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SUPPLEMENTARY MATERIAL

Exploring the pathogenesis of renal cell carcinoma: pathway and bioinformatics analysis of dysregulated genes and proteins

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The following is extracted from our recent publication:
Differential Protein Expressions in Renal Cell Carcinoma: New Biomarker Discovery by Mass Spectrometry. K.W. Michael Siu, Leroi V. DeSouza, Andreas Scorilas, Alexander D. Romaschin, R. John Honey, Robert Stewart, Kenneth Pace, Youssef Youssef, George M. Yousef, J. Proteome Res., in press.

iTRAQ Sample Preparation Procedure

We utilized a tissue preparation protocol that was previously used for biomarker studies in endometrial cancer. In summary, cell debris from the tissue homogenates was removed by centrifugation in a microfuge at 4°C for 30min at 14 000 rpm. The clarified supernatant was transferred to fresh microfuge tubes and the total protein content determined using a commercial Bradford assay reagent (Bio-Rad, Mississauga, ON, Canada). A standard curve for the Bradford assay was made using γ-globulin as a control. 100μg of each sample was then denatured and the cysteines blocked as described in the iTRAQ protocol (Applied Biosystems, Foster City, CA, USA). Each sample was then digested with trypsin as recommended in the iTRAQ protocol and labeled with the iTRAQ tags as follows: non-cancer, diseased kidney, iTRAQ114; normal kidney, iTRAQ115; and the two kidney cancer samples, iTRAQ116 and iTRAQ117. The labeled samples were then pooled and mixed with Eluent A (10 mM KH_2PO_4 solution in 25% acetonitrile and 75% deionized water acidified to a pH of 3.0 with phosphoric acid) to a total volume of 1.0 ml for strong cation exchange (SCX) chromatography. This diluted sample was further acidified using 5 μl of concentrated phosphoric acid, after which the contents were manually injected onto a 200 μl bed volume strong cation exchange (SCX) cartridge (Applied Biosystems Inc.). Separation was effected

by first a wash with 1.0 ml of Eluent A and then ten step-elutions using 0.5 ml each of Eluent A with increasing concentrations of KCl. The ten salt concentrations used were 10 mM, 50 mM, 100 mM, 150 mM, 200 mM, 250 mM, 300 mM, 350 mM, 500 mM and 1 M KCl. Following fractionation, the samples were dried by speed-vacuuming and stored at -20°C. Prior to reverse phase nanobore liquid chromatography-tandem mass spectrometric (nanoLC MS/MS) analysis, these fractions were redissolved in 10μL of an aqueous solution of 1.0% formic acid.

Nanobore LC-MS/MS

We used a nanobore LC system from LC Packings (Amsterdam, The Netherlands) consisting of a Famos autosampler and an Ultimate Nano LC system. The LC system was interfaced to an API QSTAR Pulsar-i hybrid quadrupole/time-of-flight (QqTOF) tandem mass spectrometer (Applied Biosystems/MDS Sciex, Foster City, CA, USA) equipped with a Protana NanoES ion source (Protana Engineering A/S, Odense, Denmark). The spray capillary was a PicoTip SilicaTip emitter with a 10-μm ID tip (New Objective, Woburn, MA, USA). The nanobore LC column was 75-μm ID × 150-mm length reverse-phase nano capillary column packed in-house with 3μm C_{18} beads with 100Å pores (Kromasil). One μl of sample was injected via the 'μL-pick-up' mode. Separation was performed using a binary mobile-phase gradient at a total flow rate of 200 nl/min. For nanospray analysis, the following source conditions were used: a curtain-gas setting of 20 and an ionspray voltage of 1800-3000V, Q0 declustering potential of 65V, and a focusing potential 265V. Nitrogen was used as the collision gas (CAD setting = 5) for both TOF MS and MS/MS scans. All nanoLC MS/MS data were acquired in information-dependent acquisition (IDA) mode using Analyst QS 1.1 (Applied Biosystems/MDS SCIEX). We performed two sets of analysis for each fraction. MS cycles comprised a TOF MS survey scan with an *m*/*z* range of 400-1500Th for 1 s, followed by five product ion scans with an *m*/*z* range of 80-200 Th for 2 s each. Collision energy (CE) was automatically controlled by the IDA CE Parameters script. Switching criteria were set to ions greater than 400 Th and smaller than 1500 Th with a charge state of 2 to 5 and an abundance of ≥10 counts/s. Former target ions were excluded for 30 s and ions within a 4-Th window were ignored. In addition, the IDA Extensions II script was set to no repetitions before dynamic exclusion. In all experiments, the script was set to select a precursor ion nearest to a threshold of 15 count/s every 4 cycles. These settings ensured examination of not only high abundance ions, but low abundance ones as well.

