-like	28
B5DFU2	283	Hypoxanthine phosphoribosyltransferase	25
D0QEL0	284	Protein disulfide-isomerase	55
B5XBE3	285	Mitochondrial 2-oxoglutarate/malate carrier protein	27
B5DG72	286	Phosphoglucomutase-1	61
B5X2C8	287	Cold-inducible RNA-binding protein	21
B9EL90	288	Programmed cell death protein 5	16
B5X4I3	289	SH3 domain-binding glutamic acid-rich-like protein 3	10
B5DFU8	290	Member RAS oncogene family	24
B5X5R2	291	Profilin	15
C0H9W4	292	Thimet oligopeptidase	78
C0PUD4	293	26S proteasome non-ATPase regulatory subunit 11 (Fragment)	46
B5XA59	294	Proteasome subunit alpha type	29
B5X1I2	296	Natterin-like protein	34
B5X0X5	297	Hematological and neurological expressed 1-like protein	22
B5X5W4	298	Acyl-CoA-binding protein	11
B5X8K6	299	NEDD8	10

B5X6W2	300	Cystatin-B	11
B5X837	301	Branched-chain-amino-acid aminotransferase	43
Q2V6Q7	302	Anterior gradient-2-like protein 2	20
B5RI51	303	Barrier-to-autointegration factor	11
B5X5I0	304	26S protease regulatory subunit 6A	48
B5X8E1	305	3-hydroxybutyrate dehydrogenase type 2 isoform X1	26
B9EPG7	306	Thymosin beta-a	5
C0PUI7	307	Transketolase-like protein 2 (Fragment)	16
B5DH08	308	Nuclease-sensitive element-binding protein 1	33
B5XFC3	309	Tumor-associated calcium signal transducer 2 precursor	34
C0PUQ5	310	Cathepsin Z (Fragment)	33
B5XA92	311	Thioredoxin domain-containing protein 17	14
B5X8C7	312	Inorganic pyrophosphatase	33
B5XCK8	313	Prostaglandin E synthase 3	19
B5DGQ7	314	Enolase 3-2	47
C0H9F6	315	Kunitz-type protease inhibitor 1	57
B5X9Q1	316	Peroxiredoxin-6	24
B5X953	317	Stathmin	17
B9EP59	318	Glia maturation factor beta	17
C0HBN6	319	Tropomodulin-3	39
B5XGT2	321	Ribulose-phosphate 3-epimerase	25
B9EQ08	322	Phosphatidylethanolamine-binding protein 1	17
B5XGN8	324	Pirin	32
B5DGM5	325	Adenylate kinase isoenzyme 1	21
B5DGU9	326	26S proteasome non-ATPase regulatory subunit 3 isoform X1	59
B5X6M7	327	Thioredoxin	12
B3TDD9	328	Charged multivesicular body protein 2A	25
B5XFL6	329	Plastin-2	20
C7C4W8	330	L-plastin	15
C0HAC7	331	26S protease regulatory subunit 4-like	49
C0H8H4	332	Inositol polyphosphate 1-phosphatase	42
B5X4N7	334	Galactonate dehydratase	49
B5DG36	335	26S protease regulatory subunit 7	49
B5XBN2	336	26S proteasome non-ATPase regulatory subunit 6	46
B9EL48	337	Prothymosin alpha	11
Q98SJ9	338	Glycerol-3-phosphate dehydrogenase [NAD(+)]	38
B5X5N7	339	Proteasome subunit alpha type	28
B5X8V5	340	Ester hydrolase C11orf54 homolog	36
B5X6F1	341	Creatine kinase, testis isozyme	43
B5X3E4	342	T-complex protein 1 subunit gamma	60
B5X5A2	343	Nascent polypeptide-associated complex subunit alpha	23
B5X912	344	Cystatin-B	11
B5XE76	345	ATP-dependent RNA helicase DDX39	49

