

**Carcinogenic liver fluke secretes extracellular vesicles that promote
cholangiocytes to adopt a tumorigenic phenotype**

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ABSTRACT (200 words)

Background

Throughout Asia there is an unprecedented link between cholangiocarcinoma and infection with the liver fluke *Opisthorchis viverrini*. Multiple processes including chronic inflammation and secretion of parasite proteins into the biliary epithelium drive infection towards cancer. Until now, the mechanism and effects of parasite protein entry into cholangiocytes was unknown.

Methods

Various microscopy techniques were used to identify *O. viverrini* extracellular vesicles (EVs) and their internalization by human cholangiocytes. Using mass spectrometry we characterised the EV proteome and associated changes in cholangiocytes after EV uptake, and detected EV proteins in bile of infected hamsters and humans. Cholangiocyte proliferation and IL-6 secretion was measured to assess the impact of EV internalization.

Results

EVs were identified in fluke culture medium and bile of infected hosts. EVs internalized by cholangiocytes drove cell proliferation and IL-6 secretion and induced changes in protein expression associated with endocytosis, wound repair and cancer. Antibodies to an *O. viverrini* tetraspanin blocked EV uptake and IL-6 secretion by cholangiocytes.

Conclusions

This is the first time that EVs from a multicellular pathogen have been identified in host tissues. Our findings imply a role for *O. viverrini* EVs in pathogenesis and highlight an approach to vaccine development for this infectious cancer.

Keywords: extracellular vesicles; *Opisthorchis viverrini*; cholangiocarcinoma; liver fluke; cancer

FOOTNOTES

Conflict of interest

All authors: No reported conflicts.

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Introduction (3487 words)

The liver fluke, *Opisthorchis viverrini*, is classified as a group 1 carcinogen by the International Agency for Research on Cancer, and is a major public health problem in many parts of Southeast Asia. In Northeast Thailand alone, more than 8 million people harbour the parasite [1] due to traditional dietary preferences for eating uncooked fish that harbour the infective stage of the fluke [2]. Upon ingestion of infected fish, the metacercariae excyst in the duodenum and migrate to the bile ducts of the definitive host where they feed on the biliary epithelia. Infection is associated with a spectrum of hepatobiliary abnormalities including bile duct cancer or cholangiocarcinoma (CCA) [2, 3]. The incidence of CCA in Northeast Thailand is substantially higher than elsewhere in the world, and associates strongly with the prevalence of *O. viverrini* infection [4].

The mechanisms involved in liver fluke-driven tumorigenesis are multi-factorial, with apparent roles for (i) mechanical damage caused by parasites grazing on the biliary epithelium; (ii) chronic immunopathologic processes that are dominated by pro-inflammatory cytokines such as IL-6 [1]; (iii) the active release of parasite-derived excretory/secretory (ES) products into the bile ducts that drive unchecked cell proliferation [2, 5-7]. Intriguingly, some of these ES products have been identified inside cholangiocytes of experimentally infected hamsters [6, 8, 9], akin to the intracellular presence of the CagA protein from another carcinogenic pathogen, *Helicobacter pylori* [10]. Until now, the mechanisms by which liver fluke ES proteins are internalized by cholangiocytes, and the ramifications of this process for the host cell, have remained unknown.

Recent reports have highlighted the presence of secreted extracellular vesicles (EVs) from parasites of both unicellular [11, 12] and multicellular (helminths) [13-15] origin, and provide a plausible explanation for the abundance in helminth ES products of apparently “intracellular” proteins [16]. EVs are small membrane-enclosed structures that are released by many different cell types [17, 18]. EVs from unicellular parasites have been shown to

influence host physiological processes, including immunomodulation, and adherence and communication between host and parasite [12, 19, 20]. A recent report described the uptake of parasitic platyhelminth EVs by host cell lines *in vitro* using low resolution fluorescence microscopy [13], but the molecular impact of EV uptake on the recipient cell, and detection of helminth EVs *in vivo* has until now, not been reported.

Here we show that *O. viverrini* secretes EVs that induce a pro-inflammatory/tumorigenic phenotype in human cholangiocytes. We also show that cellular uptake of *O. viverrini* EVs can be blocked by antibodies to an EV recombinant tetraspanin, highlighting the potential utility of EV proteins as vaccines to prevent fluke infection and associated cholangiocarcinogenesis.

Materials and Methods

Ethics statement

Hamsters were maintained at Khon Kaen University (KKU), Thailand. The study was approved by the KKU Animal Ethics Committee (AEKKU 55/2554). Human bile was collected under an approved protocol (HE 521209) from the KKU Institutional Review Board.

Parasite material, isolation of ES products and EV purification

Parasites were obtained from experimentally infected hamsters and ES products were isolated as described [8]. EVs were purified from ES products using differential ultracentrifugation following a modified protocol [21]. Briefly, parasite culture media was centrifuged at 2,000 g for 30 min at 4°C to remove larger debris; supernatant was further centrifuged at 15,000 g for 30 min at 4°C. ES supernatants were filtered using a 0.2 µm membrane (Schleicher and Schuell Bioscience) then ultracentrifuged at 110,000 g for 2 h at 4°C. The pellet was washed in PBS containing protease inhibitor cocktail (Roche) and

ultracentrifuged for 1 h. Crude pellet was resuspended in 200 µl PBS/ protease inhibitor cocktail and stored at 4°C.

Preparation of EVs for Transmission Electron Microscopy

Five µl of purified EVs was applied to a carbon-formvar coated grid and air dried. Grids were negatively stained in 2% uranyl acetate for 15 secs. Stained grids were viewed in a JEM1011 transmission electron microscope (JEOL) equipped with a Morada side-mounted digital camera (Olympus).

Fluorescence labelling of EVs membranes

EVs were labelled with Alexa Fluor 488 5-SDP Ester (AF488) (Life Technologies) following the manufacturer's protocol. EV pellets were resuspended in 400 µl of PBS and mixed with 50 µg of AF488 for 1 h at 4°C. The samples were collected by ultracentrifugation at 110,000 g for 2 h to remove excess dye, washed twice and resuspended in 400 µl of PBS.

Cell co-cultures and fluorescence microscopy

To investigate internalization of EVs by mammalian cells, normal immortalized human cholangiocytes (H69) were grown to 80% confluence as described [22]. Cells were starved of FCS overnight, incubated with AF488-EVs for 6 h, and analysed by fluorescence microscopy. Cell nuclei were stained with Hoechst dye and visualized using an AxioImager M2 ApoTome fluorescence microscope (Zeiss). Two technical and 2 biological replicates were performed and at least 5 fields were analysed in each replicate. Fluorescence was quantified using ImageJ.

Ultra-resolution microscopy

To convincingly demonstrate internalization of *O. viverrini* EVs by cholangiocytes, we used 3D-Structured Illumination microscopy (3D-SIM). H69 cholangiocytes were grown to 50% confluence and co-cultured with AF488-EVs or an equivalent amount (based on fluorescence) of ES products (10 µg/ml) for up to 6 h. Treated cells were fixed in 4% paraformaldehyde, permeabilised in 0.1% Triton X-100 in PBS and stained with Alexa Fluor 568 Phalloidin (Life Technologies). Specimens were mounted in 5% N-propyl-Gallate (Sigma) and 3D-SIM was performed on isolated single cells using a DeltaVision OMX 3D-SIM system (Applied Precision Inc, GE Healthcare). Solid state lasers (405, 488, 593 nm) provided wide-field illumination and multi-channel images were captured simultaneously using three 512× 512 pixel size PCO edge scientific CMOS cameras. All data capture used a 60× 1.4 NA oil objective and standard excitation and emission filter sets (in nm, 405 EX / 419-465 EM, 488 EX / 500-550 EM and 592.5 EX / 608-648 EM). 3D-SIM images were sectioned using a 125 nm Z-step size. Raw 3-phase images were reconstructed as previously described [23]. Reconstructed images were rendered in 3D using IMARIS version 7.X (Bitplane Scientific).

Proteomic analysis of EVs

Sample preparation for proteomic analysis was performed as described [13]. Peptides were resuspended in 5% formic acid and analysed by LC-MS/MS. Ten microliters was injected onto a C18 trap column (Thermo Scientific Acclaim) and flushed into an analytical column (Agilent) and eluted via a mobile phase gradient: 5–80% solvent B over 120 min. The eluted material was directly applied to the nanospray source of a QSTAR Elite instrument (Applied Biosystems), and data analysis was conducted with Analyst 2.0 (Applied Biosystems).

iTRAQ analysis

H69 cells were co-cultured with the quantity of EVs that corresponded to 1.2 µg/ml of ES protein in PBS for 30 min, 3 h and 16 h. Cells were washed using PBS containing protease inhibitor cocktail and lysed in 5 M urea, 2 M thiourea, 0.1% SDS, 1% triton X-100 and 40 mM Tris (pH 7.4). Each sample was ground with a TissueLyser II (QIAGEN) and centrifuged at 12,000 g for 20 min. The protein supernatant was precipitated with cold methanol, centrifuged at 8,000 g and air dried pellets re-dissolved in 0.5 M triethylammonium bicarbonate (TEAB)/0.05% SDS, then centrifuged at 12,000 g. Samples were resuspended in 0.5 M TEAB prior to reduction, alkylation, digestion and iTRAQ labelling (AB Sciex) then analysed on a 5600 TripleTOF mass spectrometer as described [24].

Bioinformatic analysis of protein expression data

For proteomic characterization of *O. viverrini* EV proteins, the *O. viverrini* genome database [25] was interrogated using MASCOT (Matrix-Science) allowing two missed cleavages and mass tolerance of 1.2 Da in MS mode and 0.8 Da on MS/MS product ions. Probability ($P < 0.05$) of FDR was calculated for every search using the MASCOT decoy database facility. For iTRAQ, two biological and two technical replicates were conducted. Database searches were performed against NCBI nr using MASCOT allowing two missed cleavages and a mass tolerance of 0.1 Da on MS and MS/MS modes, and results were validated using Scaffold v.4.2.1 (Proteome Software). Differentially expressed (dysregulated) proteins were determined using a Kruskal-Wallis test and results expressed in log₂ ratios. Only proteins whose expression level underwent a significant ($P < 0.05$) log₂ fold-change of >0.6 or <-0.6 for upregulated and downregulated proteins respectively were further considered. KEGG and Reactome functional enrichment analyses for dysregulated proteins were performed using KEGGMapper and DAVID [26]. Protein-protein interaction analysis was performed using String [27].

Detection of EV proteins in bile of *O. viverrini*-infected humans and hamsters

Bile was collected from *O. viverrini*-infected humans by aspiration of resected gallbladders, and experimentally infected and uninfected hamsters (controls) by puncture of the gallbladder from euthanized animals, and EVs isolated as described above. Selected Reaction monitoring (SRM) was performed on a 5600 TripleTOF to identify *O. viverrini* EV proteins in bile. All analyses were performed using SRM-initiated IDA experiments in which a SRM survey scan triggered the acquisition of MS/MS spectra. Skyline 3.1 was used to generate SRM transitions and for data analysis.

Cell proliferation

H69 cholangiocytes were cultured as described above until 80% confluent. Cells were starved of FCS overnight and cultured with the amount of EVs that corresponded to 1.2 µg/ml of ES protein over 72 h at 37°C. Control cells were incubated with 1.2 µg/ml of ES products (not ultra-centrifuged) or 1.2 µg/ml BSA for the negative control group. Cell proliferation was assessed by measuring cell index (CI) values in real time using an xCELLigence SP system and E plates (Acea). Three biological replicates were analysed and a 2-way ANOVA was performed.

Blocking internalization of EVs with anti-Ov-TSP-1 recombinant Ov-TSP-1

AF488-EVs were incubated with mouse anti-Ov-TSP-1 serum [28] or normal mouse serum (NMS) at different dilutions (1:2.5, 1:5, 1:20) at RT for 1 h. EV:antibody complexes were added to H69 cells and co-cultured for 6 h. Images were obtained using an ECLIPSE Ni-u confocal microscope (Nikon) at 60× magnification. Thirty fields from 2 biological replicates were analysed and a 1-way ANOVA was performed. Cell fluorescence was quantified using ImageJ.

IL-6 detection

H69 cholangiocytes were cultured as above to monitor cell proliferation over 24 h. Culture media were collected and centrifuged at 2000 *g* for 10 min to remove cell debris. IL-6 levels were quantified using an IL6-ELISA kit (R&D System) following the manufacturer's instructions. Three biological replicates were analysed and statistical analysis was performed using a 2-way ANOVA.

Results

Excretory/secretory products from O. viverrini contain EV-like vesicles

After filtration and ultracentrifugation of ES products from adult *O. viverrini* we identified microvesicular structures using negative staining in transmission electron microscopy (Figure 1). These spherical vesicles had an external diameter of 40-180 nm, resembling EVs recently reported from other trematodes [13, 14].

Proteomic analysis of O. viverrini EVs reveals conserved and novel proteins

O. viverrini EVs were digested with trypsin and submitted to LC-MS/MS. We identified 108 different proteins (Supplementary Table 1), 42 of which were homologous to mammalian EV proteins in Exocarta [29], including proteins that are diagnostic of mammalian exosomes such as tetraspanins, HSP-70, cytoskeletal, regulatory and trafficking proteins. Gene Ontology (GO) analysis of the proteins (Supplementary Figure 1) returned 212 biological process terms. Pfam analysis identified proteins with an EF hand domain as the most frequently represented (Supplementary Figure 1).

O. viverrini exosome proteins are identified in bile of infected hosts

SRM analysis confirmed the presence of specific EV proteins in the bile of *O. viverrini* infected humans and hamsters. Seven of the top 15 proteins identified in the EV proteomic

analysis (based on number of peptides identified) were successfully quantified (Supplementary Figure 2).

