Electronic Supplementary Material (ESI) for Environmental Science: Nano.

Supplementary Information

Silver nanoparticle-protein interactions in intact rainbow trout gill cells

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This supplementary material contains the following sections:

Figure S1. Intracellular silver content in RTgill-W1cells as determined by ICP-MS.

Figure S2. Schematic overview of AgNP-protein corona separation workflow.

Figure S3. Cell organelles in isolated fractions stained with LysoTracker.

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Table S5: Corona proteins belonging to the cell membrane.

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Table S8: Corona proteins belonging to lysosome compartment.

SI_Spectral counts of proteins identified from AgNP-protein corona (separate file).

SI_Cysteine abundance analysis (separate file).

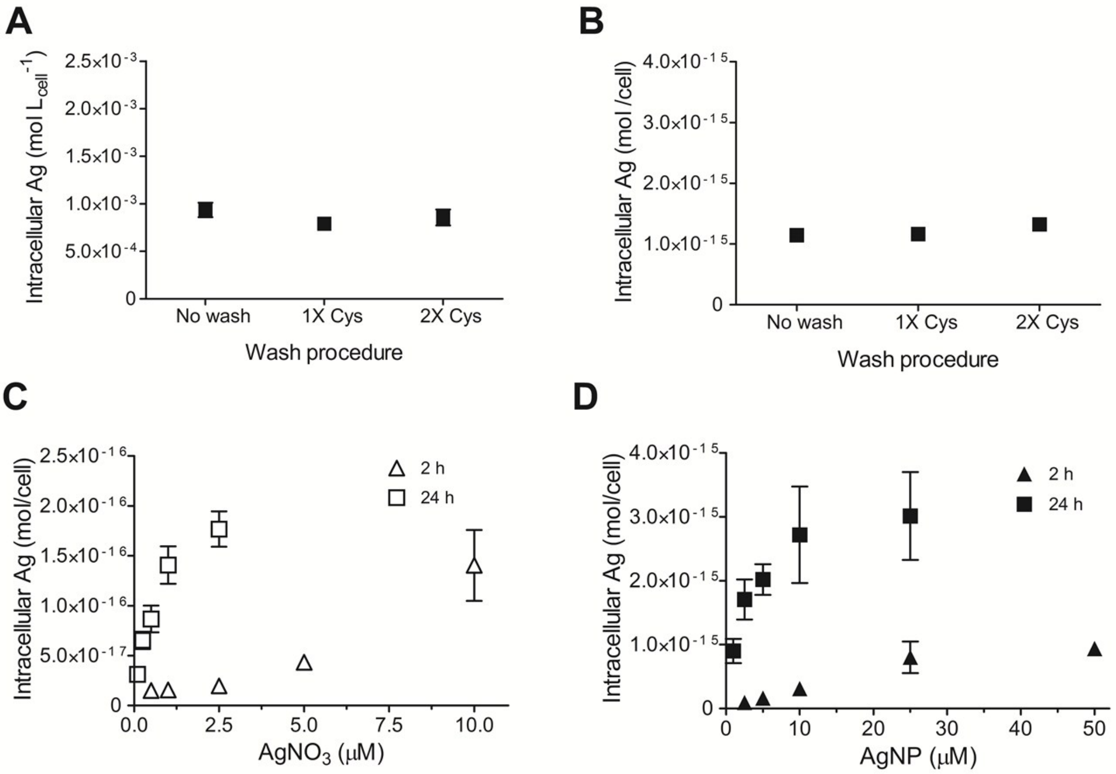
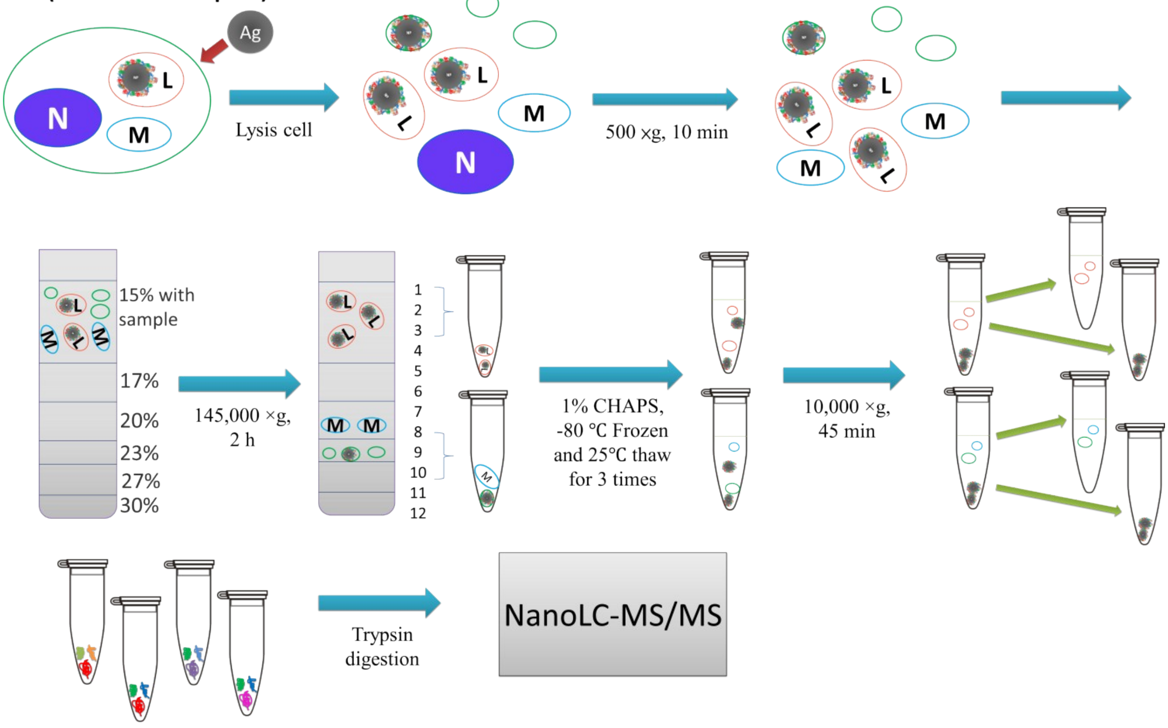
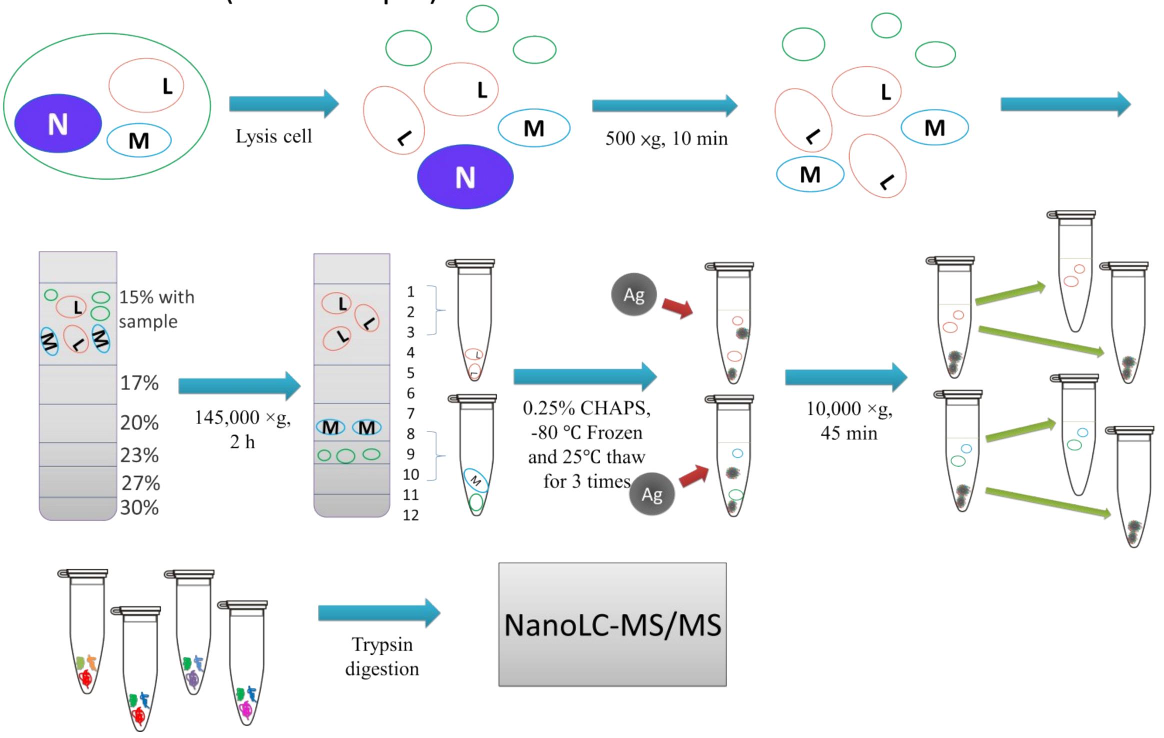


Figure S1. Intracellular silver content in RTgill-W1cells as determined by ICP-MS. A and B: RTgill-W1 cells were exposed to 10 µM AgNP for 24 h and then not washed or washed once or twice with 0.5 mM Cys solution; internal silver content is presented as mol/L_{cell} (A) and mol/cell (B). Internal silver (mol/cell) after exposure of RTgill-W1 cells to $AgNO_3$ (C) and AgNP (D) for 2 h and 24 h, determined after one wash with 0.5 mM Cys. Average and standard deviation of three independent experiments is shown (n=3).



