

Characterization of carbon nanotube protein corona by using quantitative proteomics

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Abstract

The protein corona of a nanomaterial is a complex layer of proteins spontaneously and stably formed when the material is exposed to body fluids or intracellular environments. In this study, we utilised stable isotope labeling by amino acids in cell culture (SILAC)-based quantitative proteomics to characterise the binding of human cellular proteins to two forms of carbon nanoparticles: namely multi-walled carbon nanotubes (MWCNTs) and carbon black (CB). The relative binding efficiency of over 750 proteins to these materials is measured. The data indicate that MWCNTs and CB bind to vastly different sets of proteins. The molecular basis of selectivity in protein binding is investigated. This study is the first large-scale characterisation of protein corona on CNT, providing the biochemical basis for the assessment of the suitability of CNTs as biomedical tools, and as an emerging pollutant.

From the Clinical Editor: This team of investigators performed the first large-scale characterization of protein corona on carbon nanotubes, studying 750 proteins and assessing the suitability of CNTs as biomedical tools and as an emerging pollutant.

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Key words: Nanomaterials; Quantitative-proteomics; Carbon-black; Carbon-nanotubes

Abbreviations: ATCC, American type culture collection; CB, Carbon black; CID, Collision induced dissociation; CNTs, Carbon nanotubes; CVD, Chemical vaporization deposition; DMEM, Dulbecco's modified eagle's medium; ECL, Enhanced chemiluminescence; emPAI, empirical peptide abundance index; FBS, Fetal bovine serum; HSP, Heat shock protein; LC-MS/MS, Liquid chromatography-Mass spectrometry/Mass spectrometry; MS, Mass Spectrometry; MWCNTs, Multi-walled carbon nanotubes; NaCl, Sodium chloride; PMSF, Phenylmethanesulfonylfluoride; PVDF, Polyvinylidene fluoride; PBS, Phosphate buffer saline; PDB, Protein data bank; SDS-PAGE, Sodium dodecyl sulfate polyacrylamide gel electrophoresis; SILAC, Stable isotope labelling by amino acids in cell culture; SPIO, Superparamagnetic iron oxide nanoparticles; TEM, Transmission electron microscope.

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Carbon nanotubes (CNTs) are cylindrical graphene structures closed at either end with caps that contain pentagonal rings.¹ A plethora of research over the past 20 years has revealed many chemical and physical properties of this nanomaterial that are both academically fascinating and commercially appealing. Many applications of CNTs involve direct contact of these materials with biological systems, either in the form of therapeutic treatments² or as a result of unintentional exposure.³ Biological consequences of CNT exposure have received increasing attention over the past decade. For instances, many in vitro studies have indicated that various forms of CNTs can penetrate the plasma membrane of mammalian cells and induce cytotoxicity.^{4,5} In addition, in vivo studies have revealed the involvement of CNT exposure in inflammation, epithelioid granulomas, fibrosis, and biochemical/toxicological changes in the lungs.⁶

Like other nanoparticles, CNTs are known to absorb a mixture of proteins to form a 'protein corona'.^{7–14} The binding of cellular proteins to CNTs and the subsequent alterations of protein structure and function may provide a molecular explanation of the physiological responses to CNT administration. Existing data

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indicate that the binding efficiency of proteins is not merely related to their abundance in the given sample, which may be due to the protein size or charge.¹⁵ The interactions of bacteriorhodopsin¹² and bovine serum albumin¹³ with CNTs are accompanied by changes in molecular conformation, and the CNT binding of ribonuclease A,¹⁴ R-chymotrypsin and soybean peroxidase¹⁶ leads to a reduction in the enzymatic activity of these proteins. These examples suggest that, at least in vitro, CNT binding can affect protein structures and functions. Furthermore, the cytotoxicity of CNTs is attenuated after the binding of proteins.¹⁷ When a mixture of proteins is exposed to CNTs, some proteins show preferential CNT binding.¹⁸ For instance, lipoproteins and coagulation-related proteins like antithrombin and coagulation factor V have a high affinity to CNTs, whereas immunoglobulin and acute response proteins like fibronectin and haptoglobin related protein demonstrate a lower affinity.¹⁵ The CNT affinity of a protein may be influenced by the abundance of certain amino acid residues in the protein that have physiochemical properties conducive to CNT interaction. Peptides rich in amino acids histidine, tryptophan and phenylalanine have been shown to bind to CNTs preferably.^{19,20}

Mass spectrometry (MS)-based proteomics is beginning to unravel the formation and composition of protein corona on nanomaterials. Plasma proteins that stably bind to different types of polystyrene nanoparticles have been analysed by MS²¹ with the identification of 36 to 58 proteins bound to each type of nanoparticle. Similarly, MS proteomics has identified 23 plasma proteins that adhere to superparamagnetic iron oxide (SPIO) nanoparticles.²² These studies demonstrate the feasibility of using MS-based proteomics to characterise the protein corona of nanomaterial. However, none of the studies are characterizing the protein absorption of the CNT has not been quantitatively documented, despite the popularity of this class of nanomaterial. To fill this knowledge gap, we employed a comprehensive approach to investigate the biochemical properties of the protein corona of CNTs and carbon black (CB) by using stable isotope labelling by amino acids in cell culture (SILAC) proteomics. This technique not only allows the identification of proteins in the corona, but also the measurement of the enrichment level of each protein by the material.²³ To our knowledge this is the first comprehensive study in adopting a SILAC based MS in documenting the interaction of human cellular proteins with the carbon nanoparticles.

Methods

Carbon nanomaterials

Different types of CNTs with various diameters and lengths made by a chemical vaporization deposition (CVD) method were purchased from Nanotech Port Co Ltd (Shenzhen, China). Properties of the CNTs used in this study are summarised in SI Table 1. The CNTs and CBs were put onto a copper grid which was covered with carbon film and observed under a transmission electron microscope (TEM), as described.²⁴

Protein lysate preparation

HeLa cells were from the ATCC collection and were maintained in DMEM medium (high glucose) supplemented

with 10% fetal bovine serum and 5% Anti-Anti (Gibco, Invitrogen). Cells were harvested by trypsinization, washed with phosphate buffered saline (PBS), and incubated in lysis buffer (100 mM NaCl; 25 mM Tris pH 7.3; 1 mM EDTA; 0.1% Triton-X-100, complete protease inhibitor cocktail (Roche)) was added. Typically, 2 ml of lysis buffer was used for 5×10^7 cells. The cells were sonicated for 1 min (in 5 s pulses) on ice with a 3 mm probe sonicator (Ultrasonic processor, 70–100 W). Then, the lysates were centrifuged at 21,000 g, 15 min, 4 °C and collected the clear supernatant for further proteomics analysis.

Zebrafish embryos were collected and cultured after hatching and the embryos were examined every day and the abnormal ones were discarded. The 50 fishes were lysed 72 hrs after hatching by homogenization in 500 µl of lysis buffer that contained a complete protease inhibitor cocktail (1:25 diluted, Roche Diagnostic) and 0.5 M phenylmethanesulfonylfluoride (PMSF, Sigma) on ice for 15 min. Then, the lysates were clarified by centrifugation (21,000 g, 15 min, 4 °C). Mouse liver was freshly dissected from a four-month old C57WT female mouse, weight 1.2 g, after homogenizing with 4.5 ml of lysis buffer for 5 min on ice, 21,000 g for 15 min at 4 °C. The supernatant was transferred to a new tube and the protein concentration was detected with a Bradford assay.

Three liters of *Thalassiosira pseudonana* were spun down and harvested for cell lysis, 8.5 ml of cell lysis buffer and were added into the collected algae. The extracted algae were sonicated for 1 min, 4 times (20 amplitudes, 9 pulses), cells were then vortexed by 0.5 cm diameter glass beads for 1 min each time for 4 times. The lysates were clarified by centrifugation, (21,000 g, 15 min, 4 °C). The supernatant (protein solution) was transferred to a new tube. Fifty adult *Drosophila* were anaesthetized by carbon dioxide for 1 min, 2 ml of cell lysis buffer and 80 µl of 25× protease inhibitor cocktail were added. The *Drosophila* and buffer were homogenized by a homogenizer for 3 min, and the cells were lysed for 2 hrs at 4 °C. Then, the lysates were centrifuged (21,000 g, 15 min, 4 °C). The supernatant was transferred to a new tube.

Protein corona isolation

Cell lysates were incubated with 5 mg of CNTs or CB for 3 hrs at 4 °C. After centrifugation at 800 g (3 min, 4 °C), the pellets were thoroughly washed with washing buffers (100 mM NaCl; 25 mM Tris-HCl pH 7.3; 1 mM EDTA, complete protease inhibitors) until the OD280 of the supernatant was less than 0.1. The bound proteins were eluted by heating the pellets in 50 µl of LDS sample buffer (Invitrogen) to 70 °C for 10 min. In some experiments, 5 mg of 7 CNTs of different sizes were incubated with the same amount of FBS (4 mg) or cell lysate proteins (5 mg), and then followed a standard pull-down experiment. In some experiments, lysates were adjusted to pH 7.2 and pH 11, and then incubated with CNTs, and washed with a washing buffer of pHs 7.2 and 11, respectively. Three-way SILAC encoding of HeLa cells was done as described.²³ Equal protein amounts (as measured by a Bradford assay) of the control cell lysate (light) and MWCNT (diameter 20–40 nm)-binding proteins (medium) were mixed together, CB-binding proteins (heavy) were then added into the mixture with the same

volume as CNT-binding proteins. The mixed protein samples were electrophoresed, gel-sliced and digested as described previously.^{23,25}

Mass spectrometry

Mass spectrometry was performed on an LTQ-orbitrap mass spectrometer system (ThermoElectron, Bremen, Germany) coupled to a Dionex 3000 nano-LC system (Camberley, UK) A 100×0.075 mm Agilent C18 column (3.5 μm particle diameter) with an A mobile phase of 0.1% formic acid in water and B mobile phase of 0.1% formic acid in acetonitrile were used. The peptides were eluted using a 13.5-cm-long, 75-μm-inner diameter tip column (YMC-Gel, Liquid Chromatography). The pump flow rate was set at 0.3 μl/min, and peptide elution was achieved using a linear gradient of 5% to 40% B in A for the first 40 min followed by a rapid increase to 95% B for the next 20 min. Conventional MS spectra (a survey scan) were acquired at high resolution ($M/\Delta M$, 60,000 full width half maximum) over the acquisition range m/z 200–2000 and a series of precursor ions were selected for the MS/MS scan. The former examined the accurate mass and charge state of the selected precursor ions and the latter acquired the spectrum (CID spectrum or MS/MS spectrum) of the fragment ions generated by collision-induced dissociation as described.²³

The MS/MS spectra were searched against the UniProt human database with the Mascot search engine (Matrix Science) setting with the following criteria: peptide tolerance=10 ppm; trypsin as the enzyme; carboxyamidomethylation of cysteine as a fixed modification and oxidation of methionine as variable modifications; medium SILAC labels were: label 13C(6) (R), and label 2 H(4) K; and heavy SILAC labels were: label 13C(6) 15 N(4)(R), and label 13C(4) 15 N (4) K. The MS-Quant programme^{23,26} was used for quantitation; the peptide ratio calculation carried on for each arginine- and/or lysine- containing peptide, and the peak area of labelled arginine/lysine divided by the peak area of non-labelled arginine/lysine were calculated for each single scan mass spectrum. The ratio of each protein was the average of the peptide ratios for all arginine- and lysine-containing peptides sequenced from this protein. The criteria of protein validation were as follows: only individual peptide with Mascot score of at least 25, and total protein score of at least 60 were used. Only proteins with two unique peptides were considered. This filter results in a false-positive rate of below 0.7%.²⁷

Western blotting

Following an SDS-PAGE, the proteins were transferred to a hydrated polyvinylidene fluoride (PVDF) membrane at 100 V for 1 hr by using the Western blot system (Bio-rad). The membrane was blocked with 5% skim milk powder in a washing buffer (0.1%, v/v Tween 20 in PBS, pH 7.2) for 40 min. The blot was then incubated with mouse anti-β-Actin antibody (Sigma Inc.Cat.No.A5441), 1:10000 dilution in blocking buffer (5% milk, 0.1%, v/v Tween 20 in PBS, pH 7.2) for 60 min at R.T., washed four times in the washing buffer for 25 min and incubated with secondary antibody goat anti-mouse IgG (H+L) (Zymed, Cat. No. 62 -6520), 1:10000 dilution in blocking buffer

for 1 hr at R.T., and then, washed 3 times in a washing buffer for 10 min each. The membrane was developed by using an ECL Western blotting kit (Amersham Biosciences). Mouse anti-β-tubulin antibody (1:5000, Sigma Inc. Cat.No.T4026), HSP60 (1:500, sigma Inc. Cat.No.H3524), and HSP70 (1:5000, Sigma Inc. Cat.No.H5147) were used to detect the specific proteins by following the same steps.

Data analysis

Protein Center (Thermo), a proteomics data mining and management software, was used to eliminate redundancy and compare datasets, and to convert protein IDs to gene symbols and obtain gene ontology and sequence length information. Theoretical pI, the Kyte-Doolittle hydrophobicity and amino acid usages of the identified proteins were analysed by using PROMPT software.²⁸ Protein secondary structure information was obtained from the PDB.²⁹

Results

Protein corona of carbon nanoparticles

To test the binding of a complex mixture of proteins to CNTs, we incubated pristine multi-wall CNTs (MWCNTs) with a mean diameter of 20–40 nm with a cell lysate prepared from the human cell line HeLa. Proteins from HeLa cells were chosen because they provide a representative source of the human proteome. In parallel, CB, a pure elemental carbon in the form of colloidal nanoparticles, was also tested for the binding capacity for the same protein mixture. The same amount of HeLa cell lysate proteins was used in the binding assay (Figure 1, A). Both MWCNT and CB formed loose agglomerates that could be collected by low-speed centrifugations after protein binding. The proteins that bound stably to these carbon matrices were eluted after extensive washing and then analyzed by SDS-PAGE. Remarkably, MWCNTs bound to a significant amount of HeLa cell proteins, whereas much less proteins were pulled down by the same amount of CB (Figure 1, B). By comparing the coomassie-blue staining intensities of the eluted proteins with that of the input, we estimated that about 1.5% of the entire pool of HeLa cell proteins in the incubation reaction are able to bind to the MWCNTs after 3 hrs of incubation, but only less than 0.1% of these proteins are able to bind to the same amount of CB. The efficient interaction of proteins with CNTs is not restricted to proteins from cultured human carcinoma cells, protein extracts prepared from zebrafish, mouse, drosophila and algae also demonstrated a substantial affinity to CNTs (Figure S1).