O. viverrini EVs are internalized by human cholangiocytes

We monitored the uptake of AF488-EVs by human cholangiocytes *in vitro*. Within 60 min punctate fluorescent structures were detected, the number of which increased markedly over 6 h (Figure 2A). Cell fluorescence of all fields from the two biological replicates revealed fluorescence coverage of $62.44 \pm 9.52\%$ and $90.57 \pm 4.58\%$ at 0.5 h and 6 h respectively. 3D-SIM analysis confirmed the intracellular presence of AF488-EVs within the cytoskeletal network of well-separated individual cells as evidenced by their position between the basal and apical membranes outlined with phalloidin (Figure 2B, C, Supplementary Movie). We attempted to co-localize EVs to defined organelles using specific fluorescent markers but did not observe co-localization (not shown), suggestive of a cytoplasmic location.

O. viverrini EVs promote cell proliferation and stimulate wound healing and tumorigenic pathways in cholangiocytes

H69 cholangiocytes were incubated for 72 h with (i) crude ES products, (ii) EVs purified from crude ES products, or (iii) an irrelevant protein control, Bovine Serum Albumin (BSA). We chose BSA as a control rather than EVs from another source because H69 cholangiocytes produce (and uptake) their own exosomes in culture [30]. ES and EVs both induced significant ($P < 0.05$) cell proliferation compared to BSA-treated control cells (Figure 3). A total of 705 proteins containing at least 2 peptides were identified and quantified with a 99.9% protein threshold and 1.2% false discovery rate (FDR) from 6,863 unique peptides (peptide threshold = 95% and 0.82% FDR) from H69 cholangiocytes that were co-cultured with EVs (Supplementary Table 2); a total of 396 proteins from

cholangiocytes co-cultured with EVs were differentially expressed ($P < 0.05$ as determined using a Kruskal-Wallis test) and presented a fold-difference ≥ 1.5 ($\log_2 \geq 0.6$) at ≥ 1 time point (Supplementary Table 2). The greatest changes in protein expression in EV-co-cultured cells compared to control cells occurred after 3 h, where 238 (60.1%) proteins were differentially expressed (fold-difference ≥ 1.5 ($\log_2 \geq 0.6$)) in cells incubated with EVs (Figure 4A).

A total of 274 proteins from EV-treated cells matched homologous proteins in the KEGG database associated with 186 distinct biological pathways; 171 of these proteins were assigned to 14 Reactome pathways (Supplementary Table 3). The 25 KEGG and Reactome pathways associated with the largest numbers of proteins differentially expressed after incubation with EVs are shown in Figure 4B and C respectively. The expression of proteins linked to four pathways implicated in cancer and wound healing was significantly modified by EVs (Figure 4B). Supplementary Table 4 highlights all cholangiocyte proteins and KEGG pathways related to cancer and wound healing and their expression following co-culture with EVs. A total of 7 proteins involved in the Phagosome pathway were differentially expressed following exposure of human cholangiocytes to EVs (Supplementary Figure 3, Supplementary Table 5).

When differentially expressed proteins were assigned to Reactome pathways, those associated with Apoptosis, Regulation of activated PAK-2p34 by proteasome, and Cdh1-mediated degradation of Skp2 pathways were differentially regulated in cholangiocytes co-cultured with EVs (Figure 4C). Expression of 17 proteins associated with Apoptosis was regulated by EVs, and protein-protein interactions revealed that the majority of dysregulated cholangiocyte proteins formed a cluster belonging to the proteasome complex (Supplementary Figure 4).

Uptake of EVs and pro-inflammatory cytokine production by cholangiocytes can be blocked with antibodies to an O. viverrini EV tetraspanin

Due to the roles of tetraspanins in the formation of EVs by mammalian cells and their subsequent uptake by recipient cells [31], and the recent identification of the *Ov*-TSP-1 tetraspanin on the surface of *O. viverrini* [28], we explored the role of *Ov*-TSP-1 in the uptake of EVs by cholangiocytes. Antiserum to recombinant *Ov*-TSP-1 blocked the uptake of EVs by cholangiocytes compared to normal mouse serum ($P < 0.001 - P < 0.0001$) (Figure 5). ES and EVs both stimulated the secretion of significantly more IL-6 from cholangiocytes than did control cells incubated with media alone ($P < 0.01 - P < 0.001$; Figure 7), and IL-6 secretion was significantly reduced when EV internalisation was blocked by antiserum to *Ov*-TSP-1 ($P < 0.05$; Figure 6).

Discussion

While the mechanisms that drive chronic liver fluke infection towards cancer are multi-factorial, a pivotal role for fluke ES products in promoting a tumorigenic phenotype has been demonstrated [7]. The intracellular localization of *O. viverrini* ES proteins in cholangiocytes of infected hosts has prompted speculation on the mechanisms underlying this process of parasite protein internalization and its potential pathologic and carcinogenic consequences [6, 7]. Herein we show that *O. viverrini* secretes EVs that are internalized by human cholangiocytes *in vitro* and trigger a cascade of inflammatory and pro-tumorigenic changes within the cell, thereby providing a plausible mechanism by which ES proteins are taken up by biliary cells of infected hosts and contribute to the development of CCA in infected individuals.

Investigations on the interactions between EVs derived from single celled parasites and the cells that they encounter in an infected host have shed light on a novel means of host-parasite cellular communication [11, 12]. Protozoan parasite EVs are also capable of

modulating pro-inflammatory immune responses and inducing production of regulatory cytokines in recipient cells [19]. EV production by helminth parasites however has received considerably less attention. A seminal study recently showed that the parasitic nematode *Heligmosomoides polygyrus* secretes exosomes that contain microRNAs which suppress type 2 innate responses [15]. However, little is known about the production and particularly the biological effects of EVs from parasitic flatworms (platyhelminths). EVs were reported in the ES products from the flatworms *Fasciola hepatica* and *Echinostoma caproni* [13], and more recently *Dicrocoelium dendriticum* [14], and while the authors showed binding of fluke EVs to cell lines, neither the functional implications nor *in vivo* evidence of EV uptake by tissues of infected hosts were addressed. We show here for the first time that helminth EVs are unequivocally internalized by host cells, and major EV proteins can be detected in the bile of naturally infected humans and experimentally infected hamsters. From proteomic analyses, we identified 108 proteins from *O. viverrini* EVs, and only a handful (13) of these had been previously identified in a proteomic analysis of the ES products of the fluke [32].

Cholangiocytes line the bile ducts and provide the first line of defence against pathogens in the biliary system. We show here that *O. viverrini* EVs drive production of IL-6 from recipient human cholangiocytes, implicating these EVs in the hepatic disease process. IL-6 has been associated with chronic periductal fibrosis and CCA in opisthorchiasis patients [33], and IL-6 has been implicated in the maintenance of a chronic inflammatory milieu that could lead to tumorigenesis [34]. *O. viverrini* EVs were also capable of driving proliferation of cholangiocytes, a phenomenon that has been convincingly documented in the hamster infection model [35]. This relentless cell proliferation, coupled with other carcinogenic insults such as chronic immunopathology and elevated intake of dietary nitrosamines [2] culminates in the establishment of an environment that is conducive to malignant changes.

Uptake of EVs by cholangiocytes resulted in dysregulated expression of proteins with documented roles in wound healing and cancer. Indeed, wound repair has long been

implicated in tumorigenesis, and there are striking histological and molecular similarities between tumor stroma and wounded tissues [36]. Nineteen KEGG pathways related to cancer and wound healing were affected by EVs in human cholangiocytes. Among the proteins significantly regulated we found different tropomyosin isoforms, PAK-2 and the tight junction protein ZO-2. PAK-2 is an important kinase that mediates tumor cell invasion [37]. We also noted that PAK-2 could play an important role in tumour progression by interacting with different components of the proteasome and with vimentin, a protein involved in maintaining cellular integrity and providing resistance against stress in several epithelial cancers [37]. Moreover, tight junction proteins play important roles in cell-cell junction assembly and organization, and are up-regulated during cell proliferation and wound healing [38].

Other important cholangiocyte proteins underwent dysregulated expression after co-culture with EVs, notably proteins involved in the proteasome complex. Most of the proteins involved in this complex were upregulated in cholangiocytes exposed to EVs and are known to interact with other proteins involved in cancer and wound healing processes. The proteasome complex regulates directly or indirectly many important cellular processes, and has been suggested as a therapeutic target for cancer [39, 40].

EV uptake by dendritic cells can be blocked with antibodies to EV tetraspanins [41]. Tetraspanins are thought to be involved in the regulation of protein assembly and microRNA recruitment in mammalian exosomes [31] and influence cell selectivity [42]. Our findings highlight an important role for *Ov*-TSP-1 in *O. viverrini* EV uptake by cholangiocytes. Although tetraspanins are found on the surface membranes of all exosomes, their discovery here is particularly pertinent due to their abundance on the surface membranes of parasitic helminths [43] and their importance in the development of the *O. viverrini* tegument [28]. Tetraspanins are efficacious helminth vaccine antigens [44-46], and our findings here suggest that the mechanism of vaccine efficacy is linked to interruption of parasite EV uptake by

recipient host cells *in vivo* and subsequent disruption of key physiological (and pathological) processes.

Our study describes for the first time the release of EVs in the secreted products of the carcinogenic liver fluke, *O. viverrini*, and highlights the role of fluke EVs in promoting an inflammatory yet simultaneously modulatory (wound healing) environment that ultimately facilitates the development of biliary cancer. Our findings do however offer hope for the eventual control of this debilitating neglected tropical disease by highlighting a key physiological process that can be potentially interrupted via subunit vaccines targeting key EV surface molecules.

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CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

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520

521

522

FIGURE LEGENDS

Figure 1. Extracellular vesicles (EVs) secreted by *Opisthorchis viverrini*. Transmission

electron micrograph showing the presence of microvesicles after ultracentrifugation of *O.*

viverrini excretory/secretory products. EV-like microvesicles of 40-100 nm can be observed.

Figure 2. Internalization of *Opisthorchis viverrini* secreted extracellular vesicles (EVs) by

human cholangiocytes. Fluorescence images of Alexa Fluor 488-labeled EVs (green)

internalized by H69 cholangiocytes (A). Cholangiocytes internalized the EVs within 1 h of

co-culture and maximum internalization was observed by 6 h. Control cells were incubated

with PBS. Hoescht dye (blue) was employed to label cell nuclei (A). 3D-Structured

Illumination microscopy (3D-SIM) fluorescence image of the edge of a well-separated

individual cholangiocyte after 6 h incubation with Alexa Fluor 488-stained EVs (green) (B).

Lateral (xy) overview of cell showing EVs present within the cytoskeletal actin network (red)

of the cell (B). Rendered axial (xz) view of inset in panel A revealed EVs between the apical

and basal surfaces of the cell that were stained by phalloidin (red) (C).

Figure 3. *Opisthorchis viverrini* extracellular vesicles (EVs) drive proliferation of human

cholangiocytes. *O. viverrini* EVs (open triangles) and excretory/secretory (ES) products

(closed circles) promoted the proliferation of human cholangiocytes. Asterisks represent the

time-point from which cell growth remained significantly different between test and control

groups after each treatment. * $P < 0.05$.

Figure 4. Comparison of proteins that were significantly regulated, and biological

pathways regulated in cholangiocytes co-cultured with *Opisthorchis viverrini*

extracellular vesicles (EVs). (A) Heatmap of the proteins from human cholangiocytes with a

significant fold regulation after Kruskal-Wallis test and that underwent a 2-fold-change

(log₂=1.5) in at least one of the time-points assessed after incubation with EVs from *O. viverrini*. (B) Top 25 Kyoto Encyclopedia of Genes and Genomes (KEGG) pathways regulated after incubation with EVs. (C) Reactome pathways regulated after incubation with EVs. Pathways that are involved in wound healing and cancer are indicated by red font.

Figure 5. Blockade of uptake of *Opisthorchis viverrini* extracellular vesicles (EVs) by antibodies to recombinant Ov-TSP-1. Mouse antibodies raised to recombinant Ov-TSP-1 blocked the uptake of Alexa Fluor 488-labeled *O. viverrini* EVs by H69 cholangiocytes. Fluorescence micrographs of internalized EVs co-cultured with H69 cholangiocytes in the presence of anti-Ov-TSP-1 serum (A) or normal mouse serum (NMS) (B) at different dilutions. A□□□—Ov-TSP-1 significantly reduced the binding and internalization of EVs at all serum dilutions when measured as fluorescence intensity (C) when compared to NMS (D). ****P*<0.001; *****P*<0.0001.

Figure 6. IL-6 production by human cholangiocytes after internalisation of *Opisthorchis viverrini* extracellular vesicles (EVs). Human cholangiocytes produce significantly greater levels of IL-6 after co-culture with *O. viverrini* EVs. IL-6 production was partially blocked when EVs were incubated with antibodies against recombinant Ov-TSP-1 prior to cell culture. **P*<0.05; ***P*<0.01; ****P*<0.001.

Supplementary Materials.

Figure S1. Gene Ontology and Pfam analysis of proteins in *Opisthorchis viverrini* extracellular vesicles (EVs). Gene Ontology terms according to biological process (A), molecular function (B) and cellular component (C) assigned to the proteins present in *O. viverrini* EVs. Bar graph showing the most frequently represented protein families (Pfam) in *O. viverrini* EVs (D).

