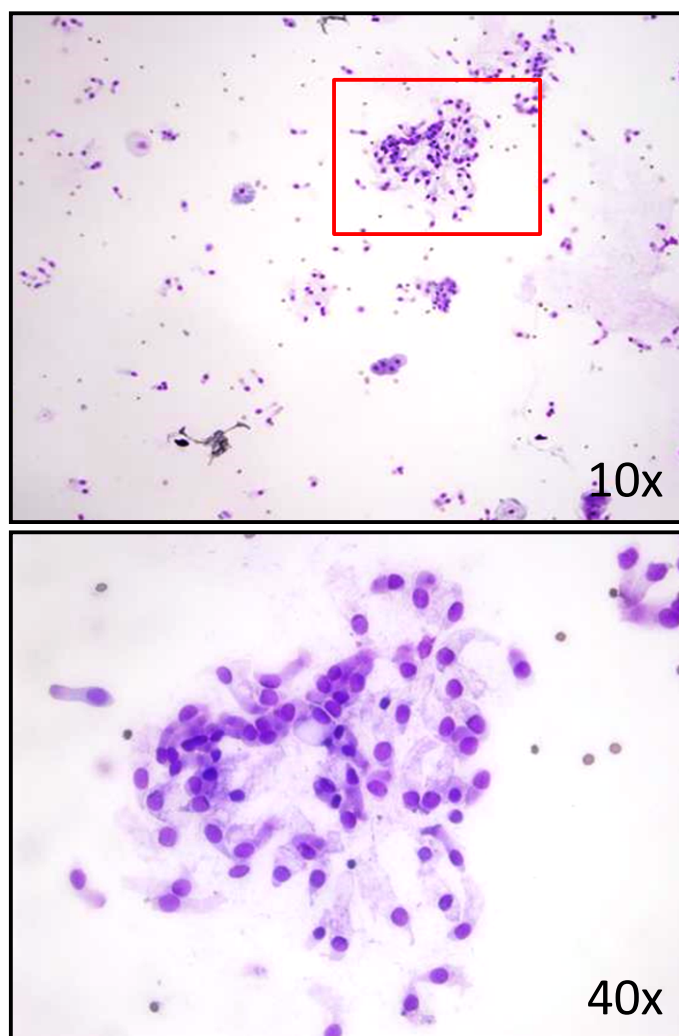


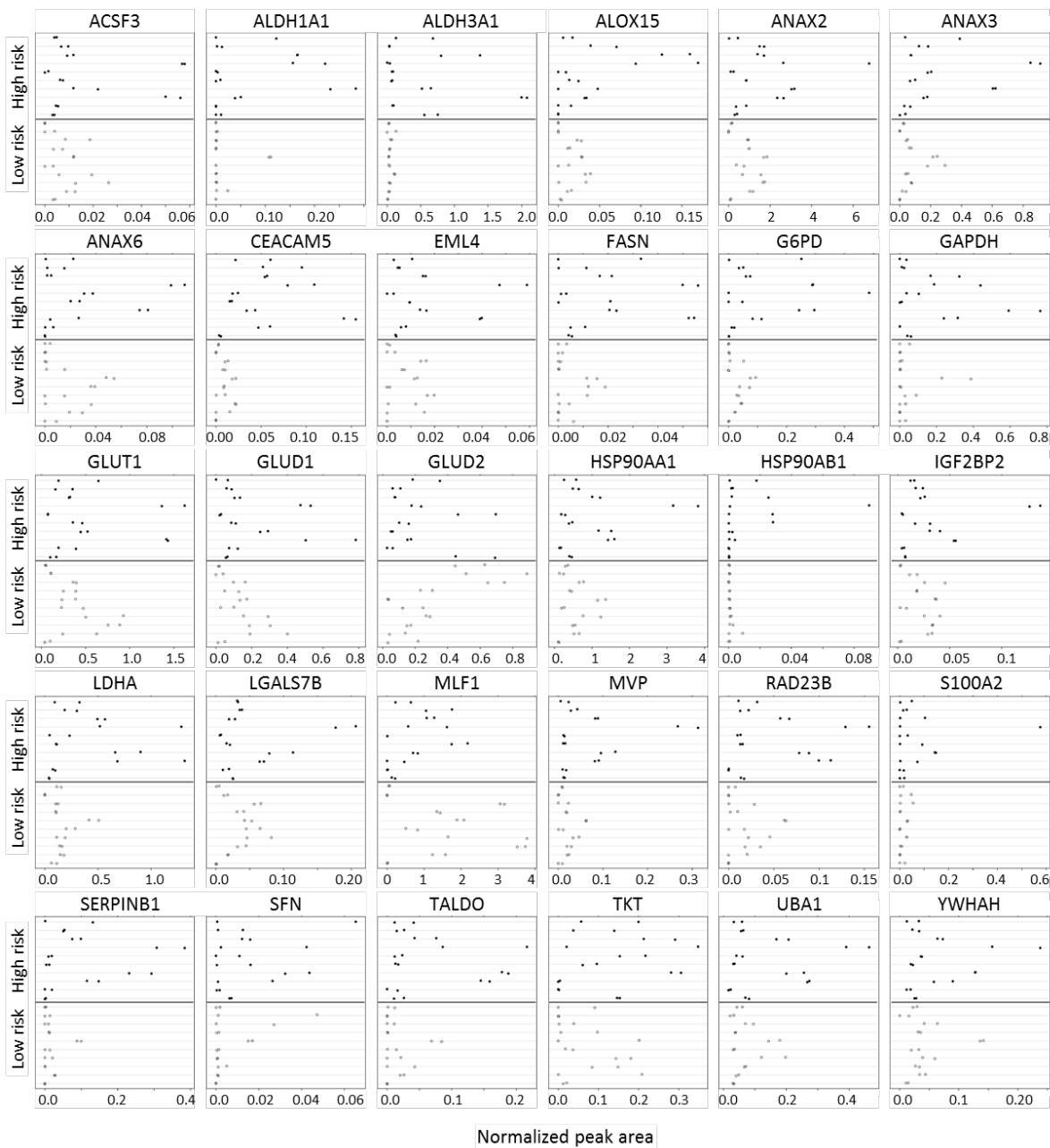
Supplemental Figure 1



Supplemental Figure S1

Representative Hematoxyline and eosin stained cytospin preparations of a bronchial brushings specimen from a healthy individual.

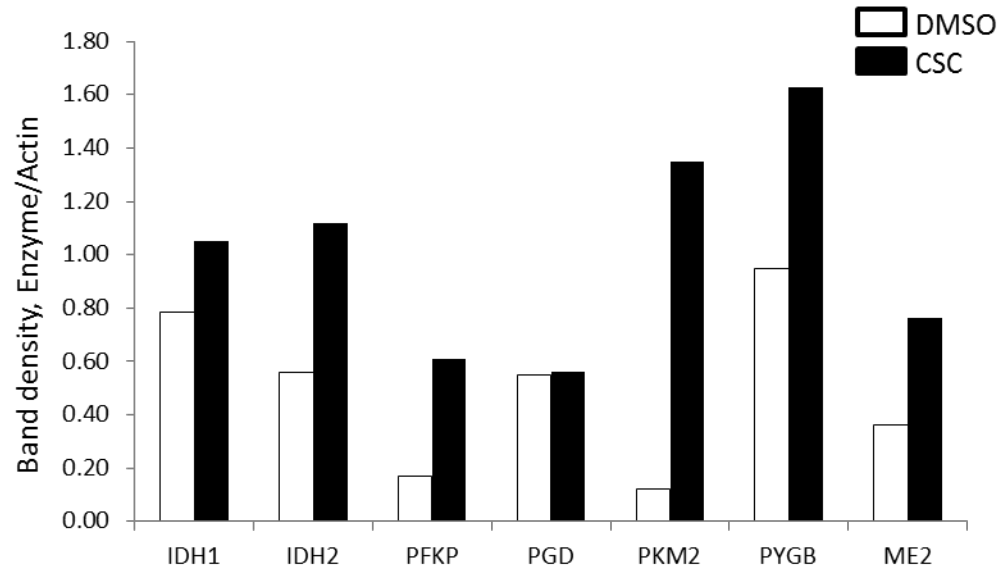
Supplemental Figure 2



Supplemental Figure S2

Quantitative measurements of selected proteins by PRM MS in a validation set of individual bronchial brushing specimens. PRM MS results of 13 carbohydrate metabolic enzymes shown in Figure 2B are not included. Two replicates of each specimen from low risk individuals were compared to that of the high risk individuals.