We examined the MWCNT and CB used in the protein binding experiments by using transmission electron microscopy (Figure 1, C and D). The diameters of CBs appear significantly smaller than MWCNTs. This suggests the dimensions of carbon nanomaterials may affect the formation of protein corona. We further characterized the possible influence of CNT length and dimension on its protein binding capacity. Fetal bovine serum (FBS) proteins were incubated with CNTs of various types, diameters and lengths (Table S1 and Figure 2, A) and the

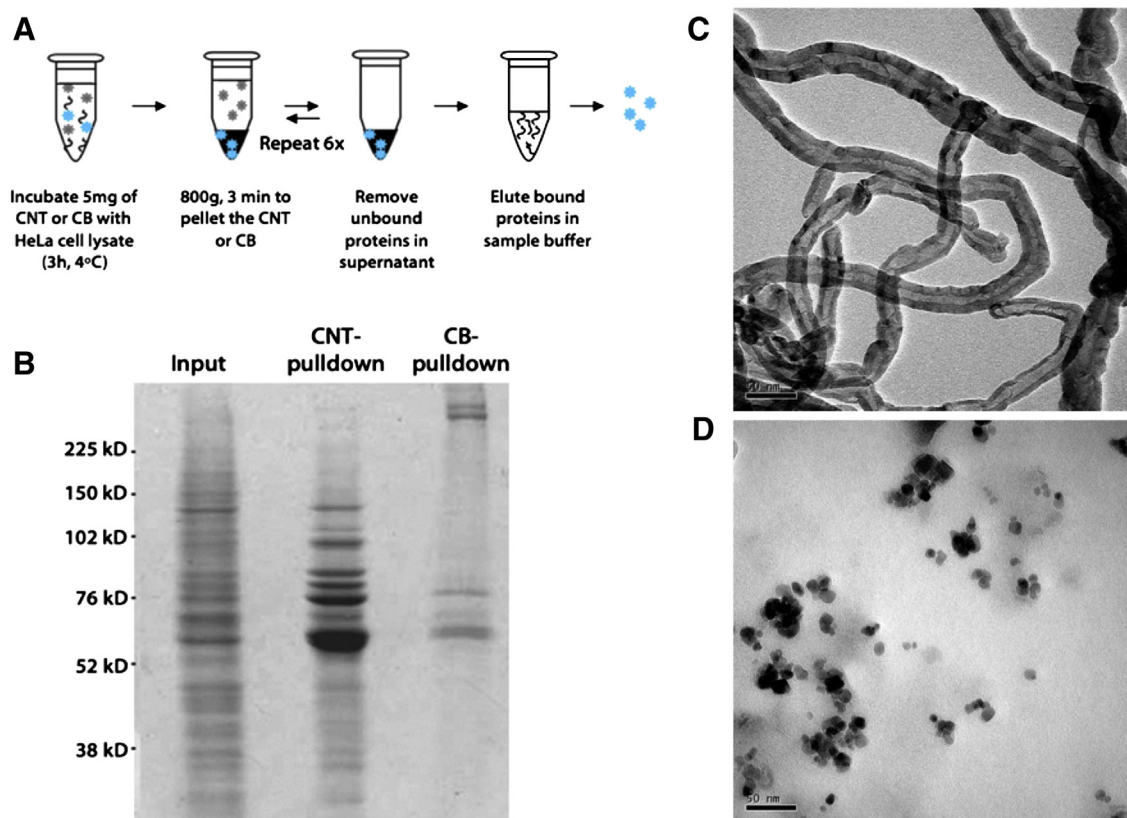


Figure 1. Protein binding assay to study MWCNT- and CB-protein corona. **(A)** Scheme of carbon nanoparticle pull-down experiment. **(B)** Proteins from HeLa cell lysate pulled down by MWCNTs and CB were separated by SDS-PAGE and stained by coomassie blue. **(C–D)** Transmission electron micrographs of the MWCNTs **(C)** and CNTs **(D)** used in this study (Bars: 50 nm).

recovery of proteins in the CNT pull-downs was studied. MWCNTs of diameters of 20–40 nm or above could pull-down a significant amount of proteins (Figure 2, B, lanes 5–8), whereas those with diameters less than 10 nm bound to virtually no proteins (Figure 2, B lanes 3–4). Single walled CNTs, typically with diameters less than 2 nm, also show no significant protein binding (Figure 2, B, Lane 2). For MWCNTs that are wider than 20 nm, an increase in nanotube diameter did not further increase the protein binding capacity, as the amount of proteins pulled down by CNTs with diameters from 20–100 nm is essentially the same (Figure 2, B, Lanes 6, 8). This result confirms the roles of the size of carbon nanomaterials in protein binding, and is consistent with previous studies where protein binding was more efficient with larger CNTs¹³ or nanoparticles²¹ than smaller ones.

Next, we asked whether the observed protein binding reflects a specific interaction of proteins with CNTs, or if it is merely a result of non-specific trapping of proteins by the CNT and CB agglomerates. We compared the protein binding capacity of MWCNTs that had similar diameters, but different averaged lengths (Figure 2, C), as short MWCNTs do not form agglomerates as efficiently as long MWCNTs. MWCNTs of different lengths bind to a similar amount of proteins (Figure 2, B, Lanes 5, 6 and 7, 8). This further supports the notion that protein interactions with CNTs is likely to be determined by

factors such as surface curvature and area, or lumen dimensions, but not by the level of agglomeration.

Systematic characterization of carbon nanoparticle-protein corona

A comparison of the gel electrophoretic profiles of total HeLa cell lysate and the proteins pulled down by MWCNTs indicated that some proteins were selectively enriched into the CNT-protein corona (Figure 1, B). This suggests that, in a complex protein mixture, some proteins are able to bind more efficiently and/or more stably with MWCNTs. It is important to identify the proteins that bind to MWCNTs specifically. In order to accomplish this, we performed proteomics analysis to identifying the proteins that selectively bind to MWCNT of diameters of 20–40 nm. We also aimed to compare the types of proteins that bound to this preparation of MWCNT with those that bound to CB. Cell lysates were prepared from three populations of HeLa cells that had been metabolically encoded using three different SILAC media (“light”, “medium” and “heavy”, Figure 3, A and Methods). A CNT pull-down was performed on the “medium” lysate, and a CB pull-down was performed on the “heavy” lysate. Equal volumes of proteins eluted from these pull-down experiments were mixed. The mixture was also spiked with an equal amount of unfractionated “light” lysate. The mixtures were then separated by SDS-PAGE, and

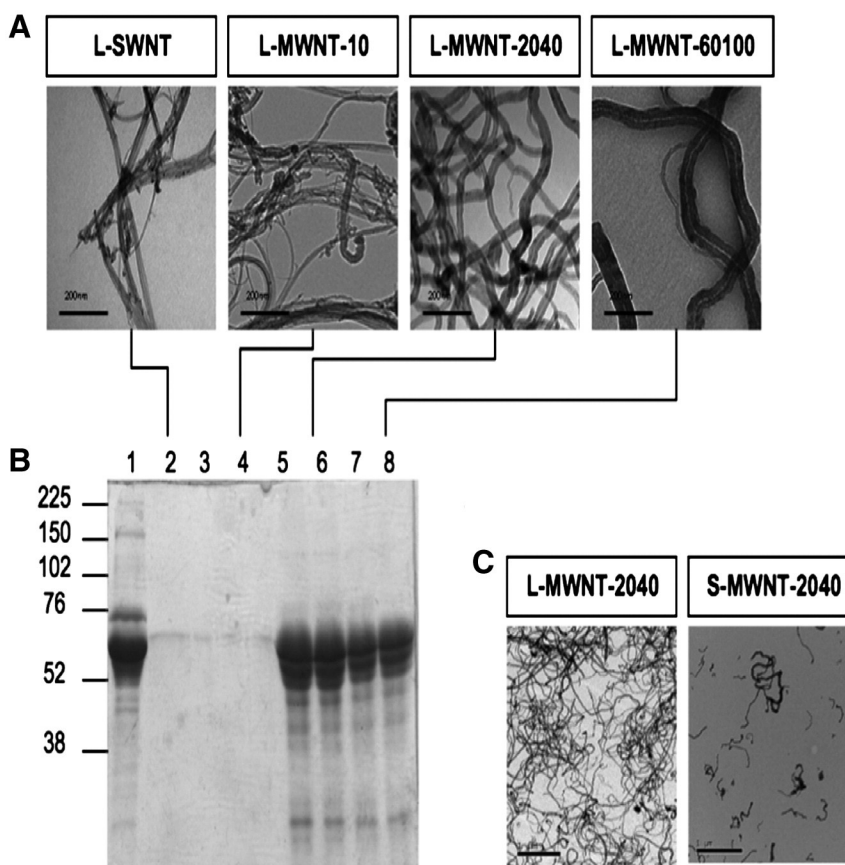


Figure 2. CNTs of different sizes exhibit different protein-binding capacities with. **(A)** TEM images of CNTs (length: 5–15 μ m) with different diameters (Magnification 87000 $\times$). From left to right: L-SWNT with diameter <2 nm; L-MWNT-10 with diameter <10 nm; L-MWNT-2040 with diameter in range of 20–40 nm; L-MWNT-60100 with diameter in range of 60–100 nm. **(B)** FBS pulled down by CNTs of different sizes. Lane1: FBS; Lane2: SWNT; Lane3: S-MWNT-10; Lane4: L-MWNT-10; Lane5: S-MWNT-2040; Lane6: L-MWNT-2040; Lane7: S-MWNT-60100; Lane8: L-MWNT-60100. **(C)** MWNTs-2040 of different length. L-MWNT-2040, length: 5–15 μ m; S-MWNT-2040, length: 1–2 μ m.

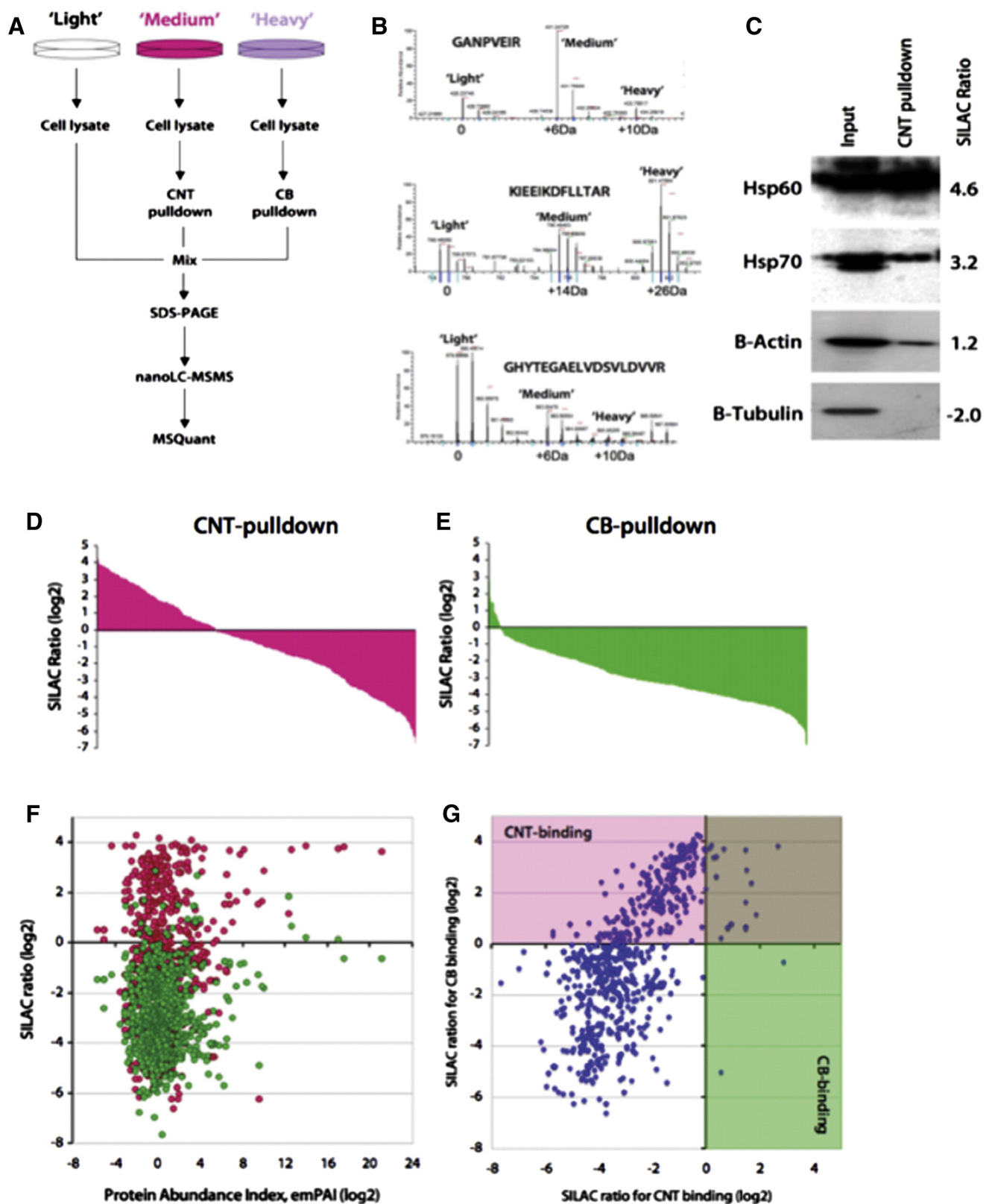
analyzed with the “gel-LC-MS/MS” approach. More than 9,000 unique peptides were unambiguously mapped to more than 1,750 human proteins. The abundance distribution of each identified peptide among the “light”, “medium” and “heavy” categories was quantified by the MSQuant programme.²⁴ In total, 778 proteins were accurately quantified (Table S2). This three-way SILAC protocol allows a comparison of the binding efficiencies of each protein to MWCNTs (medium to light ratios), and to CB (heavy to light ratios). The mass spectra of representative peptides are shown in Figure 3, B. Furthermore, to validate the MS data, we performed Western blotting analyses on HSP60, HSP70, β -actin and tubulin. Quantitative proteomic data show that HSP60, HSP70 and β -actin, but not tubulin, were enriched in the MWCNT pull-down. Western blotting results also showed an enrichment of HSP60, HSP70, and actin in the pull-down, while tubulin was only detectable in cell lysate input, but not in the pull-down (Figure 3, C).

Our MS analysis confirmed that the number of proteins enriched by MWCNT-binding is much higher than that enriched by CB (Figures 3, D and E). An examination of the SILAC ratio of each quantified protein and its empirical peptide abundance index (emPAI), a semi-quantitative indication of the overall abundance of protein in the mixture,³⁰ reveals no strong correlation between the MWCNT- and CB-binding efficiencies

of a protein and its abundance in the lysate (Figure 3, F). The relative abundance of the MWCNT-binding proteins spread over 8 orders of magnitude. Some of the proteins with the highest binding efficiencies, as indicated by the SILAC ratios, are low abundance proteins. This suggests that protein binding to MWCNTs is unlikely to be a non-specific aggregation of the highly abundant proteins with MWCNTs. Instead, the binding of proteins to MWCNT and CB appears to be protein-selective. We compared the MWCNT- and CB-binding efficiencies of all the quantitated proteins (Figure 3, G), and observed that while a small number of CB-binding proteins also bind to MWCNTs, there is no apparent correlation between the binding efficiencies of proteins to these two materials. In fact, most of the proteins with high CB-binding efficiencies bind to MWCNTs only marginally or not at all. This indicates that MWCNTs and CB not only have different protein binding capacities, but also different protein binding specificities.

Functional classification of the carbon nanotube-protein corona

To correlate the MWCNT-binding property of proteins with their functions, we grouped the quantitated proteins into 15 bins; each contained 50 proteins (except for the last bin which



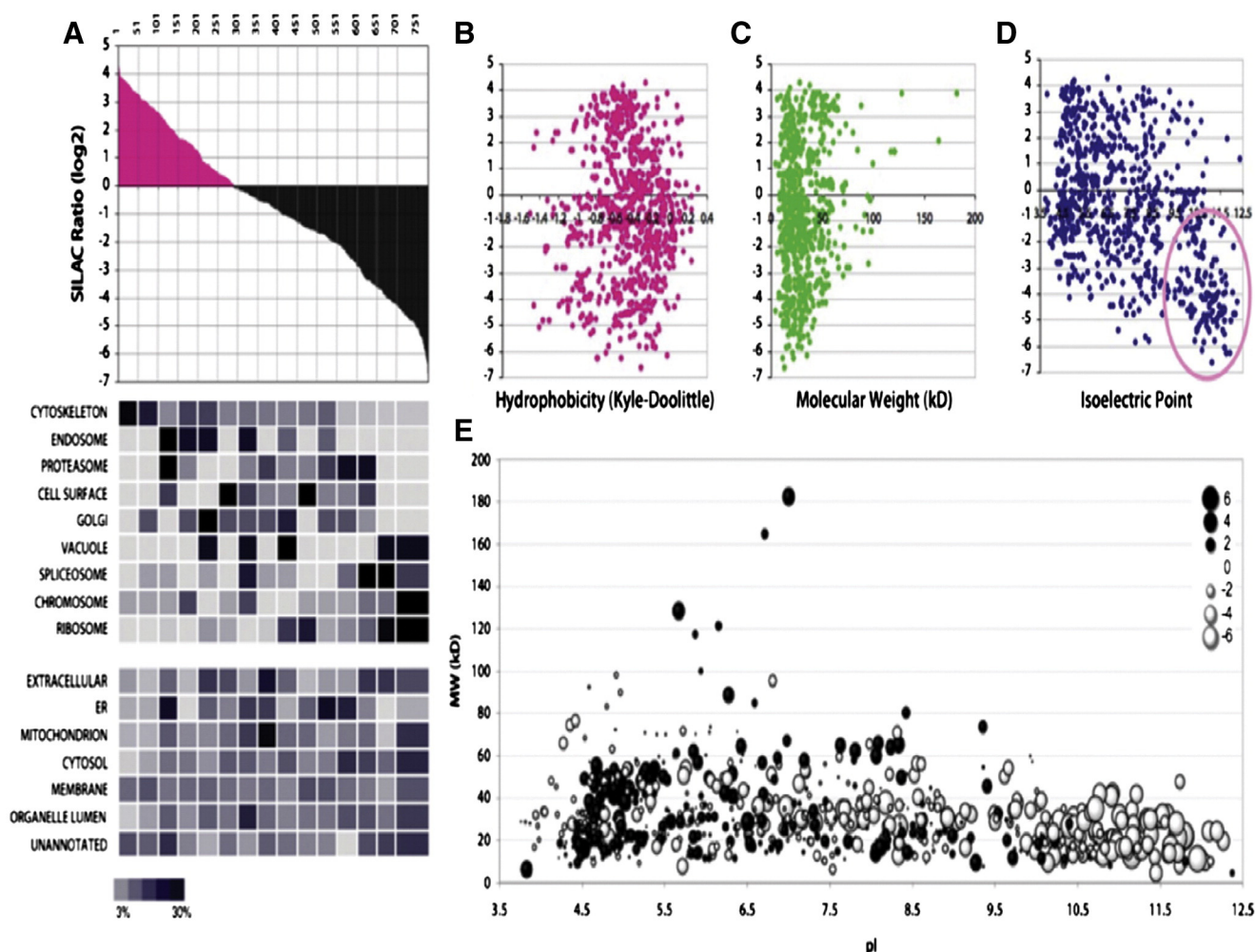


Figure 4. Correlation of MWCNT-binding with functional and physical properties. (A) Proteins are grouped according to their SILAC ratios and the percentage of proteins in each functional category is indicated. (B–D) Scatter plots of the SILAC ratio and hydrophobicity, molecular weight and isoelectric point of each quantitated protein. (E) The molecular weight and isoelectric point of each quantitated protein are shown. The SILAC ratios are indicated by the size and colour of the dots.