575

576 **Figure S2. Single Reaction Monitoring (SRM) analysis confirms the presence of specific**
577 **extracellular vesicle (EV) proteins in the bile of *Opisthorchis viverrini* infected humans**
578 **and hamsters.** The peak area for each transition analysed in the different proteins is shown.
579 Seven of the top 15 proteins identified in the EV proteomic analysis (based on number of
580 peptides identified) were successfully quantified, including a tetraspanin-family member
581 (TSP-2B). Protein names and target peptide sequences for SRM are indicated at the top and
582 the bottom of each graph, respectively. The transitions identified are also indicated in each
583 graph. Only proteins and peptides identified by LC-MS/MS in the proteomic analysis from
584 EVs secreted by *O. viverrini* were pre-selected for the SRM analysis. The software Skyline®
585 was used to select the best peptides and transitions based on default parameters. Peptides
586 analysed were the following: Annexin (EGVSSILDMAK, VGQDVADIYDAGVGK),
587 Hypothetical protein (FAQHGDQGLRRR), Myosin heavy chain (ANGMASQLER,
588 MQGELQQLR, DVEDLESSLQK), Myosin regulatory chain (LDYNEFVTLIK),
589 Taurocyamine kinase (LANAISELGK, TSFGGSLAQCVSHNAR), Tetraspanin 2-B
590 (KLIDLIQK), Tubulin alpha (DAIDTISVIK).

591

592 **Figure S3. Expression of cholangiocyte proteins in the phagosome pathway was altered**
593 **by co-culture with *Opisthorchis viverrini* extracellular vesicles (EVs).** Phagosome pathway
594 mapping of significantly regulated ($\log_2=0.6$) proteins (red boxes) identified from human
595 cholangiocytes after incubation with EVs from *Opisthorchis viverrini* using the Kyoto
596 Encyclopedia of Genes and Genomes (KEGG). Green boxes represent proteins in the
597 phagosome pathway that were not identified or were identified but not significantly regulated
598 by co-culture with EVs.

599

Figure S4. Functional interactions of cholangiocyte proteins associated with the “Apoptosis” pathway whose expression was affected by co-culture with *Opisthorchis viverrini* extracellular vesicles (EVs). STRING database [27] was used to identify protein-protein interactions associated with the apoptosis pathway for proteins from human cholangiocytes that were significantly regulated ($\log_2=0.6$) after incubation with *O. viverrini* EVs.

Table S1. Proteins identified in extracellular vesicles of *Opisthorchis viverrini*. Mascot was used as the search engine; spectra were searched against the *O. viverrini* genome database [25] and hits were annotated using Blast2GO [47].

Table S2. Quantitative protein and peptide report of human cholangiocyte proteins after incubation with extracellular vesicles from *Opisthorchis viverrini*. Scaffold-generated report of the iTRAQ results showing the proteins identified by MASCOT and X! Tandem and peptides matching each protein.

Table S3. Reactome pathway. Human cholangiocyte proteins associated with Reactome pathways after incubation with *Opisthorchis viverrini* extracellular vesicles (EVs).

Table S4. Phagosome pathway. Human cholangiocyte proteins involved in the Phagosome pathway after incubation with *Opisthorchis viverrini* extracellular vesicles (EVs).

Table S5. Proteins related to wound healing and cancer pathways that were differentially regulated in human cholangiocytes after co-culture with extracellular vesicles (EVs) from *Opisthorchis viverrini*. Proteins significantly up- or downregulated in

626 cholangiocytes after incubation with EVs were subjected to functional enrichment analysis
627 using the Kyoto Encyclopedia of Genes and Genomes (KEGG). A $\log_2=0.6$ corresponding to
628 a 1.5-fold change in proteins with P -value <0.05 was considered to be significant.

629

630 **Supplementary Movie.** 3D-Structured Illumination microscopy (3D-SIM) fluorescence
631 video of an individual cholangiocyte after 6 h incubation with Alexa Fluor 488-stained EVs
632 (green). Cytoskeletal actin network was stained by phalloidin (red).

633

Figure 1
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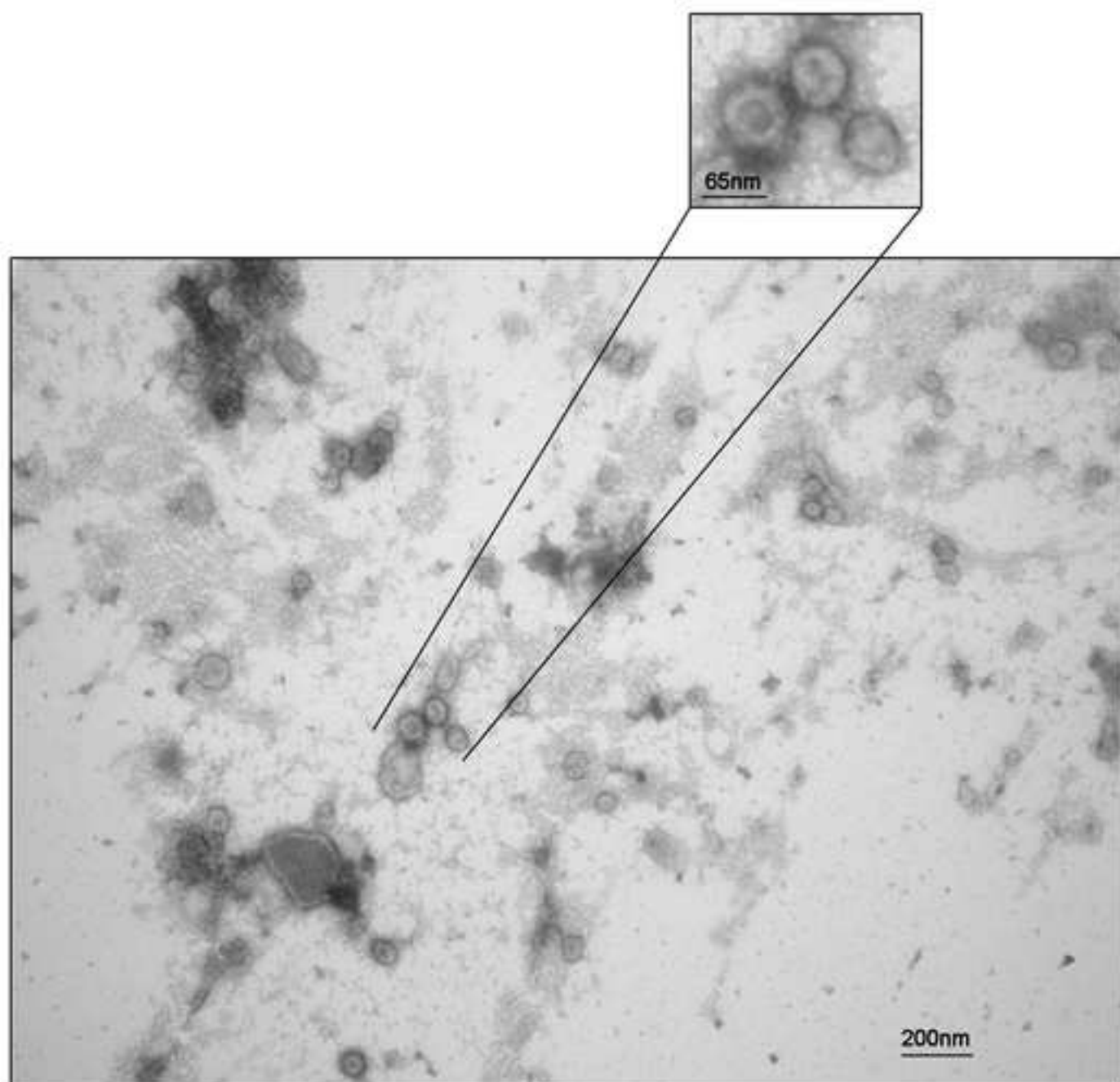


Figure 2
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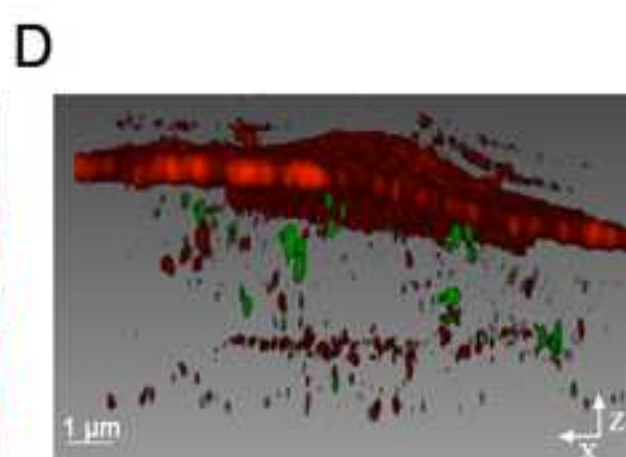
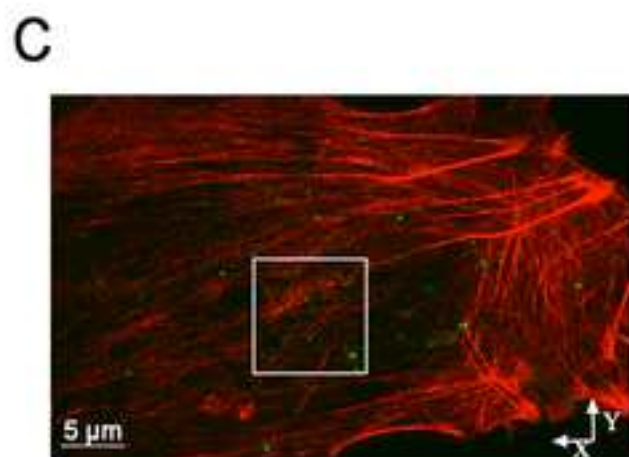
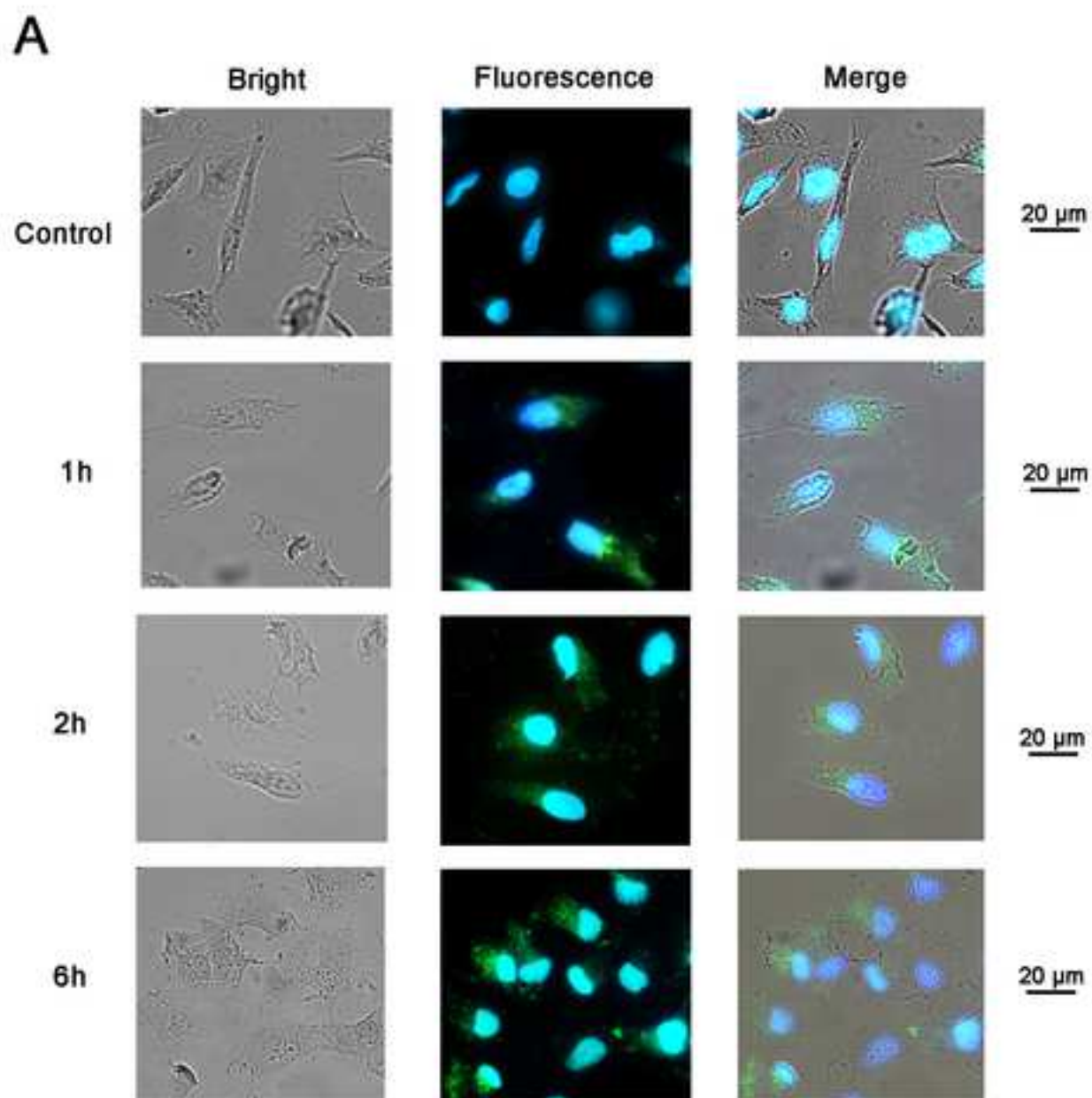