C0H7J1	346	FucU homolog	17
B5DGC5	347	Cold-inducible RNA-binding protein	15
C0HAK6	349	Ras-related protein Rab-1A	19
C0PUQ2	350	Eukaryotic translation initiation factor 4B (Fragment)	62
B5X3M6	351	Epoxide hydrolase 2	62
B5XAZ4	353	Alpha-aspartyl dipeptidase	27
B5DG30	354	Heat shock protein 70 isoform 3	71
E0R8Z1	355	Cold-inducible RNA-binding protein	13
C0H844	358	Heterogeneous nuclear ribonucleoprotein A/B	37
B5X3F9	361	Ras-related protein Rab-14	24
B5X3C0	363	Glutathione reductase	55
B5X1E2	365	PolyrC-binding protein 2	34
B9EPG1	366	Thioredoxin	12
B5XFZ3	367	Actin, adductor muscle	42
B5DGU7	368	Proteasome (Prosome, macropain) 26S subunit, non-ATPase, 13	42
B9ENB1	369	Proteasome activator complex subunit 1	29
C0HAR0	370	Coronin	53
B5X958	371	Osteoclast-stimulating factor 1	24
C0HBL4	373	Tubulin beta chain	51
B9ELR1	374	Cysteine-rich protein 1	9
B5X2G2	375	Serine/threonine-protein phosphatase	57
B5X888	377	Eukaryotic translation initiation factor 6	27
B5XCC9	378	Lactoylglutathione lyase	23
B5DFV6	379	Cathepsin D	43
B5X2Y7	380	Ras-related protein Rab-3D	25
B5X373	383	Adenylosuccinate synthetase	52
B5XDZ7	384	Catechol-O-methyltransferase domain-containing protein 1	27
B5X7L3	385	Fatty acid-binding protein, brain	15
B9ELG6	386	Elongation factor 1-delta	31
B5XBC8	387	Retinoblastoma-binding protein 9	21
B9EN25	389	Core histone macro-H2A	40
B5X0S8	390	Acyl-protein thioesterase 2	25
C0HBD9	391	Elongation factor 2	96
B5X205	392	Aspartate aminotransferase	46
B9EMV4	393	Eukaryotic translation initiation factor 5A	17
B5XCB2	394	Glutamine synthetase	42
C0PUK2	395	Nardilysin (Fragment)	71
B9EP38	396	Thiosulfate sulfurtransferase KAT	13
B9EM12	397	Cofilin-2	19
B5XA06	398	Prefoldin subunit 3	23
C0HAU7	399	Lupus La protein homolog B	46
B5X9Y8	400	Glutathione transferase omega-1	28
B5X8R5	403	Peptide methionine sulfoxide reductase	26

C0H966	406	Interferon-induced guanylate-binding protein 1	71
ENSA	409	Alpha-endosulfine	13
B5XDX4	410	Profilin	15
C0PUA0	411	Serine/threonine-pro. phosphatase 2A 65 kDa reg sub A β iso (Frag)	28
B5X293	412	Lumican	38
B5DGE3	416	Protein arginine methyltransferase 1	40
B9EL89	417	U6 snRNA-associated Sm-like protein LSm3	12
C0H8A6	418	Tubulin beta chain	50
C0H944	419	Obg-like ATPase 1	45
B5X1M6	420	Acetyl-CoA acetyltransferase, cytosolic	41
B5X0S3	423	Porphobilinogen deaminase	39
ABRAL	425	Costars family protein ABRACL	9
B5X4P4	426	Cathepsin B precursor	36
B5X1G4	427	Cysteinyl-tRNA synthetase, cytoplasmic	62
C0H8E0	428	Actin-related protein 2/3 complex subunit 5	17
B9EN91	429	Acidic leucine-rich nuclear phosphoprotein 32 family member E	28
B5X7C5	430	Plasma retinol-binding protein 1	22
B5X5H7	431	40 kDa peptidyl-prolyl cis-trans isomerase	41
B5X330	433	14-3-3 protein eta-like	28
C0H8W2	436	Autophagy-related protein 7	79
B5RI16	437	Proteasome (Prosome, macropain) 26S sub, ATPase, 6 (Fragment)	44
C0HAY4	438	Kunitz-type protease inhibitor 1	57
B5X3A3	440	Cold-inducible RNA-binding protein	17
C0HA53	441	Granulins	96
B5X8U9	442	Probable thiopurine S-methyltransferase	27
B9ELE1	443	Protein S100	11
B5X0W0	444	Serine/threonine-protein phosphatase	37
B5X2M4	448	Serine/threonine-protein phosphatase 2A activator	37
C0H8F9	449	Ras-related protein Rap-1b	21
B9EL42	451	BolA-like protein 2	10
B5X8V4	452	Vasodilator-stimulated phosphoprotein	6
B5XBJ5	456	Small ubiquitin-related modifier 2	14
C0PUH3	459	F-actin-capping protein subunit alpha-2 (Fragment)	32
B9EQK6	460	Actin-related protein 2/3 complex subunit 3	20
HBA	461	Hemoglobin subunit alpha	15
B9ELX0	462	Prostaglandin E synthase 3	18
C0PUG5	463	Heat shock 70 kDa protein 4	25
B5DGJ9	467	S100 calcium binding protein V2-like	11
B9ELZ2	468	Beta-2-microglobulin	13
B5DFZ9	469	Lactoylglutathione lyase	20
C0H8V3	470	Pyruvate kinase	58
B5X469	471	Peptidyl-prolyl isomerase	24
B5XEC5	473	Pyridoxal phosphate homeostasis protein	31