Data Analysis

Data analysis for the iTRAQ experiments were performed with ProteinPilot version 2.0.1 (Applied Biosystems) using a human Celera protein sequence database (human KBMS 20041109) provided by Applied Biosystems that contained a total of 178 239 protein sequences and comprised sequences from NCBI's nr, refseq, SwissProt, TrEMBL and Celera databases. ProteinPilot utilizes the Paragon algorithm for assigning sequence identity. Redundancy between proteins identified is minimized using a grouping function, which assigns an 'unused score' to the peptides that are unique to a protein or group of redundant proteins. The cut-off unused score used for assessing detection was 1.3, which corresponds to a confidence of 95%. Relative quantification of proteins in the case of iTRAQ is performed on the MS/MS scans and is the ratio of the areas under the peaks at 114, 115, 116, and 117Da which are the masses of the tags that correspond to the iTRAQ reagents. The protein ratios are calculated using the individual ratios of the peptides with a weighting factor incorporated based on the confidence of the matching peptide. Normalization of the ratio is performed by the ProteinPilot using the median ratio obtained across all the proteins identified in a run. This normalization is based on the assumption that most proteins will not show significant differential expression between the samples. The normalization factor is termed the 'Applied bias' and is calculated for each pair of samples.

A complete list of the differentially expressed (upregulated and downregulated) proteins identified, based on a fold change cut-off value of 1.5

SwissProt ID	Gene symbol	Protein name	Average fold change	Regulation
Q9H1B7	C14orf4	Chromosome 14 open reading frame 4	**4.8624**	UP
Q04917	YWHAH	tyrosine 3/tryptophan 5 -monooxygenase activation protein	**4.2912**	UP
P04632	CAPNS1	Calpain, small subunit 1	**3.9777**	UP
Q96FE0	SERPING1	Serpin peptidase inhibitor, clade G (C1 inhibitor), member 1	**3.6651**	UP
O60701	UGDH	UDP-glucose dehydrogenase	**3.3497**	UP
P00338	LDHA	Lactate dehydrogenase A	**3.3210**	UP
P40261	NNMT	Nicotinamide N-methyltransferase	**3.2572**	UP
Q7Z3T2	GSTO1	Glutathione S-transferase omega 1	**3.1252**	UP
Q6PKG5	PCBP2	Poly(rC) binding protein 2	**3.0866**	UP
P61204	ARF3	ADP-ribosylation factor 3	**3.0753**	UP
Q6P5S8	IGK@	IGK@ protein	**2.9837**	UP
P07355	ANXA2	annexin A2 isoform 1	**2.9206**	UP
P27824	CANX	Calnexin	**2.8414**	UP
O95861	BPNT1	3'(2'), 5'-bisphosphate nucleotidase 1	**2.7755**	UP
Q9H047	FABP7	Fatty acid binding protein 7, brain	**2.7722**	UP
P21964	COMT	In multiple clusters	**2.7512**	UP
O14556	GAPDHS	Glyceraldehyde-3-phosphate dehydrogenase, spermatogenic	**2.6716**	UP
Q6P452	ANXA4	Annexin A4	**2.6156**	UP
Q7Z2Y7	SERPINB6	Serpin peptidase inhibitor, clade B (ovalbumin), member 6	**2.5934**	UP
Q9HC35	EML4	Echinoderm microtubule associated protein like 4	**2.5750**	UP
P00352	ALDH1A1	aldehyde dehydrogenase 1A1	**2.5428**	UP
Q7Z4X1	DYNC1I2	Dynein, cytoplasmic 1, intermediate chain 2	**2.5234**	UP
P04632	CAPNS1	Calpain, small subunit 1	**2.5198**	UP
P09210	GSTA2	Glutathione S-transferase A2	**2.4979**	UP
P02511	CRYAB	Crystallin, alpha B	**2.4895**	UP
Q6P0L5	ALDOC	Aldolase C, fructose-bisphosphate	**2.4321**	UP
P31150	GDI1	GDP dissociation inhibitor 1	**2.4198**	UP
Q9BUB1	PRKAR2A	Protein kinase, cAMP-dependent, regulatory, type II, alpha	**2.4146**	UP
O00299	CLIC1	Chloride intracellular channel 1	**2.4112**	UP
Q8WW95	PBEF1	Pre-B-cell colony enhancing factor 1	**2.4046**	UP
P08758	ANXA5	In multiple clusters	**2.3679**	UP
P04406	GAPDH	In multiple clusters	**2.3475**	UP
Q6N089	IGHG1	Immunoglobulin heavy constant gamma 1 (G1m marker)	**2.3351**	UP
P01042	KNG1	Kininogen 1	**2.3289**	UP
Q01813	PFKP	6-phosphofructokinase type C	**2.3220**	UP
P00354	GAPDH	In multiple clusters	**2.2959**	UP
P08670	VIM	In multiple clusters	**2.2893**	UP
Q9BW30	TPPP3	Tubulin polymerization-promoting protein family member 3	**2.2885**	UP