Supplemental Figure 3



Supplemental Figure S3

Densitometry analysis of the Western blotting of metabolic enzymes. The ratio of the intensities of enzyme bands and beta actin bands is presented. Open bars represent the intensities of the enzymes in cultures treated with DMSO and closed bars represent the intensities of the enzymes in cultures treated with CSC.

Supplemental Table S1. Characteristics of individual volunteers providing bronchial brushings.

Group	Pt ID	Age	Gender	Smoking status	Lung Cancer status	Histology subtype of lung cancer
Low risk	7036	55	Male	Never	No	not applicable
	7044	58	Female	Never	No	not applicable
	7071	60	Male	Never	No	not applicable
	7163	53	Male	Never	No	not applicable
	7143	65	Male	Never	No	not applicable
Medium risk	7030	64	Male	Former	No	not applicable
	7047	55	Male	Former	No	not applicable
	7178	59	Female	Former	No	not applicable
	7222	74	Female	Former	No	not applicable
	7228	45	Female	Former	No	not applicable
High risk	7018	68	Male	Former	No	not applicable
	7032	77	Female	Former	No	not applicable
	7089	68	Female	Current	No	not applicable
	7083	78	Male	Former	No	not applicable
	7072	68	Male	Former	No	not applicable
Never smoker, Lung cancer	7448	56	Female	Never	Yes	Bronchioalveolar Carcinoma
	7485	59	Female	Never	Yes	Adenocarcinoma
	7522	65	Male	Never	Yes	Adenocarcinoma
	7617	80	Female	Never	Yes	Adenocarcinoma
	7657	63	Female	Never	Yes	Adenocarcinoma
Smoker, Lung cancer	7016	60	Male	Former	Yes	Large Cell Neuroendocrine
	6820	59	Female	Current	Yes	Squamous Cell Carcinoma
	7080	72	Male	Former	Yes	Adenocarcinoma
	7176	52	Female	Current	Yes	Large Cell Neuroendocrine
	7182	85	Male	Former	Yes	Adenocarcinoma
	7010	69	Female	Former	Yes	Squamous Cell Carcinoma
	7023	66	Male	Former	Yes	Squamous Cell Carcinoma
	7134	63	Male	Current	Yes	Non-Small Cell Lung Cancer
	7053	68	Male	Former	Yes	Squamous Cell Carcinoma
	7116	77	Male	Former	Yes	Adenocarcinoma

Supplemental Table S2. Number of identified protein groups and spectral counts in risk groups

Risk Group	Distinct Peptides	Spectral counts	Protein Groups
Low	5,812	24,637	2,116
Medium	5,115	24,530	1,949
High	9,579	36,598	2,771

Supplemental Table S3. Number of identified protein groups and spectral counts in the replicates of risk groups

Risk groups	Distinct Peptides	Spectral counts	Protein Groups
Low	5,812	24,637	2,116
Replicate 1	4,218	9,036	1,689
Replicate 2	3,967	8,546	1,581
Replicate 3	3,127	7,055	1,357
Medium	5,115	24,530	1,949
Replicate 1	3,586	8,617	1,459
Replicate 2	3,835	9,419	1,531
Replicate 3	2,653	6,494	1,189
High	9,579	36,598	2,771
Replicate 1	6,697	13,153	2,316
Replicate 2	6,470	12,536	2,273
Replicate 3	5,674	10,909	2,046

Supplemental Table S4. Proteins identified by shotgun proteomic analysis demonstrating significant trend direction

Gene symbol	RefSeq ID	Protein name	Total spectral count	Trend p value	Trend direction
ACSF3	NP_777577	acyl-CoA synthetase family member 3	1207	0.020	down
ACTN4	NP_004915	actinin, alpha 4	405	0.035	up
ADSS	NP_001117	adenylosuccinate synthase	22	0.035	up
AKR1B10	NP_064695	aldo-keto reductase family 1, member B10 (aldose reductase)	27	0.046	up
ALDH1A1	NP_000680	aldehyde dehydrogenase 1 family, member A1	179	0.035	up
ALDH3A1	NP_000682	aldehyde dehydrogenase 3 family, member A1	268	0.035	up
ALOX15	NP_001131	arachidonate 15-lipoxygenase	323	0.011	down
ANP32A	NP_006296	acidic (leucine-rich) nuclear phosphoprotein 32 family, member A	40	0.020	up
ANXA2	NP_001129487	annexin A2	1262	0.035	down
ANXA3	NP_005130	annexin A3	74	0.020	up
ANXA6	NP_001146	annexin A6	109	0.011	up
ANXA8L2	NP_001621	annexin A8-like 2	7	0.046	up
AP1B1	NP_663782	adaptor-related protein complex 1, beta 1 subunit	28	0.020	up
AP2B1	NP_001273	adaptor-related protein complex 2, beta 1 subunit	23	0.020	up
ARCN1	NP_001646	archain 1	5	0.046	up
ARF3	NP_001650	ADP-ribosylation factor 3	36	0.011	up
ARF5	NP_001653	ADP-ribosylation factor 5	13	0.046	up
ARFGAP2	NP_115765	ADP-ribosylation factor GTPase activating protein 2	8	0.046	up
ARFGAP3	NP_055385	ADP-ribosylation factor GTPase activating protein 3	7	0.046	up
ARFIP2	NP_001229783	ADP-ribosylation factor interacting protein 2	8	0.046	up
ASS1	NP_446464	argininosuccinate synthase 1	13	0.046	up
ATP12A	NP_001667	ATPase, H ⁺ /K ⁺ transporting, nongastric, alpha polypeptide	7	0.046	up
ATP5D	NP_001678	ATP synthase, H ⁺ transporting, mitochondrial F1 complex, delta subunit	109	0.011	down
ATP5O	NP_001688	ATP synthase, H ⁺ transporting, mitochondrial F1 complex, O subunit	28	0.035	up
BAG3	NP_004272	BCL2-associated athanogene 3	5	0.046	up
BAG5	NP_001015048	BCL2-associated athanogene 5	5	0.046	up
BANF1	NP_003851	barrier to autointegration factor 1	6	0.046	up
BAX	NP_004315	BCL2-associated X protein	7	0.046	up
BBS2	NP_114091	Bardet-Biedl syndrome 2	9	0.035	up
BCAM	NP_005572	basal cell adhesion molecule (Lutheran blood group)	38	0.035	up
BCAS1	NP_003648	breast carcinoma amplified sequence 1	27	0.020	up
BNIP1	NP_001196	BCL2/adenovirus E1B 19kDa interacting protein 1	6	0.046	up