contained 78 proteins). The distribution of gene functions, as defined by slimmed-down gene ontology categories (Table S4), in each bin was then compared (Figure 4, A). Cytoskeletal proteins were dramatically over-represented among the MWCNT-binding proteins, as Bins 1 and 2 (proteins with the highest binding efficiency with MWCNTs) contain more than 50% of all the cytoskeletal proteins identified and quantified in the entire experiment. Endosomal proteins were also significantly enriched by MWCNTs. By contrast, nuclear proteins, such as chromatin, ribosomal and spliceosomal proteins, were over-represented in proteins with very low SILAC ratios, *i.e.*, proteins that do not bind effectively to MWCNTs. Proteins in other gene ontology categories, *e.g.*,

mitochondrial and membrane proteins, exhibit no preference in terms of CNT-binding. The strong preference of cytoskeletal and endosomal proteins to CNT interactions suggests a possible link between MWCNTs to these intracellular structures. A recent study has revealed the striking ability of pristine CNT to interfere with actin organization.³¹ The preferential binding of cytoskeletal proteins to CNTs may be a biochemical basis for CNT cytotoxicity.

Physiochemical properties of CNT-binding proteins

We next studied the possible correlation of physiochemical properties of proteins with their MWCNT-binding efficiencies.

Figure 3. Characterisation of MWCNT- and CB-protein corona by SILAC proteomics. (A) Experimental design. (B) Sample mass spectra of selected peptides that show various degrees of MWCNT- enrichment and CB-enrichment. (C) Western blotting analysis of MWCNT-pull-down by using antibodies against selected proteins. (D) Histogram of the SILAC ratio ("medium" vs "light", log2) of 778 quantitated proteins. A positive ratio for a protein indicates an enrichment of this protein in the MWCNT pull-down. (E) Histogram of the SILAC ratio ("heavy" vs "light", log2) of the quantitated proteins, which indicates the relative enrichment in the CB pull-down. (F) Scatter plot that shows the SILAC ratio and the protein abundance index of each quantitated protein (pink: MWCNT pull-down; green: CB pull-down). (G) SILAC ratio of each quantitated protein with respect to the MWCNT- and CB-pull-downs.

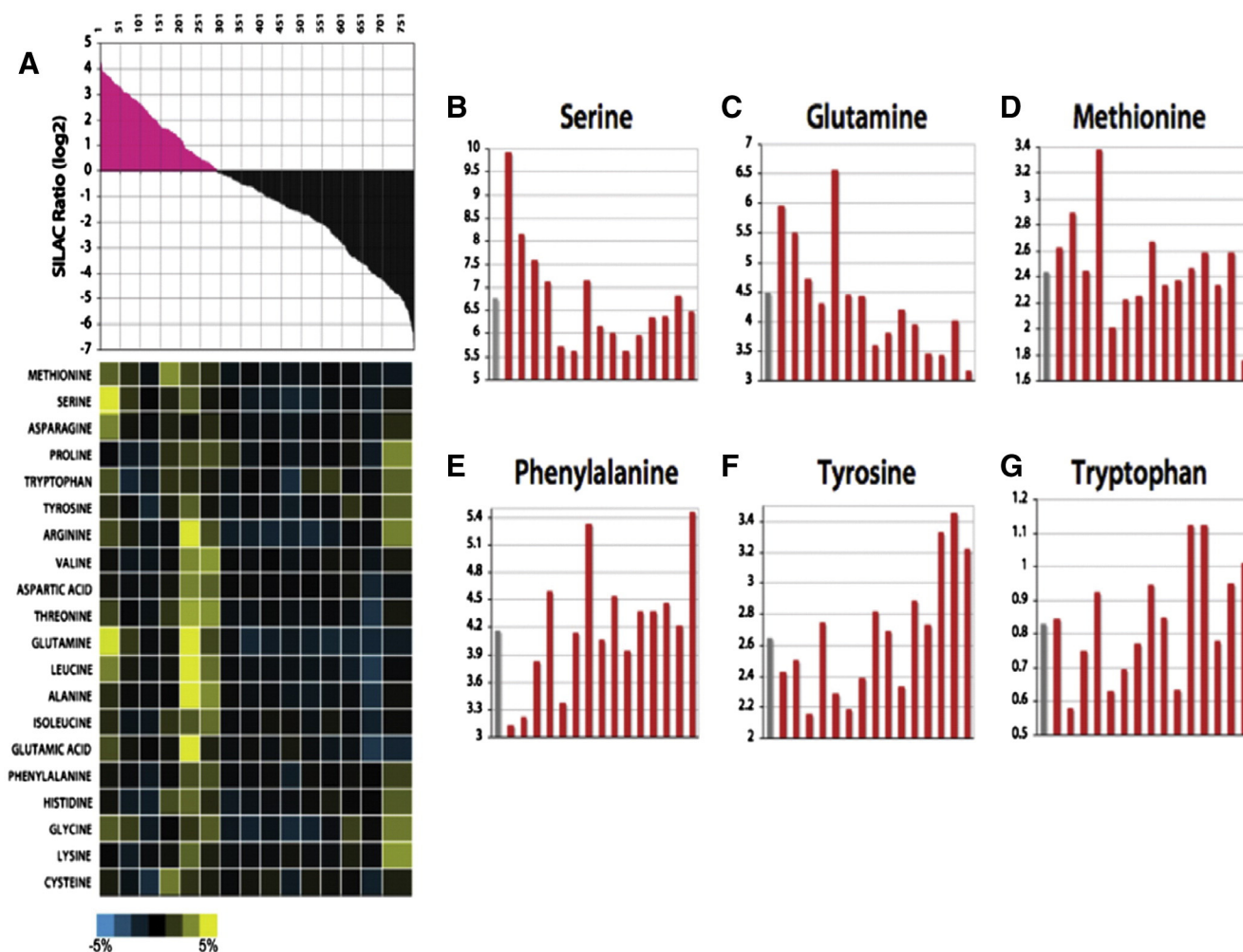


Figure 5. Amino acid usage within the proteins pulled down by MWCNTs. **(A)** Proteins are grouped according to their SILAC ratios and the amino acid usage within the proteins in each group is calculated. The colours of the boxes indicate the derivation of the measured amino acid usage from the average usage of each amino acid in the human proteome. **(B–G)** Usage of selected amino acids in each SILAC ratio group (same grouping as in 4A). Grey bars: average usage of amino acid in human proteins.

First, the overall Kyle-Doolittle hydrophobicity of proteins was plotted against the SILAC ratios (Figure 4, B and Table S4). The scatter plot indicated that there is no obvious correlation between the hydrophobicity of a protein and its CNT affinity. We did not observe a preference of MWCNTs to bind hydrophobic proteins, despite previous studies indicating that hydrophobic interactions are an important factor of peptide binding to CNTs.^{19,20} A survey of the molecular weights of quantitated proteins (Figure 4, C and Table S4) also indicated a lack of correlation between molecular sizes and MWCNT-binding, except for the under-representation of proteins over 50 kDa among the ones with very low SILAC ratios. An investigation of the distribution of isoelectric points (pI, Figure 4, D and Table S4) indicated that the majority of non-CNT-binding proteins were very basic (circled). Taken together, a theoretical 2D gel (Figure 4, E) shows a strong bias in CNT-binding efficiencies against small, basic proteins. This supports the hypothesis that interactions between MWCNTs and proteins might be modulated by electrostatic forces.¹³ Remarkably, the protein binding of

MWCNTs also appears to depend on the pH in the incubation buffer (Figure S2).

Previous studies have suggested that the peptides rich in aromatic amino acids have a higher affinity to CNTs.^{19,20} We tested this hypothesis by examining the amino acid usage of proteins with different MWCNT affinities (Figure 5, A). CNT-binding efficiency correlates well with the frequencies of serine, and to a lesser extent, methionine, glutamine and asparagine. For example, the frequency of serine in proteins with the highest affinity to MWCNTs is more than 1.5 folds higher than the serine usage in all the quantitated proteins (Figure 5, B). Unexpectedly, all three aromatic amino acids are over-represented in proteins found not to bind to MWCNTs (Figures 5, E–G), which suggests that proteins rich in these amino acids are less prone to CNT binding.

To study the potential correlation between MWCNT-binding affinity and the secondary structure of proteins, we cross-referenced the quantitated proteins in this study with the Protein Data Bank (PDB). Out of 778 proteins, 269 are found to have

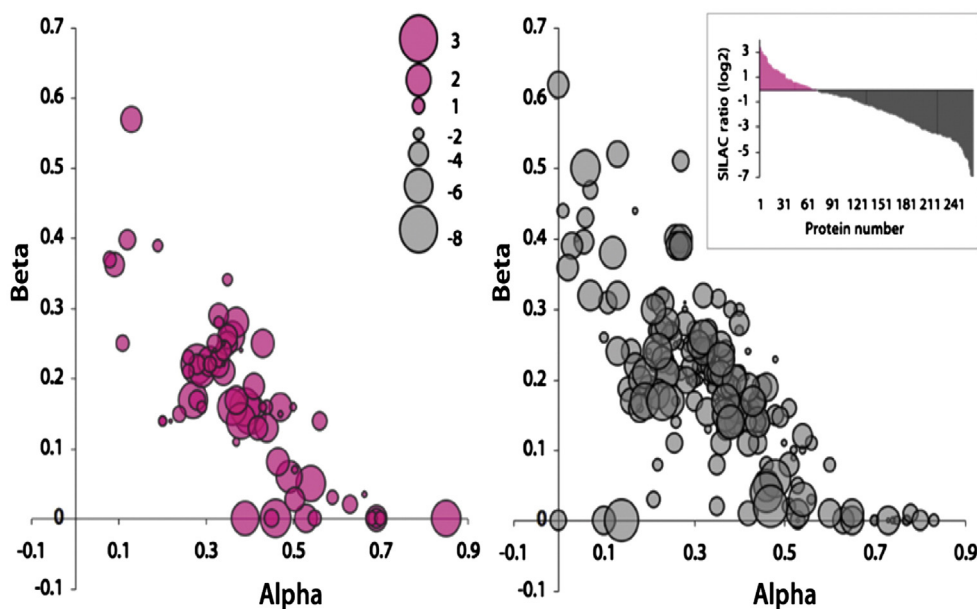


Fig. 6. Correlation of secondary structures and MWCNT-binding. The relative proportions of alpha helical and beta strand contents of a subset of proteins identified in this study were obtained from the Protein Data Bank. The SILAC ratios of the selected subset are shown in the inset. The alpha helical and beta strand content of proteins with positive SILAC ratios (MWCNT-binding, pink data) and negative SILAC ratios (non-CNT-binding, grey data) are shown as bubble plots, with the values of the SILAC ratios indicated by the bubble sizes.

information on their secondary structure (Figure 6 inset and Table S4). The theoretical proportions of alpha helical and beta strand content of each protein was calculated. Proteins found to bind MWCNTs (Figure 6, pink data) appeared to show a slight bias towards having high alpha helix content, while those with beta strand content was under-represented among the CNT-binding proteins. In contrast, among the proteins that did not bind to MWCNTs (grey data), such a bias toward alpha helical structure was not observed.

Discussion

Until recently, studies on the nanomaterial interactions with biomolecules have been limited to the use of purified proteins or peptides. In the present study we exposed CNTs to a complex protein mixture, and report the large-scale identification of the resulting corona proteins. A complete protein lysate of HeLa cells was used as an archetypal human proteome, which provided the representative inventory of proteins for the binding assay. Our quantitative approach not only allowed the identification of proteins associated with nanoparticles, as have been done previously,^{21,22,32,33} but also measured each protein's level of enrichment in the binding assay. Though not a direct measurement of binding coefficients, our data provides an unprecedented assessment of the efficiency and specificity of the protein binding to two nano materials, namely MWCNT and CB.

We observed that MWCNTs bind to a large amount of proteins. Some proteins apparently bound to CNT highly efficiently, with 44 proteins found to be enriched by over 10 fold in MWCNT after the binding assay. In comparison, much less proteins can bind to sepharose and magnetic bead

matrices.²³ Interestingly, both the protein binding capacity and specificity of MWCNTs are highly distinct from those of CB. This suggests that the protein-CNT interaction depends on the 3-dimensional arrangement of carbon atoms in CNTs, and not on the chemical properties of carbon itself. A recent study of mice treated with CNT, asbestos and CB³⁴ showed that CNTs inflict a much more serious effect on protein expression in the lungs than CB. Our results seem to provide an explanation for this difference in molecular perturbation.

The physical nature of protein-CNT interaction is not well understood. Recently, a study by Zhang et al. demonstrated that the protein-binding patterns onto the nanoparticle correspond closely to the nanoparticle surface properties, size as well as properties of proteins.³⁵ Our data show that effective protein binding was possible only if the CNT exceeds a certain size threshold. Our findings commensurate with the several findings that the particle size can play a sizeable role in determining the protein binding and the formation of corona.^{21,36–39} However, we do not see a correlation between protein sizes and binding efficiencies, implying that proteins might not be trapped in the CNT lumen. More likely, protein binding may require a suitable surface curvature, as have been previously suggested.¹³ By measuring the protein selectivity of MWCNT, we were able to test various hypotheses on the nature of protein-CNT interactions, and this yielded surprising results. Our results disagree with the reported preference towards hydrophobic proteins, or peptides containing aromatic amino acids during MWCNT binding.²⁰ The use of purified proteins or peptides, which were often applied at high concentrations, with nanoparticles may not reflect the physiological situation where proteins interact with CNTs in a complex mixture. The peptide motifs found by these studies to efficiently bind to CNTs may be not

accessible for binding or may be differently folded when present in a complex mixture of proteins in vivo.

Taken together, we have demonstrated that CNTs are able to selectively enrich some specific proteins from protein mixtures, and specific CNT protein binding capacities may be a general phenomenon that should provide new insights into the study and application of CNTs. This study helps to broaden future CNT studies in at least two aspects. Firstly, proteins with a high affinity to bind with CNTs are potential targets after the latter enters the cell. The conformation and functions of these proteins may be affected, resulting in disruptions to cellular structure and functioning. A recent cytotoxicity study showed that MWCNTs with larger diameters exhibit a higher level of toxicity to cells.³⁹ As we observed a higher level of protein binding in larger MWCNTs, the apparent link between CNT protein binding and toxicity will be an important topic for future studies. Interestingly, the toxicity of CNT was found to decrease after the binding of serum proteins,¹⁷ probably because these proteins have saturated the protein binding sites of the CNT and prevented further interactions of cellular proteins. Secondly, the identification of CNT-binding proteins may have implications on the future applications of CNTs. The binding of these proteins to CNTs could complicate the efficacy of CNTs as biosensing probes or delivery tools for therapeutic cargos. Our study has provided an inventory of proteins with high affinity to CNT. This inventory will offer future directions for the surface modification and the blocking procedures that will minimise these non-specific protein interactions. The proteomic approach developed in this study can also provide a convenient technical platform for the evaluation and optimisation of these procedures.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <http://dx.doi.org/10.1016/j.nano.2012.09.004>.