Q8TCD5	NT5C	5'(3')-deoxyribonucleotidase, cytosolic type	**2.2738**	UP
P14618	PKM2	Pyruvate kinase, muscle	**2.2725**	UP
Q6I9V1	DPEP1	Dipeptidase 1 (renal)	**2.2614**	UP
P04083	ANXA1	Annexin A1	**2.2523**	UP
P09525	ANXA4	Annexin A4	**2.2381**	UP
P02790	HPX	Hemopexin	**2.2292**	UP
P51148	RAB5C	RAB5C, member RAS oncogene family	**2.2070**	UP
Q15365	PCBP1	Poly(rC) binding protein 1	**2.1984**	UP
Q96MH4	UBC	Ubiquitin C	**2.1816**	UP
Q9BR91	PFKL	Phosphofructokinase, liver	**2.1690**	UP
P09496	CLTA	Clathrin, light chain (Lca)	**2.1186**	UP
P05783	KRT18	Keratin 18	**2.1134**	UP
P02787	TF	Transferrin	**2.0909**	UP
Q16543	CDC37	Cell division cycle 37 homolog (S. cerevisiae)	**2.0713**	UP
Q8TBV2	ANXA2	Annexin A2	**2.0569**	UP
P06733	ENO1	Enolase 1, (alpha)	**2.0265**	UP
P21810	BGN	Biglycan [Precursor]	**2.0104**	UP
Q6N093	IGHG1	Immunoglobulin heavy constant gamma 1 (G1m marker)	**1.9924**	UP
P02656	APOC3	Apolipoprotein C-III	**1.9728**	UP
Q8IZK5	LDHD	Lactate dehydrogenase D	**1.9721**	UP
P30041	PRDX6	In multiple clusters	**1.9705**	UP
O14818	PSMA7	Proteasome (prosome, macropain) subunit, alpha type, 7	**1.9593**	UP
P61026	RAB10	In multiple clusters	**1.9520**	UP
P53396	ACLY	ATP citrate lyase	**1.9435**	UP
P06744	GPI	Glucose phosphate isomerase	**1.9418**	UP
P09104	ENO2	Enolase 2 (gamma, neuronal)	**1.9308**	UP
Q9Y696	CLIC4	Chloride intracellular channel 4	**1.9177**	UP
P13929	ENO3	Enolase 3 (beta, muscle)	**1.8805**	UP
P02768	ALB	Albumin	**1.8791**	UP
Q9UI17	DMGDH	Dimethylglycine dehydrogenase	**1.8735**	UP
P47897	QARS	Glutaminyl-tRNA synthetase	**1.8728**	UP
P60709	ACTB	In multiple clusters	**1.8686**	UP
Q6IQ15	EEF1A1	In multiple clusters	**1.8649**	UP
P29218	IMPA1	Inositol(myo)-1(or 4)-monophosphatase 1	**1.8561**	UP
P36871	PGM1	Phosphoglucomutase 1	**1.8528**	UP
P04083	ANXA1	annexin I	**1.8510**	UP
Q96KP4	CNDP2	CNDP dipeptidase 2	**1.8460**	UP
Q9UEK8	UBB	Ubiquitin B	**1.8409**	UP
P19971	ECGF1	Endothelial cell growth factor 1 (platelet-derived)	**1.8340**	UP
Q8NI87	PGK1	Phosphoglycerate kinase 1	**1.8338**	UP
P14550	AKR1A1	Aldo-keto reductase family 1, member A1 (aldehyde reductase)	**1.8214**	UP
Q9BUQ0	PTBP1	Polypyrimidine tract binding protein 1	**1.8200**	UP
P09104	ENO2	Enolase 2 (gamma, neuronal)	**1.8115**	UP
P05218	TUBB	In multiple clusters	**1.8108**	UP
Q8N959	NDRG1	In multiple clusters	**1.8022**	UP