BRCA2	NP_000050	breast cancer 2, early onset	3771	0.035	down
BRK1	NP_060932	BRICK1, SCAR/WAVE actin-nucleating complex subunit	7	0.046	up
C14orf166	NP_057123	chromosome 14 open reading frame 166	16	0.046	up
C1orf31	NP_001193570	chromosome 1 open reading frame 31	15	0.026	up
C1orf87	NP_689590	chromosome 1 open reading frame 87	44	0.035	down
C9orf142	NP_899064	chromosome 9 open reading frame 142	11	0.046	up
C9orf171	NP_997300	chromosome 9 open reading frame 171	13	0.026	up
CALU	NP_001186601	calumenin	31	0.011	up
CAND1	NP_060918	cullin-associated and neddylation-dissociated 1	74	0.035	up
CAND2	NP_036430	cullin-associated and neddylation-dissociated 2 (putative)	7	0.046	up
CAPN1	NP_005177	calpain 1, (mu/I) large subunit	77	0.020	up
CAPN2	NP_001739	calpain 2, (m/II) large subunit	41	0.035	up
CAPS	NP_004049	calcyphosine	570	0.020	up
CBR1	NP_001748	carbonyl reductase 1	57	0.035	up
CBR3	NP_001227	carbonyl reductase 3	25	0.026	up
CCDC113	NP_054876	coiled-coil domain containing 113	3	0.046	up
CCDC17	NP_001108410	coiled-coil domain containing 17	24	0.011	down
CCT6A	NP_001753	chaperonin containing TCP1, subunit 6A (zeta 1)	104	0.035	up
CCT7	NP_006420	chaperonin containing TCP1, subunit 7 (eta)	29	0.008	up
CD2AP	NP_036252	CD2-associated protein	6	0.046	up
CDC37	NP_008996	cell division cycle 37 homolog (S. cerevisiae)	7	0.035	up
CDIPT	NP_006310	CDP-diacylglycerol--inositol 3-phosphatidyltransferase	7	0.046	up
CEACAM5	NP_004354	carcinoembryonic antigen-related cell adhesion molecule 5	32	0.046	up
CETN2	NP_004335	centrin, EF-hand protein, 2	38	0.046	up
CHCHD1	NP_976043	coiled-coil-helix-coiled-coil-helix domain containing 1	3	0.046	up
CHCHD3	NP_060282	coiled-coil-helix-coiled-coil-helix domain containing 3	88	0.005	up
CHCHD6	NP_115719	coiled-coil-helix-coiled-coil-helix domain containing 6	3	0.046	up
CLMN	NP_079010	calmin (calponin-like, transmembrane)	14	0.035	down
CLTA	NP_001171690	clathrin, light chain A	33	0.035	up
CORO1B	NP_065174	coronin, actin binding protein, 1B	23	0.046	up
COX2	YP_003024029	cytochrome c oxidase subunit II	100	0.035	up
CPOX	NP_000088	coproporphyrinogen oxidase	8	0.046	up
CRAT	NP_000746	carnitine O-acetyltransferase	14	0.020	up
CSNK2A2	NP_001887	casein kinase 2, alpha prime polypeptide	3	0.046	up
CTBP1	NP_001319	C-terminal binding protein 1	10	0.046	up
CUX1	NP_852477	cut-like homeobox 1	14	0.011	down
CYP1A1	NP_000490	cytochrome P450, family 1, subfamily A, polypeptide 1	6	0.046	up
CYP1B1	NP_000095	cytochrome P450, family 1, subfamily B,	16	0.046	up

		polypeptide 1			
DCAF12L1	NP_848565	DDB1 and CUL4 associated factor 12-like 1	13	0.035	down
DCTN4	NP_057305	dynactin 4 (p62)	3773	0.035	down
DCXR	NP_057370	dicarbonyl/L-xylulose reductase	8	0.046	up
DDI2	NP_115717	DNA-damage inducible 1 homolog 2 (S. cerevisiae)	19	0.046	up
DEFA1B	NP_001035965	defensin, alpha 1B	175	0.003	down
DGKA	NP_963848	diacylglycerol kinase, alpha 80kDa	4	0.046	up
DHX9	NP_001348	DEAH (Asp-Glu-Ala-His) box polypeptide 9	87	0.035	down
DIP2B	NP_775873	DIP2 disco-interacting protein 2 homolog B (Drosophila)	24	0.046	up
DLG5	NP_004738	discs, large homolog 5 (Drosophila)	90	0.011	down
DLST	NP_001924	dihydrolipoamide S-succinyltransferase (E2 component of 2-oxo-glutarate complex)	92	0.011	up
DNAH5	NP_001360	dynein, axonemal, heavy chain 5	263	0.035	down
DNAJA1	NP_001530	DnaJ (Hsp40) homolog, subfamily A, member 1	24	0.020	down
DNAJB1	NP_006136	DnaJ (Hsp40) homolog, subfamily B, member 1	11	0.046	up
DPP7	NP_037511	dipeptidyl-peptidase 7	14	0.046	up
DPYSL3	NP_001184223	dihydropyrimidinase-like 3	18	0.020	up
DYNC1H1	NP_001367	dynein, cytoplasmic 1, heavy chain 1	255	0.011	up
DYNC1LI1	NP_057225	dynein, cytoplasmic 1, light intermediate chain 1	22	0.011	up
EFHD2	NP_077305	EF-hand domain family, member D2	27	0.020	up
EIF3F	NP_003745	eukaryotic translation initiation factor 3, subunit F	9	0.046	up
EIF5	NP_001960	eukaryotic translation initiation factor 5	10	0.046	up
EML2	NP_036287	echinoderm microtubule associated protein like 2	23	0.005	up
EML4	NP_061936	echinoderm microtubule associated protein like 4	28	0.003	up
FAF2	NP_055428	Fas associated factor family member 2	8	0.046	up
FAM213A	NP_001230707	family with sequence similarity 213, member A	6	0.046	up
FASN	NP_004095	fatty acid synthase	40	0.005	up
FBLN1	NP_006477	fibulin 1	10	0.046	up
FGA	NP_000499	fibrinogen alpha chain	2598	0.005	down
FGB	NP_005132	fibrinogen beta chain	1313	0.003	down
FGG	NP_000500	fibrinogen gamma chain	1318	0.035	down
FNTA	NP_002018	farnesyltransferase, CAAX box, alpha	5	0.046	up
FTH1	NP_002023	ferritin, heavy polypeptide 1	37	0.011	up
FUBP3	NP_003925	far upstream element (FUSE) binding protein 3	5	0.046	up
GADD45GIP1	NP_443082	growth arrest and DNA-damage-inducible, gamma interacting protein 1	6	0.046	up
GALNT12	NP_078918	UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-	9	0.020	up

		acetylgalactosaminyltransferase 12 (GalNAc-T12)			
GBA	NP_001005742	glucosidase, beta, acid	9	0.046	up
GCLC	NP_001489	glutamate-cysteine ligase, catalytic subunit	11	0.046	up
GDI1	NP_001484	GDP dissociation inhibitor 1	21	0.035	up
GDI2	NP_001485	GDP dissociation inhibitor 2	59	0.011	up
GLB1	NP_000395	galactosidase, beta 1	11	0.046	up
GLIPR2	NP_071738	GLI pathogenesis-related 2	42	0.026	down
GLTSCR1	NP_056526	glioma tumor suppressor candidate region gene 1	5	0.035	down
GMDS	NP_001491	GDP-mannose 4,6-dehydratase	16	0.015	up
GNA11	NP_002058	guanine nucleotide binding protein (G protein), alpha 11 (Gq class)	19	0.035	up
GNAI2	NP_002061	guanine nucleotide binding protein (G protein), alpha inhibiting activity polypeptide 2	76	0.035	up
GOLM1	NP_057632	golgi membrane protein 1	42	0.035	up
GSN	NP_001121134	gelsolin	141	0.035	up
H1FO	NP_005309	H1 histone family, member O	185	0.035	down
H2AFV	NP_036544	H2A histone family, member V	73	0.035	down
HARS2	NP_036340	histidyl-tRNA synthetase 2, mitochondrial	4	0.046	up
HBE1	NP_005321	hemoglobin, epsilon 1	58	0.003	down
HBG1	NP_000550	hemoglobin, gamma A	191	0.020	down
HIST1H1C	NP_005310	histone cluster 1, H1c	700	0.020	down
HIST1H1D	NP_005311	histone cluster 1, H1d	484	0.035	down
HIST1H1E	NP_005312	histone cluster 1, H1e	688	0.035	down
HIST1H2AC	NP_003503	histone cluster 1, H2ac	401	0.020	down
HIST1H4D	NP_003530	histone cluster 1, H4d	1210	0.035	down
HLA-DRB1	NP_002115	major histocompatibility complex, class II, DR beta 1	57	0.020	up
HMGCS2	NP_005509	3-hydroxy-3-methylglutaryl-CoA synthase 2 (mitochondrial)	8	0.046	up
HP1BP3	NP_057371	heterochromatin protein 1, binding protein 3	71	0.003	up
HSP90AA1	NP_001017963	heat shock protein 90kDa alpha (cytosolic), class A member 1	825	0.035	up
HSP90AB1	NP_031381	heat shock protein 90kDa alpha (cytosolic), class B member 1	820	0.020	up
HSPA4	NP_002145	heat shock 70kDa protein 4	66	0.020	up
HSPE1	NP_002148	heat shock 10kDa protein 1 (chaperonin 10)	113	0.035	down
HSPH1	NP_006635	heat shock 105kDa/110kDa protein 1	90	0.020	up
IDH1	NP_005887	isocitrate dehydrogenase 1 (NADP+), soluble	55	0.011	up
IDH2	NP_002159	isocitrate dehydrogenase 2 (NADP+), mitochondrial	193	0.035	up
IFT122	NP_443715	intraflagellar transport 122 homolog (Chlamydomonas)	6	0.046	up
IFT81	NP_001137251	intraflagellar transport 81 homolog (Chlamydomonas)	15	0.046	up