A: Isolation of AgNP-protein corona from AgNP treated intact cells. (Intact sample)



B: Isolation of AgNP-protein corona from AgNP-organelle extraction incubation. (Extra sample)

Figure S2. Schematic overview of AgNP-protein corona separation workflow. A: Separating corona proteins from AgNP upon exposure of RTgill-W1 cells to 20 µM AgNP for 2 h. B: Separating corona proteins from AgNP (0.1 mg/mL) upon incubation of isolated cell fractions (1 mg/mL) for 2 h in 19 °C.

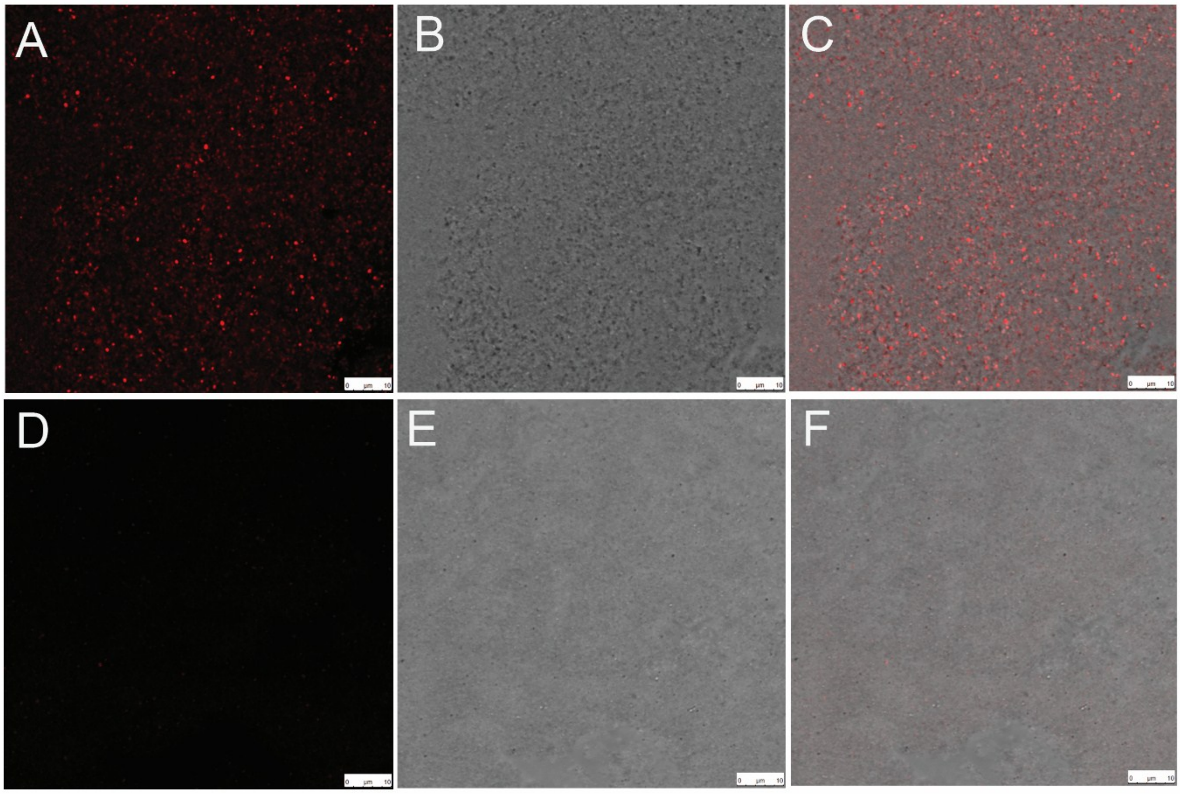


Figure S3. Cell organelles in isolated fractions stained with LysoTracker. A-C: samples from fraction 1-3, endosome-lysosome fractions. D-F: samples from fraction 8-10, cell membrane-mitochondria-nucleus fractions. A and D: LysoTacker red fluorescence images. B and E: Bright field images. C and F: merger of fluorescence image with bright field image.

Table S1. Formulation of d-L-15/ex exposure medium.*

Ion species/compound	**Concentration (mM)**
Cl^-	0.5
Ca^{2+}	0.6
Mg^{2+}	1.5
Na^+	63.3
K^+	2.4
PO_4^{3-}	0.8
SO_4^{2-}	1.5
NO_3^-	65.8
Galactose	2.3
Sodium Pyruvate	2.3
Ionic strength#	**72.0**

* The formulation of d-L-15/ex medium was from previous work.[1] This medium is a simple buffer containing only salts, sodium pyruvate and galactose, which supports short-term RTgill-W1 cell viability and is designed to mimic the aquatic environment a gill cell would face.

\# Ionic strength was calculated by Visual MINTEQ, ver. 3.0.

Reference:

1. Y. Yue, R. Behra, L. Sigg, P. Fernández Freire, S. Pillai and K. Schirmer, *Nanotoxicology*, 2015, 9, 54-63.

Table S2. EC50 Values, Corresponding 95% Confidence Intervals, Hill slope and R^2 of AgNP and $AgNO_3$ concentration-response curves obtained after 2 h of exposure.

		EC50 (µM)	**95% confidence interval**	**Hill Slope**	**R^2**
AgNP	Metabolic activity	54.20	48.11-61.06	-1.519	0.9760
	Cell membrane integrity	64.89	59.70-70.54	-1.195	0.9888
	Lysosomal membrane integrity	65.83	49.76-87.08	-0.838	0.8849
$AgNO_3$	Metabolic activity	9.681	8.916-10.51	-1.167	0.9885
	Cell membrane integrity	22.00	18.91-25.59	-0.917	0.9636
	Lysosomal membrane integrity	11.26	9.085-13.95	-0.754	0.9317

Table S3. Percentage of dissolved silver in AgNP suspension in d-L-15/ex medium incubated with RTgill-W1 cells for 2 h.

Dissolved silver	25 uM	100 uM
Centrifugal Ultrafiltration	0.57%	0.26%
Ultra-centrifugation	6.87%	3.23%
Average	2.73%	

Table S4. DAVID ontology analysis of proteins that were enriched > 2-fold in the AgNP sample compared to the $AgNO_3$ sample. Total: 35 clusters.

Annotation Cluster 1	**Enrichment Score: 18.75**				
Category	Term	Count	*P* Value	Fold Enrichment	Benjamini
SP_PIR_KEYWORDS	mitochondrion	59	3.7E-25	5.13	6.6E-23
GOTERM_CC_FAT	GO:0044429~mitochondrial part	55	4.8E-23	4.94	1.7E-20
GOTERM_CC_FAT	GO:0005739~mitochondrion	71	2.6E-21	3.49	4.6E-19
GOTERM_CC_FAT	GO:0031967~organelle envelope	53	1.2E-20	4.57	1.5E-18
GOTERM_CC_FAT	GO:0031975~envelope	53	1.4E-20	4.56	1.3E-18
GOTERM_CC_FAT	GO:0031090~organelle membrane	70	1.9E-20	3.42	1.3E-18
GOTERM_CC_FAT	GO:0031966~mitochondrial membrane	41	7.8E-19	5.57	4.6E-17
GOTERM_CC_FAT	GO:0005740~mitochondrial envelope	42	1.0E-18	5.36	5.2E-17
GOTERM_CC_FAT	GO:0019866~organelle inner membrane	32	8.2E-14	5.20	3.6E-12
GOTERM_CC_FAT	GO:0005743~mitochondrial inner membrane	29	2.9E-12	5.07	1.0E-10
Annotation Cluster 2	**Enrichment Score: 10.81**				
Category	Term	Count	*P* Value	Fold Enrichment	Benjamini
SP_PIR_KEYWORDS	mitochondrion	59	3.7E-25	5.13	6.6E-23
GOTERM_CC_FAT	GO:0044429~mitochondrial part	55	4.8E-23	4.94	1.7E-20
GOTERM_CC_FAT	GO:0005739~mitochondrion	71	2.6E-21	3.49	4.6E-19
SP_PIR_KEYWORDS	transit peptide	34	2.2E-14	5.17	2.6E-12
UP_SEQ_FEATURE	transit peptide:Mitochondrion	32	5.3E-13	4.92	4.6E-10
GOTERM_CC_FAT	GO:0031980~mitochondrial lumen	22	1.5E-09	5.18	4.7E-08
GOTERM_CC_FAT	GO:0005759~mitochondrial matrix	22	1.5E-09	5.18	4.7E-08
GOTERM_CC_FAT	GO:0070013~intracellular organelle lumen	51	1.6E-03	1.53	1.6E-02
GOTERM_CC_FAT	GO:0031974~membrane-enclosed lumen	52	2.4E-03	1.50	2.2E-02
GOTERM_CC_FAT	GO:0043233~organelle lumen	51	2.6E-03	1.50	2.4E-02
GOTERM_CC_FAT	GO:0031981~nuclear lumen	23	8.7E-01	0.85	1.0E+00
Annotation Cluster 3	**Enrichment Score: 7.04**				
Category	Term	Count	*P* Value	Fold Enrichment	Benjamini
SP_PIR_KEYWORDS	nucleotide-binding	65	4.2E-14	2.79	3.0E-12
GOTERM_MF_FAT	GO:0000166~nucleotide binding	78	1.1E-11	2.14	1.4E-09
GOTERM_MF_FAT	GO:0017076~purine nucleotide binding	70	2.6E-11	2.25	2.7E-09
GOTERM_MF_FAT	GO:0032555~purine ribonucleotide binding	66	2.5E-10	2.21	2.2E-08
GOTERM_MF_FAT	GO:0032553~ribonucleotide binding	66	2.5E-10	2.21	2.2E-08
SP_PIR_KEYWORDS	atp-binding	40	5.8E-06	2.18	9.5E-05
GOTERM_MF_FAT	GO:0001883~purine nucleoside binding	50	6.2E-06	1.92	4.6E-04
GOTERM_MF_FAT	GO:0001882~nucleoside binding	50	7.4E-06	1.91	4.9E-04
GOTERM_MF_FAT	GO:0030554~adenyl nucleotide binding	48	2.0E-05	1.87	9.7E-04
GOTERM_MF_FAT	GO:0005524~ATP binding	44	8.6E-05	1.83	3.5E-03
GOTERM_MF_FAT	GO:0032559~adenyl ribonucleotide binding	44	1.2E-04	1.81	4.1E-03
UP_SEQ_FEATURE	nucleotide phosphate-binding region:ATP	24	7.8E-03	1.79	3.6E-01
Annotation Cluster 4	**Enrichment Score: 6.58**				
Category	Term	Count	*P* Value	Fold Enrichment	Benjamini
SP_PIR_KEYWORDS	P-loop	19	3.0E-14	11.84	2.7E-12
SP_PIR_KEYWORDS	nucleotide binding	18	1.1E-13	12.16	6.4E-12
GOTERM_MF_FAT	GO:0005525~GTP binding	31	3.0E-13	5.13	1.6E-10