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Supplementary Table 2: Data reported in Figure 3

Column explanation:

Accession number (1)	Accession number (2)	Gene symbol	Gene name	No of detected peptide	Total Mascot score	smPAI	Medium:Light ratio	StDev	Heavy:Light ratio	StDev	log2(M/L)	log2(H/L)
Accession numbers of identified proteins in IPi (International Protein Index)				Accession numbers of identified proteins in other commonly used formats (as recommended by the Proteincenter database)								
Gene symbols of the identified proteins (pls note some identified proteins have no official gene symbols)				Commonly used gene names of the identified proteins								
No of detected peptides				Number of quantified peptides								
Total Mascot score				Combined Mascot scores of the identified proteins								
smPAI				Empirical Protein Abundance Indices of the identified proteins								
Medium:Light ratio				SILAC ratio of the identified proteins (medium isotope: light isotope). Average of all the ratios of the detected peptides for the proteins. StDev are the standard deviations for the averaged ratios.								
log2(M/L)				Log2 of the above ratio								
Heavy:Light ratio				SILAC ratio of the identified proteins heavy isotope: light isotope). Average of all the ratios of the detected peptides for the proteins. StDev are the standard deviations for the averaged ratios.								
log2(H/L)				Log2 of the above ratio								

Accession number (1)	Accession number (2)	Gene symbol	Gene name	No of detected peptide	Total Mascot score	empPA	Medium:Light ratio	StDev	Heavy:Light ratio	StDev	log2(M/L)	log2(H/L)
IP00167259	Q8N7Q0	FLJ40504	cDNA FLJ40504 fs, clone TEST02045509, highly	3	103	0.25	19.278	3.56	0.795	0.23	4.268883482	-0.33097323
IP00814197	ABMY52		Uncharacterized protein ENSP00000380179	5	215	1.11	10.017	5.46	0.86	0.48	4.11226904	-0.2159144
IP00873425	ABMZU		Uncharacterized protein ENSP00000380005	7	334	8.98	16.84	7.64	0.727	0.25	4.07382023	-0.45097273
IP00869238	IP00869238.1	PTPN14	Similar to Keratin 18	6	291	3.14	15.272	7.1	0.706	0.51	3.932817103	-0.50252591
IP00217437	Q8MWY7	TTBK2	Tau-tubulin kinase	5	192	0.13	14.673	6.65	0.729	0.35	3.875091965	-0.45600928
IP00871933	ABMWZ1	KRT18	Uncharacterized protein ENSP00000381433	6	329	3.96	14.665	7.52	0.75	0.51	3.874305166	-0.4150375
IP00554788	P05783		Keratin, type I cytoskeletal 18	51	2175	16164.62	14.504	17.46	1.147	1.5	3.8583718925	-1.97865391
IP00871144	ABMVV2		Uncharacterized protein ENSP00000380940	8	380	2.54	14.471	5.94	0.529	0.2	3.855092716	-0.91866037
IP00170800	Q7RTW8	OTOA	Otoacortin	2	69	0.05	14.437	0.28	0.014	0.05	3.851699077	-1.27229733
IP00879559	IP00879559.1		17 kDa protein	3	101	0.2	14.419	5.63	0.546	0.21	3.849899208	-0.87302714
IP00795725	IP00795725.1	KRT8	17 kDa protein	19	1184	186987.9	14.046	8.91	0.638	0.3	3.812087435	-0.64837167
IP00871514	ABMWY4		Uncharacterized protein ENSP00000382824	13	624	13.03	14.023	5.21	6.385	20.12	3.809723119	2.67468662
IP00005859	B4DQJ4	KRT75	cDNA FLJ36809, highly similar to Homo sapiens c	9	372	1.12	13.736	6.62	0.742	0.51	3.779890039	-0.50430891
IP00872547	ABMYN2		Uncharacterized protein ENSP00000381396	5	250	1.41	13.732	8.11	0.716	0.24	3.779496857	-0.48196851
IP00737822	B9047319	KRT18P8	PREDICTED: similar to Keratin, type I cytoskeletal	3	128	5.72	13.613	1.44	0.494	0.02	3.766913134	-1.01741705
IP00554648	P05787		Keratin, type I cytoskeletal 8	59	3472	130673	13.492	7.64	1.094	2.26	3.754032318	0.12961278
IP00871700	Q9H552	KRT18P11	Keratin-8-like protein 1.	14	756	20.59	13.482	4.3	0.568	0.2	3.752962625	-0.81603717
IP00794807	IP00794807.1	KRT18	15 kDa protein	15	1012	6322.95	13.144	7.6	1.571	2.26	3.71633248	0.651683181
IP00306959	P08729	KRT7	Keratin, type II cytoskeletal 7	23	1323	6.77	13.083	7.34	0.945	1.12	3.709621491	-0.08161377
IP00787323	IP00787323.2	DECRL	Similar to Keratin, type I cytoskeletal 8	26	1566	273.13	13.057	8.11	0.563	0.25	3.707611554	-0.62878317
IP00873523	ABMW44		Uncharacterized protein ENSP00000380980	8	406	11.23	13.018	4.94	0.543	0.2	3.702435914	-0.8809759
IP00787392	113420397	HCG_1988300	PREDICTED: similar to Keratin, type I cytoskeletal	1011	111.51	12.724	8.89	0.533	0.28	0.366940372	-0.90779256	
IP00872735	ABMY66		Uncharacterized protein ENSP00000381884	8	409	5.03	12.618	3.23	0.498	0.12	3.657411351	-1.00578235
IP00793572	IP00793572.1	KRT7	6 kDa protein	2	169	1.45	12.558	3.44	2.733	3.01	3.650534812	1.45048546
IP00847342	IP00847342.1	KRT7	keratin 7	23	1780	12.492	12.492	6.52	0.985	1.14	3.642932569	-0.02180437
IP00792642	IP00792642.1	KRT8	25 kDa protein	28	1780	2254683	12.418	7.02	0.646	0.31	3.634360932	-0.63039393
IP00796330	IP00796330.1	KRT6A	18 kDa protein	6	283	4.53	12.099	4.06	0.59	0.21	3.596815906	-0.76121314
IP00872585	ABMW47		Uncharacterized protein ENSP00000381179	12	555	6.69	11.794	4.72	0.58	0.22	3.5599861194	-0.78587519
IP00794122	IP00794122.1	KRT7	13 kDa protein	5	159	5.58	11.594	4.79	0.737	0.24	3.553530648	-0.44026348
IP00009867	P13641	KRT5	Keratin, type I cytoskeletal 5	17	401	0.55	11.565	7.79	0.534	0.28	3.531393631	-0.90508835
IP00294649	94538345	KRT35	keratin 35	3	117	0.56	11.424	5.52	0.315	0.21	3.513995979	-1.66657627
IP00871464	ABMU77		Uncharacterized protein ENSP00000383774	17	985	221.39	11.401	6.04	0.54	0.2	3.511088466	-0.88896869
IP00299145	P48668	KRT6C	Keratin, type II cytoskeletal 6C	10	436	1.76	10.752	3.03	0.511	0.16	3.426533138	-0.9686048
IP00300725	P00339	KRT6A	Keratin, type II cytoskeletal 6A	10	436	1.75	10.752	3.03	0.511	0.16	3.426533138	-0.9686048
IP00297452	Q8TDJ3	TFG	Tyrosine-protein kinase receptor	11	561	0.6	10.65	5.44	1.307	1.57	3.412781525	0.38259141
IP00796921	Q05BK6	TFG	TFG protein	11	561	1.77	10.65	5.44	1.307	1.57	3.412781525	0.38259141
IP00013164	P14129	PRPH	Peripherin	4	261	1.17	10.591	5.18	0.4	0.25	3.40476691	-1.32192809
IP00294619	Q9CT34	TFG	TFG protein	12	615	2.01	10.4	5.23	1.194	1.53	3.378511623	0.255802837
IP00220007	IP00220007.6	APOL2	cDNA FLJ55764, highly similar to Apolipoprotein-I	9	401	0.57	10.383	4.93	0.66	0.65	3.376151442	-0.59946207
IP00106913	32483352	DHRS4	peroxisomal short-chain alcohol dehydrogenase	4	259	0.38	10.359	7.44	0.447	0.44	3.372812835	-1.16165326
IP00793646	IP00793646.1		cDNA FLJ61294, highly similar to Keratin, type I c	5	198	0.93	10.352	3.41	0.782	0.31	3.371837617	-0.35475949
IP00168554	Q9BYN0	SRXN1	Sulfiredoxin-1	4	214	1.93	10.258	5.45	0.267	0.31	3.358677571	-1.90580835
IP00241841	Q04K45	KRT79	Keratin, type II cytoskeletal 79	9	401	0.57	10.211	5.04	0.61	0.17	3.352052222	-0.78805955
IP00873742	ABMWV3		Uncharacterized protein ENSP00000382295	12	688	18.63	10.2	5.5	0.507	0.21	3.350497247	-0.97994235
IP00290078	109255249	KRT4	keratin 4	4	219	0.49	9.919	1.15	0.58	0.22	3.31019468	-0.78587519
IP00376379	194018511	KRT77	keratin 77	3	159	0.37	9.893	1.12	0.451	0.04	3.304480747	-1.14880066
IP00300552	KRT84		Keratin, type II cuticular Hb4	3	142	0.56	9.851	1.79	0.413	0.01	3.300270184	-1.27578631
IP00642542	IP00642542.1	CNN3	DJ359P13.2.2	3	180	0.85	9.806	2.18	0.357	0.13	3.293664762	-1.48600402
IP00642078	Q5TDQ0	TPD52L1	Tumor protein D52-like 1	3	193	1.16	9.806	6.3	0.953	0.42	3.293664762	-0.6945188
IP00032831	Q95721	SNAP29	Synaptosomal-associated protein 29	5	300	0.55	9.667	5.66	0.54	0.51	3.273068242	-0.88896869
IP00166205	25140706	KRT78	TPA: TPA_exp: keratin 5b	2	84	0.18	9.547	1.4	0.482	0.11	3.255047459	-1.05284994
IP00308359	Q001546	TFG	Keratin, type II cytoskeletal 2 oral	4	214	0.34	9.448	1.1	0.435	0.04	3.244009895	-1.20091269
IP00290857	P12035	KRT3	Keratin, type II cytoskeletal 3	5	166	0.35	9.448	1.1	0.435	0.04	3.240008965	-1.20091269
IP00787216	113414151	LOC650864	PREDICTED: similar to Keratin, type II cytoskeletal	4	238	7.25	9.212	2.57	0.443	0.1	3.203514411	-1.1746214
IP00794644	IP00794644.1	KRT19	21 kDa protein	5	264	4.16	8.725	5.79	0.428	0.39	3.125155131	-1.2243173
IP00791852	IP00791852.1	KRT17	42 kDa protein	19	1013	4.83	8.723	3.28	0.722	0.34	3.14248493	-0.46949262
IP00412076	ABMU17		Putative uncharacterized protein TPD52L1	4	214	0.57	8.57	0.9	0.35	0.2	3.082026202	-0.10780329
IP00009866	P13646	KRT13	Keratin, type I cytoskeletal 13	5	229	0.38	8.568	5.4	0.398	0.08	3.08985848	-1.37706965
IP00060181	Q96C19	EFHD2	EF-hand domain-containing protein D2	9	483	3.12	8.41	4.39	0.51	0.09	3.07721058	-2.73695955
IP00225363	P14136	GFAP	Glia fibrillary acidic protein	5	267	0.67	8.378	1.72	0.378	0.26	3.06665884	-1.40354186
IP00303815	P14136-2	GFAP	Isform 2 of Gial fibrillary acidic protein	5	267	0.67	8.378	1.72	0.378	0.26	3.06665884	-1.40354186
IP00443478	P14136-3	GFAP	Isform 3 of Gial fibrillary acidic protein	5	267	0.67	8.378	1.72	0.378	0.26	3.06665884	-1.40354186
IP00180956	ABMW45	LOC650611	Uncharacterized protein ENSP00000382160	10	495	0.93	8.337	4.11	0.628	0.31	3.059528335	-0.67116354
IP00171196	IP00171196.2	KRT13	keratin 13 isoform b	6	273	0.63	8.306	4.44	0.331	0.13	3.054153872	-1.59509688
IP00015262	Q9B439	CNN2	Calponin-2	6	158	0.66	8.257	3.16	0.724	0.96	3.045641705	-0.46466384
IP00065671	Q9BZC2	UCK2	Uridine-cytidine kinase 2	4	252	1.93	8.251	4.29	0.351	0.27	3.044568691	-1.5102106
IP00465084	P17661	DES	Desmin	7	359	1.45	8.218	5.23	0.355	0.23	3.038787331	-1.49410907
IP00450768	Q04695	KRT17	Keratin, type I cytoskeletal 17	29	1510	7.36	8.175	3.88	0.618	0.33	3.033334895	-0.64611216
IP00240503	IP00240503.7		48 kDa protein	11	473	1.21	8.175	3.88	0.618	0.3	3.032128731	-0.69432126
IP00877836	IP00877836.1	SNAP29	21S protein	3	210	0.68	8.054	5.1	0.602	0.61	3.009705472	-0.73216461
IP00873410	IP00873410.1	CNN3	46 kDa protein	7	507	0.88	7.935	3.1	0.432	0.32	2.98230223	-1.21089678
IP00745035	IP00745035.2		15 kDa protein	2	73	0.51	7.889	0.52	0.237	0.1	2.979842438	-0.20770414
IP00747707	47939651	KRT17	KRT17 protein	22	1213	6.78	7.888	3.03	0.623	0.32	2.979695952	-0.68269593
IP00787127	Q9B727	KRT18	Keratin, type I cytoskeletal 18	7	338	1.38	7.681	7.53	0.401	0.35	2.94129415	-1.31835686
IP00025277	Q7S340	PCDC6	Programmed cell death protein 6	7	342	7.5	7.349	5.47	0.476	0.62	2.877547592	-1.07096652
IP00465084	P17661	DES	Desmin	7	359	1.45	8.218	5.23	0.355	0.23	2.871494916	-1.30673373
IP00446474	Q9Y5V2	NBP2	Nucleotide-binding protein 2	2	121	0.24	7.314	1.68	2.817	3	2.870660622	1.494159504
IP00418471	P08670	VM	Vimentin	48	2842	1007.01	7.203	2.45	0.283	0.16	2.848597904	-1.82112604
IP00023640	O14737	PCD	Programmed cell death protein 5	5	350	4.51	7.124	3.28	0.098			