IGF2BP2	NP_006539	insulin-like growth factor 2 mRNA binding protein 2	8	0.046	up
IMPA1	NP_005527	inositol(myo)-1(or 4)-monophosphatase 1	12	0.026	up
ITIH1	NP_002206	inter-alpha-trypsin inhibitor heavy chain 1	21	0.026	up
KARS	NP_005539	lysyl-tRNA synthetase	52	0.020	up
KIAA1324	NP_065826	KIAA1324	5	0.046	up
KIF1C	NP_006603	kinesin family member 1C	7	0.046	up
KIF5B	NP_004512	kinesin family member 5B	76	0.035	up
KIF9	NP_001128350	kinesin family member 9	5	0.046	up
KRT1	NP_006112	keratin 1	1385	0.003	down
KRT10	NP_000412	keratin 10	887	0.003	down
KRT17	NP_000413	keratin 17	2644	0.020	down
KRT2	NP_000414	keratin 2	677	0.035	down
KRT31	NP_002268	keratin 31	84	0.035	down
KRT33B	NP_002270	keratin 33B	68	0.035	down
KRT34	NP_066293	keratin 34	72	0.035	down
KRT36	NP_003762	keratin 36	28	0.046	down
KRT38	NP_006762	keratin 38	14	0.020	down
KRT7	NP_005547	keratin 7	1413	0.005	down
KRT79	NP_787028	keratin 79	306	0.020	down
KRT8	NP_002264	keratin 8	4203	0.005	down
KRT83	NP_002273	keratin 83	88	0.003	down
KRT85	NP_002274	keratin 85	94	0.005	down
KRT86	NP_002275	keratin 86	107	0.003	down
LBR	NP_919424	lamin B receptor	9	0.035	up
LCORL	NP_710153	ligand dependent nuclear receptor corepressor-like	60	0.035	down
LDHB	NP_002291	lactate dehydrogenase B	163	0.020	up
LGALS7B	NP_001035972	lectin, galactoside-binding, soluble, 7B	62	0.020	up
LIMK1	NP_002305	LIM domain kinase 1	5	0.046	down
LLGL2	NP_001026973	lethal giant larvae homolog 2 (Drosophila)	17	0.035	up
LMO7	NP_005349	LIM domain 7	13	0.026	up
LRRFIP1	NP_004726	leucine rich repeat (in FLII) interacting protein 1	33	0.005	up
LRRFIP2	NP_006300	leucine rich repeat (in FLII) interacting protein 2	11	0.046	up
LSS	NP_002331	lanosterol synthase (2,3-oxidosqualene-lanosterol cyclase)	25	0.020	up
LUZP1	NP_361013	leucine zipper protein 1	3	0.046	up
LYN	NP_002341	v-yes-1 Yamaguchi sarcoma viral related oncogene homolog	11	0.046	up
MAN2A1	NP_002363	mannosidase, alpha, class 2A, member 1	6	0.035	up
MANF	NP_006001	mesencephalic astrocyte-derived neurotrophic factor	31	0.020	up
MAOA	NP_000231	monoamine oxidase A	43	0.020	up
MBOAT7	NP_001139555	membrane bound O-acyltransferase domain containing 7	14	0.020	up
MCU	NP_612366	mitochondrial calcium uniporter	10	0.046	up

ME2	NP_002387	malic enzyme 2, NAD(+)-dependent, mitochondrial	32	0.020	up
MKRN3	NP_005655	makorin ring finger protein 3	51	0.046	down
MLF1	NP_001123629	myeloid leukemia factor 1	29	0.035	down
MOGS	NP_006293	mannosyl-oligosaccharide glucosidase	16	0.046	up
MRPL43	NP_115488	mitochondrial ribosomal protein L43	35	0.035	down
MSH6	NP_000170	mutS homolog 6 (E. coli)	3	0.046	up
MSN	NP_002435	moesin	107	0.020	up
MTHFD1	NP_005947	methylenetetrahydrofolate dehydrogenase (NADP+ dependent) 1, methenyltetrahydrofolate cyclohydrolase, formyltetrahydrofolate synthetase	15	0.015	up
MVP	NP_005106	major vault protein	240	0.035	up
MYH10	NP_001242941	myosin, heavy chain 10, non-muscle	89	0.003	up
MYH9	NP_002464	myosin, heavy chain 9, non-muscle	691	0.003	up
MYL1	NP_524146	myosin, light chain 1, alkali; skeletal, fast	22	0.020	up
MYL6	NP_524147	myosin, light chain 6, alkali, smooth muscle and non-muscle	195	0.005	up
MYO1C	NP_203693	myosin IC	15	0.003	up
NAE1	NP_003896	NEDD8 activating enzyme E1 subunit 1	5	0.046	up
NCL	NP_005372	nucleolin	97	0.035	up
NDUFAF3	NP_951032	NADH dehydrogenase (ubiquinone) complex I, assembly factor 3	6	0.046	up
NDUFV1	NP_001159574	NADH dehydrogenase (ubiquinone) flavoprotein 1, 51kDa	16	0.026	up
NFKB1	NP_003989	nuclear factor of kappa light polypeptide gene enhancer in B-cells 1	8	0.046	up
NLRP12	NP_653288	NLR family, pyrin domain containing 12	22	0.003	down
NUP85	NP_079120	nucleoporin 85kDa	7	0.046	up
OAS1	NP_001027581	2'-5'-oligoadenylate synthetase 1, 40/46kDa	1201	0.020	down
ODF2L	NP_065780	outer dense fiber of sperm tails 2-like	14	0.035	up
OPA1	NP_056375	optic atrophy 1 (autosomal dominant)	25	0.035	up
PACIN3	NP_057307	protein kinase C and casein kinase substrate in neurons 3	8	0.046	up
PAFAH1B1	NP_000421	platelet-activating factor acetylhydrolase 1b, regulatory subunit 1 (45kDa)	4	0.046	up
PBLD	NP_071412	phenazine biosynthesis-like protein domain containing	12	0.046	up
PCCA	NP_000273	propionyl CoA carboxylase, alpha polypeptide	18	0.026	up
PCYT1B	NP_004836	phosphate cytidyltransferase 1, choline, beta	11	0.046	up
PDLIM4	NP_003678	PDZ and LIM domain 4	9	0.035	up
PEBP1	NP_002558	phosphatidylethanolamine binding protein 1	86	0.020	up
PFKL	NP_002617	phosphofructokinase, liver	9	0.046	up