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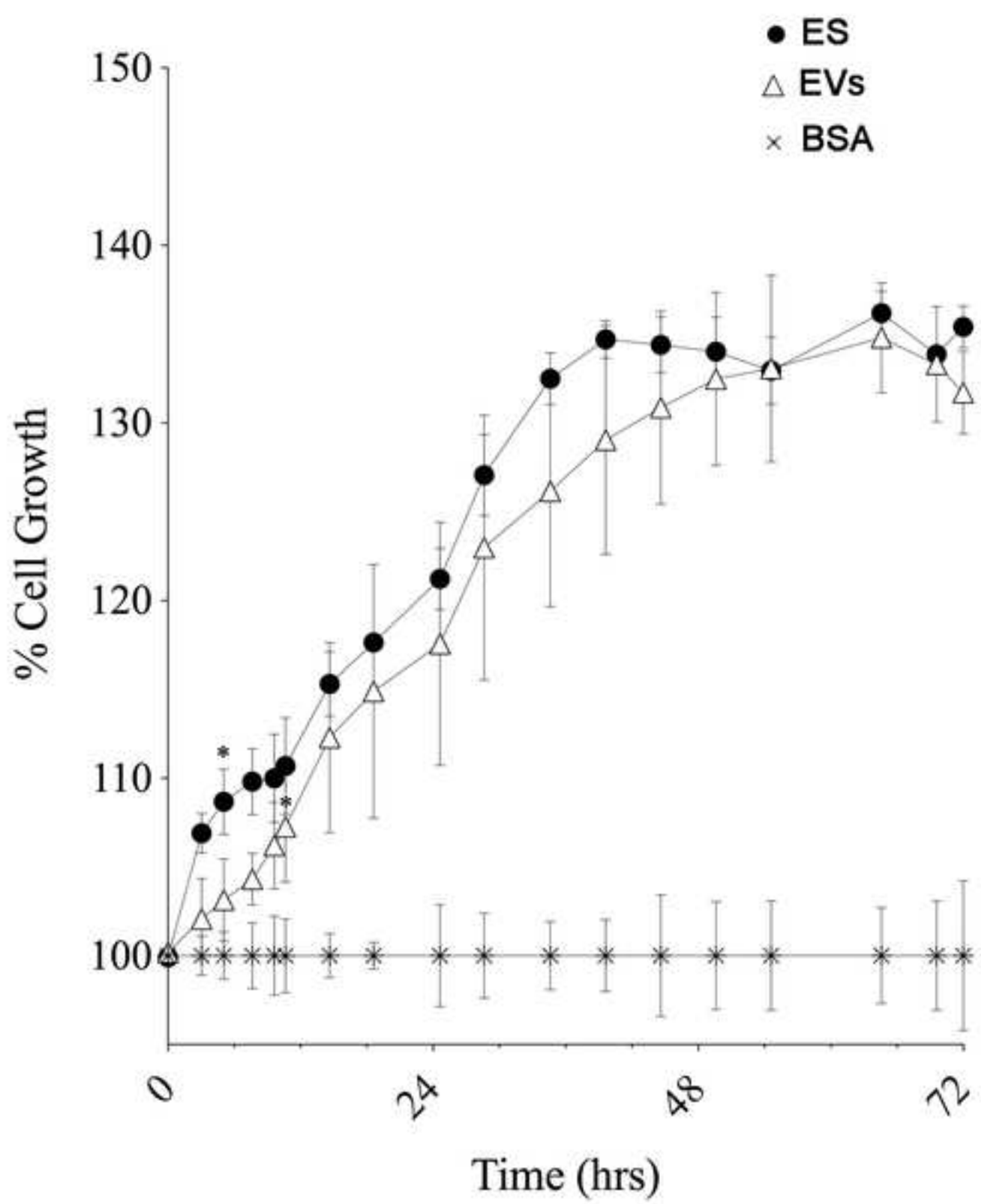


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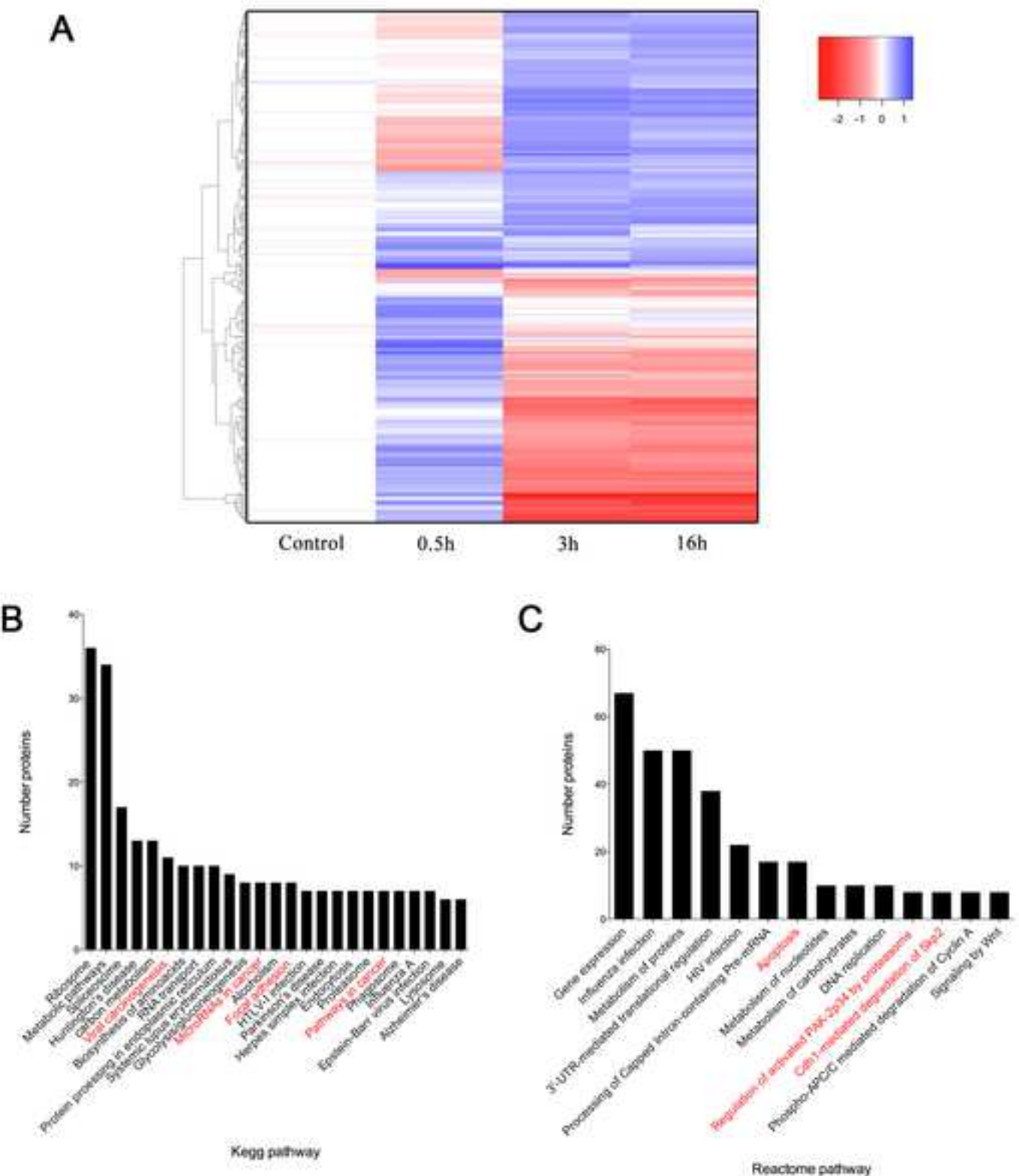


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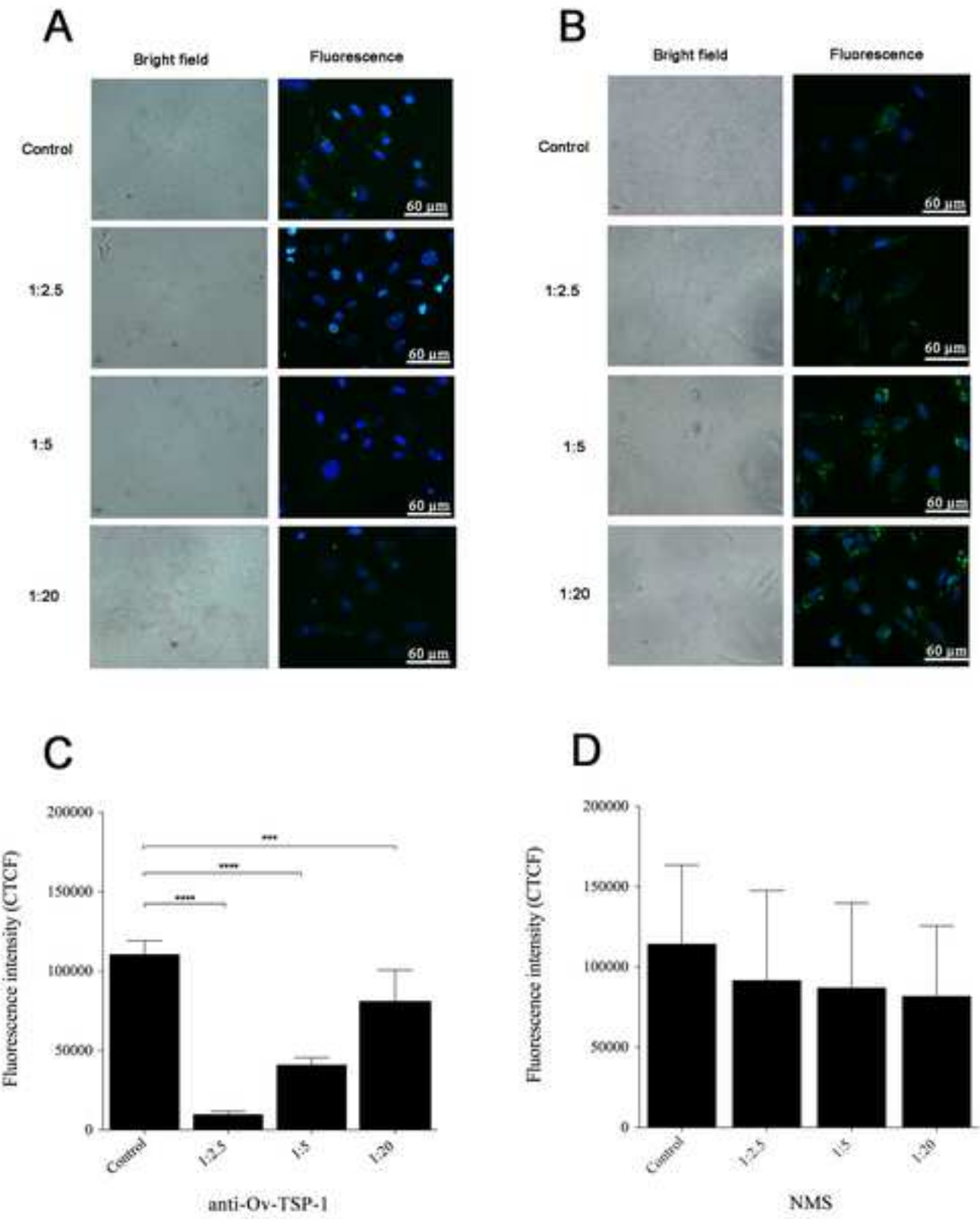
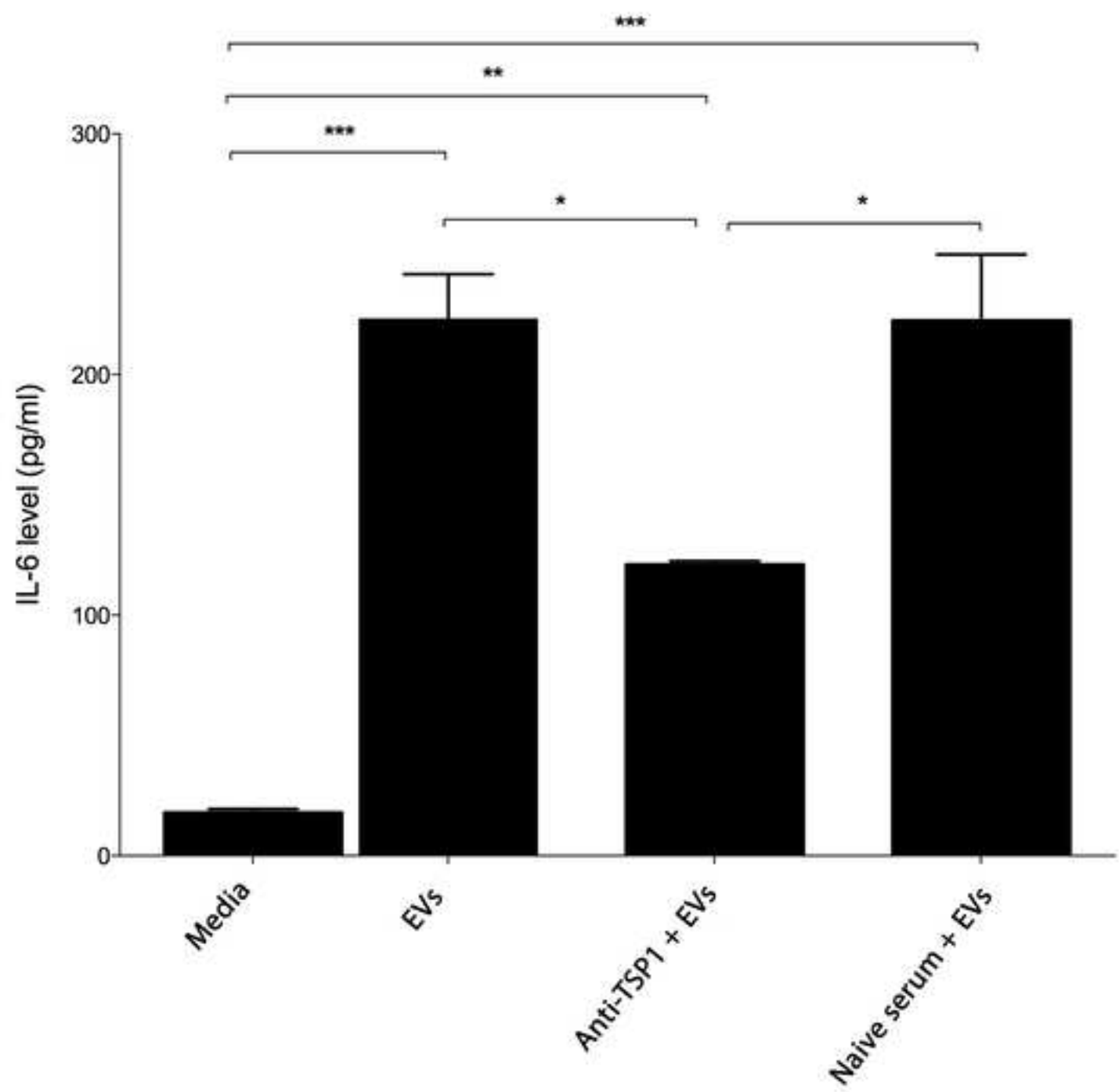
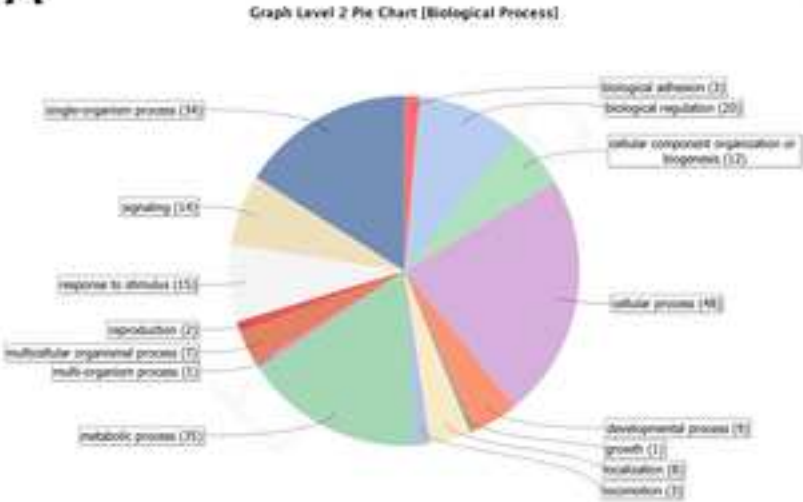