GOTERM_MF_FAT	GO:0019001~guanyl nucleotide binding	31	5.9E-13	4.99	1.6E-10
GOTERM_MF_FAT	GO:0032561~guanyl ribonucleotide binding	31	5.9E-13	4.99	1.6E-10
GOTERM_MF_FAT	GO:0003924~GTPase activity	23	3.5E-12	6.71	6.2E-10
SP_PIR_KEYWORDS	gtp-binding	26	5.1E-12	5.71	2.3E-10
SP_PIR_KEYWORDS	GTP binding	14	6.3E-12	15.11	2.5E-10
UP_SEQ_FEATURE	nucleotide phosphate-binding region:GTP	21	6.0E-09	5.11	2.6E-06
SP_PIR_KEYWORDS	prenylated cysteine	8	1.8E-08	25.15	4.5E-07
SP_PIR_KEYWORDS	prenylation	14	2.6E-07	6.49	5.8E-06
UP_SEQ_FEATURE	short sequence motif:Effector region	11	8.0E-07	8.32	2.3E-04
SP_PIR_KEYWORDS	methylation	16	1.4E-06	4.78	2.7E-05
UP_SEQ_FEATURE	lipid moiety-binding region:S-geranylgeranyl cysteine	11	1.5E-06	7.75	3.3E-04
INTERPRO	IPR005225:Small GTP-binding protein	14	2.0E-06	5.41	3.8E-04
GOTERM_BP_FAT	GO:0007264~small GTPase mediated signal transduction	19	5.0E-06	3.63	8.6E-04
INTERPRO	IPR001806:Ras GTPase	12	7.9E-06	5.74	1.1E-03
INTERPRO	IPR013753:Ras	11	2.4E-05	5.68	2.8E-03
SMART	SM00175:RAB	7	8.5E-05	9.47	3.7E-03
SP_PIR_KEYWORDS	lipoprotein	23	8.6E-05	2.59	1.2E-03
INTERPRO	IPR003579:Ras small GTPase, Rab type	7	3.5E-04	7.41	2.8E-02
BIOCARTA	h_rabPathway:Rab GTPases Mark Targets In The Endocytotic Machinery	5	5.2E-04	11.74	7.1E-02
SP_PIR_KEYWORDS	membrane trafficking	4	1.3E-03	18.08	1.3E-02
GOTERM_CC_FAT	GO:0009898~internal side of plasma membrane	15	2.4E-03	2.54	2.2E-02
GOTERM_BP_FAT	GO:0007242~intracellular signaling cascade	35	4.7E-03	1.62	1.3E-01
INTERPRO	IPR002078:RNA polymerase sigma factor 54, interaction	3	1.2E-02	17.61	2.8E-01
UP_SEQ_FEATURE	propeptide:Removed in mature form	7	1.0E-01	2.20	9.1E-01
GOTERM_CC_FAT	GO:0031225~anchored to membrane	5	5.9E-01	1.22	9.3E-01
Annotation Cluster 5	**Enrichment Score: 6.36**				
Category	Term	Count	*P* Value	Fold Enrichment	Benjamini
GOTERM_CC_FAT	GO:0042470~melanosome	18	5.1E-13	10.82	2.0E-11
GOTERM_CC_FAT	GO:0048770~pigment granule	18	5.1E-13	10.82	2.0E-11
GOTERM_CC_FAT	GO:0031410~cytoplasmic vesicle	27	1.6E-04	2.25	2.4E-03
GOTERM_CC_FAT	GO:0031982~vesicle	27	3.1E-04	2.16	3.8E-03
GOTERM_CC_FAT	GO:0016023~cytoplasmic membrane-bounded vesicle	23	6.2E-04	2.24	6.8E-03
GOTERM_CC_FAT	GO:0031988~membrane-bounded vesicle	23	9.4E-04	2.17	9.7E-03
Annotation Cluster 6	**Enrichment Score: 5.47**				
Category	Term	Count	*P* Value	Fold Enrichment	Benjamini
INTERPRO	IPR016040:NAD(P)-binding domain	15	8.4E-08	6.46	4.9E-05
SP_PIR_KEYWORDS	nad	14	2.3E-06	5.36	4.1E-05
UP_SEQ_FEATURE	nucleotide phosphate-binding region:NAD	9	1.0E-05	8.51	1.5E-03
UP_SEQ_FEATURE	binding site:NAD	7	6.4E-05	10.06	7.9E-03
Annotation Cluster 7	**Enrichment Score: 5.37**				
Category	Term	Count	*P* Value	Fold Enrichment	Benjamini
SP_PIR_KEYWORDS	mitochondrion outer membrane	12	2.9E-09	12.40	8.1E-08
GOTERM_CC_FAT	GO:0005741~mitochondrial outer membrane	12	8.4E-07	7.13	2.3E-05
GOTERM_CC_FAT	GO:0031968~organelle outer membrane	12	3.6E-06	6.17	8.4E-05
GOTERM_CC_FAT	GO:0019867~outer membrane	12	5.2E-06	5.94	1.1E-04