B5X2M9	475	Cell division control protein 42 homolog	21
B5XGF2	476	Hemoglobin subunit beta-1	16
B5X448	479	Splicing factor, arginine/serine-rich 9	29
B5XCW1	481	Peptidyl-prolyl isomerase	25
B9EN63	483	protein DJ-1 precursor	18
C0HBQ0	484	Uridine 5-monophosphate synthase	53
B9EPN7	488	Eukaryotic translation initiation factor 2 subunit 2	38
KFA	489	Kynurenine formamidase	33
B5XCE5	490	F-actin-capping protein subunit beta	31
B5X0T7	491	Heterogeneous nuclear ribonucleoprotein A0	31
B5X3H7	493	Tubulin beta chain	50
B5XEV0	495	Troponin C-akin-1 protein precursor	20
B9EPE3	496	GTP-binding nuclear protein Ran	24
RBM8A	497	RNA-binding protein 8A	20
B9EP10	498	Sorting nexin-12	19
B5XAB2	500	26S proteasome non-ATPase regulatory subunit 8	31
B5X6D2	505	Prefoldin subunit 4	15
C0HBR6	507	Actin-related protein 2/3 complex subunit	42
B5X386	508	26S proteasome non-ATPase regulatory subunit 12	53
Q91470	512	Beta-globin	16
B5X475	513	Aldehyde dehydrogenase	55
B5XF63	514	Nattectin	20
B5X1I0	516	S-adenosylmethionine synthase	44
B9ELB6	520	Charged multivesicular body protein 5	25
B5X4R2	521	Glucosamine-6-phosphate isomerase	31
B5XFN3	528	Myosin light polypeptide 6B	24
B9EP02	530	Prothymosin alpha	12
B5DGS5	531	Malate dehydrogenase	35
B5X4E1	533	MAP kinase-activated protein kinase 2-like isoform X1	44
B5X5H3	534	Ubiquitin carboxyl-terminal hydrolase	40
B5X7F2	537	Transgelin	22
B5XDJ1	538	Peptidyl-prolyl isomerase	19
B9EM96	540	Glutathione S-transferase A	26
B5X5H1	542	Epididymal secretory protein E1	16
B5X466	548	Cell division control protein 42 homolog	21
B5X976	549	Adenosine deaminase	40
B5X3N8	550	3-hydroxyisobutyrate dehydrogenase	35
B5X8I8	551	Ubiquitin-conjugating enzyme E2 variant 1	16
B9ELQ5	555	Autophagy-related protein 3	27
B9EN06	556	Ubiquitin-conjugating enzyme E2 D2	17
UFC1	557	Ubiquitin-fold modifier-conjugating enzyme 1	19
B9EM22	569	Phosphoglycerate mutase 1	6
C0HB49	570	protein TFG isoform X1	44