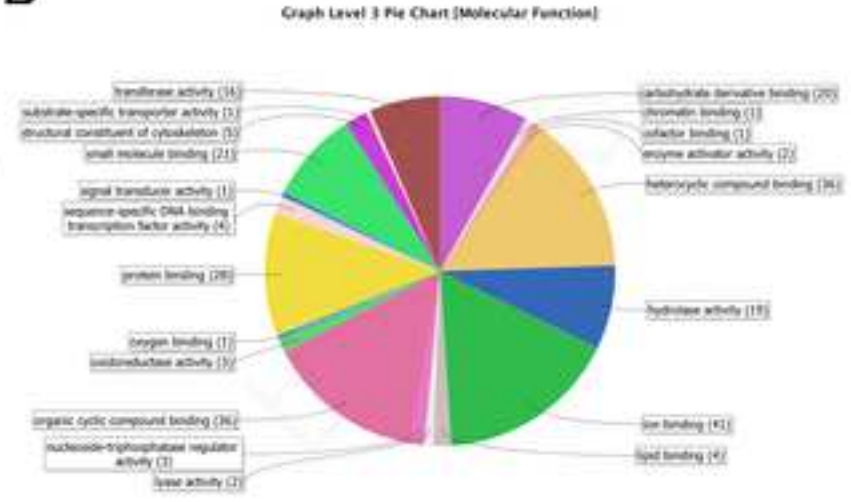
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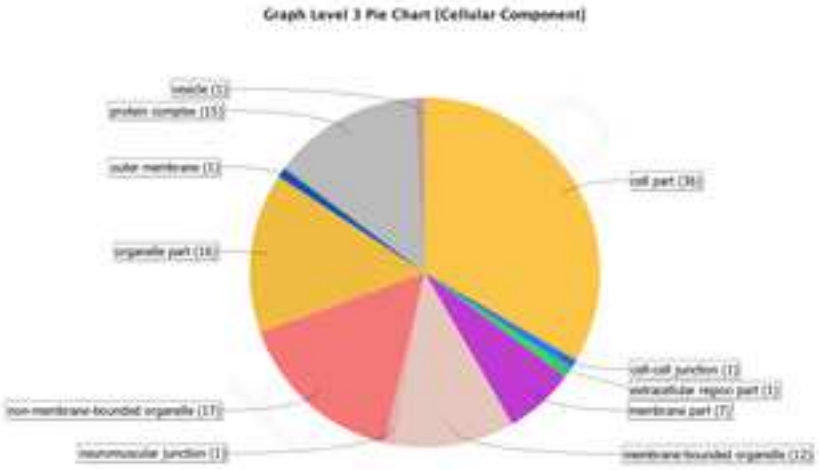
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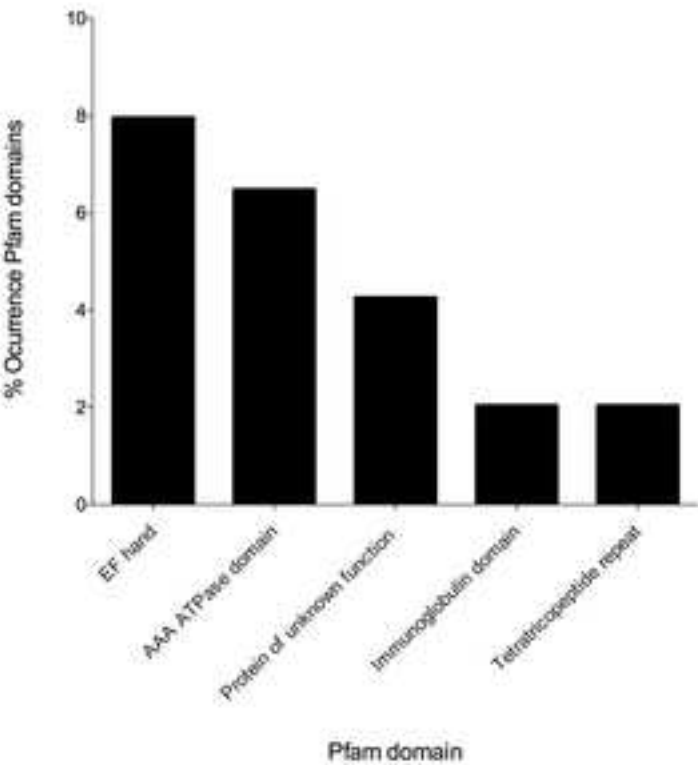
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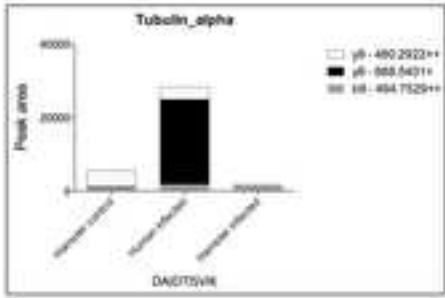
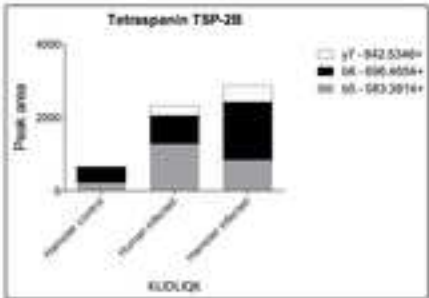
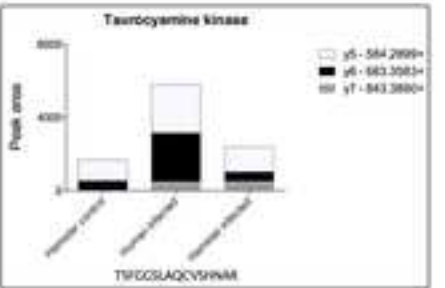
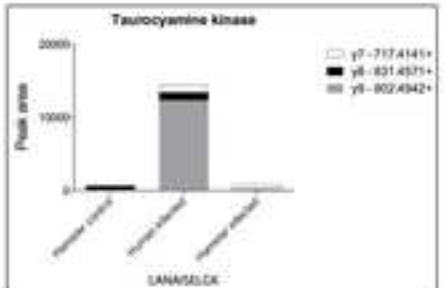
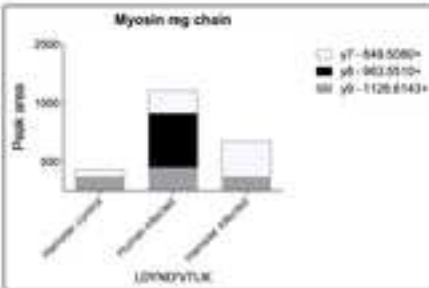
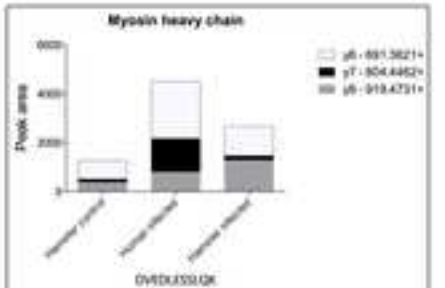
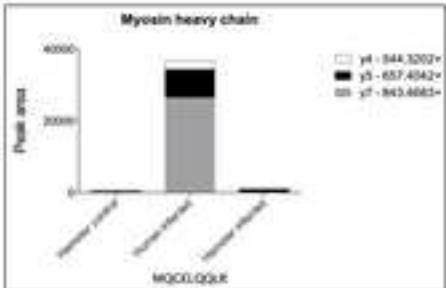
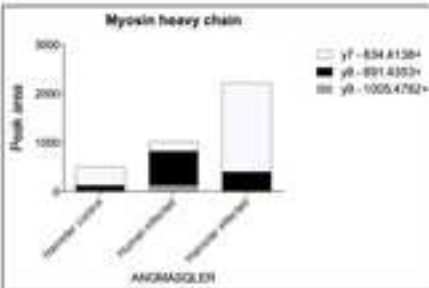
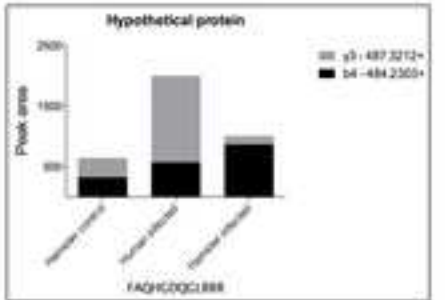
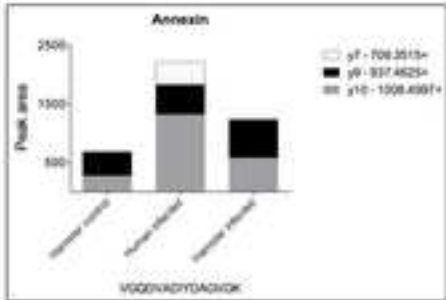
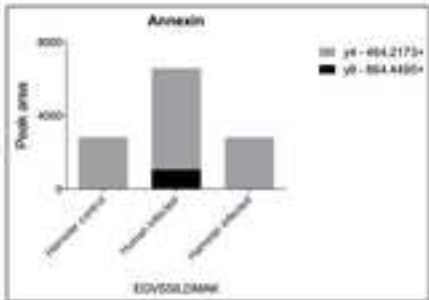


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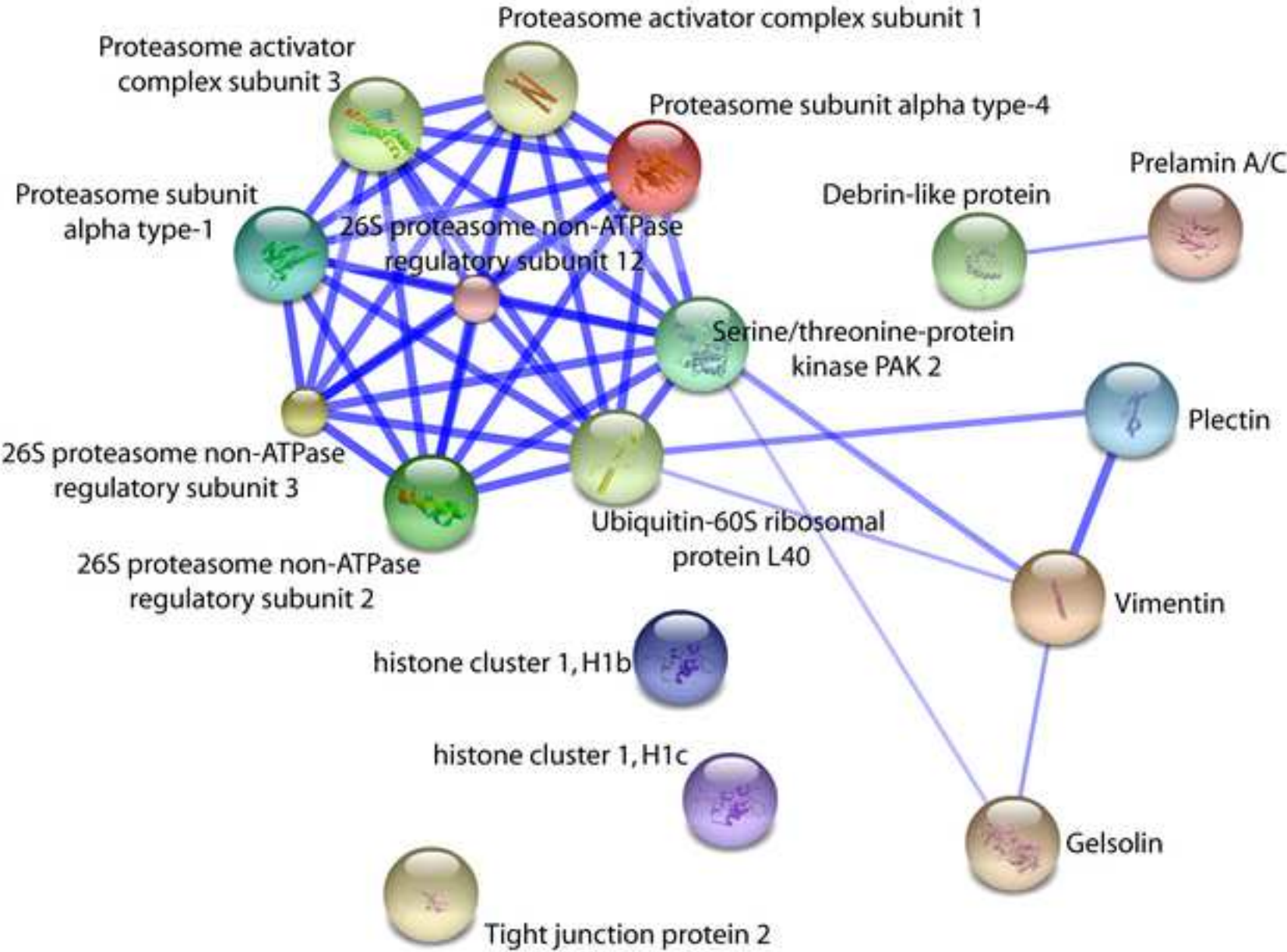