P00558	PGK1	Phosphoglycerate kinase 1	**1.7954**	UP
Q9H4A4	RNPEP	Arginyl aminopeptidase (aminopeptidase B)	**1.7781**	UP
P06744	GPI	Glucose-6-phosphate isomerase	**1.7733**	UP
P62269	RPS18	ribosomal protein S18	**1.7658**	UP
Q9BQ80	RNH1	Ribonuclease/angiogenin inhibitor 1	**1.7619**	UP
Q8TAA3	PSMA8	Proteasome (prosome, macropain) subunit, alpha type, 8	**1.7547**	UP
O95153	BZRAP1	Benzodiazapine receptor (peripheral) associated protein 1	**1.7455**	UP
Q9BUS0	ZYX	Zyxin	**1.7400**	UP
P50238	CRIP1	Cysteine-rich protein 1 (intestinal)	**1.7271**	UP
Q14240	EIF4A2	In multiple clusters	**1.7252**	UP
Q6B051	TPSAB1	tryptase alpha/beta 1 precursor	**1.7213**	UP
Q92793	CREBBP	CREB binding protein (Rubinstein-Taybi syndrome)	**1.7207**	UP
Q14764	MVP	Major vault protein	**1.6983**	UP
P07339	CTSD	In multiple clusters	**1.6960**	UP
O15511	ARPC5	Actin related protein 2/3 complex, subunit 5, 16kDa	**1.6913**	UP
Q14011	CIRBP	Cold-inducible RNA-binding protein	**1.6874**	UP
Q13347	EIF3I	Eukaryotic translation initiation factor 3, subunit I	**1.6859**	UP
Q15701	DYNLL1	Dynein, light chain, LC8-type 1	**1.6832**	UP
P28072	PSMB6	Proteasome (prosome, macropain) subunit, beta type, 6	**1.6816**	UP
P20042	EIF2S2	Eukaryotic translation initiation factor 2, subunit 2 beta	**1.6782**	UP
Q9NUQ9	FAM49B	Family with sequence similarity 49, member B	**1.6778**	UP
P62241	RPS8	Ribosomal protein S8	**1.6688**	UP
Q9BWL9	HNRPM	In multiple clusters	**1.6687**	UP
Q99541	ADFP	Adipose differentiation-related protein	**1.6629**	UP
Q6IPK9	CES2	Carboxylesterase 2 (intestine, liver)	**1.6606**	UP
Q9UKL9	AKR1C3	Aldo-keto reductase family 1, member C3	**1.6519**	UP
Q13561	DCTN2	Dynactin 2 (p50)	**1.6500**	UP
Q6P5V6	SNX5	Sorting nexin 5	**1.6494**	UP
P14618	PKM2	Pyruvate kinase, muscle	**1.6428**	UP
Q6ICQ3	PPP2R1A	Protein phosphatase 2, regulatory subunit A , alpha isoform	**1.6403**	UP
Q6FG59	CDC37	Cell division cycle 37 homolog (S. cerevisiae)	**1.6370**	UP
P07205	PGK2	Phosphoglycerate kinase 2	**1.6323**	UP
Q15274	QPRT	Quinolinate phosphoribosyltransferase	**1.6276**	UP
P05787	KRT8	In multiple clusters	**1.6169**	UP
P05787	KRT8	In multiple clusters	**1.6089**	UP
Q96DV6	RPS6	Ribosomal protein S6	**1.6056**	UP
Q6DN90	IQSEC1	IQ motif and Sec7 domain 1	**1.6010**	UP
Q9NYR7	HBA2	Hemoglobin, alpha 2	**1.5715**	UP
P35030	PRSS3	Protease, serine, 3 (mesotrypsin)	**1.5712**	UP
Q6N0A0	CLTC	In multiple clusters	**1.5695**	UP
Q9BW18	CPSF6	Cleavage and polyadenylation specificity factor subunit 6	**1.5613**	UP
P60903	S100A10	Protein S100-A10	**1.5554**	UP
P61158	ACTR3	ARP3 actin-related protein 3 homolog (yeast)	**1.5547**	UP
Q96AU2	HNRPF	In multiple clusters	**1.5536**	UP