IP00399053	Q9BU61	C3orf50	Uncharacterized protein C3orf50	4	229	0.85	4.097	1.61	0.433	0.29	2.034567893	-1.20756107
IP00420084	P59597-2	BID	Isoform 2 of BH3-interacting domain death agonist	3	222	0.6	4.078	1.09	0.332	0.13	2.027861775	-1.59074485
IP00784154	P10089	HSPD1	60 kDa heat shock protein, mitochondrial	45	343	337.11	4.067	1.43	0.328	0.46	2.023964981	-1.60823228
IP00880053	IP00880053.1		Mitochondrial heat shock 60kD protein 1 variant 1	18	1064	6.61	4.057	1.48	0.226	0.27	2.020413303	-2.14566532
IP00016339	P51148	RAB5C	Ras-related protein Rab-5C	10	604	6.42	4.028	0.78	0.266	0.24	2.010063683	-1.91050185
IP00854538	AY543	TPD52	CLIMPRPS28 fusion protein	6	444	1.49	3.908	0.62	0.331	0.22	1.966430467	-1.59509688
IP00018398	P17980	PSMC3	26S protease regulatory subunit 6A	14	795	3.17	3.902	1.49	0.255	0.18	1.964213778	-1.97143085
IP00787692	169211725	LOC6420788	PREDICTED: similar to 40S ribosomal protein S2i	2	130	8.45	3.852	1.074	0.02	0.12	1.945607103	-3.75623092
IP00023510	P20339	RAB5A	Ras-related protein Rab-5A	7	371	3.29	3.805	1.7	0.284	0.27	1.927896454	-1.81603717
IP00794769	IP00794769.1	HSPD1	18 kDa protein	14	882	103.06	3.674	1.08	0.198	0.26	1.977351626	-2.33642766
IP00794046	CC174		20 kDa protein	5	262	2.57	3.664	0.59	0.566	0.88	1.873419503	-0.82112604
IP00003419	C00193	C11orf58	Small acidic protein	2	111	0.17	3.522	0.02	1.308	0.34	1.815394909	-1.69899774
IP00519951	7060814		tumor protein D52 isoform 2	9	359	3.63	3.519	1.09	0.48	0.31	1.815165514	-1.05889369
IP00873344	Q9UCX8	TPD52	N8 protein long isoform	9	580	2.7	3.519	1.09	0.48	0.31	1.815165514	-1.05889369
IP00844412	A4D286		Similar to Nuclear protein Hcc-1 (HSPC316) (Proti	3	194	0.57	3.512	2.58	0.719	1.1	1.812292485	-0.47593632
IP00017344	P61020	RAB5B	Ras-related protein Rab-5B	6	315	1.88	3.451	1.03	0.174	0.11	1.771084474	-2.52284079
IP00030354	P61289	PSME3	Proteasome activator complex subunit 3	10	572	2.6	3.291	0.49	0.253	0.25	1.718526026	-1.98279071
IP00021945	P61289-2	PSME3	Isoform 2 of Proteasome activator complex subunit	10	572	2.41	3.291	0.49	0.253	0.25	1.718526026	-1.98279071
IP00076042	Q96R13	LOC642237	Short heat shock protein 60 Hsp60s2	8	491	6.2	3.276	1.13	0.294	0.32	1.711935357	-1.76611194
IP00554681	Q15718	NUDFA5	NADH dehydrogenase lubeinone1 alpha subcc	2	106	0.57	3.263	0.43	0.319	0.02	1.706189887	-1.64837167
IP00795769	119617241		NC02016179, isoform CRA_c	6	305	0.36	3.227	1.93	0.517	0.65	1.687084688	-0.95176381
IP00060650	Q8WW12-2	PCPN	Isoform 2 of PEST proteolytic signal-containing nu	2	85	0.57	3.211	0.86	0.148	0.01	1.683022665	-2.75633092
IP00796456	IP00796456.1	PCPN	Isoform 1 of PEST proteolytic signal-containing nu	2	85	0.39	3.211	0.86	0.148	0.01	1.683022665	-2.75633092
IP00505746	Q9Y266	NUDC	Nuclear migration protein nudC	8	457	1.11	3.2	0.81	0.143	0.09	1.678071905	-2.80591295
IP00298559	Q9BU61.8	POD101	Programmed cell death protein 10	4	249	1.91	3.191	0.49	0.29	0.15	1.674036619	-1.78591619
IP00022462	P02786	TFRC	Transferrin receptor protein 1	3	193	0.12	3.173	1.84	0.142	0.03	1.665847521	-2.81603717
IP00334190	Q9JUZ1	STOML2	Stomatin-like protein 2	3	199	0.39	3.168	0.51	0.868	1.16	1.663572335	-0.20423305
IP00073655	113413200	LOC653781	PREDICTED: similar to protein expressed in prost	7	327	0.64	3.155	0.98	0.286	0.05	1.676400005	-1.80591295
IP00786945	Q56217	LOC6277848	PREDICTED: similar to actin-like protein	7	247	0.57	3.155	0.78	0.286	0.05	1.676400005	-1.80591295
IP00790339	IP00790339.1	ACTG1	22 kDa protein	9	549	173.56	3.118	0.91	0.297	0.07	1.640620928	-1.75146516
IP00796881	IP00796881.1	ACTG1	16 kDa protein	9	549	889.49	3.118	0.91	0.297	0.07	1.640620928	-1.75146516
IP00555809	IP00555809.3	TBC1D22A	Pseudogene candidate	2	67	0.13	3.109	0.23	2.763	3.46	1.638450617	-1.466235562
IP00740545	88953571	LOC653269	PREDICTED: similar to protein expressed in prost	8	397	0.75	3.103	0.92	0.286	0.05	1.633663697	-1.79585928
IP00784029	AB757	HTATP2	cDNA FLJ75232, highly similar to Homo sapiens I	6	295	0.76	3.086	0.48	0.283	0.07	1.625713802	-1.82112604
IP00739539	AS4362	POTEF	ANKRD26-like family C member 1B	8	459	0.94	3.084	0.93	0.278	0.05	1.624802765	-1.85725983
IP00016610	Q15365	PCBP1	Putative (Poly)C-binding protein 1	14	834	4.43	3.082	1.45	0.235	0.22	1.623866862	-2.08926734
IP00021370	P16086	UBE2K	Ubiquitin-conjugating enzyme E2 K	4	230	0.52	3.072	0.81	0.376	0.13	1.619178216	-1.41119543
IP00478743	Q56217	POTEE	ANKRD26-like family C member 1A	10	521	1.57	3.069	0.59	0.283	0.05	1.617288483	-1.8312604
IP00030297	P50991	CC174	T-complex protein 1 subunit delta	24	1300	6.72	2.978	1	0.24	0.37	1.574343754	-2.05889369
IP00027681	P40261	NNMT	Nicotinamide N-methyltransferase	4	217	0.38	2.94	0.41	0.151	0.12	1.555816155	-2.72737955
IP00038365	Q9BUP3-2	HTATP2	Isoform 2 of Oxidoreductase HTATP2	4	183	0.85	2.903	0.45	0.31	0.06	1.537544572	-1.68965988
IP00008603	P62736	ACT1	Actin, aortic smooth muscle	16	837	80.28	2.88	0.78	0.585	1.23	1.526068812	-0.77349147
IP00025416	P62736	ACTG2	Actin, gamma-enteric smooth muscle	16	837	80.28	2.88	0.78	0.585	1.23	1.526068812	-0.77349147
IP00021428	P68133	ACTA1	Actin, alpha skeletal muscle	17	885	107.75	2.876	0.75	0.57	1.2	1.524063676	-0.81096618
IP00023006	P68032	ACT1	Actin, alpha cardiac muscle 1	17	885	109.08	2.876	0.75	0.57	1.2	1.524063676	-0.81096618
IP00084058	IP00084058.1	ACTB	Actin, cytoplasmic 2	22	1454	716.06	2.858	0.64	0.411	0.38	1.510505916	-1.2827897
IP00078919	Q56217	LOC6389036	Actin-like protein	2	88	3.85	2.785	0.3	0.322	0.03	1.482848283	-1.63486741
IP00877144	Q56217	P70P4P	Actin-like protein	2	88	3.79	2.795	0.3	0.322	0.03	1.482848283	-1.63486741
IP00640817	Q57987	AK1	Adenylylate kinase 1	5	319	2.8	2.786	0.67	0.182	0.15	1.478195258	-1.54798964
IP00010158	Q9NRG0	CHRA21	Chromatin accessibility complex protein 1	2	88	0.52	2.777	0.29	0.211	0.22	1.473527177	-2.2446851
IP00555900	Q9Y8Y7	ACTBL3	Kappa-actin	5	297	2.92	2.766	0.56	0.289	0.05	1.467801156	-1.7308586
IP00024095	P12129	ANKA3	Annexin A3	4	249	0.89	2.762	0.9	0.06	0.34	1.467801156	-1.7308586
IP00000643	Q56816	BAG2	BAG family molecular chaperone regulator 2	8	317	1.52	2.755	1.33	0.331	0.29	1.462052319	-1.59509688
IP00030143	A7YDY3	BOLA2B	BoA homolog 2 (E. coli)	4	174	1.49	2.726	0.05	0.466	0.39	1.446785562	-1.10159814
IP00791573	Q9Y22D-2	SUGT1	Isoform 2 of Suppressor of G2 allele of SKP1 hom	2	76	0.18	2.628	0.48	0.259	0.26	1.391217808	-1.948976
IP00412525	ABWZ1	LOC61757335	Actin-like protein Rap-1b-like protein	4	347	2.45	2.599	0.34	0.389	0.05	1.377985698	-1.8312604
IP00016179	Q96858	S100A13	Calyculin A-inhibited protein 3	4	165	1.87	2.524	0.3	0.115	0.02	1.33571191	-3.12029423
IP00167750	IP00167750.5	PCBP3	Poly(C)-binding protein 3 (Alpha-CP3), isoform 5	5	218	0.53	2.483	0.84	0.155	0.1	1.312084262	-2.68956988
IP00505365	IP00505365.2	PCBP3	Putative uncharacterized protein PCBP3	5	218	0.52	2.483	0.84	0.155	0.1	1.312084262	-2.68956988
IP00003269	Q562R1	ACTBL2	Beta-actin-like protein 2	7	357	12.17	2.482	0.35	0.282	0.03	1.311503115	-1.82623293
IP00015148	P16121	RAP1B	Ras-related protein Rap-1b	4	294	3.48	2.467	0.38	0.414	0.05	1.302757716	-1.72729733
IP00019345	P62834	RAP1A	Ras-related protein Rap-1A	4	294	3.41	2.467	0.38	0.414	0.05	1.302757716	-1.72729733
IP00877120	Q5U0C3	RAP1A	RAP1A, member of RAS oncogene family	4	294	3.41	2.467	0.38	0.414	0.05	1.302757716	-1.72729733
IP00874082	ABMY02		Uncharacterized protein ENSNP000382574	2	77	0.59	2.438	0.33	0.02	0.28	1.256988126	-1.59946027
IP00018671	Q9Y8Y7	DUSP3	Dual specificity protein phosphatase 3	3	184	0.58	2.401	0.19	0.121	0.05	1.236355404	-3.04692105
IP000218395	196533965	PSMC6	Proteasome 26S, AT1Pase subunit 6	24	1300	6.72	2.375	1	0.24	0.37	1.247927513	-2.73291647
IP00030882	Q60664	MPRBP1	Mannose-6-phosphate receptor-binding protein 1	7	521	0.84	2.312	0.56	0.315	0.16	1.209141398	-1.66657627
IP00797742	IP00797742.1	CIFP29	5 kDa protein	2	82	2.29	2.288	0.08	0.201	0.18	1.194087052	-2.31473259
IP00789551	ABMXP9	MATR3	Putative uncharacterized protein MATR3	2	161	0.17	2.255	0.57	0.161	0.1	1.173127433	-2.63486741
IP00030319	Q9Y8Y7	FAM49B	Protein FAM49B	6	227	2.27	2.222	0.7	0.321	0.09	1.151858891	-3.04692105
IP00215790	P63173	RPL38	60S ribosomal protein L38	7	421	551.556	2.195	0.59	0.391	0.41	1.134220094	-1.84385653
IP00100796	Q9NZ23	CHMP5	Charged multivesicular body protein 5	3	123	0.29	2.168	1.96	0.047	0.34	1.113646757	-1.08620104
IP00004902	P38117	ETFB	Electron transfer flavoprotein subunit beta	3	107	0.57	2.04	0.71	0.101	0.01	1.028699152	-3.7075728
IP00554512	P38117	ETFB	Isoform 2 of Electron transfer flavoprotein subunit I	3	107	0.4	2.04	0.71	0.101	0.01	1.028699152	-3.7075728
IP00798442	IP00798442.1	PCBP2	Putative uncharacterized protein PCBP2	5	107	0.4	1.995	0.78	0.076	0.04	0.986389746	-3.73291647
IP00798360	IP00798360.1	CIFP29	18 kDa protein	4	187	1.33	1.978	1.41	0.128	0.14	0.984042426	-2.96578478
IP00016372	P51151	RAB9A	Ras-related protein Rab-9A	3	88	0.31	1.835	1.7	0.245	0.24	0.975780063	-2.02914635
IP000218918	P40483	ANXA1	Annexin A1	11	786	1.59	1.826	0.47	0.117	0.19	0.888868765	-1.90541957
IP00012066	ABWZ1	LOC6177432	highly similar to Homo sapiens I	11	600	1.15	1.826	0.47	0.117	0.19	0.888868765	-1.90541957
IP000184525	Q9BV20-2	MGC3207	Isoform 2 of Translation initiation factor eIF-2B sub	2	115	0.32	1.802	0.19	0.126	0	0.849599011	-2.98850436
IP00006052	Q9UHV9	PFDC2	Prefoldin subunit 2	2	151	1.1	1.794	0.29	0.082	0.04	0.84317989	-3.08223228
IP000329801	P08758	ANXA5	Annexin A5	20	1170	39.54	1.793	0.49	0.151	0.22	0.842375488	-2.72737955
IP00029508	Q9Y8Y7	SRFBP8	Signal recognition particle receptor subunit beta	3	177	0.34	1.787	0.43	0.082	0.06	0.837539634	-1.00862042
IP00022597	P16081	UBE2M	NEDD8-conjugating enzyme UbcL2	4	177	0.82	1.778	0.47	0.13	0.07	0.830255324	-2.94341647
IP00033143	Q9UBQ5	EIF3K	Eukaryotic translation initiation factor 3 subunit K	3	223	0.87	1.742	0.32	0.049	0.01	0.800744624	-3.5107444
IP00505363	P37802	TAGLN2	Transgelin-2	10	638	130.06						