C0PUP3	571	AP-2 complex subunit beta-1	27
C0HA45	573	Alpha-galactosidase	46
CALUB	578	Calumenin-B	37
B5X9M2	584	Acyl-CoA-binding protein	10
B5X7A8	585	Ras-related C3 botulinum toxin substrate 2	21
B5DH20	586	60S acidic ribosomal protein P1-like	11
B5X8L9	587	mRNA cap guanine-N7 methyltransferase	18
B5XEE5	588	Regucalcin	33
B5X786	592	Apoptosis-associated speck-like protein containing a CARD	23
B9ELH2	597	Cofilin-2	19
B5XCU8	598	Annexin	38
C0PU36	599	Serine/threonine-protein phosphatase (Fragment)	35
B5X326	600	Plasminogen activator inhibitor 1 RNA-binding protein	47
B5X4X9	601	Nucleolin	47
B5X3X4	605	Phosphatase 1G	58
B5X7L8	607	Actin-related protein 2/3 complex subunit 4	20
B5X9K1	608	Phosphoserine phosphatase	27
B5XG88	609	PolyADP-ribose glycohydrolase ARH3	41
B5X4L8	611	14-3-3 protein epsilon isoform X1	29
B5X365	614	C7orf57 homolog	18
B5X229	620	Rho-related GTP-binding protein RhoC	22
Q9DDK2	621	Elongation factor 1-alpha	50
B5DFT8	622	Malate dehydrogenase	36
Q6ZZX5	623	Heterogeneous nuclear ribonucleoprotein (Fragment)	13
A7KIJ4	624	Tubulin beta chain	50
B5XEY5	641	Histone H2B	17
B9EQN9	642	Plastin-2	24
B9EL16	644	Tubulin beta-2C chain	23
B5XFE9	649	Tubulin alpha chain	50
B9EPF6	650	Astrocytic phosphoprotein PEA-15	15
B5XC59	651	Ubiquitin-conjugating enzyme E2 N	17
B5X127	652	Ras-related protein Rab-7a	23
B9ENI2	653	Coactosin-like	9
B9ENH7	654	Proteasome activator complex subunit 2	28
C0H894	663	Superoxide dismutase	25
B5X420	664	Transforming protein RhoA	22
B5DGJ5	665	Calpain small subunit 1	24
B5XB18	674	Adenosine deaminase	14
B5XCG1	693	Programmed Cell death protein 5	14
B5XEX6	694	Butyrophilin subfamily 2 member A2	17
B5DG91	704	Apoptosis-associated speck-like protein containing a CARD	22
B5X5C7	714	Nuclear transport factor 2	15
B5XE86	715	Thioredoxin	12

B9EQH8	716	Ubiquitin thioesterase	31
B5XFB2	719	Flavin reductase	23
B5X2K6	726	Interleukin enhancer-binding factor 2 homolog	43
B5X1K6	730	ADP-ribosylation factor 4-like	20
B5X7A4	749	Protein S100	10
B5DH09	751	Y-box binding protein-2	33
B5XB79	752	Thymosin beta-11	5
B5X3Y4	755	Farnesyl pyrophosphate synthetase	41
B5DGK5	782	Inosine triphosphate pyrophosphatase	23
B5XH75	793	HN1-like protein	23

*UniProt, with ending _SALSA
#ID in result protein list after filtering with Scaffold Viewer

Supplementary Table 3

a) Most discriminant proteomic and metabolomic features separating Cl0-E17 vs. Cl0-R21 as identified by S-plot analysis.

Accession number*	Protein name	Molecular weight [kDa]	Sequence coverage#¤ [%]	Identification probability¤ [%]	vs. E17
B5X6G0	SH3 domain-bind. glutamic acid-rich-like protein 3	10.27	74.7	100	↑
C0HAA7	Alpha-galactosidase	48.48	33.6	100	↓
B5X931	Carbonyl reductase 1	30.07	44.2	100	↓
B5XF51	Aldose reductase	35.54	20.8	100	↑
A6PZ97	Lysozyme g	21.96	43.0	100	↑
B5XBK0	Malate dehydrogenase	35.38	38.3	100	↑
B5XCG6	Tumor protein D52	20.99	38.3	100	↑
B9EPE7	SH3 domain-bind. glutamic acid-rich-like protein	12.91	27.8	100	↓
B5X3B0	Ras-related C3 Botulinum toxin substrate 1	21.42	16.1	100	↑
B5XFL6	Plastin-2	20.44	45.1	100	↑
B5XE76	ATP-dependent RNA helicase DDX39	48.33	12.6	100	↑
C0HAK6	Ras-related protein Rab-1A	18.74	37.1	99.8	↓
C0H844	Heterogeneous nuclear ribonucleoprotein A/B	36.85	14.0	100	↑
B5X3C0	Glutathione reductase	54.53	5.98	100	↑
C0HBD9	Elongation factor 2	95.61	39.5	100	↑
B5X1M6	Acetyl-CoA acetyltransferase, cytosolic	41.23	13.2	100	↑
C0H8E0	Actin-related protein 2/3 complex subunit 5	16.65	39.3	100	↑
C0HAY4	Kunitz-type protease inhibitor 1	56.75	1.9	100	↓
B5X8V4	Vasodilator-stimulated phosphoprotein	6.27	42.9	100	↑
B5XFN3	Myosin light polypeptide 6B	23.51	32.2	99.9	↑
B5X7F2	Transgelin	22.50	57.4	95.7	↑
Q9DDK2	Elongation factor 1-alpha	50.16	39.7	95.1	↑
B5X127	Ras-related protein Rab-7a	23.13	19.0	98.5	↑