GOTERM_BP_FAT	GO:0007005~mitochondrion organization	7	3.1E-02	2.96	4.2E-01
Annotation Cluster 8	**Enrichment Score: 4.85**				
Category	Term	Count	*P* Value	Fold Enrichment	Benjamini
SMART	SM00244:PHB	6	2.7E-07	38.09	2.4E-05
INTERPRO	IPR001107:Band 7 protein	6	9.8E-07	29.80	2.8E-04
PIR_SUPERFAMILY	PIRSF005651:membrane protease subunits, stomatin/prohibitin homologs	3	1.1E-02	18.11	6.1E-01
Annotation Cluster 9	**Enrichment Score: 4.77**				
Category	Term	Count	*P* Value	Fold Enrichment	Benjamini
GOTERM_CC_FAT	GO:0005626~insoluble fraction	37	2.1E-06	2.36	5.3E-05
GOTERM_CC_FAT	GO:0000267~cell fraction	43	3.7E-06	2.12	8.1E-05
GOTERM_CC_FAT	GO:0005624~membrane fraction	35	6.6E-06	2.31	1.3E-04
GOTERM_CC_FAT	GO:0005792~microsome	15	1.4E-04	3.38	2.3E-03
GOTERM_CC_FAT	GO:0042598~vesicular fraction	15	1.9E-04	3.29	2.8E-03
Annotation Cluster 10	**Enrichment Score: 4.51**				
Category	Term	Count	*P* Value	Fold Enrichment	Benjamini
GOTERM_BP_FAT	GO:0006091~generation of precursor metabolites and energy	24	4.0E-09	4.47	6.2E-06
GOTERM_BP_FAT	GO:0009060~aerobic respiration	9	1.0E-07	14.99	5.2E-05
SP_PIR_KEYWORDS	tricarboxylic acid cycle	7	2.9E-07	24.10	5.9E-06
GOTERM_BP_FAT	GO:0045333~cellular respiration	12	7.8E-07	7.21	2.4E-04
GOTERM_BP_FAT	GO:0046356~acetyl-CoA catabolic process	7	1.8E-06	17.75	4.1E-04
GOTERM_BP_FAT	GO:0006099~tricarboxylic acid cycle	7	1.8E-06	17.75	4.1E-04
GOTERM_BP_FAT	GO:0009109~coenzyme catabolic process	7	4.0E-06	15.70	7.7E-04
GOTERM_BP_FAT	GO:0015980~energy derivation by oxidation of organic compounds	13	6.6E-06	5.26	1.0E-03
UP_SEQ_FEATURE	nucleotide phosphate-binding region:NAD	9	1.0E-05	8.51	1.5E-03
GOTERM_BP_FAT	GO:0051187~cofactor catabolic process	7	1.2E-05	13.17	1.5E-03
GOTERM_BP_FAT	GO:0006084~acetyl-CoA metabolic process	7	1.2E-05	13.17	1.5E-03
GOTERM_BP_FAT	GO:0043648~dicarboxylic acid metabolic process	7	2.1E-05	12.01	2.3E-03
KEGG_PATHWAY	hsa00020:Citrate cycle (TCA cycle)	7	8.7E-05	9.11	1.2E-02
GOTERM_BP_FAT	GO:0051186~cofactor metabolic process	13	1.3E-04	3.89	1.3E-02
GOTERM_BP_FAT	GO:0006734~NADH metabolic process	4	2.6E-04	29.16	2.2E-02
GOTERM_BP_FAT	GO:0006732~coenzyme metabolic process	11	3.0E-04	4.19	2.4E-02
GOTERM_BP_FAT	GO:0043603~cellular amide metabolic process	7	3.7E-04	7.29	2.8E-02
GOTERM_BP_FAT	GO:0006103~2-oxoglutarate metabolic process	4	5.4E-04	23.32	3.6E-02
GOTERM_BP_FAT	GO:0046496~nicotinamide nucleotide metabolic process	6	5.6E-04	8.75	3.5E-02
GOTERM_BP_FAT	GO:0006769~nicotinamide metabolic process	6	5.6E-04	8.75	3.5E-02
GOTERM_BP_FAT	GO:0009820~alkaloid metabolic process	6	6.3E-04	8.53	3.8E-02
GOTERM_BP_FAT	GO:0019362~pyridine nucleotide metabolic process	6	7.1E-04	8.33	4.1E-02
GOTERM_BP_FAT	GO:0019674~NAD metabolic process	5	7.9E-04	11.66	4.3E-02
GOTERM_BP_FAT	GO:0006733~oxidoreduction coenzyme metabolic process	6	1.9E-03	6.73	7.2E-02
GOTERM_BP_FAT	GO:0019748~secondary metabolic process	7	2.3E-03	5.17	8.1E-02
Annotation Cluster 11	**Enrichment Score: 4.46**				
Category	Term	Count	*P* Value	Fold Enrichment	Benjamini
SP_PIR_KEYWORDS	oxidoreductase	33	1.1E-11	4.25	4.0E-10

GOTERM_BP_FAT	GO:0055114~oxidation reduction	33	4.2E-08	3.01	3.2E-05
INTERPRO	IPR016040:NAD(P)-binding domain	15	8.4E-08	6.46	4.9E-05
UP_SEQ_FEATURE	binding site:Substrate	17	4.3E-06	4.11	7.4E-04
SP_PIR_KEYWORDS	nadp	10	3.2E-04	4.64	4.0E-03
INTERPRO	IPR002347:Glucose/ribitol dehydrogenase	6	1.3E-03	7.31	6.7E-02
INTERPRO	IPR002198:Short-chain dehydrogenase/reductase SDR	6	2.1E-03	6.57	9.0E-02
PIR_SUPERFAMILY	PIRSF000092:short-chain dehydrogenase	4	3.1E-03	13.00	4.1E-01
UP_SEQ_FEATURE	active site:Proton acceptor	15	7.7E-02	1.64	8.8E-01
UP_SEQ_FEATURE	nucleotide phosphate-binding region:NADP	4	7.8E-02	3.99	8.7E-01
Annotation Cluster 12	**Enrichment Score: 4.35**				
Category	Term	Count	*P* Value	Fold Enrichment	Benjamini
GOTERM_MF_FAT	GO:0050662~coenzyme binding	14	7.6E-06	4.76	4.4E-04
GOTERM_MF_FAT	GO:0048037~cofactor binding	16	1.3E-05	3.95	6.8E-04
GOTERM_MF_FAT	GO:0051287~NAD or NADH binding	6	9.3E-04	7.85	2.6E-02
Annotation Cluster 13	**Enrichment Score: 3.49**				
Category	Term	Count	*P* Value	Fold Enrichment	Benjamini
SP_PIR_KEYWORDS	tricarboxylic acid cycle	7	2.9E-07	24.10	5.9E-06
GOTERM_BP_FAT	GO:0006099~tricarboxylic acid cycle	7	1.8E-06	17.75	4.1E-04
GOTERM_BP_FAT	GO:0046356~acetyl-CoA catabolic process	7	1.8E-06	17.75	4.1E-04
GOTERM_BP_FAT	GO:0009109~coenzyme catabolic process	7	4.0E-06	15.70	7.7E-04
GOTERM_BP_FAT	GO:0006084~acetyl-CoA metabolic process	7	1.2E-05	13.17	1.5E-03
GOTERM_BP_FAT	GO:0051187~cofactor catabolic process	7	1.2E-05	13.17	1.5E-03
KEGG_PATHWAY	hsa00020:Citrate cycle (TCA cycle)	7	8.7E-05	9.11	1.2E-02
GOTERM_MF_FAT	GO:0051287~NAD or NADH binding	6	9.3E-04	7.85	2.6E-02
UP_SEQ_FEATURE	site:Critical for catalysis	3	1.9E-03	43.11	1.4E-01
INTERPRO	IPR019818:Isocitrate/isopropylmalate dehydrogenase, conserved site	3	2.3E-03	38.74	8.5E-02
GOTERM_MF_FAT	GO:0004448~isocitrate dehydrogenase activity	3	2.5E-03	36.92	6.4E-02
GOTERM_BP_FAT	GO:0006102~isocitrate metabolic process	3	2.8E-03	34.99	9.0E-02
INTERPRO	IPR001804:Isocitrate/isopropylmalate dehydrogenase	3	3.4E-03	32.28	1.2E-01
UP_SEQ_FEATURE	metal ion-binding site:Magnesium or manganese	3	2.3E-02	12.68	5.9E-01
SP_PIR_KEYWORDS	manganese	4	3.5E-01	1.90	7.8E-01
GOTERM_MF_FAT	GO:0030145~manganese ion binding	4	4.6E-01	1.60	9.9E-01
Annotation Cluster 14	**Enrichment Score: 3.24**				
Category	Term	Count	*P* Value	Fold Enrichment	Benjamini
GOTERM_CC_FAT	GO:0012505~endomembrane system	32	5.4E-05	2.19	9.9E-04
GOTERM_CC_FAT	GO:0005783~endoplasmic reticulum	35	2.1E-04	1.95	2.9E-03
GOTERM_CC_FAT	GO:0044432~endoplasmic reticulum part	18	2.7E-04	2.77	3.4E-03
SP_PIR_KEYWORDS	endoplasmic reticulum	23	3.8E-04	2.33	4.4E-03
GOTERM_CC_FAT	GO:0005789~endoplasmic reticulum membrane	13	4.6E-03	2.58	3.8E-02
GOTERM_CC_FAT	GO:0042175~nuclear envelope-endoplasmic reticulum network	13	7.0E-03	2.45	5.1E-02
Annotation Cluster 15	**Enrichment Score: 3.14**				
Category	Term	Count	*P* Value	Fold Enrichment	Benjamini
GOTERM_CC_FAT	GO:0030062~mitochondrial tricarboxylic acid cycle enzyme complex	4	1.2E-04	35.65	2.0E-03
GOTERM_CC_FAT	GO:0045239~tricarboxylic acid cycle enzyme complex	4	2.1E-04	30.56	2.8E-03