IP000301277	P34931	HSPA1L	Heat shock 70 kDa protein 1L	6	453	0.58	1.102	0.29	0.095	0.07	0.140124224	-0.39592868
IP000300341	Q15369	TCEB1	Transcription elongation factor B polypeptide 1	3	101	0.63	1.098	0.19	0.064	0.04	0.134878054	-0.96578428
IP000109551	P07455/2735	EPK1	epikotin 1	4	222	0.93	1.021	0.21	0.164	0.12	0.125651102	-0.60823228
IP000085529	P05387	RPLP2	60S acidic ribosomal protein P2	7	432	0.25	1.093	0.33	0.041	0.09	0.125651102	-0.82623305
IP000295386	P16152	SETD4	Carbonyl reductase [NADPH] 1	7	500	2.14	1.081	0.29	0.68	1.33	0.112366523	-0.55639335
IP000169383	P00558	PGK1	Phosphoglycerate kinase 1	24	1290	46.23	1.067	0.26	0.104	0.26	0.093560176	-0.26534457
IP000212347	P68036	UBE2L3	Ubiquitin-conjugating enzyme E2 L3	2	123	1	1.047	0.31	0.105	0.09	0.086261442	-0.32515877
IP000174448	P65240	RPS21	60S ribosomal protein S21	4	192	1.65	1.041	0.17	0.121	0.15	0.057970059	-0.34652105
IP000463115	A2A202	STMN1	Stathmin	2	85	0.97	0.981	0.21	0.09	0.11	-0.02767496	-0.34793319
IP000744618	IP000744618.2	STMN1	Stathmin	2	85	0.84	0.981	0.21	0.09	0.11	-0.02767496	-0.34793319
IP00017454	Q9H853	TUBA4B	Putative tubulin-like protein alpha-4B	3	193	2.52	0.977	0.51	0.047	0.04	-0.03366953	-0.41119543
IP000792673.1	ETFA	24 kDa protein		7	570	0.78	0.963	0.3	0.36	0.43	-0.03806332	-0.51158797
IP000216691	P07737	PFN1	Profilin-1	8	509	37.66	0.968	0.14	0.059	0.07	-0.04692105	-0.40831424
IP000024282	Q92930	RAB8B	Ras-related protein Rab-8B	2	118	0.7	0.966	0.09	0.098	0.02	-0.04904941	-0.35107444
IP000028481	P61006	RAB8A	Ras-related protein Rab-8A	2	118	0.7	0.966	0.09	0.098	0.02	-0.04904941	-0.35107444
IP000300096	Q15286	RAB35	Ras-related protein Rab-35	2	118	0.72	0.966	0.09	0.098	0.02	-0.04904941	-0.35107444
IP003363449	P59190-2	RAB15	Ras-related protein Rab-15	2	118	0.67	0.966	0.09	0.098	0.02	-0.04904941	-0.35107444
IP003394882	P59190	RAB15	Ras-related protein Rab-15	2	118	0.67	0.966	0.09	0.098	0.02	-0.04904941	-0.35107444
IP000556414	Q59EP4	RAB8A	Mel transforming oncogene variant	2	118		0.966	0.09	0.098	0.02	-0.04904941	-0.35107444
IP000790414.1	RAB8B	10 kDa protein		2	118		0.966	0.09	0.098	0.02	-0.04904941	-0.35107444
IP000791726.1	NACA	nascent polypeptide-associated complex alpha sub		7	570	0.78	0.963	0.3	0.36	0.43	-0.0542923	-1.47393119
IP00017726	Q9H744	HSO17B10	3-hydroxyacyl-CoA dehydrogenase type-2	11	884	17.65	0.953	0.2	0.1	0.08	-0.06945188	-0.32192809
IP000872214.1	IP00872214.1	TBCA	16 kDa protein	2	144	0.81	0.945	0.1	0.117	0.09	-0.08161377	-0.99541957
IP000018146	P27348	YWHAQ	14-3-3 protein theta	13	722	12.58	0.933	0.25	0.057	0.06	-0.10005107	-1.43289427
IP000740010	113451510	LOC643412	PREDICTED: similar to basic transcription factor 3	2	136	1	0.922	0.27	0.345	0.09	-0.11716134	-1.53633173
IP000211055	P20290	BTFC3	Transcription factor BTFC3	3	127	0.76	0.922	0.27	0.345	0.09	-0.11716134	-1.53633173
IP000795676	IP000795676.1	RAB11A	22 kDa protein	6	286	2.05	0.921	0.15	0.07	0.06	-0.11872694	-0.83650127
IP000798247	IP000798247.1	HSPA8	20 kDa protein	4	296	1.97	0.918	0.41	0.111	0.05	-0.12343394	-0.17136842
IP000291922	P28066	PSMA5	Proteasome subunit alpha type-5	7	317	1.3	0.914	0.36	0.079	0.06	-0.12973393	-0.66200354
IP000549240	NP1M1	Nucleophosmin		12	667	10.37	0.922	0.22	0.667	0.06	-0.13313123	-0.14560532
IP000297579	Q13185	LOC653972	Chromobox protein homolog 3	3	199	0.82	0.911	0.11	0.087	0.05	-0.13447704	-0.52284079
IP000658013	Q9BYG9	NP1M1	Nucleophosmin (Nucleolar phosphoprotein B23, n	11	638	14.97	0.908	0.24	0.12	0.12	-0.1392358	-0.50889369
IP000016572	P62308	SNRPG	Small nuclear ribonucleoprotein G	2	99	1	0.899	0.06	0.247	0.03	-0.15360698	-0.201741705
IP000291928	P61106	RAB1A	Ras-related protein Rab-1A	3	180	0.69	0.896	0.19	0.12	0.01	-0.15842936	-0.30889369
IP00005969	P52907	CAPZL1	F-actin-capping protein subunit alpha-1	2	112	0.82	0.884	0.25	0.057	0.02	-0.18114944	-0.21187977
IP000218667	Q93045	STMN2	Stathmin-2	2	86	0.82	0.881	0.36	0.118	0.07	-0.18278608	-0.80831424
IP000216049	P61788	HNRNPDK	Heterogeneous nuclear ribonucleoprotein K	17	1066	5.98	0.876	0.47	0.074	0.06	-0.19099723	-0.75633092
IP00013679	P33316	DUT	Deoxyuridine 5-triphosphate nucleotidohydrolase, a	4	264	1.57	0.874	0.08	0.05	0.06	-0.19429482	-0.32192809
IP000749113	P33316.1	DUT	Deoxyuridine 5-triphosphate nucleotidohydrolase, a	4	264	1.57	0.874	0.08	0.05	0.06	-0.19429482	-0.32192809
IP000793322	IP000793322.1	DUT	Deoxyuridine 5-triphosphate nucleotidohydrolase, a	4	264	1.79	0.874	0.08	0.05	0.06	-0.19429482	-0.32192809
IP000514561	Q5T6W5	HNRNPDK	Heterogeneous nuclear ribonucleoprotein K	15	997	6.01	0.871	0.49	0.079	0.09	-0.19925538	-0.66200354
IP00001639	Q14974	PKNB1	Importin subunit beta-1	4	223	0.22	0.868	0.34	0.166	0.12	-0.20423305	-0.59074485
IP000298547	Q94947	PKP1	Protein D3-1	6	295	6.64	0.865	0.15	0.11	0.08	-0.20922796	-0.17842457
IP004779997	P16649	STMN1	Stathmin	2	86	1.44	0.864	0.25	0.057	0.09	-0.21069678	-0.57158797
IP000029631	P84090	ERH	Enhancer of rudimentary homolog	2	75	0.28	0.859	0.18	0.084	0	-0.2126996	-0.57346686
IP00021700	P12004	PCNA	Proliferating cell nuclear antigen	10	544	8.99	0.855	0.19	0.136	0.08	-0.22600367	-0.27832144
IP000108010	P13804	ETFA	Electron transfer flavoprotein subunit alpha, mitocho	4	203	0.88	0.835	0.48	0.041	0.02	-0.2601519	-0.60823228
IP000419235	1180419235.4	GSTM5	Glutathione S-transferase U2 subunit	5	137	0.82	0.82	0.04	0.82	0.04	-0.2863041	-0.64365619
IP000364683	IP000364683.1	GSTM5	Glutathione S-transferase U2 subunit	5	148	0.3	0.813	0.17	0.009	0.01	-0.28867274	-0.78585028
IP00004968	Q9UM54	PRPF19	Pre-mRNA-processing factor 19	3	105	0.19	0.809	0.13	0.222	0.24	-0.30578839	-0.17136842
IP000642971	194239723	EEF1D	eukaryotic translation elongation factor 1 delta isofo	9	596	0.96	0.809	0.23	0.121	0.03	-0.30578839	-0.40692105
IP000216319	Q04917	YWHAH	14-3-3 protein eta	6	311	1.73	0.805	0.14	0.025	0.04	-0.31293931	-0.52192809
IP000640504	Q5C263	CLEC2D	Putative uncharacterized protein	8	445	0.8	0.797	0.14	0.057	0.05	-0.32192809	-0.57158797
IP000246975	P21266	GSTM3	Glutathione S-transferase Mu 3	8	418	4.91	0.797	0.23	0.08	0.09	-0.32734837	-0.64385619
IP000688801	89039164	LOC647504	PREDICTED: similar to Acidic leucine-rich nucleo	6	275	4.19	0.795	0.27	0.126	0.18	-0.33097323	-0.98850436
IP000179964	P26599	PTBP1	Poly(pyrimidine tract-binding protein 1	7	462	1.19	0.792	0.17	0.156	0.1	-0.33642766	-0.68038207
IP000872407	Q5YHAB	YWHAH	Yeast 3-monooxygenase/histidylphosphon 5-monoon	5	263	1.68	0.786	0.09	0.033	0.03	-0.34739878	-0.92139017
IP00007423	Q92682	ANP2B	Acidic leucine-rich nuclear phosphoprotein 32 fam	7	343	0.3	0.781	0.24	0.058	0.18	-0.35665055	-0.85732683
IP000010796	P07327	P4HB	Protein disulfide-isomerase	2	513	0.96	0.78	0.23	0.141	0.16	-0.35845397	-0.82623293
IP000173334	P35232	PHB	Prohibitin	8	449	2.57	0.776	0.19	0.189	0.13	-0.36587144	-0.4035147
IP000291005	P40925	MDH1	Malate dehydrogenase, cytoplasmic	9	504	2.39	0.775	0.21	0.107	0.05	-0.36771738	-0.22434161
IP000216319	Q5YHAB	YWHAH	14-3-3 protein beta/alpha	8	418	1.94	0.763	0.13	0.091	0.05	-0.36771738	-0.4035147
IP000759832	P31946-2	YWHAH	Isoform Short of 14-3-3 protein beta/alpha	15	891	20.12	0.775	0.11	0.079	0.14	-0.36771738	-0.66200354
IP000797206	IP000797206.1	CCT8	Protein	6	416	1.45	0.756	0.23	0.083	0.18	-0.40354186	-0.45008445
IP00027350	P32119	PRDX2	Peroxiredoxin-2	9	515	25.63	0.756	0.14	0.038	0.02	-0.40354186	-0.47178567
IP000878440	IP000878440.1	RANBP1	19 kDa protein	2	107	0.93	0.749	0.02	0.038	0.03	-0.41686238	-0.71785677
IP000796294	EEF1D	CCT8	cDNA FLJ57945, highly similar to Elongation fact	6	274	1.24	0.749	0.12	0.041	0.04	-0.42692547	-0.94042514
IP000220642	P61981	YWHAH	14-3-3 protein gamma	9	527	4.93	0.742	0.12	0.071	0.12	-0.43050891	-0.81603717
IP000793442	ABMUL1	PHB	Putative uncharacterized protein PHB	6	307	2	0.725	0.15	0.183	0.15	-0.4639471	-0.25008445
IP000791634	Q5QFV0	PHB	Prohibitin variant	7	359	1.6	0.725	0.15	0.183	0.15	-0.4639471	-0.25008445
IP000302925	1180302925	CCT8	Chaperonin containing TCP1, subunit 8 (theta), iso	6	245	2.46	0.725	0.12	0.126	0.15	-0.46992931	-0.87849208
IP000795516	IP000795516.1	YWHAH	cDNA FLJ51975, moderately similar to 14-3-3 pro	5	259	4.35	0.713	0.12	0.043	0.04	-0.48802602	-0.53951953
IP000869193	88952419	LOC644131	PREDICTED: similar to chaperonin containing TC	2	134	0.43	0.711	0.61	0.026	0.06	-0.49027854	-0.92139017
IP00013890	P31947	SFN	14-3-3 protein sigma	9	331	1.78	0.709	0.15	0.052	0.07	-0.49614247	-0.26534457
IP000395627	Q9H871	CACYPB	Calcycin-binding protein	2	127	0.82	0.705	0.12	0.157	0.12	-0.50430484	-0.67116354
IP000794673.1	IP000794673.1	CCT8	Chaperonin containing TCP1, subunit 8 (theta), iso	6	245	3.79	0.705	0.24	0.189	0.14	-0.50430484	-0.67116354
IP00024175	Q14818	PSMA7	Proteasome subunit alpha type-7	5	393	1.47	0.705	0.24	0.072	0.05	-0.50430484	-0.79585928
IP000100137	118604798	EEF1D1P1	hCG2000329	3	201	0.84	0.698	0.37	0.12	0.02	-0.51870106	-0.50889369
IP000159584	SAR1A	GTP-binding protein SAR1A		3	132	0.75	0.694	0.53	0.229	0.03	-0.52699243	-0.21265805
IP000032626	ST13	HSP70	HSP70-interacting protein	2	102	0.36	0.692	0.07	0.067	0.02	-0.53115606	-0.13298427
IP000218038	Q8Q2P2	FAM104A	Protein FAM104A	2	133	0.58	0.692	0.04	0.057	0.02	-0.53115606	-0.13298427
IP000216298	P10599	TXN	Thioredoxin	5	301	6.78	0.692	0.09	0.077	0.12	-0.53115606	-0.69899774
IP000448725	Q6PWK3	RAB4B	RAB4B protein	2	114	0.96	0.691	0.48	0.339	0.32	-0.53324238	-1.56064282
IP000399212	11699212.776	LOC389842	PREDICTED: similar to RanBP1	2	95	0.99	0.691	0.1	0.034	0.02	-0.53324238	-0.87832144
IP000414127	P43487	RANBP1	Ran-specific GTPase-activating protein	3	145	1.24	0.691	0.1	0.034	0.02	-0.53324238	-0.87832144
IP000878075	119623394	RANBP1	RAN binding protein 1, isoform CRA_d	3	145	1.25	0.691	0.1	0.034	0.02	-0.53324238	-0.87832144