Table S1. Proteins identified in extracellular vesicles of *Opisthorchis viverrini*

Seq. Name	BLAST Accession	BLAST hitName
T265_11028	gi 358253594	actin beta/gamma 1
T265_02106	gi 358332991	tubulin beta
T265_00284	gi 126116628	paramyosin
T265_06881	gi 22655518	AF527456_1calcium binding pr
T265_07359	gi 358336555	ubiquitin C
T265_09134	gi 358341210	annexin A7
T265_15787	gi 358334577	cathepsin D
T265_09973	gi 358340940	syntenin-1
T265_08714	gi 262213552	myosin regulatory light chain
T265_13308	gi 325513923	helminth defence molecule-1
T265_10526	gi 684407701	hypothetical protein T265_105
T265_15836	gi 684413836	hypothetical protein T265_158
T265_16303	gi 353229182	putative major vault protein
T265_08893	gi 358340880	annexin A7
T265_06253	gi 684390600	hypothetical protein T265_062
T265_03631	gi 358334667	tRNA (adenine-N(1)-)-methyltr
T265_05238	gi 684386456	hypothetical protein T265_052
T265_09955	gi 325459332	unknown transmembrane prot
T265_09952	gi 358333044	myosin heavy chain
T265_15563	gi 360043476	venom allergen-like (VAL) 8 pr
T265_15799	gi 685936383	Ras-related protein Rac1, parti
T265_03867	gi 20270894	AF461710_1myoglobin
T265_02259	gi 23428564	glutathione S-transferase
T265_08043	gi 358337609	tegumental protein
T265_08991	gi 358333925	Ras homolog gene family mem
T265_09265	gi 358337832	endophilin-B1
T265_10536	gi 684407743	hypothetical protein T265_105
T265_03615	gi 684379718	hypothetical protein T265_036
T265_04144	gi 684381871	hypothetical protein T265_041
T265_07169	gi 360044564	cript-related
T265_04047	gi 350023777	tubulin alpha chain
T265_07596	gi 358333877	taurocyamine kinase
T265_10204	gi 426308934	tetraspanin 2A
T265_13185	gi 684378098	hypothetical protein T265_131
T265_00358	gi 358253276	hypothetical protein CLF_1087
T265_01977	gi 358342015	COMPASS component SWD1
T265_04046	gi 358335874	tubulin alpha
T265_08065	gi 426308936	tetraspanin 2B
T265_09781	gi 358253835	DNA repair protein REV1, parti
T265_06356	gi 358335181	zinc finger protein 341
T265_10362	gi 226468366	Vesicle transport protein SFT2I

T265_02867	gi 358333977	myosin essential light chain str
T265_04527	gi 358332486	KRAB domain-containing zinc f
T265_08099	gi 904121	tropomyosin
T265_10125	gi 358254620	copine-8, partial
T265_08367	gi 358342140	hypothetical protein CLF_1033
T265_04851	gi 358336212	replication factor C subunit 3/5
T265_05756	gi 684388548	hypothetical protein T265_057
T265_13582	gi 58263527	14-3-3 protein
T265_07292	gi 358331798	tubulin alpha
T265_08188	gi 254587308	endonuclease-reverse transcrip
T265_10730	gi 358339096	BRO1 domain-containing protei
T265_01105	gi 358333593	beta-arrestin
T265_03959	gi 358337668	hypothetical protein CLF_1096
T265_12534	gi 358333203	serine/threonine-protein kinas
T265_13848	gi 358254343	calcium-binding protein
T265_14319	gi 358333055	cyclin-dependent kinase-like
T265_01853	gi 360044613	putative merlin/moesin/ezrin/
T265_03292	gi 358334092	U3 small nucleolar RNA-associ
T265_06061	gi 153861719	heat shock protein 70
T265_06656	gi 358333984	hypothetical protein CLF_1080
T265_10899	gi 358342418	acetyl-CoA acyltransferase
T265_13810	gi 358340653	protein unc-80 homolog
T265_14094	gi 358332850	signal-induced proliferation-as
T265_14629	gi 685962441	Regulator of G-protein signalin
T265_00300	gi 358342642	pre-mRNA-splicing factor
T265_03216	gi 360044772	putative dead box ATP-depend
T265_03979	gi 358335239	large subunit ribosomal protei
T265_08081	gi 358254618	coiled-coil domain-containing
T265_09935	gi 358336872	transitional endoplasmic reticu
T265_11598	gi 358253589	hypothetical protein CLF_1103
T265_11632	gi 358340214	spectrin beta chain
T265_14214	gi 358253196	calpain
T265_14955	gi 358332908	hypothetical protein CLF_1062
T265_01157	gi 358336587	sterol regulatory element-bind
T265_01206	gi 358253741	gamma-tubulin complex comp
T265_01323	gi 358332388	cullin 1
T265_01951	gi 358253292	serine/threonine-protein phos
T265_03269	gi 358336101	innexin unc-9
T265_05027	gi 353228659	putative serine-rich repeat pro
T265_06464	gi 358254922	protein tyrosine phosphatase
T265_06544	gi 358334779	protocadherin-9
T265_06597	gi 358340957	protein CIP2A
T265_07346	gi 358341589	nuclear factor interleukin-3-re
T265_08700	gi 358332999	splicing factor arginine/serine-

T265_08792	gi 358339172	programmed cell death 6-inter
T265_09632	gi 358342856	polycomb protein Su(z)12
T265_10413	gi 358338282	integrin alpha-5
T265_15583	gi 358334974	coiled-coil domain-containing
T265_05385	gi 358254660	ecdysone-induced protein 78C
T265_06055	gi 358338672	ankyrin repeat domain-contair
T265_09823	gi 358338574	patatin-like phospholipase dor
T265_12442	gi 358342089	exocyst complex component 6
T265_14563	gi 358336386	terminal uridylyltransferase 7
T265_14630	gi 358338747	zinc finger CCCH domain-conta
T265_15132	gi 358333293	ATPase family AAA domain-coi
T265_15342	gi 358341675	cell division cycle 2-like
T265_00630	gi 358340488	telomerase protein componen
T265_00976	gi 358252933	FH1/FH2 domain-containing pr
T265_02851	gi 358335297	neurofibromin 1
T265_04878	gi 684384900	hypothetical protein T265_048
T265_05525	gi 358340495	DNA polymerase alpha subunit
T265_11520	gi 358338356	Ca(2+)/calmodulin-responsive
T265_12500	gi 358340364	striated muscle preferentially e
T265_13055	gi 353229947	putative spectrin beta chain, b
T265_14174	gi 358254651	plectin, partial
T265_14303	gi 358255157	rootletin
T265_15051	gi 358342072	twitchin, partial

ini are diagnostic features of exosomes. Mascot was used as the search engine; spectra were search

BLAST Organism	SignalP	TMHMM	Exocarta homologu	Present in <i>O. viverrini</i>	E-#GOs
Clonorchis sinensis	N	N	Yes	No	7
Clonorchis sinensis	N	N	Yes	Yes	8
Clonorchis sinensis	N	N	No	Yes	3
Clonorchis sinensis	N	N	No	Yes	1
Clonorchis sinensis	N	N	Yes	No	1
Clonorchis sinensis	N	N	Yes	No	2
Clonorchis sinensis	N	N	Yes	No	2
Clonorchis sinensis	N	N	No	No	1
Fasciola hepatica	N	N	Yes	No	8
Fasciola hepatica	N	N	Yes	No	5
Opisthorchis viverrini	N	N	No	No	0
Opisthorchis viverrini	N	N	No	No	0
Schistosoma mansoni	N	N	Yes	Yes	3
Clonorchis sinensis	N	N	Yes	No	2
Opisthorchis viverrini	N	N	No	No	0
Clonorchis sinensis	N	N	No	No	4
Opisthorchis viverrini	N	N	No	No	0
Clonorchis sinensis	N	Y	No	No	0
Clonorchis sinensis	N	N	Yes	No	6
Schistosoma mansoni	N	N	No	Yes	1
Schistosoma haematobium	N	N	Yes	No	6
Clonorchis sinensis	N	N	No	Yes	5
Opisthorchis viverrini	N	N	Yes	Yes	2
Clonorchis sinensis	N	N	No	Yes	3
Clonorchis sinensis	N	N	No	No	20
Clonorchis sinensis	N	N	Yes	Yes	2
Opisthorchis viverrini	N	N	No	No	0
Opisthorchis viverrini	N	N	No	No	0
Opisthorchis viverrini	N	Y	No	No	0
Schistosoma mansoni	N	N	No	No	0
Clonorchis sinensis	N	N	Yes	No	8
Clonorchis sinensis	N	N	No	No	6
Opisthorchis viverrini	N	Y	Yes	No	1
Opisthorchis viverrini	Y	N	No	No	0
Clonorchis sinensis	N	N	No	No	1
Clonorchis sinensis	N	N	No	No	1
Clonorchis sinensis	N	N	Yes	No	8
Opisthorchis viverrini	N	Y	Yes	No	1
Clonorchis sinensis	N	N	No	No	3
Clonorchis sinensis	N	N	No	No	7
Schistosoma japonicum	N	Y	No	No	2

Clonorchis sinensis	N	N	Yes	No	1
Clonorchis sinensis	N	N	Yes	No	2
Clonorchis sinensis	N	N	Yes	No	0
Clonorchis sinensis	N	N	Yes	No	4
Clonorchis sinensis	N	N	No	No	0
Clonorchis sinensis	N	N	Yes	No	3
Opisthorchis viverrini	N	N	No	No	0
Fasciola gigantica	N	N	Yes	Yes	2
Clonorchis sinensis	N	N	Yes	No	12
Schistosoma japonicum	N	N	No	No	4
Clonorchis sinensis	N	N	Yes	No	1
Clonorchis sinensis	N	N	No	No	1
Clonorchis sinensis	N	N	No	No	0
Clonorchis sinensis	N	N	Yes	No	4
Clonorchis sinensis	N	N	Yes	Yes	2
Clonorchis sinensis	N	N	Yes	No	3
Schistosoma mansoni	N	N	No	Yes	7
Clonorchis sinensis	N	N	Yes	No	2
Fasciola hepatica	N	N	Yes	No	2
Clonorchis sinensis	N	N	No	No	1
Clonorchis sinensis	N	N	Yes	No	14
Clonorchis sinensis	N	N	No	No	0
Clonorchis sinensis	N	N	No	No	3
Schistosoma haematobium	N	N	No	No	1
Clonorchis sinensis	N	N	No	No	3
Schistosoma mansoni	N	N	Yes	No	4
Clonorchis sinensis	N	N	Yes	No	2
Clonorchis sinensis	N	N	No	No	4
Clonorchis sinensis	N	N	No	No	3
Clonorchis sinensis	N	N	No	No	1
Clonorchis sinensis	N	N	Yes	No	2
Clonorchis sinensis	N	N	Yes	Yes	4
Clonorchis sinensis	N	Y	No	No	0
Clonorchis sinensis	N	N	No	No	35
Clonorchis sinensis	N	N	No	No	3
Clonorchis sinensis	N	N	No	No	6
Clonorchis sinensis	N	N	Yes	No	1
Clonorchis sinensis	N	Y	No	No	1
Schistosoma mansoni	N	N	No	No	0
Clonorchis sinensis	N	N	No	No	3
Clonorchis sinensis	N	Y	No	No	4
Clonorchis sinensis	N	N	No	No	8
Clonorchis sinensis	N	N	No	No	3
Clonorchis sinensis	N	N	No	No	0

Clonorchis sinensis	N	N	Yes	No	1
Clonorchis sinensis	N	N	No	No	5
Clonorchis sinensis	Y	N	Yes	No	3
Clonorchis sinensis	N	N	No	No	5
Clonorchis sinensis	N	Y	No	No	8
Clonorchis sinensis	N	N	No	No	1
Clonorchis sinensis	N	N	Yes	No	2
Clonorchis sinensis	N	N	No	No	4
Clonorchis sinensis	N	N	No	No	3
Clonorchis sinensis	N	N	No	No	8
Clonorchis sinensis	N	N	Yes	No	4
Clonorchis sinensis	N	N	No	No	4
Clonorchis sinensis	N	N	No	No	3
Clonorchis sinensis	N	N	No	No	8
Clonorchis sinensis	Y	N	No	No	4
Opisthorchis viverrini	N	N	No	No	0
Clonorchis sinensis	N	N	No	No	5
Clonorchis sinensis	N	Y	No	No	3
Clonorchis sinensis	N	N	No	No	6
Schistosoma mansoni	N	N	No	No	31
Clonorchis sinensis	N	N	Yes	No	9
Clonorchis sinensis	Y	N	Yes	No	2
Clonorchis sinensis	N	N	No	No	5

shed against the *O. viverrini* genome database [65] and hits were annotated using Blast2GO