PFKP	NP_002618	phosphofructokinase, platelet	23	0.020	up
PGD	NP_002622	phosphogluconate dehydrogenase	134	0.020	up
PGK1	NP_000282	phosphoglycerate kinase 1	113	0.020	up
PGM1	NP_002624	phosphoglucomutase 1	13	0.020	up
PIR	NP_001018119	pirin (iron-binding nuclear protein)	6	0.046	up
PITRM1	NP_055704	pitrilysin metalloproteinase 1	22	0.020	up
PKM	NP_002645	pyruvate kinase, muscle	318	0.003	up
PKP3	NP_009114	plakophilin 3	29	0.020	up
PLSCR1	NP_066928	phospholipid scramblase 1	10	0.046	up
POF1B	NP_079197	premature ovarian failure, 1B	18	0.035	down
POR	NP_000932	P450 (cytochrome) oxidoreductase	23	0.035	down
PPIF	NP_005720	peptidylprolyl isomerase F	20	0.046	up
PPIH	NP_006338	peptidylprolyl isomerase H (cyclophilin H)	7	0.046	up
PPIL1	NP_057143	peptidylprolyl isomerase (cyclophilin)-like 1	6	0.046	up
PPP2R4	NP_066954	protein phosphatase 2A activator, regulatory subunit 4	12	0.026	up
PPP2R5E	NP_006237	protein phosphatase 2, regulatory subunit B', epsilon isoform	7	0.046	up
PRB3	NP_006240	proline-rich protein BstNI subfamily 3	9	0.026	up
PRDX6	NP_004896	peroxiredoxin 6	104	0.035	up
PRMT1	NP_001527	protein arginine methyltransferase 1	13	0.046	down
PRPF6	NP_036601	PRP6 pre-mRNA processing factor 6 homolog (S. cerevisiae)	10	0.046	up
PSMD13	NP_002808	proteasome (prosome, macropain) 26S subunit, non-ATPase, 13	15	0.020	up
PSMD6	NP_055629	proteasome (prosome, macropain) 26S subunit, non-ATPase, 6	12	0.035	up
PTCD3	NP_060422	pentatricopeptide repeat domain 3	6	0.046	up
PTGES2	NP_079348	prostaglandin E synthase 2	4	0.046	up
PYGB	NP_002853	phosphorylase, glycogen; brain	28	0.026	up
RAB21	NP_055814	RAB21, member RAS oncogene family	10	0.046	up
RABAC1	NP_006414	Rab acceptor 1 (prenylated)	8	0.046	up
RAD23B	NP_002865	RAD23 homolog B (S. cerevisiae)	25	0.008	up
RBBP4	NP_001128728	retinoblastoma binding protein 4	30	0.020	up
RBMXL1	NP_062556	RNA binding motif protein, X-linked-like 1	184	0.035	down
RGPD3	NP_001137485	RANBP2-like and GRIP domain containing 3	83	0.035	down
RHOB	NP_004031	ras homolog family member B	22	0.035	up
RPL11	NP_000966	ribosomal protein L11	32	0.011	up
RPL14	NP_003964	ribosomal protein L14	60	0.035	up
RPL27	NP_000979	ribosomal protein L27	43	0.035	up
RPL27A	NP_000981	ribosomal protein L27a	18	0.026	down
RPL5	NP_000960	ribosomal protein L5	16	0.046	up
RPS13	NP_001008	ribosomal protein S13	102	0.020	down
RPS16	NP_001011	ribosomal protein S16	18	0.020	up
RPS19	NP_001013	ribosomal protein S19	66	0.020	up
RPS4X	NP_000998	ribosomal protein S4, X-linked	30	0.011	down
RSPH9	NP_689945	radial spoke head 9 homolog	55	0.011	down

		(Chlamydomonas)			
S100A2	NP_005969	S100 calcium binding protein A2	16	0.035	up
SCGB1A1	NP_003348	secretoglobin, family 1A, member 1 (uteroglobin)	189	0.020	down
SCRIB	NP_874365	scribbled homolog (Drosophila)	11	0.046	up
SEC62	NP_003253	SEC62 homolog (S. cerevisiae)	4	0.046	up
SERPINB1	NP_109591	serpin peptidase inhibitor, clade B (ovalbumin), member 1	109	0.035	up
SF3A3	NP_006793	splicing factor 3a, subunit 3, 60kDa	16	0.046	up
SF3B14	NP_057131	splicing factor 3B, 14 kDa subunit	11	0.035	up
SFN	NP_006133	stratifin	35	0.008	up
SFTPB	NP_000533	surfactant protein B	45	0.003	down
SH3GL1	NP_001186872	SH3-domain GRB2-like 1	6	0.046	up
SH3GLB2	NP_064530	SH3-domain GRB2-like endophilin B2	7	0.046	up
SHROOM3	NP_065910	shroom family member 3	25	0.046	down
SIRT5	NP_112534	sirtuin 5	13	0.020	up
SLC25A11	NP_003553	solute carrier family 25 (mitochondrial carrier; oxoglutarate carrier), member 11	20	0.011	down
SMARCC2	NP_001123892	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily c, member 2	7	0.046	up
SMARCE1	NP_003070	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily e, member 1	13	0.046	up
SMC4	NP_005487	structural maintenance of chromosomes 4	31	0.003	down
SNRPA1	NP_003081	small nuclear ribonucleoprotein polypeptide A'	14	0.020	down
SNX6	NP_689419	sorting nexin 6	6	0.046	up
SPRYD4	NP_997227	SPRY domain containing 4	11	0.046	up
SRP54	NP_003127	signal recognition particle 54kDa	13	0.046	up
SRP68	NP_055045	signal recognition particle 68kDa	13	0.046	up
STIP1	NP_006810	stress-induced-phosphoprotein 1	49	0.003	up
STT3A	NP_689926	STT3, subunit of the oligosaccharyltransferase complex, homolog A (S. cerevisiae)	40	0.035	up
STUB1	NP_005852	STIP1 homology and U-box containing protein 1, E3 ubiquitin protein ligase	6	0.046	up
SUGT1	NP_001124384	SGT1, suppressor of G2 allele of SKP1 (S. cerevisiae)	15	0.035	up
TBL2	NP_036585	transducin (beta)-like 2	4	0.046	up
TCERG1	NP_006697	transcription elongation regulator 1	169	0.003	down
TEKT1	NP_444515	tektin 1	75	0.035	up
TIAL1	NP_001029097	TIA1 cytotoxic granule-associated RNA binding protein-like 1	10	0.035	up
TM2D3	NP_510883	TM2 domain containing 3	1200	0.020	down
TMEM231	NP_001070884	transmembrane protein 231	24	0.035	down
TMEM48	NP_060557	transmembrane protein 48	4	0.046	up
TMX4	NP_066979	thioredoxin-related transmembrane protein	8	0.046	up

		4			
TNPO1	NP_002261	transportin 1	24	0.035	up
TOP2B	NP_001059	topoisomerase (DNA) II beta 180kDa	32	0.046	up
TPGS1	NP_277048	tubulin polyglutamylase complex subunit 1	7	0.046	up
TPM3	NP_705935	tropomyosin 3	225	0.035	up
TRA2B	NP_001230808	transformer 2 beta homolog (Drosophila)	4	0.046	up
TRIM2	NP_056086	tripartite motif containing 2	11	0.046	up
TST	NP_003303	thiosulfate sulfurtransferase (rhodanese)	15	0.046	up
TUBA1A	NP_006000	tubulin, alpha 1a	655	0.020	down
TUBB1	NP_110400	tubulin, beta 1 class VI	199	0.035	down
TUBGCP3	NP_006313	tubulin, gamma complex associated protein 3	7	0.046	up
UBA1	NP_695012	ubiquitin-like modifier activating enzyme 1	189	0.035	up
UCHL3	NP_005993	ubiquitin carboxyl-terminal esterase L3 (ubiquitin thiolesterase)	8	0.046	up
UFSP2	NP_060829	UFM1-specific peptidase 2	10	0.046	up
UGP2	NP_006750	UDP-glucose pyrophosphorylase 2	16	0.020	up
UHRF1BP1L	NP_055869	UHRF1 binding protein 1-like	110	0.011	down
UNC45A	NP_061141	unc-45 homolog A (C. elegans)	7	0.046	up
UPK3BL	NP_001107875	uroplakin 3B-like	7	0.046	up
UQCRH	NP_005995	ubiquinol-cytochrome c reductase hinge protein	5	0.046	up
VAMP2	NP_055047	vesicle-associated membrane protein 2 (synaptobrevin 2)	16	0.035	up
VPS28	NP_057292	vacuolar protein sorting 28 homolog (S. cerevisiae)	7	0.046	up
WARS	NP_004175	tryptophanyl-tRNA synthetase	47	0.015	up
WDR35	NP_065830	WD repeat domain 35	12	0.046	up
XPO1	NP_003391	exportin 1 (CRM1 homolog, yeast)	15	0.008	up
XRN2	NP_036387	5'-3' exoribonuclease 2	7	0.046	up
YWHAH	NP_003396	tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, eta polypeptide	82	0.011	up
ZNF281	NP_036614	zinc finger protein 281	30	0.020	down