P58546	MTPN	Myotrophin	**1.5455**	UP
P30740	SERPINB1	Serpin peptidase inhibitor, clade B (ovalbumin), member 1	**1.5436**	UP
O00231	PSMD11	Proteasome (prosome, macropain) 26S subunit, non-ATPase, 11	**1.5426**	UP
P20071	FKBP1A	FK506 binding protein 1A, 12kDa	**1.5380**	UP
Q9BVU3	AHNAK	AHNAK nucleoprotein	**1.5348**	UP
P25787	PSMA2	Proteasome (prosome, macropain) subunit, alpha type, 2	**1.5327**	UP
P13639	EEF2	Eukaryotic translation elongation factor 2	**1.5269**	UP
Q6GMY2	IGHG1	Immunoglobulin heavy constant gamma 1 (G1m marker)	**1.5265**	UP
Q9NNW7	TXNRD2	Thioredoxin reductase 2, mitochondrial [Precursor]	**1.5261**	UP
P02765	AHSG	Alpha-2-HS-glycoprotein	**1.5236**	UP
Q96BB9	IGHG1	Immunoglobulin heavy constant gamma 1 (G1m marker)	**1.5196**	UP
P62333	PSMC6	Proteasome (prosome, macropain) 26S subunit, ATPase, 6	**1.5075**	UP
Q9BQE3	TUBA1C	Tubulin, alpha 1c	**1.5072**	UP
Q9Y371	SH3GLB1	SH3-domain GRB2-like endophilin B1	**0.6666**	DOWN
Q02818	NUCB1	Nucleobindin 1	**0.6650**	DOWN
Q9BTA4	CSRP1	Cysteine and glycine-rich protein 1	**0.6627**	DOWN
P63208	SKP1	S-phase kinase-associated protein 1A	**0.6627**	DOWN
P14314	PRKCSH	Protein kinase C substrate 80K-H	**0.6619**	DOWN
P17174	GOT1	Glutamic-oxaloacetic transaminase 1, soluble	**0.6579**	DOWN
Q6PJX7	KHDRBS1	KH domain containing, RNA binding, signal transduction associated 1	**0.6532**	DOWN
Q6NWQ3	HIST1H2BM	Histone cluster 1, H2bm	**0.6531**	DOWN
Q96CU2	EEF1G	In multiple clusters	**0.6449**	DOWN
P06748	NPM1	Nucleophosmin (nucleolar phosphoprotein B23, numatrin)	**0.6440**	DOWN
P51148	RAB5C	RAB5C, member RAS oncogene family	**0.6423**	DOWN
Q96I99	SUCLG2	Succinate-CoA ligase, GDP-forming, beta subunit	**0.6389**	DOWN
Q13200	PSMD2	Proteasome (prosome, macropain) 26S subunit, non-ATPase, 2	**0.6382**	DOWN
Q96H89	ANXA8L2	Annexin A8-like 2	**0.6357**	DOWN
P07108	ACBP	Acyl-CoA-binding protein	**0.6348**	DOWN
P17980	PSMC3	Proteasome (prosome, macropain) 26S subunit, ATPase, 3	**0.6326**	DOWN
Q96SJ5	MASTL	Microtubule associated serine/threonine kinase-like	**0.6324**	DOWN
A4D2P0	RAC1	Ras-related C3 botulinum toxin substrate 1	**0.6300**	DOWN
Q7Z4J4	TPT1	Tumor protein, translationally-controlled 1	**0.6288**	DOWN
P35558	PCK1	Phosphoenolpyruvate carboxykinase 1 (soluble)	**0.6285**	DOWN
Q9Y5X6	PGCP	Plasma glutamate carboxypeptidase	**0.6271**	DOWN
P15374	UCHL3	Ubiquitin carboxyl-terminal esterase L3 (ubiquitin thiolesterase)	**0.6256**	DOWN
P27816	MAP4	Microtubule-associated protein 4	**0.6252**	DOWN
P00918	HCA2	Carbonic Anhydrase II (Mutant V143G)	**0.6246**	DOWN
Q7Z4L1	EIF5A	Eukaryotic translation initiation factor 5A	**0.6179**	DOWN
Q8N448	LNX2	Ligand of Numb protein X 2	**0.6164**	DOWN