GOs	Enzyme Codes	InterProScan score	Number peptides	Score	emPAI
P:sarcomere -	IPR004000 (PF 728.783	9	1040	1.05	
C:microtubul -	Coil (COILS); II 846.655	8	852	0.94	
C:myofibril; C -	Coil (COILS); C 1540.4	13	945	0.52	
F:calcium ion -	IPR002048 (SF 133.265	1	32	0.45	
F:protein binding	IPR019956 (PF 303	2	147	0.43	
F:calcium ion -	IPR001464 (PF 678.707	4	213	0.39	
F:aspartic-tyr EC:3.4.23	IPR001461 (PF 141.739	1	17	0.36	
F:protein binding	IPR001478 (SF 287	3	216	0.34	
P:DNA duple; EC:3.6.1	Coil (COILS); II 311.997	3	201	0.33	
C:retromer complex; P:vacuola	Coil (COILS); II 50.447	2	84	0.32	
-	no IPS match 100	1	14	0.31	
-	no IPS match 99	1	38	0.31	
P:eye develop -	IPR002499 (PF 206	1	40	0.3	
F:calcium ion -	IPR001464 (PF 653.67	3	199	0.28	
-	no IPS match 117	1	17	0.26	
P:methylation -	IPR007316 (PF 207.223	1	15	0.24	
-	no IPS match 134	1	27	0.24	
-	Coil (COILS); C 191	5	261	0.22	
C:myosin fila -	Coil (COILS); C 3319.25	13	509	0.21	
C:extracellular region	IPR001283 (PF 134.42	2	134	0.21	
F:GTP binding; P:small GTPase	IPR001806 (PF 143	1	44	0.21	
F:heme bindi -	IPR011406 (PI 256.144	1	200	0.2	
F:transferase -	IPR004046 (PF 342.813	1	52	0.17	
F:calcium ion -	IPR011992 (PF 306.22	1	98	0.17	
P:oviposition -	IPR001806 (PF 293.123	1	20	0.17	
C:cytoplasm; -	Coil (COILS); II 263.848	1	50	0.17	
-	no IPS match 188	1	15	0.17	
-	no IPS match 182	1	25	0.16	
-	CYTOPLASMIC 191	1	18	0.16	
-	IPR019367 (PF 92	1	16	0.16	
C:microtubul -	Coil (COILS); II 800.431	2	56	0.14	
F:metal ion b EC:2.7.3.4	IPR022413 (G 567	3	70	0.14	
C:integral to membrane	IPR000301 (PF 178.333	1	114	0.14	
-	SIGNAL_PEPTI 211	1	44	0.14	
F:zinc ion bin -	IPR000433 (PF 368.622	1	23	0.13	
F:protein binding	IPR001680 (SF 269	2	14	0.13	
C:microtubul -	Coil (COILS); II 753.051	2	44	0.13	
C:integral to -	IPR000301 (PF 336.265	1	39	0.13	
P:DNA repair; F:DNA-directed C	no IPS match 91.2781	1	33	0.13	
F:translation EC:2.7.7.49	no IPS match 182.57	1	14	0.12	
C:integral to -	IPR007305 (PF 148.288	1	19	0.11	

F:calcium ion -	IPR011992 (G 370.933	1	147	0.1
F:nucleic acid -	IPR015880 (S 226.868	1	17	0.1
-	Coil (COILS); C 279	1	44	0.1
F:RNA binding EC:2.7.7.49	IPR010734 (P 213.001	1	18	0.1
-	no IPS match 322	1	26	0.09
F:nucleoside- EC:3.6.1.15	PF13177 (PFA 622.854	1	23	0.08
-	no IPS match 354	1	32	0.08
F:protein domain -	IPR000308 (P 338.191	1	46	0.08
C:cilium; F:protein -	Coil (COILS); I 840.491	1	55	0.07
F:RNA binding; P:RNA-dependent	no IPS match 101.679	1	13	0.07
C:membrane	IPR004328 (S 286.96	1	34	0.07
P:signal transduction -	IPR000698 (P 788.104	1	17	0.06
-	Coil (COILS); C 316	1	38	0.06
P:protein phosphorylation EC:2.7.11	IPR000095 (S 891.338	1	13	0.06
C:membrane -	IPR002048 (S 688.723	1	77	0.06
P:protein phosphorylation EC:2.7.11	no IPS match 181.8	1	18	0.06
F:RNA-directed EC:2.7.7.49	Coil (COILS); C 355.14	2	76	0.05
C:intracellular -	Coil (COILS); C 946.806	1	17	0.05
F:ATP binding -	IPR013126 (P 1083.94	1	54	0.05
F:protein tyrosine phosphatase	IPR028472 (P 415	1	19	0.05
C:mitochondrial EC:4.2.1.17; EC:1.	IPR002155 (T 573.933	1	19	0.05
-	Coil (COILS); P 344	1	14	0.05
F:GTPase activity -	no IPS match 996.882	1	21	0.05
P:termination of G-protein coupling	IPR000342 (P 185	1	27	0.05
P:mRNA processing -	IPR003107 (S 1461.82	1	28	0.04
F:helicase activity -	IPR001650 (S 716.457	1	17	0.04
C:ribosome; I-	Coil (COILS); I 780.015	1	17	0.04
C:cytoplasm; C:cytoskeleton; P:	Coil (COILS); C 78.1814	1	15	0.04
F:nucleoside- EC:3.6.1.15	IPR003338 (S 1365.9	1	28	0.04
C:cell wall	TRANSMEMBI 58.5362	2	29	0.04
F:actin binding -	Coil (COILS); C 1178.7	2	20	0.04
C:intracellular -	Coil (COILS); I 1535.39	1	28	0.04
-	CYTOPLASMIC 375	1	16	0.04
F:sequence-specific EC:3.1.4.11	Coil (COILS); I 817.765	1	19	0.03
C:microtubule -	no IPS match 1664.82	1	18	0.03
C:SCF ubiquitin -	IPR016158 (S 1125.92	1	17	0.03
F:calcium ion -	IPR011992 (P 1578.15	1	24	0.03
C:gap junction -	IPR000990 (P 803.897	1	30	0.03
-	no IPS match 323	1	14	0.03
F:protein tyrosine phosphorylation EC:3.1.3.48	IPR000980 (P 1274.61	1	14	0.03
C:integral to -	IPR002126 (P 1865.51	1	33	0.03
F:RNA binding EC:2.7.7.49	Coil (COILS); I 207.608	1	28	0.03
F:sequence-specific -	Coil (COILS); C 1566.21	1	16	0.03
-	Coil (COILS); C 365	1	17	0.03

F:protein binding	Coil (COILS); II 334	1	41	0.03
F:binding; P:r -	IPR019135 (PF 159.844	1	17	0.03
C:integrin coi -	IPR000413 (PF 1672.14	1	16	0.03
P:system dev -	Coil (COILS); C 330.872	1	17	0.03
P:steroid hor -	IPR000008 (PF 804.668	1	22	0.02
F:protein binding	IPR002110 (SF 846	1	14	0.02
P:phosphatid EC:3.1.1.5	IPR000595 (SF 2380.13	1	19	0.02
P:vesicle docl -	IPR007225 (PF 1456.04	1	18	0.02
F:zinc ion bin -	IPR001878 (SF 3256.08	1	31	0.02
F:RNA-direct EC:2.7.7.49	Coil (COILS); II 1535.78	1	18	0.02
F:nucleoside- EC:3.6.1.15	Coil (COILS); II 1464.51	1	18	0.02
P:protein phc EC:2.7.11	IPR002290 (SF 1755.34	1	20	0.02
F:RNA bindin -	IPR001680 (SF 580.096	1	18	0.01
P:cell migrati -	Coil (COILS); C 3016.1	1	20	0.01
C:intracellula -	IPR001936 (SF 4016.08	1	19	0.01
-	no IPS match 2654	1	24	0.01
F:DNA-direct EC:2.7.7.7	Coil (COILS); C 2401.71	1	20	0.01
P:intracellula -	IPR001054 (SF 5421.67	1	20	0.01
F:Rho guanyl -	Coil (COILS); C 5958.64	1	22	0.01
P:axon midlir -	Coil (COILS); C 3063.86	1	20	0.01
P:anatomical -	Coil (COILS); C 4715.6	1	21	0.01
P:centrosom -	Coil (COILS); C 1859.73	1	13	0.01
F:protein binding; F:ATP bindin	PR00014 (PRII 20387	2	18	0.01

[66].

Seq. Length	#Hits	min. eValue	mean Similarity
358	20	0	93.80%
474	20	0	91.50%
871	20	0	93.05%
70	20	3.23E-40	67.50%
152	20	2.40E-103	99.95%
342	20	0	68.90%
86	3	7.42E-56	78.67%
302	20	0	61.45%
295	20	0	90.30%
202	17	4.42E-146	66.24%
100	1	8.01E-64	100.00%
99	2	5.38E-64	89.50%
101	20	4.75E-68	79.55%
354	20	0	69.45%
117	1	4.07E-82	100.00%
124	20	1.42E-84	69.70%
134	1	8.74E-79	100.00%
727	20	0	55.45%
1932	20	0	84.95%
298	20	0	61.20%
142	20	2.35E-99	72.10%
150	20	1.67E-104	66.00%
177	20	2.23E-126	63.20%
175	20	1.81E-112	59.80%
175	20	1.45E-111	80.40%
173	20	2.45E-95	57.90%
188	20	3.13E-135	74.00%
182	20	3.13E-127	71.35%
191	5	1.02E-137	82.00%
186	20	7.69E-135	85.10%
435	20	0	94.15%
655	20	0	82.50%
223	20	4.71E-154	66.35%
211	4	3.53E-154	70.25%
218	9	3.90E-149	64.89%
477	20	0	80.45%
473	20	0	90.00%
230	20	3.20E-149	66.00%
230	20	2.45E-170	73.40%
233	20	3.28E-159	83.50%
279	20	0	82.35%

300	20	0	85.80%
291	20	0	71.00%
284	20	7.91E-152	90.35%
314	20	0	77.30%
322	20	0	57.65%
367	20	0	80.10%
354	5	5.95E-136	66.60%
355	20	0	79.65%
451	20	0	93.15%
397	20	0	62.95%
436	20	0	60.25%
469	20	0	51.85%
499	20	0	54.65%
478	20	0	67.00%
516	20	0	77.65%
483	2	0	95.50%
1059	20	0	86.60%
561	20	0	62.50%
653	20	0	95.00%
553	20	0	78.15%
584	20	0	81.80%
610	20	0	78.20%
608	20	0	75.55%
628	20	0	54.05%
763	20	0	81.95%
744	20	0	66.60%
801	20	0	57.35%
648	20	0	56.80%
827	20	0	90.05%
1567	20	0	59.85%
1305	20	0	58.55%
756	20	0	73.05%
756	7	0	66.71%
1060	20	0	76.65%
918	20	0	68.45%
966	20	0	64.85%
929	20	0	79.25%
969	20	0	81.05%
895	5	0	67.60%
860	20	0	65.50%
1115	20	0	47.10%
1136	20	0	85.20%
936	20	0	75.30%
975	20	0	65.90%

1068	20	0	57.00%
1163	20	0	55.15%
1021	20	0	59.95%
969	20	0	58.45%
1255	20	0	54.50%
1991	20	0	56.55%
1619	20	0	62.65%
1660	20	0	58.60%
1835	20	0	54.90%
1736	20	0	95.10%
1613	20	0	69.25%
1571	20	0	88.35%
3231	20	0	56.05%
2026	20	0	64.15%
3568	20	0	72.90%
2654	2	0	74.50%
3052	20	0	62.65%
3148	20	0	58.00%
5487	20	0	53.75%
2421	20	0	77.70%
3288	20	0	56.55%
2198	20	0	59.90%
6861	1	0	100%

Table S2. Quantitative protein and peptide report of human cholangiocyte proteins after in

Microvesicles Quantitative Sample report created on 26/08/2014

Experiment: Microvesicles

Identification Criteria: unknown

Scaffold Version: Scaffold_4.2.1

Quantification Type: iTRAQ 8-Plex

Peak Quantitation Measurement: Centroided Peak Intensity

Peak List Generator: Analyst

Version: 2.0

Charge States Calculated: True

Deisotoped: True

Textual Annotation: unknown

Database Set: 2 Databases

Database Name: a subset of the SwissProt_2013_09 da

Version: 2013_09

Taxonomy: All Entries

Number of Proteins: 17420

Database Name: the SwissProt_2013_09 database

Version: 2013_09

Taxonomy: Homo sapiens

Number of Proteins: 20272

Does database contain common contaminants?: Yes

Search Engine Set: 2 Search Engines

Search Engine: Mascot

Version: 2.4.0

Samples: All Samples

Fragment Tolerance: 0.50 Da (Monoisotc

Parent Tolerance: 0.50 Da (Monoisotopic

Fixed Modifications: +304 on Kn (iTRAQ8

Variable Modifications: +16 on M (Oxidat

Database: the SwissProt_2013_09 databa

Digestion Enzyme: Trypsin

Max Missed Cleavages: 2

Probability Model:

mascot_daemon_merge (e

mascot_daemon_merge (e

Search Engine: X! Tandem

Version: CYCLONE (2010.12.01.1)

Samples: All Samples

Fragment Tolerance: 0.50 Da (Monoisotc

Parent Tolerance: 0.50 Da (Monoisotopic

Fixed Modifications: +304 on Kn (iTRAQ8

Variable Modifications: -18 on n (Glu->py

Database: a subset of the SwissProt_201

Digestion Enzyme: Trypsin

Max Missed Cleavages: 2

Probability Model:

mascot_daemon_merge (e

mascot_daemon_merge (e

Scaffold: Version: Scaffold_4.2.1

Modification Metadata Set: 1541 modifications

Source: C:\Program Files\Scaffold 4\para

Comment:

Protein Grouping Strategy: Experiment-wide grouping

Peptide Thresholds: 95.0% minimum

Protein Thresholds: 99.9% minimum and 2 peptides m

Peptide FDR: 0.8% (Decoy)

Protein FDR: 1.2% (Decoy)

Purity Correction Set: unknown

Default iTRAQ 8-Plex Purity Correction:

Purity Correction Values: [0.000,0.000,0.929,0.0689,0.0

Samples Applied To: All Samples

Quantitation Preferences: unknown

Minimum Value Preference:

Use Minimum Absolute Intensity: false

Minimum Absolute Intensity: 0.0

Minimum Value: 0.01

Model Preference:

Model Type: Intensity-Based Normalization

Condenser Preference:

Use Intensity Weighting: true

Use Standard Deviation Estimation: true

Use Non-Exclusive Peptides: false

Intensity-Based Normalization Preference:

Calculation Type: Median

Quant Uniqueness Model: Unique Peptides

Use Inter Experiment Normalization: true

Use Intra Sample Normalization: true

Use Peptide Normalization: true

Use Protein Reference Normalization: true

Use Protein Average As Reference: true

Use Iterative Normalization: true

View Preference:

View Type: Log2 Ratio

Normalization Factors: unknown

Inter-Experiment Normalization Factors:

Javi_microvesicles: -0.000

Intra-Sample Normalization Factors:

Javi_microvesicles: [0.609,1.40,55.7,55.7,-1.14,55.7,-1.