Supplemental Table S5. Enriched pathways from shotgun proteomics data

	Gene symbol	Protein
Metabolic pathways		
1	UGP2	UDP-glucose pyrophosphorylase 2
2	PRDX6	peroxiredoxin 6
3	PCYT1B	phosphate cytidyltransferase 1, choline, beta
4	PAFAH1B1	platelet-activating factor acetylhydrolase 1b, regulatory subunit 1 (45kDa)
5	GALNT12	UDP-N-acetyl-alpha-D-galactosamine:polypeptide N- acetylglactosaminyltransferase 12 (GalNAc-T12)
6	DGKA	diacylglycerol kinase, alpha 80kDa
7	MOGS	mannosyl-oligosaccharide glucosidase
8	ASS1	argininosuccinate synthase 1
9	IDH2	isocitrate dehydrogenase 2 (NADP+), mitochondrial
10	CDIPT	CDP-diacylglycerol--inositol 3-phosphatidyltransferase
11	ALOX15	arachidonate 15-lipoxygenase
12	NDUFV1	NADH dehydrogenase (ubiquinone) flavoprotein 1, 51kDa
13	CYP1A1	cytochrome P450, family 1, subfamily A, polypeptide 1
14	PFKL	phosphofructokinase, liver
15	ALDH3A1	aldehyde dehydrogenase 3 family, member A1
16	MAN2A1	mannosidase, alpha, class 2A, member 1
17	GMDS	GDP-mannose 4,6-dehydratase
18	LDHB	lactate dehydrogenase B
19	MTHFD1	methylenetetrahydrofolate dehydrogenase (NADP+ dependent) 1, methenyltetrahydrofolate cyclohydrolase, formyltetrahydrofolate synthetase
20	IMPA1	inositol(myo)-1(or 4)-monophosphatase 1
21	PGM1	phosphoglucomutase 1
22	GCLC	glutamate-cysteine ligase, catalytic subunit
23	PCCA	propionyl CoA carboxylase, alpha polypeptide
24	CPOX	coproporphyrinogen oxidase
25	AKR1B10	aldo-keto reductase family 1, member B10 (aldose reductase)
26	FASN	fatty acid synthase
27	GBA	glucosidase, beta, acid
28	HMGCS2	3-hydroxy-3-methylglutaryl-CoA synthase 2 (mitochondrial)
29	PKM	pyruvate kinase, muscle
30	DLST	dihydrolipoamide S-succinyltransferase (E2 component of 2-oxo-glutarate complex)
31	IDH1	isocitrate dehydrogenase 1 (NADP+), soluble
32	PTGES2	prostaglandin E synthase 2
33	ATP5D	ATP synthase, H+ transporting, mitochondrial F1 complex, delta subunit
34	TST	thiosulfate sulfurtransferase (rhodanese)
35	PGD	phosphogluconate dehydrogenase
36	ADSS	adenylosuccinate synthase
37	LSS	lanosterol synthase (2,3-oxidosqualene-lanosterol cyclase)
38	CBR1	carbonyl reductase 1
39	PGK1	phosphoglycerate kinase 1
40	DCXR	dicarbonyl/L-xylulose reductase
41	STT3A	STT3, subunit of the oligosaccharyltransferase complex, homolog A (<i>S. cerevisiae</i>)
42	MAOA	monoamine oxidase A
43	GLB1	galactosidase, beta 1
44	UQCRH	ubiquinol-cytochrome c reductase hinge protein
45	CBR3	carbonyl reductase 3

- 46 ALDH1A1 aldehyde dehydrogenase 1 family, member A1
- 47 ATP5O ATP synthase, H⁺ transporting, mitochondrial F1 complex, O subunit
- 48 PFKP phosphofructokinase, platelet

Protein processing in endoplasmic reticulum

- 1 CAPN2 calpain 2, (m/II) large subunit
- 2 STUB1 STIP1 homology and U-box containing protein 1, E3 ubiquitin protein ligase
- 3 HSPH1 heat shock 105kDa/110kDa protein 1
- 4 STT3A STT3, subunit of the oligosaccharyltransferase complex, homolog A (*S. cerevisiae*)
- 5 HSP90AB1 heat shock protein 90kDa alpha (cytosolic), class B member 1
- 6 SEC62 SEC62 homolog (*S. cerevisiae*)
- 7 RAD23B RAD23 homolog B (*S. cerevisiae*)
- 8 BAX BCL2-associated X protein
- 9 MOGS mannosyl-oligosaccharide glucosidase
- 10 HSP90AA1 heat shock protein 90kDa alpha (cytosolic), class A member 1
- 11 DNAJB1 DnaJ (Hsp40) homolog, subfamily B, member 1
- 12 DNAJA1 DnaJ (Hsp40) homolog, subfamily A, member 1
- 13 CAPN1 calpain 1, (mu/I) large subunit

Ribosome

- 1 RPS4X ribosomal protein S4, X-linked
- 2 RPS16 ribosomal protein S16
- 3 RPL27 ribosomal protein L27
- 4 RPS19 ribosomal protein S19
- 5 RPL14 ribosomal protein L14
- 6 RPL27A ribosomal protein L27a
- 7 RPL5 ribosomal protein L5
- 8 RPL11 ribosomal protein L11
- 9 RPS13 ribosomal protein S13

Galactose metabolism

- 1 GLB1 galactosidase, beta 1
- 2 PGM1 phosphoglucomutase 1
- 3 UGP2 UDP-glucose pyrophosphorylase 2
- 4 PFKL phosphofructokinase, liver
- 5 PFKP phosphofructokinase, platelet

Glycolysis / Gluconeogenesis

- 1 PGM1 phosphoglucomutase 1
- 2 PKM pyruvate kinase, muscle
- 3 PGK1 phosphoglycerate kinase 1
- 4 PFKL phosphofructokinase, liver
- 5 ALDH3A1 aldehyde dehydrogenase 3 family, member A1
- 6 PFKP phosphofructokinase, platelet
- 7 LDHB lactate dehydrogenase B

Spliceosome

- 1 SNRPA1 small nuclear ribonucleoprotein polypeptide A'
- 2 SF3B14 splicing factor 3B, 14 kDa subunit
- 3 TRA2B transformer 2 beta homolog (*Drosophila*)

- | | | |
|---|--------|---|
| 4 | SF3A3 | splicing factor 3a, subunit 3, 60kDa |
| 5 | PPIL1 | peptidylprolyl isomerase (cyclophilin)-like 1 |
| 6 | PPIH | peptidylprolyl isomerase H (cyclophilin H) |
| 7 | PRPF6 | PRP6 pre-mRNA processing factor 6 homolog (S. cerevisiae) |
| 8 | TCERG1 | transcription elongation regulator 1 |
| 9 | RBMXL1 | RNA binding motif protein, X-linked-like 1 |

Pentose phosphate pathway

- | | | |
|---|------|--------------------------------|
| 1 | PGM1 | phosphoglucomutase 1 |
| 2 | PFKL | phosphofructokinase, liver |
| 3 | PFKP | phosphofructokinase, platelet |
| 4 | PGD | phosphogluconate dehydrogenase |

Fructose and mannose metabolism

- | | | |
|---|---------|---|
| 1 | GMDS | GDP-mannose 4,6-dehydratase |
| 2 | PFKL | phosphofructokinase, liver |
| 3 | PFKP | phosphofructokinase, platelet |
| 4 | AKR1B10 | aldo-keto reductase family 1, member B10 (aldose reductase) |

Phenylalanine metabolism

- | | | |
|---|---------|--|
| 1 | MAOA | monoamine oxidase A |
| 2 | PRDX6 | peroxiredoxin 6 |
| 3 | ALDH3A1 | aldehyde dehydrogenase 3 family, member A1 |

Tryptophan metabolism

- | | | |
|---|--------|---|
| 1 | MAOA | monoamine oxidase A |
| 2 | CYP1A1 | cytochrome P450, family 1, subfamily A, polypeptide 1 |
| 3 | WARS | tryptophanyl-tRNA synthetase |
| 4 | CYP1B1 | cytochrome P450, family 1, subfamily B, polypeptide 1 |