P38117	ETFB	Electron-transfer-flavoprotein, beta polypeptide	**0.6160**	DOWN
O60506	SYNCRIP	Synaptotagmin binding, cytoplasmic RNA interacting protein	**0.6144**	DOWN
Q6DKQ7	DYNC1H1	Dynein, cytoplasmic 1, heavy chain 1	**0.6142**	DOWN
Q96H54	ECHS1	Enoyl Coenzyme A hydratase, short chain, 1, mitochondrial	**0.6089**	DOWN
Q86VC7	BCAM	Basal cell adhesion molecule (Lutheran blood group)	**0.6084**	DOWN
Q96FH6	HBG1	Hemoglobin, gamma A	**0.6079**	DOWN
P00919	HCA3	Carbonic Anhydrase II (Mutant A65S)	**0.6064**	DOWN
Q8IYQ0	LTB4DH	Leukotriene B4 12-hydroxydehydrogenase	**0.6062**	DOWN
P30048	PRDX3	In multiple clusters	**0.6061**	DOWN
O75880	SCO1	SCO cytochrome oxidase deficient homolog 1 (yeast)	**0.6045**	DOWN
P62805	H4	Histone H4	**0.6041**	DOWN
P13798	APEH	N-acylaminoacyl-peptide hydrolase	**0.6022**	DOWN
Q01995	TAGLN	Transgelin	**0.5929**	DOWN
P24752	ACAT1	Acetyl-Coenzyme A acetyltransferase 1	**0.5894**	DOWN
Q6NZA7	ADH1C	Alcohol dehydrogenase 1C (class I), gamma polypeptide	**0.5891**	DOWN
O15145	ARPC3	Actin related protein 2/3 complex, subunit 3, 21kDa	**0.5884**	DOWN
P09493	TPM1	Tropomyosin 1 (alpha)	**0.5819**	DOWN
Q8NHX1	MAPK3	Mitogen-activated protein kinase 3	**0.5813**	DOWN
P82909	MRPS36	Mitochondrial ribosomal protein S36	**0.5776**	DOWN
Q96EZ9	ECH1	Enoyl Coenzyme A hydratase 1, peroxisomal	**0.5771**	DOWN
P48735	IDH2	Isocitrate dehydrogenase 2 (NADP+), mitochondrial	**0.5759**	DOWN
Q86TY5	LGALS3	Lectin, galactoside-binding, soluble, 3	**0.5749**	DOWN
Q96FH7	HBG1	Hemoglobin, gamma A	**0.5743**	DOWN
Q7Z2L6	DCI	Dodecenoyl-Coenzyme A delta isomerase	**0.573**	DOWN
P29034	S100A2	S100 calcium binding protein A2	**0.56985**	DOWN
Q8N3B3	BSCL2	Bernardinelli-Seip congenital lipodystrophy 2 (seipin)	**0.5691**	DOWN
P01008	SERPINC1	Serpin peptidase inhibitor, clade C (antithrombin), member 1	**0.5673**	DOWN
P07951	TPM2	Tropomyosin beta chain	**0.5657**	DOWN
Q9UDX0	OGDH	Oxoglutarate (alpha-ketoglutarate) dehydrogenase	**0.5653**	DOWN
Q6IBE1	HMGB1	In multiple clusters	**0.5638**	DOWN
Q8IUL9	HBB	Hemoglobin, beta	**0.5636**	DOWN
Q15843	NEDD8	Neural precursor cell expressed, developmentally down-regulated 8	**0.56235**	DOWN
P05937	CALB1	Calbindin 1, 28kDa	**0.5621**	DOWN
P62820	RAB1A	Ras-related protein Rab-1A	**0.5619**	DOWN
Q6NUS1	PDCD6IP	Programmed cell death 6 interacting protein	**0.5592**	DOWN
P00915	CA1	Carbonic anhydrase I	**0.5585**	DOWN
P30048	PRDX1	Thioredoxin-dependent peroxide reductase, mitochondrial [Precursor]	**0.558**	DOWN
O75347	TBCA	Tubulin folding cofactor A	**0.5542**	DOWN
Q6V962	RARA	Retinoic acid receptor, alpha	**0.5498**	DOWN
Q7LDY7	DLST	Dihydrolipoamide S-succinyltransferase	**0.54615**	DOWN
P02042	HBD	Hemoglobin Delta	**0.5448**	DOWN
P14174	MIF	Macrophage migration inhibitory factor	**0.5438**	DOWN
Q96HK1	SUMO2	SMT3 suppressor of mif two 3 homolog 2 (S. cerevisiae)	**0.5437**	DOWN