GOTERM_CC_FAT	GO:0045240~dihydrolipoyl dehydrogenase complex	3	3.3E-03	32.09	2.8E-02
GOTERM_CC_FAT	GO:0005947~mitochondrial alpha-ketoglutarate dehydrogenase complex	3	3.3E-03	32.09	2.8E-02
Annotation Cluster 16	**Enrichment Score: 2.89**				
Category	Term	Count	*P* Value	Fold Enrichment	Benjamini
GOTERM_BP_FAT	GO:0046395~carboxylic acid catabolic process	10	1.2E-04	5.25	1.2E-02
GOTERM_BP_FAT	GO:0016054~organic acid catabolic process	10	1.2E-04	5.25	1.2E-02
GOTERM_BP_FAT	GO:0009083~branched chain family amino acid catabolic process	4	7.3E-04	21.20	4.1E-02
GOTERM_BP_FAT	GO:0009081~branched chain family amino acid metabolic process	4	2.3E-03	14.58	7.9E-02
KEGG_PATHWAY	hsa00280:Valine, leucine and isoleucine degradation	6	4.2E-03	5.50	6.3E-02
GOTERM_BP_FAT	GO:0009063~cellular amino acid catabolic process	6	6.1E-03	5.15	1.5E-01
GOTERM_BP_FAT	GO:0009310~amine catabolic process	6	1.1E-02	4.49	2.2E-01
Annotation Cluster 17	**Enrichment Score: 2.87**				
Category	Term	Count	*P* Value	Fold Enrichment	Benjamini
SP_PIR_KEYWORDS	transport	53	1.8E-08	2.29	4.4E-07
SP_PIR_KEYWORDS	protein transport	24	2.9E-07	3.58	6.1E-06
GOTERM_BP_FAT	GO:0016192~vesicle-mediated transport	29	5.9E-07	2.94	2.3E-04
GOTERM_BP_FAT	GO:0008104~protein localization	37	8.9E-07	2.45	2.3E-04
GOTERM_BP_FAT	GO:0045184~establishment of protein localization	32	7.2E-06	2.43	1.0E-03
GOTERM_BP_FAT	GO:0015031~protein transport	31	1.6E-05	2.37	1.9E-03
GOTERM_BP_FAT	GO:0046907~intracellular transport	26	1.5E-04	2.31	1.3E-02
GOTERM_BP_FAT	GO:0034613~cellular protein localization	17	1.9E-03	2.41	7.3E-02
GOTERM_BP_FAT	GO:0070727~cellular macromolecule localization	17	2.0E-03	2.39	7.5E-02
GOTERM_BP_FAT	GO:0006605~protein targeting	10	1.2E-02	2.71	2.3E-01
GOTERM_BP_FAT	GO:0006886~intracellular protein transport	14	1.2E-02	2.18	2.3E-01
GOTERM_BP_FAT	GO:0033365~protein localization in organelle	8	1.3E-02	3.20	2.4E-01
GOTERM_BP_FAT	GO:0017038~protein import	7	2.5E-02	3.12	3.7E-01
GOTERM_BP_FAT	GO:0006839~mitochondrial transport	5	3.0E-02	4.23	4.2E-01
GOTERM_BP_FAT	GO:0051170~nuclear import	5	6.4E-02	3.31	6.0E-01
GOTERM_BP_FAT	GO:0006626~protein targeting to mitochondrion	3	1.1E-01	5.15	7.3E-01
GOTERM_BP_FAT	GO:0070585~protein localization in mitochondrion	3	1.1E-01	5.15	7.3E-01
GOTERM_BP_FAT	GO:0006606~protein import into nucleus	4	1.8E-01	2.71	8.5E-01
GOTERM_BP_FAT	GO:0034504~protein localization in nucleus	4	2.2E-01	2.48	8.8E-01
GOTERM_BP_FAT	GO:0006913~nucleocytoplasmic transport	5	2.8E-01	1.87	9.1E-01
GOTERM_BP_FAT	GO:0051169~nuclear transport	5	2.8E-01	1.85	9.2E-01
Annotation Cluster 18	**Enrichment Score: 2.70**				
Category	Term	Count	*P* Value	Fold Enrichment	Benjamini
UP_SEQ_FEATURE	repeat:Solcar 1	7	9.9E-05	9.31	1.1E-02
UP_SEQ_FEATURE	repeat:Solcar 2	7	9.9E-05	9.31	1.1E-02
INTERPRO	IPR018108:Mitochondrial substrate/solute carrier	7	2.2E-04	8.07	2.1E-02
UP_SEQ_FEATURE	repeat:Solcar 3	6	6.9E-04	8.45	6.4E-02
INTERPRO	IPR001993:Mitochondrial substrate carrier	6	1.2E-03	7.45	6.7E-02
GOTERM_BP_FAT	GO:0055085~transmembrane transport	20	4.1E-03	2.05	1.2E-01
INTERPRO	IPR002067:Mitochondrial carrier protein	4	8.1E-03	9.57	2.1E-01

INTERPRO	IPR002113:Adenine nucleotide translocator 1	3	6.0E-02	7.45	6.8E-01
PIR_SUPERFAMILY	PIRSF002458:ADP,ATP carrier protein	3	1.6E-01	4.23	1.0E+00
Annotation Cluster 19	**Enrichment Score: 2.60**				
Category	Term	Count	*P* Value	Fold Enrichment	Benjamini
GOTERM_CC_FAT	GO:0005856~cytoskeleton	45	2.5E-04	1.74	3.2E-03
GOTERM_CC_FAT	GO:0043232~intracellular non-membrane-bounded organelle	65	8.2E-03	1.34	5.9E-02
GOTERM_CC_FAT	GO:0043228~non-membrane-bounded organelle	65	8.2E-03	1.34	5.9E-02
Annotation Cluster 20	**Enrichment Score: 2.54**				
Category	Term	Count	*P* Value	Fold Enrichment	Benjamini
SP_PIR_KEYWORDS	mitochondrion inner membrane	18	1.6E-09	6.74	4.7E-08
GOTERM_CC_FAT	GO:0044455~mitochondrial membrane part	14	5.6E-07	5.99	1.6E-05
GOTERM_MF_FAT	GO:0015077~monovalent inorganic cation transmembrane transporter activity	10	4.6E-05	5.92	2.0E-03
GOTERM_MF_FAT	GO:0015078~hydrogen ion transmembrane transporter activity	9	1.0E-04	6.15	3.8E-03
GOTERM_MF_FAT	GO:0022890~inorganic cation transmembrane transporter activity	11	1.7E-04	4.48	5.6E-03
KEGG_PATHWAY	hsa05012:Parkinson's disease	11	1.1E-03	3.47	5.0E-02
KEGG_PATHWAY	hsa00190:Oxidative phosphorylation	11	1.2E-03	3.41	3.4E-02
SP_PIR_KEYWORDS	oxidative phosphorylation	5	1.3E-03	10.33	1.3E-02
GOTERM_BP_FAT	GO:0006119~oxidative phosphorylation	8	1.4E-03	4.76	6.1E-02
KEGG_PATHWAY	hsa04260:Cardiac muscle contraction	8	2.8E-03	4.14	4.9E-02
SP_PIR_KEYWORDS	respiratory chain	6	3.0E-03	6.11	2.5E-02
KEGG_PATHWAY	hsa05016:Huntington's disease	12	4.5E-03	2.69	5.6E-02
SP_PIR_KEYWORDS	membrane-associated complex	4	9.5E-03	9.04	6.5E-02
GOTERM_MF_FAT	GO:0004129~cytochrome-c oxidase activity	4	1.0E-02	8.79	1.6E-01
GOTERM_MF_FAT	GO:0015002~heme-copper terminal oxidase activity	4	1.0E-02	8.79	1.6E-01
GOTERM_MF_FAT	GO:0016676~oxidoreductase activity, acting on heme group of donors, oxygen as acceptor	4	1.0E-02	8.79	1.6E-01
GOTERM_MF_FAT	GO:0016675~oxidoreductase activity, acting on heme group of donors	4	1.0E-02	8.79	1.6E-01
GOTERM_CC_FAT	GO:0070469~respiratory chain	6	1.3E-02	4.28	8.4E-02
KEGG_PATHWAY	hsa05010:Alzheimer's disease	10	1.8E-02	2.48	1.7E-01
SP_PIR_KEYWORDS	mitochondrial inner membrane	3	2.8E-02	11.42	1.5E-01
GOTERM_CC_FAT	GO:0005746~mitochondrial respiratory chain	5	3.1E-02	4.18	1.6E-01
GOTERM_BP_FAT	GO:0022900~electron transport chain	6	4.6E-02	3.07	5.2E-01
SP_PIR_KEYWORDS	electron transport	5	5.0E-02	3.62	2.2E-01
GOTERM_BP_FAT	GO:0022904~respiratory electron transport chain	4	9.6E-02	3.64	7.0E-01
SP_PIR_KEYWORDS	electron transfer	3	1.5E-01	4.34	4.9E-01
GOTERM_BP_FAT	GO:0042775~mitochondrial ATP synthesis coupled electron transport	3	2.5E-01	3.12	9.0E-01
GOTERM_BP_FAT	GO:0042773~ATP synthesis coupled electron transport	3	2.5E-01	3.12	9.0E-01
Annotation Cluster 21	**Enrichment Score: 2.28**				
Category	Term	Count	*P* Value	Fold Enrichment	Benjamini
SP_PIR_KEYWORDS	cytoskeleton	21	5.4E-04	2.39	5.9E-03
SP_PIR_KEYWORDS	actin binding	5	2.2E-03	9.04	1.9E-02
GOTERM_MF_FAT	GO:0008092~cytoskeletal protein binding	18	3.4E-03	2.20	8.2E-02
SP_PIR_KEYWORDS	actin-binding	10	7.4E-03	2.93	5.4E-02