Vasopressin-regulated water reabsorption

- | | | |
|---|----------|---|
| 1 | DYNC1H1 | dynein, cytoplasmic 1, heavy chain 1 |
| 2 | VAMP2 | vesicle-associated membrane protein 2 (synaptobrevin 2) |
| 3 | DYNC1LI1 | dynein, cytoplasmic 1, light intermediate chain 1 |
| 4 | DCTN4 | dynactin 4 (p62) |

Protein export

- | | | |
|---|-------|-----------------------------------|
| 1 | SRP54 | signal recognition particle 54kDa |
| 2 | SRP68 | signal recognition particle 68kDa |
| 3 | SEC62 | SEC62 homolog (S. cerevisiae) |

Huntington's disease

- | | | |
|---|--------|--|
| 1 | AP2B1 | adaptor-related protein complex 2, beta 1 subunit |
| 2 | CLTA | clathrin, light chain A |
| 3 | UQCRH | ubiquinol-cytochrome c reductase hinge protein |
| 4 | NDUFV1 | NADH dehydrogenase (ubiquinone) flavoprotein 1, 51kDa |
| 5 | ATP5O | ATP synthase, H+ transporting, mitochondrial F1 complex, O subunit |
| 6 | DCTN4 | dynactin 4 (p62) |
| 7 | BAX | BCL2-associated X protein |
| 8 | ATP5D | ATP synthase, H+ transporting, mitochondrial F1 complex, delta subunit |

Glutathione metabolism

- | | | |
|---|------|---|
| 1 | IDH2 | isocitrate dehydrogenase 2 (NADP+), mitochondrial |
| 2 | IDH1 | isocitrate dehydrogenase 1 (NADP+), soluble |
| 3 | GCLC | glutamate-cysteine ligase, catalytic subunit |
| 4 | PGD | phosphogluconate dehydrogenase |
-

Supplemental Table S6: Selected candidates for validation by Parallel Reaction Monitoring Mass Spectrometry

Candidate	Criteria for selection: pathways; dataset from previous studies	Trend p value	up/ down
ACSF3	Lipid metabolism	0.0196	down
ALDH1A1	Alcohol and aldehyde metabolism; ¹ Massion, MCP	0.0348	up
ALDH3A1	Alcohol and aldehyde metabolism; Massion, MCP; Crystal, BMC, Spira, PNAS	0.0348	up
ALOX15	Lipid metabolism	0.0106	down
ANXA2	Massion, MCP; Crystal, BMC	0.0348	down
ANXA3	Massion, MCP; Spira, PNAS	0.0196	up
ANXA6	Massion, MCP	0.0106	up
CEACAM5	Cancer biomarker; Massion, MCP	0.0455	up
DLST	Carbohydrate metabolism	0.0106	up
EML4	Absent in control. EML4/ALK translocation in NSCLC; Massion, MCP	0.0027	up
FASN	Lipid metabolism; Massion, MCP	0.0055	up
GLB1	Carbohydrate metabolism	0.0455	up
HSP90AA1	candidate biomarker, ATPase activity, chaperone; Massion, MCP	0.0348	up
HSP90AB1	candidate biomarker, ATPase activity, chaperone; Massion, MCP	0.0196	up
IDH1	Carbohydrate metabolism; Massion, MCP	0.0106	up
IDH2	Carbohydrate metabolism; Massion, MCP	0.0348	up
IGF2BP2	Hepatocellular Carcinoma Autoantigen P62	0.0455	up
LDHB	Carbohydrate metabolism; Massion, MCP	0.0196	up
LGALS7B	hypopharynx carcinoma, laryngeal squamous cell carcinoma	0.0196	up
ME2	Carbohydrate metabolism; Massion, MCP	0.0196	up
MLF1	p53 regulator, Transcription factor	0.0348	down
MVP	Massion, MCP	0.0348	up
PFKL	Carbohydrate metabolism	0.0455	up
PFKP	Carbohydrate metabolism; Massion, MCP	0.0196	up
PGD	Carbohydrate metabolism; Massion, MCP	0.0196	up
PGK1	Carbohydrate metabolism; Massion, MCP	0.0196	up
PGM1	Carbohydrate metabolism	0.0196	up
PKM2	Carbohydrate metabolism	0.0027	up
PYGB	Carbohydrate metabolism; Massion, MCP	0.0263	up
RAD23B	DNA repair function	0.0077	up
S100A2	Undetected in control, Tumor suppressor; Massion, MCP	0.0348	up
SERPINB1	Massion, MCP	0.0348	up
SFN	Undetected in control, lung nodule metastasis; Massion, MCP; Spira, PNAS	0.0077	up
UBA1	Massion, MCP	0.0348	up
YWHAH	Massion, MCP	0.0106	up
<u>Trend p >0.05</u>			
G6PD	glucose-6-phosphate dehydrogenase	0.1824	up
GAPDH	glyceraldehyde-3-phosphate dehydrogenase	0.5785	down
GLUD1	glutamate dehydrogenase 1	0.2216	up
GLUD2	glutamate dehydrogenase 2	² n/a	² n/a
GLUT1/SLC2A1	solute carrier family 2 (facilitated glucose transporter), member 1	0.0589	up
LDHA	lactate dehydrogenase A	0.7389	down
TALDO1	transaldolase 1	0.2216	up
TKT	transketolase	0.0956	up

¹Massion MCP (Mol Cell Prot. 2014), Crystall BMC (BMC Genomics 2012), Spira PNAS (Proc. Natl. Acad. Sci. 2004)²Not identified by shotgun analysis

Supplemental Table S7: Peptide sequences used for Parallel Reaction Monitoring Mass Spectrometry