Q8N1C8	HSPA9	Heat shock 70kDa protein 9 (mortalin)	**0.5436**	DOWN
Q6FHZ0	MDH2	Malate dehydrogenase 2, NAD (mitochondrial)	**0.5417**	DOWN
P00734	F2	Prothrombin [Precursor]	**0.5399**	DOWN
P99999	CYCS	In multiple clusters	**0.5374**	DOWN
P80723	BASP1	Brain abundant, membrane attached signal protein 1	**0.5346**	DOWN
P40926	MDH2	Malate dehydrogenase	**0.534**	DOWN
Q6VUD1	ENSA	Endosulfine alpha	**0.5325**	DOWN
Q8WZA9	IRGQ	Immunity-related GTPase family, Q	**0.5311**	DOWN
P61604	HSPE1	Heat shock 10kDa protein 1 (chaperonin 10)	**0.5267**	DOWN
P20810	CAST	calpastatin,	**0.5246**	DOWN
Q9NVE2	MOBKL1B	MOB1, Mps One Binder kinase activator-like 1B (yeast)	**0.5245**	DOWN
Q9H6S3	EPS8L2	EPS8-like 2	**0.5209**	DOWN
Q8IXV2	ATP5A1	ATP synthase, H+ transporting, mitochondrial F1 complex, alpha subunit 1	**0.5138**	DOWN
Q6FHH6	LANCL1	LanC lantibiotic synthetase component C-like 1 (bacterial)	**0.5127**	DOWN
P48735	IDH2	Isocitrate dehydrogenase 2 (NADP+), mitochondrial	**0.5062**	DOWN
Q9C0C2	TNKS1BP1	Tankyrase 1 binding protein 1, 182kDa	**0.503**	DOWN
P14174	MIF	Macrophage migration inhibitory factor	**0.5029**	DOWN
P02023	HBB	Hemoglobin, beta	**0.5008**	DOWN
O75947	ATP5H	ATP synthase, H+ transporting, mitochondrial F0 complex, subunit d	**0.4986**	DOWN
Q9Y5Z5	HEBP1	Heme binding protein 1	**0.49855**	DOWN
Q6MZV5	ARCN1	Archain 1	**0.4937**	DOWN
P02042	HBD	Hemoglobin, delta	**0.4911**	DOWN
Q08380	LGALS3BP	Lectin, galactoside-binding, soluble, 3 binding protein	**0.4898**	DOWN
P10809	HSPD1	In multiple clusters	**0.4896**	DOWN
P30049	ATP5D	ATP synthase, H+ transporting, mitochondrial F1 complex, delta subunit	**0.4879**	DOWN
P31146	CORO1A	Coronin, actin binding protein, 1A	**0.4878**	DOWN
Q6IAT2	GCSH	Glycine cleavage system protein H (aminomethyl carrier)	**0.4873**	DOWN
Q6FI52	TAGLN	Transgelin	**0.4862**	DOWN
Q6UW93	CDH16	Cadherin 16, KSP-cadherin	**0.4818**	DOWN
Q01130	SFRS2	splicing factor, arginine/serine-rich 2	**0.4802**	DOWN
O43670	ZNF207	Zinc finger protein 207	**0.4726**	DOWN
O75531	BANF1	Barrier to autointegration factor 1	**0.4725**	DOWN
P08708	RPS17	Ribosomal protein S17	**0.4702**	DOWN
Q96FB4	ATP5A1	ATP synthase, H+ transporting, mitochondrial F1 complex, alpha subunit 1	**0.4647**	DOWN
O95994	AGR2	Anterior gradient homolog 2 (Xenopus laevis)	**0.4640**	DOWN
P62328	TMSB4X	In multiple clusters	**0.4631**	DOWN
Q7Z664	FGG	Fibrinogen gamma chain	**0.4624**	DOWN
Q6FG40	CKB	Creatine kinase, brain	**0.4589**	DOWN
Q13942	CALM2	Calmodulin 2 (phosphorylase kinase, delta)	**0.4562**	DOWN
Q6ZR40	C9orf58	Chromosome 9 open reading frame 58	**0.4479**	DOWN
P00568	AK1	Adenylate kinase isoenzyme 1	**0.4477**	DOWN
P49411	TUFM	Tu translation elongation factor, mitochondrial	**0.4476**	DOWN