SMART	SM00033:CH	5	9.8E-03	5.90	1.3E-01
GOTERM_MF_FAT	GO:0003779~actin binding	12	1.7E-02	2.26	2.3E-01
INTERPRO	IPR001715:Calponin-like actin-binding	5	2.3E-02	4.61	4.3E-01
Annotation Cluster 22	**Enrichment Score: 2.21**				
Category	Term	Count	*P* Value	Fold Enrichment	Benjamini
GOTERM_BP_FAT	GO:0030036~actin cytoskeleton organization	13	5.1E-04	3.35	3.5E-02
GOTERM_BP_FAT	GO:0030029~actin filament-based process	13	9.1E-04	3.15	4.6E-02
GOTERM_BP_FAT	GO:0007015~actin filament organization	6	7.7E-03	4.86	1.7E-01
GOTERM_BP_FAT	GO:0007010~cytoskeleton organization	16	8.0E-03	2.14	1.8E-01
GOTERM_CC_FAT	GO:0005925~focal adhesion	6	4.2E-02	3.15	2.0E-01
GOTERM_CC_FAT	GO:0005924~cell-substrate adherens junction	6	4.8E-02	3.03	2.2E-01
Annotation Cluster 23	**Enrichment Score: 2.16**				
Category	Term	Count	*P* Value	Fold Enrichment	Benjamini
GOTERM_MF_FAT	GO:0004579~dolichyl-diphosphooligosaccharide-protein glycotransferase activity	4	3.3E-04	27.35	1.0E-02
GOTERM_MF_FAT	GO:0004576~oligosaccharyl transferase activity	4	4.6E-04	24.61	1.3E-02
GOTERM_BP_FAT	GO:0018279~protein amino acid N-linked glycosylation via asparagine	4	5.4E-04	23.32	3.6E-02
GOTERM_BP_FAT	GO:0018196~peptidyl-asparagine modification	4	5.4E-04	23.32	3.6E-02
GOTERM_CC_FAT	GO:0008250~oligosaccharyltransferase complex	4	6.9E-04	21.39	7.4E-03
GOTERM_CC_FAT	GO:0005789~endoplasmic reticulum membrane	13	4.6E-03	2.58	3.8E-02
GOTERM_BP_FAT	GO:0006487~protein amino acid N-linked glycosylation	5	6.6E-03	6.63	1.6E-01
GOTERM_CC_FAT	GO:0042175~nuclear envelope-endoplasmic reticulum network	13	7.0E-03	2.45	5.1E-02
GOTERM_BP_FAT	GO:0009101~glycoprotein biosynthetic process	7	5.4E-02	2.58	5.6E-01
GOTERM_BP_FAT	GO:0009100~glycoprotein metabolic process	8	5.9E-02	2.31	5.9E-01
GOTERM_BP_FAT	GO:0006486~protein amino acid glycosylation	6	6.8E-02	2.73	6.2E-01
GOTERM_BP_FAT	GO:0070085~glycosylation	6	6.8E-02	2.73	6.2E-01
GOTERM_BP_FAT	GO:0043413~biopolymer glycosylation	6	6.8E-02	2.73	6.2E-01
KEGG_PATHWAY	hsa00510:N-Glycan biosynthesis	4	1.0E-01	3.51	5.2E-01
Annotation Cluster 24	**Enrichment Score: 2.14**				
Category	Term	Count	*P* Value	Fold Enrichment	Benjamini
SP_PIR_KEYWORDS	membrane	138	6.6E-11	1.60	2.2E-09
SP_PIR_KEYWORDS	transmembrane	82	4.7E-02	1.19	2.1E-01
UP_SEQ_FEATURE	transmembrane region	80	7.2E-02	1.17	8.9E-01
GOTERM_CC_FAT	GO:0031224~intrinsic to membrane	96	8.4E-01	0.94	9.9E-01
UP_SEQ_FEATURE	topological domain:Cytoplasmic	42	8.5E-01	0.89	1.0E+00
GOTERM_CC_FAT	GO:0016021~integral to membrane	91	8.9E-01	0.92	1.0E+00
Annotation Cluster 25	**Enrichment Score: 2.05**				
Category	Term	Count	*P* Value	Fold Enrichment	Benjamini
GOTERM_BP_FAT	GO:0046395~carboxylic acid catabolic process	10	1.2E-04	5.25	1.2E-02
GOTERM_BP_FAT	GO:0016054~organic acid catabolic process	10	1.2E-04	5.25	1.2E-02
GOTERM_BP_FAT	GO:0030258~lipid modification	7	1.1E-03	5.92	5.3E-02
GOTERM_BP_FAT	GO:0006635~fatty acid beta-oxidation	4	1.2E-02	8.33	2.3E-01
GOTERM_BP_FAT	GO:0006631~fatty acid metabolic process	9	2.1E-02	2.65	3.4E-01

GOTERM_BP_FAT	GO:0009062~fatty acid catabolic process	4	2.3E-02	6.48	3.6E-01
GOTERM_BP_FAT	GO:0034440~lipid oxidation	4	2.9E-02	5.98	4.1E-01
GOTERM_BP_FAT	GO:0019395~fatty acid oxidation	4	2.9E-02	5.98	4.1E-01
GOTERM_BP_FAT	GO:0044242~cellular lipid catabolic process	4	1.4E-01	3.07	7.9E-01
GOTERM_BP_FAT	GO:0016042~lipid catabolic process	5	3.4E-01	1.69	9.4E-01
Annotation Cluster 26	**Enrichment Score: 2.04**				
Category	Term	Count	*P* Value	Fold Enrichment	Benjamini
GOTERM_CC_FAT	GO:0032592~integral to mitochondrial membrane	4	1.2E-03	17.83	1.2E-02
GOTERM_CC_FAT	GO:0031307~integral to mitochondrial outer membrane	3	4.9E-03	26.74	4.0E-02
GOTERM_CC_FAT	GO:0031306~intrinsic to mitochondrial outer membrane	3	6.8E-03	22.92	5.2E-02
GOTERM_CC_FAT	GO:0031301~integral to organelle membrane	7	2.7E-02	3.04	1.4E-01
GOTERM_CC_FAT	GO:0031300~intrinsic to organelle membrane	7	5.5E-02	2.56	2.4E-01
Annotation Cluster 27	**Enrichment Score: 2.03**				
Category	Term	Count	*P* Value	Fold Enrichment	Benjamini
GOTERM_MF_FAT	GO:0015077~monovalent inorganic cation transmembrane transporter activity	10	4.6E-05	5.92	2.0E-03
GOTERM_MF_FAT	GO:0015078~hydrogen ion transmembrane transporter activity	9	1.0E-04	6.15	3.8E-03
GOTERM_MF_FAT	GO:0022890~inorganic cation transmembrane transporter activity	11	1.7E-04	4.48	5.6E-03
GOTERM_BP_FAT	GO:0009141~nucleoside triphosphate metabolic process	10	4.1E-04	4.45	3.0E-02
GOTERM_BP_FAT	GO:0009205~purine ribonucleoside triphosphate metabolic process	9	8.8E-04	4.49	4.6E-02
GOTERM_BP_FAT	GO:0009199~ribonucleoside triphosphate metabolic process	9	9.3E-04	4.45	4.5E-02
GOTERM_BP_FAT	GO:0009144~purine nucleoside triphosphate metabolic process	9	1.2E-03	4.30	5.3E-02
KEGG_PATHWAY	hsa00190:Oxidative phosphorylation	11	1.2E-03	3.41	3.4E-02
GOTERM_BP_FAT	GO:0006163~purine nucleotide metabolic process	11	1.4E-03	3.45	6.0E-02
GOTERM_BP_FAT	GO:0006119~oxidative phosphorylation	8	1.4E-03	4.76	6.1E-02
GOTERM_BP_FAT	GO:0009206~purine ribonucleoside triphosphate biosynthetic process	8	1.4E-03	4.76	6.1E-02
GOTERM_BP_FAT	GO:0009145~purine nucleoside triphosphate biosynthetic process	8	1.5E-03	4.71	6.3E-02
GOTERM_BP_FAT	GO:0009201~ribonucleoside triphosphate biosynthetic process	8	1.5E-03	4.71	6.3E-02
GOTERM_BP_FAT	GO:0009142~nucleoside triphosphate biosynthetic process	8	1.8E-03	4.57	7.3E-02
GOTERM_BP_FAT	GO:0046034~ATP metabolic process	8	2.1E-03	4.44	7.7E-02
GOTERM_BP_FAT	GO:0009150~purine ribonucleotide metabolic process	9	2.5E-03	3.80	8.3E-02
GOTERM_BP_FAT	GO:0009259~ribonucleotide metabolic process	9	3.7E-03	3.57	1.1E-01
GOTERM_BP_FAT	GO:0006164~purine nucleotide biosynthetic process	9	3.9E-03	3.55	1.2E-01
GOTERM_BP_FAT	GO:0009152~purine ribonucleotide biosynthetic process	8	3.9E-03	3.99	1.1E-01
GOTERM_BP_FAT	GO:0006754~ATP biosynthetic process	7	4.2E-03	4.59	1.2E-01
GOTERM_BP_FAT	GO:0009260~ribonucleotide biosynthetic process	8	5.4E-03	3.76	1.4E-01
GOTERM_MF_FAT	GO:0042625~ATPase activity, coupled to transmembrane movement of ions	6	6.9E-03	4.99	1.4E-01
GOTERM_MF_FAT	GO:0042626~ATPase activity, coupled to transmembrane movement of substances	7	8.5E-03	3.95	1.6E-01
GOTERM_MF_FAT	GO:0043492~ATPase activity, coupled to movement of substances	7	8.9E-03	3.92	1.6E-01
GOTERM_MF_FAT	GO:0016820~hydrolase activity, acting on acid anhydrides, catalyzing	7	9.3E-03	3.88	1.6E-01