IP00418813	IP00418813.2		Similar to Ribosomal protein S27a	4	188	0.87	0.472	0.09	0.036	0.04	-1.08314124	-4.79585928
IP00794205	IP00794205.1		26 kDa protein	4	188	0.84	0.472	0.09	0.036	0.04	-1.08314124	-4.79585928
IP00641244	IP00641244	PRDX1	peroxidodoxin 1	7	329	2.38	0.455	0.04	0.011	0.05	-1.08314124	-4.79585928
IP00871646	IP00871646	Q8NHV5	60S acidic ribosomal protein P0-like	6	338	1.3	0.466	0.05	0.008	0.03	-1.10159814	-3.64858610
IP00023860	IP00023860	P55209	Nucleosome assembly protein 1-like 1	4	211	0.32	0.465	0.01	0.063	0.02	-1.10469738	-3.98850436
IP000220014	IP000220014	B4E155	cDNA FLJ56330, highly similar to Homo sapiens t	3	154	0.22	0.463	0.24	0.063	0.06	-1.1109159	-3.98850436
IP00010896	IP00010896	O00299	Chloride intracellular channel protein 1	5	326	1.02	0.463	0.13	0.063	0.07	-1.1109159	-3.98850436
IP00795465.1	IP00795465.1	CLCBP	Protein	1	0.85	0.46	0.02	0.02	0.078	0.01	-1.12052943	-3.68027077
IP000218820	IP000218820	TPM2	isoform 3 of Tropomyosin beta chain	6	229	1.16	0.459	0.39	0.283	0.08	-1.12343394	-1.82112604
IP000220709	IP000220709	TPM2	isoform 2 of Tropomyosin beta chain	6	229	0.96	0.459	0.39	0.283	0.08	-1.12343394	-1.82112604
IP00793002	IP00793002.1	RPLP0	18 kDa protein	5	293	3.39	0.455	0.04	0.101	0.05	-1.13661655	-3.3075728
IP00793584	IP00793584.1	RPLP0	23 kDa protein	5	293	2.38	0.455	0.04	0.101	0.05	-1.13661655	-3.3075728
IP00686999	IP00686999	RPLP0-like	60S acidic ribosomal protein P0	4	244	1.68	0.453	0.05	0.081	0.03	-1.12421704	-3.62534328
IP00000874	IP00000874	Q06830	PRDX1	14	664	91.04	0.447	0.24	0.069	0.04	-1.16165326	-3.85725983
IP000218474	IP000218474	P13929	Beta-enolase	2	173	0.31	0.443	0.09	0.016	0.01	-1.1746214	-5.96578428
IP000216171	IP000216171	P09104	ENO2	3	201	0.5	0.443	0.09	0.016	0.01	-1.1746214	-5.96578428
IP00011229	IP00011229	P07339	Cathepsin D	5	240	0.65	0.437	0.01	0.101	0.01	-1.19429462	-3.3075728
IP00024933	IP00024933	P30050	RPL12	60S ribosomal protein L12	6	257	0.421	0.24	0.065	0.01	-1.20756107	-3.94314167
IP000215919	IP000215919	P84085	ARF5	ADP-ribosylation factor 5	7	356	4.3	0.427	0.16	0.08	-1.22769203	-3.64385619
IP000224911	IP000224911	P30040	ERP29	Endoplasmic reticulum protein ERp29	5	252	0.72	0.426	0.27	0.05	-1.23107466	-4.32192809
IP00555614	IP00555614	Q58F07	HSP90AB3P	Putative heat shock protein HSP 90-beta-3	7	275	0.33	0.424	0.18	0.08	-1.23786383	-3.47393119
IP00397609	IP00397609	166211240	LOC388339	PREDICTED: similar to ribosomal protein	6	257	4.76	0.421	0.24	0.05	-1.24810786	-1.30400519
IP00414676	IP00414676	P08238	HSP90AB1	Heat shock protein HSP 90-beta	21	1112	1.53	0.42	0.23	0.148	-1.25153877	-2.75633092
IP000216975	IP000216975	TPM4	isoform 2 of Tropomyosin alpha-4 chain	7	254	0.97	0.417	0.38	0.02	0.08	-1.26188071	-1.88363524
IP00792139	IP00792139.1	RP527A	Ubiquitin C	4	174	2.66	0.414	0.17	0.036	0.04	-1.27229733	-4.79585928
IP00010262	IP00010262	C42423	ANP32C	Acidic leucine-rich nuclear phosphoprotein 32 fam	2	86	0.12	0.413	0.08	0.23	-1.27517861	-2.19092773
IP00456429	IP00456429	Q3MH43	UBA52	Ubiquitin A-52 residue ribosomal protein fusion pr	5	232	3.27	0.412	0.12	0.026	-1.27928376	-5.26534457
IP00798823	IP00798823.1	RPS27A	16 kDa protein	5	232	2.81	0.412	0.12	0.026	0.04	-1.27928376	-5.26534457
IP00794211	IP00794211.1	RPS27A	18 kDa protein	5	232	2.43	0.412	0.12	0.026	0.04	-1.27928376	-5.26534457
IP00796600	IP00796600.1	RPS27A	18 kDa protein	5	232	2.43	0.412	0.12	0.026	0.04	-1.27928376	-5.26534457
IP00075248	IP00075248	PE2156	Calmodulin	3	131	0.73	0.401	0.07	0.912	0.12	-1.31825986	-0.13298427
IP00015018	IP00015018	Q15181	PPA1	Inorganic pyrophosphatase	5	193	0.62	0.393	0.17	0.062	-1.34739878	-0.11587977
IP00646864	IP00646864.1	SSR4	Protein	3	146	1.01	0.385	0.19	0.154	0.05	-1.37706965	-2.69899774
IP00647421	IP00647421	ANL1M8	SSR4	Putative uncharacterized protein SSR4	3	146	0.77	0.385	0.19	0.154	-1.37706965	-2.69899774
IP00013719	IP00013719	Q20422	ENO1B	Alpha-enolase, lung specific (2-phospho-D-glyceri	4	255	0.92	0.382	0.05	0.029	-1.38855546	-5.10780329
IP00793498	IP00793498	PA2G4P4	Pseudogene candidate	3	204	0.55	0.381	0.05	0.071	0.03	-1.39213171	-3.81603717
IP00794875	IP00794875.1	PA2G4	41 kDa protein	10	581	1.33	0.379	0.1	0.126	0.15	-1.39973025	-2.98850436
IP00382470	IP00382470	HSP90AA1	heat shock protein 90kDa alpha (cytosolic), class I	16	769	0.75	0.377	0.17	0.131	0.07	-1.40736357	-2.93236128
IP00799847	IP00799847.1	TPM1	Tropomyosin	16	769	0.74	0.377	0.17	0.131	0.07	-1.40736357	-2.93236128
IP00010779	IP00010779	TPM4	Tropomyosin alpha-4 chain	9	373	1.7	0.373	0.34	0.248	0.09	-1.42275246	-0.10158797
IP00477279	IP00477279	LOC464675	PREDICTED: similar to ribosomal protein L12	3	132	0.55	0.37	0.02	0.076	0.01	-1.43440282	-3.71785677
IP00738605	IP00738605	LOC463550	PREDICTED: similar to 60S ribosomal protein L12	4	154	2.5	0.37	0.02	0.076	0.01	-1.43440282	-3.71785677
IP000310121	IP000310121	SSR1	Transferrin-associated protein subunit alpha	2	134	0.34	0.366	0.05	0.09	0.01	-1.45008445	-3.47393119
IP00793851	IP00793851.1	LOC46584	17 kDa protein	3	138	0.36	0.366	0.05	0.09	0.01	-1.45008445	-3.47393119
IP00688616	IP00688616.1	LOC46584	Pseudogene candidate	3	138	4.35	0.365	0.03	0.06	0.01	-1.45403163	-0.05898369
IP00788737	IP00788737	GAPDH	39 kDa protein	17	862	11.7	0.364	0.25	0.017	0.07	-1.45798964	-2.2243173
IP00790307	IP00790307.1	PA2G4	20 kDa protein	3	111	0.59	0.362	0.14	0.215	0.26	-1.45693984	-2.21729144
IP00019370	IP00019370	RPS27A	cDNA FLJ395793, Homo sapiens ribosomal protein	7	282	2.53	0.361	7	0.14	0.023	-1.46992826	-5.44222233
IP00333476	IP00333476	ATP5B	ATP synthase subunit beta, mitochondrial	18	111	0.38	0.359	0.09	0.142	0.26	-1.47393119	-2.6346741
IP00018853	IP00018853	TPM1	Tropomyosin isoform	5	211	0.74	0.353	0.1	0.472	0.32	-1.50225991	-1.08314124
IP000216134	IP000216134	TPM1	tropomyosin 1 (alpha), isoform CRA_m	5	211	0.73	0.353	0.1	0.472	0.32	-1.50225991	-1.08314124
IP000216135	IP000216135	TPM1	isoform 3 of Tropomyosin alpha-1 chain	5	211	0.62	0.353	0.1	0.472	0.32	-1.50225991	-1.08314124
IP00745267	IP00745267	TPM1	isoform 2 of Tropomyosin alpha-1 chain	5	211	0.57	0.353	0.1	0.472	0.32	-1.50225991	-1.08314124
IP00873694	IP00873694	ANMTE8	Uncharacterized protein ENSP00000383857	2	78	0.78	0.352	0.01	0.066	0.02	-1.50635267	-3.92139017
IP00026645	IP00026645	ANMTE8	Uncharacterized protein ENSP00000375058	4	120	0.68	0.352	0.01	0.066	0.02	-1.50635267	-3.92139017
IP00078310	IP00078310	RPL12P8	PREDICTED: similar to 60S ribosomal protein L12	5	142	0.36	0.352	0.01	0.066	0.02	-1.50635267	-3.92139017
IP00791052	IP00791052.1	LOC388720	31 kDa protein	12	318	724	0.35	0.18	0.155	0.31	-1.50635267	-2.69899774
IP00791968	IP00791968	LOC388720	PREDICTED: similar to ubiquitin	3	133	2.36	0.349	0.08	0.005	0.01	-1.51870106	-3.64385619
IP00013296	IP00013296	PE2269	LOC100130553	40S ribosomal protein S18	11	549	45.05	0.348	0.26	0.328	-1.52284079	-1.60823228
IP000219018	IP000219018	P04406	GAPDH	20	1082	29.8	0.348	0.23	0.09	0.07	-1.52284079	-1.60823228
IP00790847	IP00790847.1	ATP5B	15 kDa protein	5	303	2.47	0.347	0.1	0.334	0.41	-1.52699243	-5.08277999
IP00219217	IP00219217	LDHB	L-lactate dehydrogenase B chain	10	658	11.07	0.342	0.06	0.058	0.1	-1.53535317	-1.10729299
IP00479722	IP00479722	PSME1	Proteasome activator complex subunit 1	5	262	0.93	0.342	0.05	0.095	0.07	-1.54793177	-3.95929868
IP000218319	IP000218319	TPM3	isoform 2 of Tropomyosin alpha-3 chain	11	573	2.31	0.342	0.08	0.305	0.06	-1.54793177	-1.71311885
IP00011916	IP00011916	ITVL	Multisynthetase complex auxiliary component p38	2	82	0.2	0.339	0.1	0.116	0.03	-1.56064282	-3.9024769
IP00019329	IP00019329	PE3167	Dynein light chain 1, cytoplasmic	3	99	1.38	0.337	0.3	0.05	0.01	-1.56817795	-2.05289495
IP00798157	IP00798157.1	ATP5B	ATP synthase subunit beta, mitochondrial	10	658	2.32	0.337	0.05	0.09	0.03	-1.56817795	-2.05289495
IP000220766	IP000220766	GL01	Lactylglutathione lyase	3	128	0.35	0.331	0.05	0.087	0.03	-1.59509688	-3.52284079
IP00796844	IP00796844	HSP90AA1	Full-length cDNA clone SC0CAP007YF18 of Thyr	10	478	0.91	0.331	0.15	0.068	0.06	-1.59509688	-3.52284079
IP000183968	IP000183968	TPM3	Tropomyosin 3 isoform 1	6	268	0.96	0.329	0.07	0.03	0.02	-1.60384051	-1.64385619
IP00377005	IP00377005	ANL1M8	Uncharacterized protein ENSP00000340627	6	268	0.96	0.329	0.07	0.03	0.02	-1.60384051	-1.64385619
IP00062037	IP00062037	Q96J32	DYNNL2	Dynein light chain 2, cytoplasmic	2	70	0.34	0.323	0.06	0.225	-1.63039393	-2.15200309
IP00031523	IP00031523	Q14568	HSP90AA2	Putative heat shock protein HSP 90-alpha-2	5	212	0.56	0.323	0.07	0.224	-1.63039393	-2.15200309
IP00064537	IP00064537	G3252896	TPM1	tropomyosin 1 alpha chain isoform 3	4	181	0.62	0.321	0.08	0.332	-1.6393548	-1.59074495
IP00794332	IP00794332.2	TUBA3D	Tubulin alpha-2 chain	4	288	2.45	0.321	0.08	0.332	0.08	-1.6393548	-1.59074495
IP00844078	IP00844078	ANL1M8	Uncharacterized protein ENSP00000340627	4	208	1.27	0.318	0.12	0.287	0.05	-1.65290133	-1.64385619
IP00645055	IP00645055	Q8NAH0	TPM3	cDNA FLJ353731, clone SKMUS2001.1740, highl	5	205	0.4	0.318	0.07	0.05	-1.65290133	-1.64385619
IP00083751	IP00083751	Q9UDG2	CALRETICULIN-CALCIUM binding protein	4	225	1.17	0.317	0.11	0.049	0.03	-1.65744525	-3.5107444
IP00791971	IP00791971.1	NME1	9 kDa protein	12	119	1.34	0.316	0.05	0.039	0.01	-1.66200354	-1.68038207
IP00005199	IP00005199	LF2	Interleukin enhancer-binding factor 2	4	172	0.35	0.315	0.14	0.318	0.23	-1.66200354	-1.68038207
IP00641665	IP00641665	LF2	Interleukin enhancer binding factor 2, 45kDa	4	234	1.09	0.315	0.14	0.318	0.23	-1.66657627	-1.65200133
IP0069532	IP0069532	CD42	isoform 2 of Cell division control protein 42 homol	2	112	0.55	0.314	0.03	0.121	0.09	-1.67116354	-3.04692105
IP00070778	IP00070778	119613212	LOC463751	hCG39634, isoform CRA_a	2	112	0.55	0.314	0.03	0.121	-1.67116354	-3.04692105
IP00017672	IP00017672	Q8NHV5	NP									