Q9BWB8	TP53I3	Tumor protein p53 inducible protein 3	**0.4383**	DOWN
P25325	MPST	3-mercaptopyruvate sulfurtransferase	**0.429**	DOWN
P62158	CALM2	Calmodulin 2 (phosphorylase kinase, delta)	**0.4245**	DOWN
Q9Y427	TPM1	Tropomyosin 1 (alpha)	**0.4187**	DOWN
P12277	CKB	Creatine kinase, brain	**0.4162**	DOWN
P06576	ATP5B	ATP synthase, H+ transporting, mitochondrial F1 complex, beta polypeptide	**0.4146**	DOWN
P31937	HIBADH	3-hydroxyisobutyrate dehydrogenase	**0.4132**	DOWN
Q6R7N2	HBB	Hemoglobin, beta	**0.4127**	DOWN
Q7L7L0	HIST3H2A	In multiple clusters	**0.4112**	DOWN
P27695	APEX1	APEX nuclease (multifunctional DNA repair enzyme) 1	**0.4085**	DOWN
P30042	C21orf33	Chromosome 21 open reading frame 33	**0.4084**	DOWN
P11310	ACADM	Acyl-Coenzyme A dehydrogenase, C-4 to C-12 straight chain	**0.3938**	DOWN
P05204	HMGN2	High-mobility group nucleosomal binding domain 2	**0.39295**	DOWN
P30042	C21orf33	Chromosome 21 open reading frame 33	**0.3925**	DOWN
O15372	EIF3H	Eukaryotic translation initiation factor 3, subunit H	**0.3894**	DOWN
Q6NVY1	HIBCH	3-hydroxyisobutyryl-CoA hydrolase, mitochondrial [Precursor]	**0.38065**	DOWN
Q96BK4	CALB2	Calbindin 2, 29kDa (calretinin)	**0.3772**	DOWN
O14737	PDCD5	Programmed cell death 5	**0.3623**	DOWN
Q86XE5	C10orf65	Chromosome 10 open reading frame 65	**0.3616**	DOWN
Q9UIJ7	AK3	Adenylate kinase 3	**0.3613**	DOWN
Q96EV5	C10orf65	Chromosome 10 open reading frame 65	**0.3554**	DOWN
Q15254	PTMA	Prothymosin alpha [Precursor]	**0.35495**	DOWN
P31930	UQCRC1	Ubiquinol-cytochrome c reductase core protein I	**0.3531**	DOWN
Q86YI6	PLS3	Plastin 3 (T isoform)	**0.3394**	DOWN
Q9UJZ1	STOML2	Stomatin (EPB72)-like 2	**0.3341**	DOWN
P82979	CIP29	Nuclear protein Hcc-1 (HSPC316)	**0.3316**	DOWN
Q9MYD9	HLA-DRB1	In multiple clusters	**0.3294**	DOWN
Q15293	RCN1	Reticulocalbin 1, EF-hand calcium binding domain	**0.312**	DOWN
P67809	YBX1	Y box binding protein 1	**0.31**	DOWN
Q96M02	C10orf90	chromosome 10 open reading frame 90 was suggested to discard this	**0.3077**	DOWN
Q6NUR2	CYCS	In multiple clusters	**0.2901**	DOWN
O75380	NDUFS6	NADH dehydrogenase (ubiquinone) Fe-S protein 6	**0.2759**	DOWN
Q9H895	DAK	Dihydroxyacetone kinase 2 homolog (S. cerevisiae)	**0.2717**	DOWN
P05455	SSB	Sjogren syndrome antigen B (autoantigen La)	**0.2709**	DOWN
P11177	PDHB	Pyruvate dehydrogenase (lipoamide) beta	**0.2662**	DOWN
Q9Y4F1	FARP1	FERM, RhoGEF (ARHGEF) and pleckstrin domain protein 1	**0.2628**	DOWN
Q6IV71	ALDH2	Aldehyde dehydrogenase 2 family (mitochondrial)	**0.2603**	DOWN
P06454	PTMA	prothymosin-alpha; pseudogene	**0.242**	DOWN
Q16698	DECR1	2,4-dienoyl CoA reductase 1, mitochondrial	**0.21255**	DOWN
Q6IAV5	OXCT1	3-oxoacid CoA transferase 1	**0.1973**	DOWN
Q6QN92	GCSH	Glycine cleavage system protein H (aminomethyl carrier)	**0.164**	DOWN
Q15202	PTMA	Prothymosin alpha	**0.1322**	DOWN
Q9UFK3	PDHB	Pyruvate dehydrogenase (lipoamide) beta	**0.1253**	DOWN

Q6J1Z7	HBB	Hemoglobin, beta	**0.0835**	DOWN
Q9BQI0	C9orf58	Chromosome 9 open reading frame 58	**0.0412**	DOWN