	transmembrane movement of substances				
SP_PIR_KEYWORDS	atp synthesis	3	1.3E-02	16.69	8.6E-02
GOTERM_MF_FAT	GO:0015399~primary active transmembrane transporter activity	7	1.4E-02	3.53	2.1E-01
GOTERM_MF_FAT	GO:0015405~P-P-bond-hydrolysis-driven transmembrane transporter activity	7	1.4E-02	3.53	2.1E-01
GOTERM_BP_FAT	GO:0009165~nucleotide biosynthetic process	9	1.5E-02	2.82	2.6E-01
GOTERM_BP_FAT	GO:0034404~nucleobase, nucleoside and nucleotide biosynthetic process	9	1.8E-02	2.72	3.0E-01
GOTERM_BP_FAT	GO:0034654~nucleobase, nucleoside, nucleotide and nucleic acid biosynthetic process	9	1.8E-02	2.72	3.0E-01
GOTERM_MF_FAT	GO:0019829~cation-transporting ATPase activity	4	2.0E-02	6.84	2.6E-01
GOTERM_MF_FAT	GO:0016887~ATPase activity	12	2.0E-02	2.21	2.6E-01
GOTERM_BP_FAT	GO:0044271~nitrogen compound biosynthetic process	12	2.4E-02	2.15	3.6E-01
GOTERM_MF_FAT	GO:0046933~hydrogen ion transporting ATP synthase activity, rotational mechanism	3	2.7E-02	11.54	3.2E-01
SP_PIR_KEYWORDS	Hydrogen ion transport	4	2.8E-02	6.03	1.5E-01
GOTERM_BP_FAT	GO:0015986~ATP synthesis coupled proton transport	4	3.1E-02	5.83	4.2E-01
GOTERM_BP_FAT	GO:0015985~energy coupled proton transport, down electrochemical gradient	4	3.1E-02	5.83	4.2E-01
GOTERM_MF_FAT	GO:0042623~ATPase activity, coupled	10	3.3E-02	2.26	3.5E-01
GOTERM_CC_FAT	GO:0033178~proton-transporting two-sector ATPase complex, catalytic domain	3	4.3E-02	8.91	2.0E-01
GOTERM_CC_FAT	GO:0005753~mitochondrial proton-transporting ATP synthase complex	3	4.8E-02	8.44	2.2E-01
GOTERM_BP_FAT	GO:0034220~ion transmembrane transport	4	5.1E-02	4.76	5.4E-01
GOTERM_CC_FAT	GO:0016469~proton-transporting two-sector ATPase complex	4	5.1E-02	4.75	2.3E-01
GOTERM_MF_FAT	GO:0046961~proton-transporting ATPase activity, rotational mechanism	3	5.3E-02	8.03	4.6E-01
GOTERM_CC_FAT	GO:0045259~proton-transporting ATP synthase complex	3	5.7E-02	7.64	2.4E-01
GOTERM_BP_FAT	GO:0015992~proton transport	4	8.6E-02	3.82	6.7E-01
GOTERM_BP_FAT	GO:0006818~hydrogen transport	4	9.3E-02	3.70	6.9E-01
GOTERM_BP_FAT	GO:0006811~ion transport	18	1.6E-01	1.37	8.3E-01
GOTERM_MF_FAT	GO:0015662~ATPase activity, coupled to transmembrane movement of ions, phosphorylative mechanism	3	2.1E-01	3.48	8.9E-01
SP_PIR_KEYWORDS	ion transport	11	2.8E-01	1.38	6.9E-01
GOTERM_BP_FAT	GO:0006812~cation transport	11	4.7E-01	1.16	9.8E-01
GOTERM_BP_FAT	GO:0015672~monovalent inorganic cation transport	6	6.4E-01	1.10	9.9E-01
Annotation Cluster 28	**Enrichment Score: 2.03**				
Category	Term	Count	*P* Value	Fold Enrichment	Benjamini
GOTERM_BP_FAT	GO:0016044~membrane organization	16	2.3E-03	2.45	8.0E-02
SP_PIR_KEYWORDS	endosome	10	2.5E-03	3.46	2.2E-02
GOTERM_BP_FAT	GO:0006897~endocytosis	9	3.5E-02	2.39	4.6E-01
GOTERM_BP_FAT	GO:0010324~membrane invagination	9	3.5E-02	2.39	4.6E-01
Annotation Cluster 29	**Enrichment Score: 1.97**				
Category	Term	Count	*P* Value	Fold Enrichment	Benjamini
INTERPRO	IPR012335:Thioredoxin fold	8	9.6E-04	5.11	6.0E-02
UP_SEQ_FEATURE	short sequence motif:Prevents secretion from ER	6	1.3E-03	7.31	1.1E-01
INTERPRO	IPR017936:Thioredoxin-like	5	2.2E-03	8.97	8.7E-02
INTERPRO	IPR000886:Endoplasmic reticulum, targeting sequence	5	5.0E-03	7.17	1.5E-01

GOTERM_CC_FAT	GO:0005793~ER-Golgi intermediate compartment	5	6.9E-03	6.52	5.2E-02
GOTERM_MF_FAT	GO:0003756~protein disulfide isomerase activity	3	8.7E-03	20.51	1.6E-01
GOTERM_MF_FAT	GO:0016864~intramolecular oxidoreductase activity, transposing S-S bonds	3	8.7E-03	20.51	1.6E-01
GOTERM_MF_FAT	GO:0016862~intramolecular oxidoreductase activity, interconverting keto- and enol-groups	3	1.1E-02	18.46	1.7E-01
GOTERM_CC_FAT	GO:0005788~endoplasmic reticulum lumen	6	1.7E-02	4.01	9.8E-02
SP_PIR_KEYWORDS	Redox-active center	4	2.0E-02	6.89	1.1E-01
GOTERM_BP_FAT	GO:0045454~cell redox homeostasis	5	2.3E-02	4.63	3.6E-01
INTERPRO	IPR017937:Thioredoxin, conserved site	3	6.0E-02	7.45	6.8E-01
INTERPRO	IPR013766:Thioredoxin domain	3	6.5E-02	7.17	6.9E-01
GOTERM_MF_FAT	GO:0016860~intramolecular oxidoreductase activity	3	1.3E-01	4.86	7.4E-01
Annotation Cluster 30	**Enrichment Score: 1.96**				
Category	Term	Count	*P* Value	Fold Enrichment	Benjamini
SP_PIR_KEYWORDS	calcium binding	8	5.6E-04	5.62	5.9E-03
INTERPRO	IPR018247:EF-HAND 1	12	5.7E-04	3.57	4.0E-02
INTERPRO	IPR018249:EF-HAND 2	11	1.9E-03	3.30	8.8E-02
INTERPRO	IPR011992:EF-Hand type	11	3.8E-03	3.01	1.2E-01
UP_SEQ_FEATURE	calcium-binding region:2	7	5.4E-03	4.37	2.8E-01
SMART	SM00054:EFh	7	7.4E-03	4.04	1.2E-01
UP_SEQ_FEATURE	calcium-binding region:1	7	8.3E-03	3.99	3.6E-01
SP_PIR_KEYWORDS	EF hand	5	9.4E-03	6.03	6.6E-02
UP_SEQ_FEATURE	calcium-binding region:3	4	1.3E-02	7.98	4.6E-01
UP_SEQ_FEATURE	domain:EF-hand 2	8	1.4E-02	3.16	4.5E-01
UP_SEQ_FEATURE	domain:EF-hand 1	8	1.4E-02	3.16	4.5E-01
SP_PIR_KEYWORDS	calcium	20	1.6E-02	1.80	9.8E-02
INTERPRO	IPR002048:Calcium-binding EF-hand	7	2.4E-02	3.16	4.2E-01
UP_SEQ_FEATURE	domain:EF-hand 3	5	4.2E-02	3.82	8.0E-01
UP_SEQ_FEATURE	domain:EF-hand 4	4	4.9E-02	4.87	8.2E-01
GOTERM_MF_FAT	GO:0005509~calcium ion binding	21	1.1E-01	1.41	7.1E-01
INTERPRO	IPR018248:EF hand	4	3.2E-01	1.99	9.9E-01
Annotation Cluster 31	**Enrichment Score: 1.92**				
Category	Term	Count	*P* Value	Fold Enrichment	Benjamini
KEGG_PATHWAY	hsa04670:Leukocyte transendothelial migration	10	2.3E-03	3.42	5.3E-02
KEGG_PATHWAY	hsa04360:Axon guidance	10	4.2E-03	3.13	5.8E-02
KEGG_PATHWAY	hsa04062:Chemokine signaling pathway	8	1.8E-01	1.73	6.4E-01
Annotation Cluster 32	**Enrichment Score: 1.81**				
Category	Term	Count	*P* Value	Fold Enrichment	Benjamini
INTERPRO	IPR012335:Thioredoxin fold	8	9.6E-04	5.11	6.0E-02
UP_SEQ_FEATURE	domain:GST C-terminal	4	1.1E-02	8.71	4.2E-01
INTERPRO	IPR010987:Glutathione S-transferase, C-terminal-like	3	7.3E-02	6.68	7.1E-01
INTERPRO	IPR017933:Glutathione S-transferase/chloride channel, C-terminal	3	7.8E-02	6.46	7.3E-01
Annotation Cluster 33	**Enrichment Score: 1.76**				
Category	Term	Count	*P* Value	Fold Enrichment	Benjamini
UP_SEQ_FEATURE	domain:EH	3	1.9E-03	43.11	1.4E-01
SMART	SM00027:EH	3	7.3E-03	22.51	1.5E-01