Protein	Peptide	Protein	Peptide	Protein	Peptide	Protein	Peptide
1 ACSF3	LPGSVGTPLPGVQVR	11 FASN	LQVVVDQPLPVR	21 IDH2	YFDLGLPNR	34 PKM2	LDIDSPPIR
ACSF3	SAFTLDGWFK	FASN	VLFPATGYLSIVWK	IDH2	ATDFVADR	PKM2	IYVDDGLISLQVK
		FASN	LPEDPLLSGLLDSPALK	IDH2	TIEAEAAHGTVTR	PKM2	EAEAAIYHLQLFEELR
2 ALDH1A1	VAFTGSTEVGK	FASN	FPQLDSTSFANSR			PKM2	LAPITSDPTEATAVGAVE
ALDH1A1	IFVEESIYDEFVR			22 IGF2BP2	ILVPTQFVGAIIGK	PKM2	C[+57]C[+57]SGAIIVLT
ALDH1A1	ILDIESGK	12 G6PD	GGYFDEFGIIR	IGF2BP2	IAPAECPDVSR		
ALDH1A1	ANNTFYGLSAGVFTK	G6PD	DGLLPENTFIVGYAR	IGF2BP2	TVNELQNLTSAEVIVPR	35 PYGB	GLAGLGDVAEVR
						PYGB	DYFFALAHTVR
3 ALDH3A1	FDHILYTGSTGVGK	13 GAPDH	VLAAYVK	23 LDHA	LVIITAGAR	PYGB	DFYELEPEK
ALDH3A1	VAYGGTGDAATR	GAPDH	ELSDIAHR			PYGB	LLPLVSDDEVFIR
ALDH3A1	SLEEAIQFINQR	GAPDH	LQSIGTENTEENR	24 LDHB	FIIPQIVK	PYGB	VEDVEALDR
ALDH3A1	SFETFSHR	GAPDH	GILAADESTGSIK	LDHB	SADTLWDIQR		
		GAPDH	GALQNIIPASTGAAK			36 RAD23B	IDIDPEETVK
4 ALOX15	TVGEDPQGLFQK	GAPDH	VGVNGFGR	25 LGALS7B	LDTSEVVFNSK	RAD23B	ASFNNPDR
ALOX15	LYDLPVDER	GAPDH	LVINGNPITIFQER	LGALS7B	GQPFVLIASDDGFK		
ALOX15	VDFEVSIAK			LGALS7B	AVVGDAQYHHFR	37 S100A2	ELPSFVGEK
ALOX15	SSFYAQDALR	14 GBL1	AYVAVDGIPQGVLR	LGALS7B	AVVGDAQYHHFR		
		GLB1	TEAVASSLYDILAR			38 SERPINB1	FAYGYIEDLK
5 ANXA2	AAYTNFDAER	GLB1	VNYGAYINDFK	26 ME2	IETQDIQALR	SERPINB1	IEEQLTLEK
ANXA2	DALNIETAIK			ME2	HISDSVFLEAAK	SERPINB1	LEESYTLNSDLAR
ANXA2	TPAQYDASELK	15 GLUD1	NYTDNELEK				
ANXA2	TNQELQEINR	GLUD1	HGGTIPIVPTAEFQDR	27 MLF1	SFSEPFGR	39 SFN	LGVQDLFNSSK
				MLF1	DLLSISDGR	SFN	VLSSIEQK
6 ANXA3	DYPDFSPSVDAEAIQK	16 GLUD2	YSTDVSDEVK	MLF1	VFAQSTQTR	SFN	YLAEVATGDDK
ANXA3	GAGTNEDALIEILTTR	GLUD2	YNLGLDLR				
ANXA3	SLGDDISSETSGDFR	GLUD2	TAAYVNAIEK	28 MVP	GPLEYVPSAK	40 TALDO1	VSTEVDAR
ANXA3	GIGTDEFTLNR			MVP	TAVFGFETSEAK	TALDO1	SYEPLEDPGVK
ANXA3	SEIDLLDIR	17 GLUT1	VTILELFR	MVP	IEGEGSVLQAK	TALDO1	LFVLFGAEILK
		GLUT1	TFDEIASGFR			TALDO1	LSSTWEGIQAGK
7 ANXA6	DAFVAIVQSVK			29 PFKL	SEWGSLEELVAEGK		
ANXA6	SLHQAIEGDTSGDFLK	18 HSP90AA1	APFDLFENR	PFKL	TFVLEVMGR	41 TKT	DAIAQAVR
ANXA6	SLHQAIEGDTSGDFLK	HSP90AA1	LGIHEDSQNR	PFKL	VTVLGHVQR	TKT	AVELAANTK
ANXZ6	LVFDEYK	HSP90AA1	DQVANSFAVER			TKT	IIALDGDTK
				30 PFKP	ELVVTQLGYDTR		
8 CEACAM5	SDLVNEEATGQFR	19 HSP90AB1	NPDDITQEEYGEFYK			42 UBA1	ALPAVQQNNLDEDLIR
		HSP90AB1	LGIHEDSTNR	31 PGD	VDDFLANEAK	UBA1	YDQGVAVFGSDLQEK
9 DLST	TPAFAESVTEGDVR	HSP90AB1	DIFQEIYDK	PGD	SFLEDIR	UBA1	LAGTQPLEVLEAVQR
DLST	VEGGTPLFTLR	HSP90AB1	TVEAEAAHGTVTR			UBA1	AENYDIPSADR
DLST	LGFMSAFVK			32 PGK1	YSLEPVAVELK		
		20 IDH1	HAYGDQYR	PGK1	AC[+57]ANPAAGSVILLENLR	43 YWHAH	AVTELNEPLSNEDR
10 EML4	VQQQEIDEITVLK	IDH1	VEITYTPSDGTQK			YWHAH	YLAEVASGEK
EML4	LSLPQNETVADTTLT			33 PGM1	VDLGVLGK	YWHAH	NSVVEASEAAYK
				PGM1	LSGTGSAGATIR		

Supplemental Table S8. Validation of overexpressed carbohydrate metabolic enzymes by Parallel Reaction Monitoring Mass Spectrometry

Gene	Protein name	Pathway	ICC	p value
GLB1	galactosidase, beta 1	Galactose metabolism	0.000	0.018
* PYGB	phosphorylase, glycogen; brain	Glycogenolysis	0.608	0.019
PGM1	phosphoglucomutase 1	Glucose metabolism	0.732	0.024
PGD	phosphogluconate dehydrogenase	Pentose phosphate pathway	0.534	0.008
* PFKL	phosphofructokinase, liver	Glycolysis	0.906	0.140
* PFKP	phosphofructokinase, platelet	Glycolysis	0.670	0.025
PGK1	phosphoglycerate kinase 1	Glycolysis	0.901	0.085
* PKM2	pyruvate kinase, muscle	Glycolysis	0.493	0.111
LDHB	lactate dehydrogenase B	Glycolysis	0.898	0.166
IDH1	isocitrate dehydrogenase 1 (NADP+), soluble	TCA cycle	0.980	0.062
IDH2	isocitrate dehydrogenase 2 (NADP+), mitochondrial	TCA cycle	0.953	0.100
DLST	dihydrolipoamide S-succinyltransferase	TCA cycle	0.208	0.049
ME2	malic enzyme 2, NAD(+)-dependent, mitochondrial	TCA cycle	0.965	0.170

*rate limiting enzyme

Supplemental Table S9: Expression of selected genes in the RNAseq dataset. Metabolic enzymes are in bold fonts.

Gene	Gene name	Adjusted p value
GLB1	Galactosidase, beta 1	0.0107
ALDH1A1	Aldehyde dehydrogenase 1 family, member A1	0.0447
PYGB	Phosphorylase, glycogen; brain	0.0784
LDHB	Lactate dehydrogenase B	0.0952
IDH2	Isocitrate dehydrogenase 2 (NADP+), mitochondrial	0.1206
ANXA2	Annexin A2	0.1328
PGK1	Phosphoglycerate kinase 1	0.1661
UBA1	Ubiquitin-like modifier activating enzyme 1	0.1795
UGP2	UDP-glucose pyrophosphorylase 2	0.2080
ALOX15	Arachidonate 15-lipoxygenase	0.2373
ME2	Malic enzyme 2, NAD(+)-dependent, mitochondrial	0.2892
PGD	Phosphogluconate dehydrogenase	0.2979
BRCA2	Breast cancer 2, early onset	0.2982
CAPS	Calcyphosine	0.2988
ANXA6	Annexin A6	0.3009
PFKP	Phosphofructokinase, platelet	0.3749
HSP90AB1	Heat shock protein 90kDa alpha (cytosolic), class B member 1	0.4651
HSP90AA1	Heat shock protein 90kDa alpha (cytosolic), class A member 1	0.4705
BCAS1	Breast carcinoma amplified sequence 1	0.5136
CEACAM5	Carcinoembryonic antigen-related cell adhesion molecule 5	0.5591
ALDH3A1	Aldehyde dehydrogenase 3 family, member A1	0.5715
FASN	Fatty acid synthase	0.5833
RAD23B	RAD23 homolog B (S. cerevisiae)	0.5882
SFTPB	Surfactant protein B	0.6392
PKM2	Pyruvate kinase, muscle	0.6677
SERPINB1	Serpin peptidase inhibitor, clade B (ovalbumin), member 1	0.6757
PFKL	Phosphofructokinase, liver	0.6782
PGM1	Phosphoglucomutase 1	0.7029
SFN	Stratifin	0.7152
S100A2	S100 calcium binding protein A2	0.7309
MLF1	Myeloid leukemia factor 1	0.7970
YWHAH	Tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, eta polypeptide	0.8104
CYP1B1	Cytochrome P450, family 1, subfamily B, polypeptide 1	0.8320
IDH1	Isocitrate dehydrogenase 1 (NADP+), soluble	0.9211
ANXA3	Annexin A3	0.9360
LGALS7B	Lectin, galactoside-binding, soluble, 7B	0.9406
MVP	Major vault protein	0.9628
DLG5	Discs, large homolog 5 (Drosophila)	0.9704
IGF2BP2	Insulin-like growth factor 2 mRNA binding protein 2	0.9920
DLST	Dihydrolipoamide S-succinyltransferase (E2 component of 2-oxo-glutarate complex)	0.9993
EML2	Echinoderm microtubule associated protein like 2	not detected
EML4	Echinoderm microtubule associated protein like 4	not detected
AKR1B10	Aldo-keto reductase family 1, member B10 (aldose reductase)	not detected
ACSF3	Acyl-CoA synthetase family member 3	not detected
SHROOM3	Shroom family member 3	not detected