IP00212093	P08708	TPS17	40S ribosomal protein S17	5	276	2.99	0.186	0.05	0.109	0.08	-2.42662547	-3.19759996
IP000783641	IP000783641.4	TXNRD1	Isomorph 3 of Thoredoxin reductase 1, cytoplasmic	5	274	0.2	0.184	0.14	0.105	0.1	-2.44222233	-3.25153877
IP00552072	ABMW48	CTT7	Putative uncharacterized protein CTT7	5	203	0.29	0.183	0.04	0.048	0.05	-2.45084885	-3.22139017
IP00003881	P52597	HNRNPF	Heterogeneous nuclear ribonucleoprotein F	4	248	0.52	0.177	0.11	0.036	0.02	-2.49817873	-4.79588826
IP000030296	Q9NZ66	E1FAA2	BM-010	7	447	1.07	0.177	0.05	0.026	0.02	-2.49817873	-5.26534457
IP000000811	P28072	PSMB6	Proteasome subunit beta type-6	3	145	0.28	0.176	0.01	0.056	0.01	-2.50635267	-4.15842936
IP00513829	Q5X90	GDJ2	GDP dissociation inhibitor 2	3	116	0.74	0.171	0.05	0.154	0.03	-2.54793177	-2.69899774
IP00203867	P30046	DOT	O ⁶ -dephospho decarboxylase	3	147	0.171	0.171	0.06	0.234	0.29	-2.54793177	-2.06573527
IP00395865	Q16576	RBBP7	Histone-binding protein RBBP7	2	173	0.14	0.171	0.14	0.077	0.01	-2.54793177	-3.69899774
IP00552530.2	IP00552530.2	RBBP7	Retinoblastoma binding protein 7	2	173	0.15	0.171	0.14	0.077	0.01	-2.54793177	-3.69899774
IP00646512	Q5J3P0	RBBP7	cDNA FLJ3592.5s, clone KIDNE200887, highly	2	173	0.13	0.171	0.14	0.077	0.01	-2.54793177	-3.69899774
IP00025491	E1FAA1	E1FAA1	Eukaryotic initiation factor 4A-II	17	309	0.69	0.169	0.04	0.048	0.05	-2.55480485	-4.38082178
IP00328328	Q14240	E1FAA2	Eukaryotic initiation factor 4A-II	10	148	1.62	0.168	0.05	0.024	0.01	-2.57346686	-5.38082178
IP00791157	IP00791157.1		16 kDa protein	3	174	1.63	0.162	0.05	0.148	0.05	-2.62593428	-2.75633092
IP00218493	P00492	HPRT1	Hypoxanthine-guanine phosphoribosyltransferase	5	286	0.67	0.162	0.07	0.062	0.04	-2.62593428	-4.01158797
IP00555602	B4DKP9	E1FAA1	cDNA FLJ58012, moderately similar to Eukaryotic	13	798	2.86	0.159	0.03	0.047	0.05	-2.65290133	-4.41119543
IP00186290	P12093	EEF2	Elongation factor 2	12	625	0.45	0.159	0.14	0.07	0.05	-2.66200354	-3.83650127
IP00382885	Q8WTY3	RPL27	60S ribosomal protein L27	4	174	2.08	0.155	0.15	0.046	0	-2.68965988	-4.4222233
IP00219155	P61353	RPL27	60S ribosomal protein L27	6	242	2.91	0.155	0.15	0.046	0	-2.68965988	-4.4222233
IP00788730	IP00788730.1	E1FAA2	25 kDa protein	5	269	1.1	0.155	0.03	0.021	0.02	-2.68965988	-5.57346686
IP00029733	Q04828	AKR1C1	aldo-keto reductase family 1 member C1	3	153	1.52	0.155	0.13	0.033	0.06	-2.68965988	-4.01158797
IP00607708	IP00607708	LDHA	LDHA	21	1028	28.87	0.147	0.07	0.026	0.03	-2.76611194	-3.26534457
IP00375704	31874085	PSMB1	hypothetical protein	5	343	0.73	0.142	0.12	0.075	0.02	-2.81603717	-3.73696559
IP00444262	Q6ZS99	NCL	cDNA FLJ45706.5s, clone FEBRA2028457, highly	11	616	0.79	0.141	0.13	0.088	0.09	-2.82623293	-3.50635267
IP00604620	P13338	NCL	Nucleolin	12	638	0.65	0.141	0.13	0.088	0.09	-2.82623293	-3.50635267
IP00627674.1	IP00627674.1	NCL	Nucleolin, isoform CRA_c	12	638	0.68	0.141	0.13	0.088	0.09	-2.82623293	-3.50635267
IP00217966	P00338	LDHA	L-lactate dehydrogenase A chain	24	1190	57.53	0.141	0.06	0.024	0.03	-2.82623293	-5.38082178
IP00873466	ABMSU4	HPRT1	Putative uncharacterized protein HPRT1	4	194	0.47	0.14	0.07	0.049	0.04	-2.83650127	-4.35107444
IP00789078	ABMS13	SOD1	Superoxide dismutase [Cu-Zn]	2	90	0.55	0.137	0.01	0.224	0.2	-2.8677522	-2.15842936
IP00218733	SOD1	SOD1	Superoxide dismutase [Cu-Zn]	3	159	0.79	0.137	0.224	0.07	0.2	-2.8677522	-2.15842936
IP00872233	ABMW59		Uncharacterized protein ENSP00000375452	3	146	2.85	0.135	0.13	0.079	0.26	-2.88989689	-1.39973029
IP00031461	B4DLV7	GDJ2	cDNA FLJ60299, highly similar to Rab GDP disso	5	285	0.46	0.134	0.07	0.113	0.07	-2.89969509	-3.14560532
IP00646762	ABNFX8	NUDT5	Putative uncharacterized protein NUDT5	5	205	0.83	0.129	0.07	0.108	0.07	-2.95455703	-3.21089678
IP00419373	P51991	HNRNPA3	Heterogeneous nuclear ribonucleoprotein A3	5	294	0.49	0.121	0.1	0.1	0.06	-3.04682105	-3.32192809
IP00872250	IP00872250.1	HNRNPA3	7 kDa protein	2	191	0.12	0.121	0.11	0.1	0.06	-3.04682105	-3.32192809
IP00002520	P34897	SHMT2	Serine hydroxymethyltransferase, mitochondrial	2	168	0.12	0.119	0.02	0.15	0.03	-3.07096652	-2.73696559
IP00012074	Q43390	HNRNPR	Heterogeneous nuclear ribonucleoprotein R	3	139	0.15	0.117	0.04	0.048	0.04	-3.09541957	-4.38082178
IP00000494	P48777	RPL5	60S ribosomal protein L5	4	182	0.32	0.114	0.1	0.062	0.05	-3.13289427	-4.01158797
IP00259571	IP00259571.1	RPL5	Isomorph 2 of Protein disulfide-isomerase A6	6	145	1.13	0.114	0.06	0.042	0.2	-3.13289427	-3.87823144
IP00021840	P62753	RPS56	Isomorph 1 of 60S ribosomal protein S6	7	315	0.55	0.112	0.09	0.131	0.06	-3.15842936	-2.9326128
IP00879622	IP00879622.1		18 kDa protein	2	94	2.96	0.111	0.01	0.215	0.07	-3.17136842	-2.21759144
IP00478277	169165866	LOC100128936	PREDICTED: similar to ribonucleoprotein L10a	4	217	1.78	0.108	0.05	0.04	0.03	-3.21089678	-4.05889369
IP00008433	P45872	RPS5	40S ribosomal protein S5	2	92	0.31	0.104	0.01	0.113	0.07	-3.26534457	-3.14560532
IP00101405	P14321	FDPS	Farnesyl pyrophosphate synthetase	3	144	0.43	0.104	0.04	0.032	0.02	-3.26534457	-4.86573527
IP00025019	P20618	PSMB1	Proteasome subunit beta type-1	3	135	0.43	0.104	0.03	0.18	0.2	-3.26534457	-2.74933119
IP00011913	Q13151	HNRNPA0	Heterogeneous nuclear ribonucleoprotein A0	3	207	0.36	0.103	0.04	0.054	0.03	-3.27928376	-4.21089678
IP00689502.1	IP00689502.1	TMSL3	Similar to Elongation factor 1-alpha 1	6	261	5.19	0.102	0.02	0.229	0.05	-3.29335894	-2.3075728
IP00026271	P62263	RPL1	60S ribosomal protein S1A	4	261	1.13	0.101	0.4	0.01	0.69	-3.3075728	-3.86725983
IP00027569	Q06812	HNRNPLC1	Heterogeneous nuclear ribonucleoprotein C-like 1	3	291	0.81	0.101	0.04	0.048	0.01	-3.3075728	-4.38082178
IP00735540	B2RXH8	LOC440563	LOC440563 protein	5	291	0.81	0.101	0.02	0.048	0.01	-3.3075728	-4.38082178
IP00871838	ABMW44		Uncharacterized protein ENSP00000383818	5	291	0.74	0.101	0.02	0.048	0.01	-3.3075728	-4.38082178
IP00003918	P35578	RPL4	60S ribosomal protein L4	14	571	1.09	0.1	0.06	0.113	0.07	-3.32192809	-3.14560532
IP00117964	P002319	SNRPD3	Small nuclear ribonucleoprotein Sm D3	2	193	0.93	0.099	0.102	0.127	0	-3.33642766	-2.9770996
IP00879750	IP00879750.1	SNRPD3	19 kDa protein	2	89	0.64	0.099	0.02	0.127	0	-3.33642766	-2.9770996
IP00003217	Q99436	PSMB7	Proteasome subunit beta type-7	3	150	0.52	0.099	0.01	0.052	0.01	-3.33642766	-2.6534457
IP00640006	Q5X88	GDJ2	GDP dissociation inhibitor 2 (cDNA FLJ60305, hig	4	232	0.32	0.099	0.05	0.105	0.1	-3.33642766	-3.25153877
IP00440662	Q6Q48B		Antigen MLI4-42	3	142	0.73	0.093	0.03	0.087	0.07	-3.35107444	-3.60823228
IP00029623	P62909	PSMA6	Proteasome subunit alpha type-6	4	242	0.58	0.098	0.06	0.303	0.4	-3.35107444	-1.7226103
IP00755956	P07910-4	HNRNPA3	Uncharacterized protein ENSP00000381868	9	573	2.48	0.098	0.03	0.041	0.01	-3.38082178	-4.60823228
IP00873616	ABMW42		Uncharacterized protein ENSP00000381868	2	84	0.53	0.093	0.02	0.147	0.03	-3.42662547	-2.76611194
IP00216592	P07910-2	HNRNPA3	Uncharacterized protein ENSP00000381868	10	612	2.24	0.092	0.03	0.041	0.01	-3.44222233	-4.60823228
IP00350706	Q92503	NONO	Activator of 90 kDa heat shock protein ATPase h	3	104	0.18	0.091	0.02	0.137	0	-3.45798964	-3.60823228
IP00304596	Q15233	NONO	Non-POU domain-containing octamer-binding pr	5	200	0.27	0.091	0.04	0.086	0.01	-3.45798964	-3.53951953
IP00479191	IP00479191.2	HNRNPH1	51 kDa protein	3	210	0.37	0.09	0.04	0.032	0.01	-3.47393119	-4.96578428
IP00216730	Q8U1E6	HIST2H2AB	Histone H2A type 2-B	6	346	10.02	0.09	0.09	0.087	0.07	-3.47393119	-3.52284970
IP00419585	P62937	PP1A	Peptidyl-prolyl cis-trans isomerase A	11	520	12.2	0.089	0.02	0.049	0.06	-3.49005085	-4.35107444
IP00016862	P00380	CSF1	Glucuronidase, mitochondrial	2	115	0.12	0.088	0.07	0.048	0.01	-3.50635267	-2.85725983
IP00219156	P62888	RPL30	60S ribosomal protein L30	5	218	3.16	0.088	0.07	0.138	0.01	-3.50635267	-2.85725983
IP00872940	ABMYX5	RPL30	Putative uncharacterized protein RPL30	5	218	3.11	0.088	0.07	0.138	0.01	-3.50635267	-2.85725983
IP00180730	CD138		Similar to Elongation factor 1-alpha 1	6	266	1.95	0.088	0.03	0.187	0.04	-3.50635267	-2.41889892
IP00010157	P31157	MAT2A	adenosylmethionine synthetase isomorph type-2	8	393	1.36	0.085	0.06	0.134	0.01	-3.55639335	-4.21089678
IP00514814.2	IP00514814.2	AKR1C1	Aldo-keto reductase family 1, member C1 (Dihydr	8	295	0.56	0.085	0.06	0.101	0.08	-3.55639335	-3.3075728
IP00642560	ABNHU4	AKR1C1	Putative uncharacterized protein AKR1C1	5	295	1.57	0.085	0.06	0.101	0.08	-3.55639335	-3.3075728
IP00291483	P42330	AKR1C3	Aldo-keto reductase family 1 member C3	8	246	1.36	0.085	0.06	0.101	0.08	-3.55639335	-3.3075728
IP00736657	113420853	LOC648517	PREDICTED: similar to Aldo-keto reductase fami	8	246	1.46	0.085	0.06	0.101	0.08	-3.55639335	-3.3075728
IP00219525	P52209	PCD	6-phosphogluconate dehydrogenase, decarboxyla	5	303	0.62	0.083	0.06	0.096	0.02	-3.59017444	-2.68989689
IP00688835.2	IP00688835.2		Similar to Heterogeneous nuclear ribonucleopro	5	309	0.9	0.082	0.03	0.045	0.01	-3.60823228	-4.74933119
IP00453476	ABNJ80	hCG_2015269	Uncharacterized protein ENSP00000348237	9	426	1.67	0.082	0.05	0.04	0.04	-3.60823228	-4.6435691
IP00872802	ABMU41		Uncharacterized protein ENSP00000375462	3	146	0.78	0.081	0.06	0.049	0.01	-3.62593428	-4.35107444
IP00433834	ABN299	LOC730343	Putative uncharacterized protein RPL26P6	3	263	2.29	0.081	0.06	0.049	0.01	-3.62593428	-4.35107444
IP00412579	P62906	RPL10A	60S ribosomal protein L10a	8	343	1.13	0.08	0.06	0.053	0.03	-3.64385619	-4.23786383
IP00827508	IP00827508.2	RPL10A	25 kDa protein	8	343	1.12	0.08	0.06	0.053	0.03	-3.64385619	-4.23786383
IP00215780	P39019	RPS19	40S ribosomal protein S19	8	402	3.61	0.08	0.03	0.204	0.12	-3.64385619	-2.29335894
IP00296378	HNRNPA2B1	HNRNPA2B1	Heterogeneous nuclear ribonucleoproteins A2B1	13	681	2.04	0.078	0.03	0.042	0.02	-3.66200354	-4.4222233
IP00023503	119609761	CDK5	cyclin-dependent kinase 5, isoform CRA_a	2	144	0.18	0.078	0.02	0.153	0.07	-3.68038207	-3.25153877
IP00031681	P24941	CDK2	Cell division protein kinase 2	3	188	0.						

IP00411329	A6NCA2	Uncharacterized protein ENSP0000022956	8	433	1.38	0.041	0.02	0.051	0.02	-4.60823228	-4.29335894
IP00513971	P42677	40S ribosomal protein S27	2	117	0.87	0.04	0.01	0.104	0.04	-4.64385619	-3.26534457
IP00738640	169184563	PREDICTED: similar to v-fos transformation effect	5	250	0.7	0.04	0.04	0.074	0.09	-4.64385619	-3.75633092
IP00647546	IP00647546.1	16 kDa protein	5	208	1.15	0.039	0.01	0.061	0.05	-4.68038207	-4.03504695
IP00478327	119580810	SLC5A1	6	237	0.74	0.039	0.01	0.061	0.05	-4.68038207	-4.03504695
IP00789127	IP00789127.1	LOC645001	5	295	0.52	0.038	0.02	0.053	0.02	-4.71785677	-4.23786383
IP00874005	ABMW77	Uncharacterized protein ENSP00000381249	4	165	0.32	0.037	0.02	0.046	0.02	-4.75633092	-4.44222233
IP00031804	Q9Y277	VDAC3	5	233	0.67	0.037	0.02	0.065	0.02	-4.75633092	-3.94341647
IP0029479	Q9Y277.2	VDAC3	5	233	0.67	0.037	0.02	0.065	0.02	-4.75633092	-3.94341647
IP00871813	IP00871813.1	VDAC3	5	233	0.67	0.037	0.02	0.065	0.02	-4.75633092	-3.94341647
IP00871473	ABMW77	Uncharacterized protein ENSP00000381626	3	162	0.39	0.036	0.02	0.049	0.02	-4.79585928	-4.35107444
IP00397611	169212066	PREDICTED: similar to RPL13 protein	4	153	0.39	0.036	0.02	0.019	0.01	-4.79585928	-5.71785677
IP00465361	P26373	RPL13	8	357	1.82	0.036	0.02	0.019	0.01	-4.79585928	-5.71785677
IP00144171	119616214	HCG_2015956	10	427	0.86	0.036	0.02	0.02	0.01	-4.79585928	-5.64385619
IP00472171	119607406	ribosomal protein L7, isoform CRA_a	12	527	0.99	0.036	0.02	0.02	0.01	-4.79585928	-5.64385619
IP00871827	ABMVV7	Putative uncharacterized protein RPL7	12	527	1.19	0.036	0.02	0.02	0.01	-4.79585928	-5.64385619
IP00872387	ABMY04	Uncharacterized protein ENSP00000381447	12	527	1.19	0.036	0.02	0.02	0.01	-4.79585928	-5.64385619
IP00061178	Q96E39	CCBL2	2	160	0.16	0.035	0.02	0.049	0	-4.83650127	-4.35107444
IP00643486	Q5T9T9	CCBL2	2	160	0.44	0.035	0.02	0.049	0	-4.83650127	-4.35107444
IP00304692	P38159	RBMX	3	212	0.25	0.035	0.01	0.046	0.01	-4.83650127	-4.44222233
IP00879848	119598703	HCG2022018	4	153	1.08	0.034	0.02	0.067	0.02	-4.87832144	-3.89969509
IP00847163	IP00847163.1	THOC3	3	189	1.63	0.034	0.02	0.03	0.03	-4.87832144	-5.05889369
IP00299573	P62424	RPL7A	11	521	1.58	0.033	0.02	0.278	0.39	-4.92139017	-1.84684321
IP00397676	169213130	LOC388474	7	396	1.09	0.032	0.03	0.056	0.07	-4.96578428	-4.15842936
IP00736803	119570872	HCG1988775	3	155	0.47	0.031	0.03	0.043	0.03	-5.01158797	-4.53951953
IP00645201	Q5JUR5	RPS58	7	403	2.61	0.031	0.02	1.477	3.77	-5.01158797	0.56269826
IP00790291	IP00790291.1	RPL7	5	215	1.76	0.03	0.02	0.017	0.01	-5.05889369	-5.87832144
IP00221091	P62244	RPS15A	5	216	0.85	0.03	0.02	0.037	0.01	-5.05889369	-4.75633092
IP00738970	A6NIE4	Uncharacterized protein ENSP00000304033	6	258	0.39	0.03	0.02	0.017	0.01	-5.05889369	-5.87832144
IP00879238	B5MCT8	Putative uncharacterized protein RPS9 (Ribosomu	7	317	2.04	0.03	0.02	0.047	0.04	-5.05889369	-4.41119543
IP00816796	Q8N8Y7	cDNA FLJ136696 fs, clone KIDNE2001931, highly	2	128	0.17	0.029	0.01	0.045	0.01	-5.10780329	-4.47393119
IP00556601	Q59EP7	Solute carrier family 25 member 4 variant	4	232	0.54	0.027	0.02	0.058	0.02	-5.21089678	-4.10780329
IP00398673	113429532	LOC388885	4	253	0.87	0.026	0.02	0.117	0.05	-5.26534457	-3.09541957
IP00221088	P46781	RPS9	10	409	1.64	0.026	0.02	0.041	0.04	-5.26534457	-4.60823228
IP00008293	169161603	LOC149224	3	98	0.54	0.025	0.02	0.051	0	-5.32192809	-4.29335894
IP00008438	P46783	RPS10	6	323	1.27	0.025	0.01	0.109	0.05	-5.32192809	-3.19759996
IP00011253	P23396	RPS3	16	768	4.87	0.025	0.01	0.04	0.02	-5.32192809	-4.64385619
IP00450975	Q6IPX4	RPS16	3	159	0.72	0.024	0.01	0.045	0.01	-5.38082178	-4.47393119
IP00413641	P15121	AKR1B1	6	262	0.7	0.024	0.01	0.146	0.18	-5.38082178	-2.77595973
IP00478986	IP00478986.2	CGB8	3	105	0.23	0.023	0.01	0.054	0.05	-5.44222233	-4.21089678
IP00075558	169166935	LOC152663	3	124	0.31	0.023	0.02	0.364	0.51	-5.44222233	-1.45798964
IP00012772	P62917	RPL8	8	359	0.96	0.021	0.01	0.016	0.01	-5.57346686	-5.96578428
IP00641950	37724561	GNB2L1	7	379	0.8	0.02	0.01	0.02	0.01	-5.64385619	-5.64385619
IP00847774	B40M74	RPL18A	3	125	0.79	0.018	0.01	0.022	0.02	-5.79585928	-5.50635267
IP00792352	119618921	RAN	8	454	3.69	0.018	0.01	0.121	0.02	-5.79585928	-3.04692105
IP00796462	IP00796462.1	RAN	8	454	3.61	0.018	0.01	0.121	0.02	-5.79585928	-3.04692105
IP00397017	88948852	LOC644790	3	115	0.23	0.017	0.01	0.031	0.01	-5.87832144	-5.01158797
IP00784408	38570357	GNB2L1	5	278	0.7	0.017	0.01	0.025	0	-5.87832144	-5.32192809
IP00217465	P18403	HIST1H1C	11	553	4	0.015	0.01	0.063	0.11	-6.05889369	-3.98850436
IP00010420	Q9H0C2	SLC25A31	3	180	0.31	0.014	0.01	0.043	0	-6.15842936	-4.53951953
IP00217466	P16402	HIST1H1D	7	422	2.52	0.013	0.01	0.075	0.13	-6.26534457	-3.73696559
IP00217467	P10412	HIST1H1E	10	523	3.81	0.013	0.01	0.075	0.13	-6.26534457	-3.73696559
IP00453473	P62805	HIST2H4B	10	585	765.54	0.013	0.01	0.033	0.01	-6.26534457	-4.92139017
IP00249267	IP00249267.2	13 kDa protein	3	197	2.9	0.01	0.01	0.076	0	-6.64385619	-3.71785677