SMART	SM00053:DYNc	3	1.0E-02	19.05	1.2E-01
INTERPRO	IPR000261:EPS15 homology (EH)	3	1.2E-02	17.61	2.8E-01
INTERPRO	IPR001401:Dynamin, GTPase region	3	1.7E-02	14.90	3.5E-01
UP_SEQ_FEATURE	domain:EF-hand	3	1.1E-01	5.26	9.2E-01
KEGG_PATHWAY	hsa04144:Endocytosis	8	1.7E-01	1.75	6.3E-01
Annotation Cluster 34	**Enrichment Score: 1.73**				
Category	Term	Count	*P* Value	Fold Enrichment	Benjamini
SP_PIR_KEYWORDS	endosome	10	2.5E-03	3.46	2.2E-02
GOTERM_CC_FAT	GO:0005768~endosome	13	1.5E-02	2.21	9.2E-02
KEGG_PATHWAY	hsa04144:Endocytosis	8	1.7E-01	1.75	6.3E-01
Annotation Cluster 35	**Enrichment Score: 1.72**				
Category	Term	Count	*P* Value	Fold Enrichment	Benjamini
GOTERM_CC_FAT	GO:0016323~basolateral plasma membrane	14	1.1E-04	3.69	1.9E-03
GOTERM_CC_FAT	GO:0005912~adherens junction	9	8.5E-03	3.11	5.9E-02
GOTERM_CC_FAT	GO:0070161~anchoring junction	9	1.5E-02	2.80	9.1E-02
GOTERM_CC_FAT	GO:0030055~cell-substrate junction	7	1.8E-02	3.34	1.0E-01
GOTERM_CC_FAT	GO:0005925~focal adhesion	6	4.2E-02	3.15	2.0E-01
GOTERM_CC_FAT	GO:0005924~cell-substrate adherens junction	6	4.8E-02	3.03	2.2E-01
GOTERM_CC_FAT	GO:0030054~cell junction	15	1.0E-01	1.55	3.7E-01
SP_PIR_KEYWORDS	cell junction	8	3.1E-01	1.45	7.4E-01
Annotation Cluster 73	**Enrichment Score: 0.70**				
Category	Term	Count	*P* Value	Fold Enrichment	Benjamini
SP_PIR_KEYWORDS	lysosome	6	5.6E-02	2.91	2.4E-01
GOTERM_CC_FAT	GO:0005770~late endosome	4	8.6E-02	3.82	3.3E-01
KEGG_PATHWAY	hsa04142:Lysosome	5	3.2E-01	1.72	7.8E-01
GOTERM_CC_FAT	GO:0005773~vacuole	7	3.3E-01	1.49	7.3E-01
GOTERM_CC_FAT	GO:0000323~lytic vacuole	6	3.6E-01	1.52	7.6E-01
GOTERM_CC_FAT	GO:0005764~lysosome	6	3.6E-01	1.52	7.6E-01

Table S5. Corona proteins belonging to the cell membrane. Because clusters of cell membrane proteins did not emerge in the GO analysis, the corona proteins belonging to the cell membrane were selected manually.

Protein GI number[#]	Gene Name
4502101	annexin A1
51895795	annexin A13
48255959	ATPase, Ca++ transporting, plasma membrane 4
21361181	ATPase, Na+/K+ transporting, alpha 1 polypeptide
4502281	ATPase, Na+/K+ transporting, beta 3 polypeptide
4502565	calpain, small subunit 1
16357472	cell division cycle 42 (GTP binding protein, 25kDa); cell division cycle 42 pseudogene 2
7330335	chloride intracellular channel 4
124107616	claudin 23
170650661	ectonucleotide pyrophosphatase/phosphodiesterase 1
4503571	enolase 1, (alpha)
45387945	family with sequence similarity 62 (C2 domain containing), member B
94538362	flotillin 2
73486658	glutamic-oxaloacetic transaminase 2, mitochondrial (aspartate aminotransferase 2)
21614499	hypothetical protein LOC100129652; ezrin
19743813	integrin, beta 1 (fibronectin receptor, beta polypeptide, antigen CD29 includes MDF2, MSK12)
4506787	IQ motif containing GTPase activating protein 1
5031815	lysyl-tRNA synthetase
19718759	Myoferlin
124494247	myosin IC
29171736	phosphatidic acid phosphatase type 2A
190358517	RAB11B, member RAS oncogene family
10880989	RAB18, member RAS oncogene family
16933567	RAB8A, member RAS oncogene family
7661678	RAP1B, member of RAS oncogene family
10835049	ras homolog gene family, member A
5454028	related RAS viral (r-ras) oncogene homolog
41872583	Rho-associated, coiled-coil containing protein kinase 2
166795299	solute carrier family 2 (facilitated glucose transporter), member 1
38016911	Stomatin
189217915	syntaxin binding protein 5 (tomosyn)
223029410	talin 1
4759300	vesicle-associated membrane protein 3 (cellubrevin)
4507879	voltage-dependent anion channel 1; similar to voltage-dependent anion channel 1

[#] These protein GI numbers are from the human data base.

Table S6. Corona proteins belonging to the endocytosis pathway.

Annotation Cluster 28	Enrichment Score: 2.03
GOTERM_BP_FAT	GO:0006897~endocytosis
Protein GI number[#]	Gene Name
30240932	EH-domain containing 1
21361462	EH-domain containing 2
21264315	EH-domain containing 4
10880989	RAB18, member RAS oncogene family
19923262	RAB5A, member RAS oncogene family
34147513	RAB7A, member RAS oncogene family
260436862	adaptor-related protein complex 1, beta 1 subunit
15451856	caveolin 1, caveolae protein, 22kDa
4557797	nucleoside diphosphate kinase

[#] These protein GI numbers are from the human data base.

Table S7. Corona proteins belonging to vesicle-mediated transport pathway.

Annotation Cluster 17	Enrichment Score: 2.87
GOTERM_BP_FAT	GO:0016192~vesicle-mediated transport
Protein GI number[#]	Gene Name
4502209	ADP-ribosylation factor 5
30240932	EH-domain containing 1
21361462	EH-domain containing 2
21264315	EH-domain containing 4
10880989	RAB18, member RAS oncogene family
4506365	RAB2A, member RAS oncogene family
19923262	RAB5A, member RAS oncogene family
38679888	RAB6C, member RAS oncogene family; RAB6A, member RAS oncogene family; hypothetical LOC100130819; RAB6C-like
34147513	RAB7A, member RAS oncogene family
16933567	RAB8A, member RAS oncogene family
116812591	RER1 retention in endoplasmic reticulum 1 homolog (S. cerevisiae)
260436862	adaptor-related protein complex 1, beta 1 subunit
15451856	caveolin 1, caveolae protein, 22kDa
4503015	copine III
21361625	exocyst complex component 2
31083351	exocyst complex component 3
116063573, 160420317	filamin A, alpha (actin binding protein 280)
38044288	gelsolin (amyloidosis, Finnish type)
7705636	golgi transport 1 homolog B (S. cerevisiae)
5729850	guanine nucleotide binding protein (G protein), alpha inhibiting activity polypeptide 3
4557888	keratin 18; keratin 18 pseudogene 26; keratin 18 pseudogene 19
4557797	non-metastatic cells 1, protein (NM23A) expressed in; NME1-NME2 readthrough transcript; non-metastatic cells 2, protein (NM23B) expressed in
5174655, 41393604	reticulon 3
5730031	secretory carrier membrane protein 2
28933465	syntaxin 12
189217915	syntaxin binding protein 5 (tomosyn)
98986464	transmembrane emp24-like trafficking protein 10 (yeast)
6005942	valosin-containing protein
4759300	vesicle-associated membrane protein 3 (cellubrevin)

[#] These protein GI numbers are from the human data base.

Table S8. Corona proteins belonging to lysosome compartment.

Annotation Cluster 73	Enrichment Score: 0.7
SP_PIR_KEYWORDS KEGG_PATHWAY	lysosome
Protein GI number[#]	Gene Name
8922601	ADP-ribosylation factor-like 8B
17136148	v-ATPase, H^+ transporting, lysosomal accessory protein 1 (V-type proton ATPase subunit S1)
4502679	CD63 molecule
34147513	RAB7A, member RAS oncogene family
4503143	cathepsin D
23821023	L-amino-acid oxidase isoform X2 (interleukin 4 induced 1)
5031631	lysosome membrane protein 2 (scavenger receptor class B, member 2)

[#] These protein GI numbers are from the human data base.