*UniProt, with ending _SALSA
#by proteomic analysis
¤maximum in control group Cl0-R21

Metabolite ID number*	Ion mode	Retention time	Molecular weight (*m/z*)
122_024a7_144	neg.	7.14	122.024
148_0436a12_149	neg.	12.15	148.044
174_0404a19_49	neg.	19.49	174.040
186_9649a20_017	neg.	20.02	186.965
277_034a18_422	neg.	18.42	277.034
137_0462a9_573	pos.	9.57	137.046
190_1439a12_432	pos.	12.43	190.144
205_155a22_377	pos.	22.38	205.155
324_2386a3_834	pos.	3.83	324.239
326_2539a3_912	pos.	3.91	326.254
366_152a9_673	pos.	9.67	366.152

*analysis with HILIC-HRMS/MS

b) Most discriminant proteomic and metabolomic features separating Cl_{60}-E17 vs. Cl_{60}-R21 as identified by S-plot analysis.

Accession number*	Protein name	Molecular weight [kDa]	Sequence coverage#¤ [%]	Identification probability¤ [%]	vs. R21
C0PUL2	Lysine-tRNA ligase (Fragment)	65.21	31.8	100	↑
D0QEL0	Protein disulfide-isomerase	54.96	22.5	100	↑
B5DG72	Phosphoglucomutase-1	60.84	7.3	100	↓
B5X0X5	Hematological & neurology. expressed 1-like prot.	22.31	5.6	96.2	↓
B5DGQ7	Enolase 3-2	47.29	3.2	100	↓
C0H9F6	Kunitz-type protease inhibitor 1	57.49	3.5	100	↓
B5X3E4	T-complex protein 1 subunit gamma	59.75	2.0	65.4	↑
C0HBL4	Tubulin beta chain	51.28	39.5	99.6	↑
B5XCB2	Glutamine synthetase	41.55	5.4	99.9	↑
B5XCW1	Peptidyl-prolyl isomerase	24.68	<0.5	28.3	↓
C0H789	Hemoglobin subunit alpha-4	16.04	6.3	7.5	↓
B5X4L8	14-3-3 protein epsilon isoform X1	29.09	46.7	97.5	↑

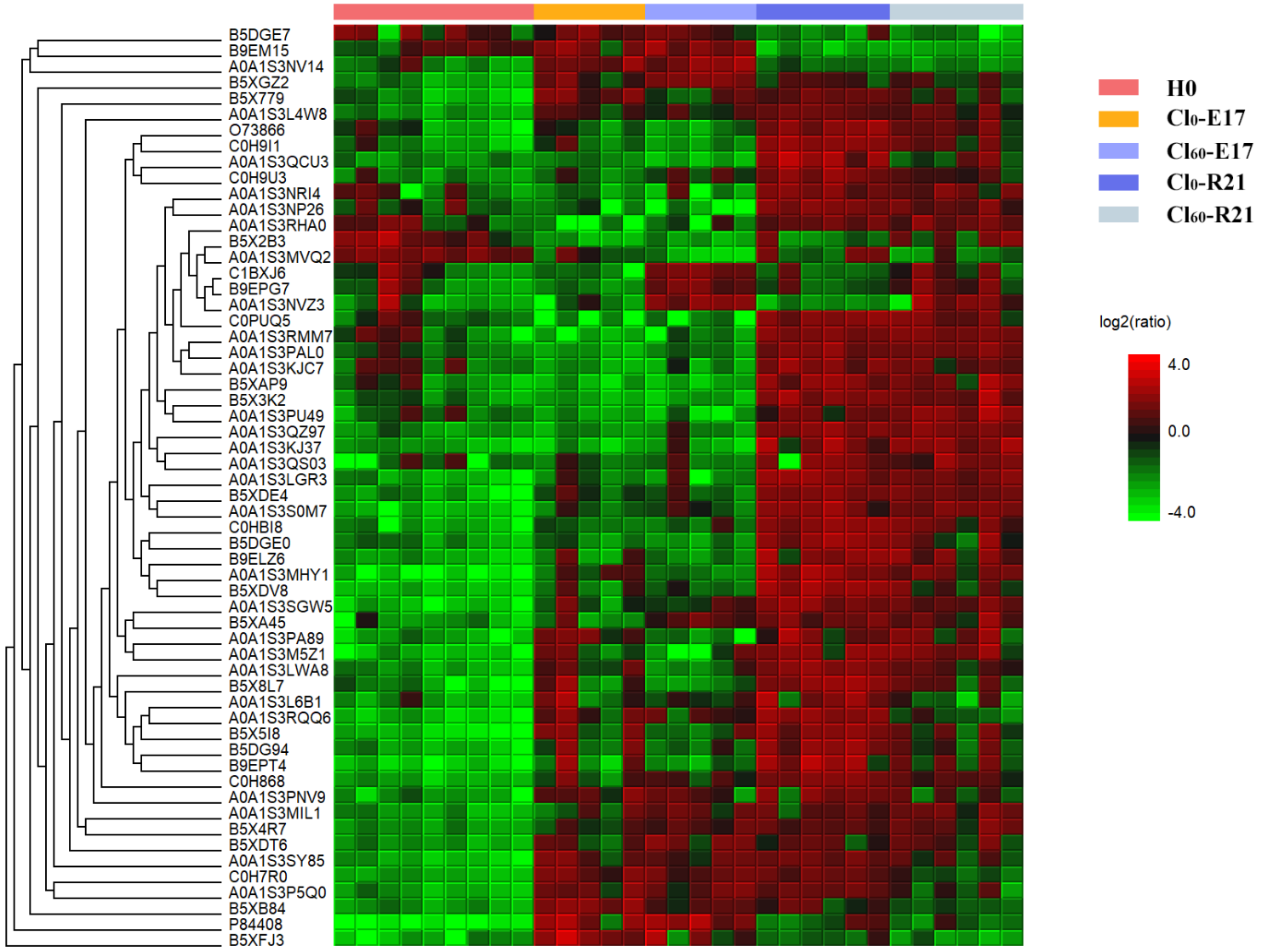
*UniProt, with ending _SALSA
#by proteomic analysis

[¤]maximum in treatment group Cl_{60}-R21

Metabolite ID number[*]	Ion mode	Retention time	Molecular weight (*m/z*)
201_113a3_502	neg.	3.50	201.113
203_0927a13_374	neg.	13.37	203.093
221_0663a8_825	neg.	8.83	221.066
221_0819a12_121	neg.	12.12	221.082
243_1238a4_123	neg.	4.12	243.124
257_0992a6_823	pos.	6.82	257.099
274_9904a17_387	pos.	17.39	274.990
386_2399a7_909	pos.	7.91	386.240

[*]analysis with HILIC-HRMS/MS

Supplementary Figure 1



Heatmap (Peak Viewer) of proteomics data from the analysis of skin mucus from chloramine-exposed and control salmon **.**

H0 = pre-exposure, Cl_0 = control fish, Cl_{60} = chloramine-exposed fish; E17 = end of 17-day exposure period; R21 = end of 21-day recovery period. The color codes indicate the relative signal strength of the protein in a sample relative to all measured proteins in the same sample and are expressed on a scale of 4 (light red) to -4 (light green) with one of the Cl0-E17 samples as the reference point. Red color means that the protein was measured with high relative signal strength and green color means that relative signal strength was low compared to the reference sample. The representative proteins are clustered if they exhibit a similar expression trend across the samples. The hierarchical clustering is generated using neighbor joining

algorithm with a Euclidean distance similarity measurement of the log2 ratios of the abundance of each sample relative to the average abundance.

Supplementary Figure 2

SUS-Plots showing results from OPLS-DA generated for the analysis of proteomics and metabolomics data comparing Cl_0-E17 vs. Cl_0-R21 and Cl_{60}-E17 vs. Cl_{60}-R21