Quantitative Test: unknown

Quantitative Test: Kruskal-Wallis Test (P-Value)

Microvesicles Displaying:Log2 Fold Change

#	Visible?	Starred?	Identified Protein Accession Number Molecular Weight Protein Group
1	TRUE	Empty	Serum albumin ALBU_HUMAN 69 kDa TRUE
2	TRUE	Empty	Cluster of Actin ACTB_HUMAN 42 kDa TRUE
3	TRUE	Empty	Cluster of Histone H2B1M_HUMAN 14 kDa TRUE
4	TRUE	Empty	Cluster of Myosin MYH9_HUMAN 227 kDa TRUE
5	TRUE	Empty	Neuroblast differentiation AHNK_HUMAN 629 kDa TRUE
6	TRUE	Empty	Cluster of Vinculin VIME_HUMAN 54 kDa TRUE
7	TRUE	Empty	Cluster of Glyceraldehyde 3-phosphate dehydrogenase G3P_HUMAN 36 kDa TRUE
8	TRUE	Empty	Cluster of Tubulin TBB5_HUMAN 50 kDa TRUE
9	TRUE	Empty	Histone H4 O H4_HUMAN 11 kDa
10	TRUE	Empty	Cluster of Heat shock protein 90B HS90B_HUMAN 83 kDa TRUE
11	TRUE	Empty	Cluster of Anion exchange protein 2 ANXA2_HUMAN 39 kDa TRUE
12	TRUE	Empty	Plectin OS=Human PLEC_HUMAN 532 kDa TRUE
13	TRUE	Empty	Cluster of Filamin FLNA_HUMAN 281 kDa TRUE
14	TRUE	Empty	Cluster of Tubulin TBA1A_HUMAN 50 kDa TRUE
15	TRUE	Empty	Cluster of Eln EF1A1_HUMAN 50 kDa TRUE
16	TRUE	Empty	Cluster of Microtubule associated protein MOES_HUMAN 68 kDa TRUE
17	TRUE	Empty	Nucleolin OS=Human NUCL_HUMAN 77 kDa TRUE
18	TRUE	Empty	Cluster of Histone H31T_HUMAN 16 kDa TRUE
19	TRUE	Empty	Cluster of Ubiquitin RL40_HUMAN 15 kDa TRUE
20	TRUE	Empty	Prelamin-A/C LMNA_HUMAN 74 kDa TRUE
21	TRUE	Empty	Cluster of Heat shock protein 70 HSP7C_HUMAN 71 kDa TRUE
22	TRUE	Empty	Cluster of Pyruvate kinase KPYM_HUMAN 58 kDa TRUE
23	TRUE	Empty	Annexin A5 CANXA5_HUMAN 36 kDa TRUE
24	TRUE	Empty	Peptidyl-prolyl isomerase PPIA_HUMAN 18 kDa TRUE
25	TRUE	Empty	10 kDa heat shock protein CH10_HUMAN 11 kDa
26	TRUE	Empty	Cluster of Keratin K1C18_HUMAN 48 kDa TRUE
27	TRUE	Empty	Cluster of Aldolase ENOA_HUMAN 47 kDa TRUE
28	TRUE	Empty	Cluster of Actin ACTN4_HUMAN 105 kDa TRUE
29	TRUE	Empty	Cluster of Histone H12_HUMAN 21 kDa TRUE
30	TRUE	Empty	Protein disulfide isomerase PDIA1_HUMAN 57 kDa TRUE
31	TRUE	Empty	60 kDa heat shock protein CH60_HUMAN 61 kDa TRUE
32	TRUE	Empty	Cluster of L-lactate dehydrogenase LDHA_HUMAN 37 kDa TRUE
33	TRUE	Empty	Spectrin alpha SPTN1_HUMAN 285 kDa TRUE
34	TRUE	Empty	Cluster of Phosphoglycerate kinase PGK1_HUMAN 45 kDa TRUE
35	TRUE	Empty	Protein disulfide isomerase PDIA3_HUMAN 57 kDa TRUE

36	TRUE	Empty	Elongation fa EF2_HUMAN 95 kDa	TRUE
37	TRUE	Empty	78 kDa glucosyl GRP78_HUMAN 72 kDa	TRUE
38	TRUE	Empty	Cluster of Tra TAGL2_HUMAN 22 kDa	TRUE
39	TRUE	Empty	Cluster of RN RBMX_HUMAN 42 kDa	TRUE
40	TRUE	Empty	Cluster of 14-1433Z_HUMAN 28 kDa	TRUE
41	TRUE	Empty	Triosephosph TPIS_HUMAN 31 kDa	
42	TRUE	Empty	ATP synthase ATPB_HUMAN 57 kDa	TRUE
43	TRUE	Empty	Nucleophosmin NPM_HUMAN 33 kDa	TRUE
44	TRUE	Empty	Microtubule- MAP4_HUMAN 121 kDa	
45	TRUE	Empty	Cluster of En ENPL_HUMAN 92 kDa	TRUE
46	TRUE	Empty	Cluster of Sta STMN1_HUMAN 17 kDa	TRUE
47	TRUE	Empty	Cluster of He HNRPC_HUMAN 34 kDa	TRUE
48	TRUE	Empty	Heterogeneous ROA2_HUMAN 37 kDa	TRUE
49	TRUE	Empty	Heterogeneous HNRPK_HUMAN 51 kDa	TRUE
50	TRUE	Empty	DNA-dependent PRKDC_HUMAN 469 kDa	TRUE
51	TRUE	Empty	Ribosome-binding RBP1_HUMAN 152 kDa	TRUE
52	TRUE	Empty	MRO2B_HUMAN MRO2B_HUMAN ?	TRUE
53	TRUE	Empty	Cluster of Cal CALM_HUMAN 17 kDa	TRUE
54	TRUE	Empty	Cluster of Sp SPTB2_HUMAN 275 kDa	TRUE
55	TRUE	Empty	Profilin-1 OS= PROF1_HUMAN 15 kDa	
56	TRUE	Empty	Cluster of 40S RS10_HUMAN 19 kDa	TRUE
57	TRUE	Empty	Calreticulin O CALR_HUMAN 48 kDa	
58	TRUE	Empty	Cluster of He ROA1_HUMAN 39 kDa	TRUE
59	TRUE	Empty	Talin-1 OS=H TLN1_HUMAN 270 kDa	TRUE
60	TRUE	Empty	Stress-induced STIP1_HUMAN 63 kDa	TRUE
61	TRUE	Empty	Heat shock protein HSPB1_HUMAN 23 kDa	
62	TRUE	Empty	Peroxiredoxin PRDX6_HUMAN 25 kDa	TRUE
63	TRUE	Empty	Peptidyl-protein PPIB_HUMAN 24 kDa	TRUE
64	TRUE	Empty	40S ribosome RS19_HUMAN 16 kDa	
65	TRUE	Empty	T-complex protein TCPG_HUMAN 61 kDa	
66	TRUE	Empty	Cluster of Fru ALDOA_HUMAN 39 kDa	TRUE
67	TRUE	Empty	ATP synthase ATPA_HUMAN 60 kDa	TRUE
68	TRUE	Empty	Histone H1.5 H15_HUMAN 23 kDa	TRUE
69	TRUE	Empty	Alpha-2-HS-glyc FETUA_HUMAN 39 kDa	
70	TRUE	Empty	40S ribosome RS9_HUMAN 23 kDa	TRUE
71	TRUE	Empty	Proteasome subunit PSME1_HUMAN 29 kDa	
72	TRUE	Empty	Cluster of Cla CLH1_HUMAN 192 kDa	TRUE
73	TRUE	Empty	Transitional epsilon TERA_HUMAN 89 kDa	TRUE
74	TRUE	Empty	Protein S100- S10A6_HUMAN 10 kDa	
75	TRUE	Empty	Cluster of AD ADT2_HUMAN 33 kDa	TRUE
76	TRUE	Empty	40S ribosome RS16_HUMAN 16 kDa	
77	TRUE	Empty	L-lactate dehydrogenase LDHB_HUMAN 37 kDa	TRUE
78	TRUE	Empty	40S ribosome RS3A_HUMAN 30 kDa	
79	TRUE	Empty	Ras GTPase-activator IQGA1_HUMAN 189 kDa	TRUE

80	TRUE	Empty	X-ray repair c XRCC6_HUM/ 70 kDa	TRUE
81	TRUE	Empty	Cluster of Hig HMGB1_HUN 25 kDa	TRUE
82	TRUE	Empty	Translational GCN1L_HUM 293 kDa	TRUE
83	TRUE	Empty	Cytoplasmic c DYHC1_HUM 532 kDa	TRUE
84	TRUE	Empty	Stress-70 pro GRP75_HUM 74 kDa	TRUE
85	TRUE	Empty	Cluster of Prc TGM2_HUM/ 77 kDa	TRUE
86	TRUE	Empty	Cluster of Hei HBA_HUMAN 15 kDa	TRUE
87	TRUE	Empty	Cluster of Col COF1_HUMA 19 kDa	TRUE
88	TRUE	Empty	40S ribosome RS18_HUMAN 18 kDa	
89	TRUE	Empty	Galectin-1 OS LEG1_HUMAN 15 kDa	
90	TRUE	Empty	Prohibitin-2 C PHB2_HUMA 33 kDa	
91	TRUE	Empty	Cluster of 40S RS4X_HUMAN 30 kDa	TRUE
92	TRUE	Empty	Calnexin OS= CALX_HUMAN 68 kDa	TRUE
93	TRUE	Empty	Heterogeneo HNRPM_HUN 78 kDa	
94	TRUE	Empty	Cluster of Lac TRFL_HUMAN 78 kDa	TRUE
95	TRUE	Empty	Cluster of His H2A2B_HUM 14 kDa	TRUE
96	TRUE	Empty	Myosin light I MYL6_HUMA 17 kDa	
97	TRUE	Empty	60S ribosome RL4_HUMAN 48 kDa	TRUE
98	TRUE	Empty	Cluster of Trc TPM3_HUMA 33 kDa	TRUE
99	TRUE	Empty	Cluster of Nu YBOX1_HUM 36 kDa	TRUE
100	TRUE	Empty	60S ribosome RL3_HUMAN 46 kDa	TRUE
101	TRUE	Empty	Cluster of Glu G6PI_HUMAN 63 kDa	TRUE
102	TRUE	Empty	Cluster of Trc TPM1_HUMA 33 kDa	TRUE
103	TRUE	Empty	Cystatin-B OS CYTB_HUMAN 11 kDa	
104	TRUE	Empty	Malate dehydrogenase MDHM_HUM 36 kDa	
105	TRUE	Empty	Protein S100- S10AA_HUM 11 kDa	TRUE
106	TRUE	Empty	Thioredoxin C THIO_HUMAN 12 kDa	
107	TRUE	Empty	Calpastatin O ICAL_HUMAN 77 kDa	
108	TRUE	Empty	Elongation factor EF1G_HUMAN 50 kDa	
109	TRUE	Empty	Neutral alpha-galactosidase GANAB_HUM 107 kDa	
110	TRUE	Empty	Serine/arginine-rich protein SRSF1_HUMA 28 kDa	TRUE
111	TRUE	Empty	60S ribosome RL6_HUMAN 33 kDa	TRUE
112	TRUE	Empty	Annexin A6 CANXA6_HUM 76 kDa	TRUE
113	TRUE	Empty	ATP-citrate synthase ACLY_HUMAN 121 kDa	TRUE
114	TRUE	Empty	40S ribosome RS7_HUMAN 22 kDa	TRUE
115	TRUE	Empty	60S ribosome RL23A_HUM/ 18 kDa	
116	TRUE	Empty	Vinculin OS=H VINC_HUMAN 124 kDa	
117	TRUE	Empty	Heterogeneo ROAA_HUMA 36 kDa	TRUE
118	TRUE	Empty	Far upstream element FUBP2_HUM 73 kDa	TRUE
119	TRUE	Empty	C-1-tetrahydropteridine C1TC_HUMAN 102 kDa	
120	TRUE	Empty	Annexin A1 CANXA1_HUM 39 kDa	TRUE
121	TRUE	Empty	Cluster of 60S RL13A_HUM/ 24 kDa	TRUE
122	TRUE	Empty	Transketolase TKT_HUMAN 68 kDa	TRUE
123	TRUE	Empty	Calumenin O= CALU_HUMA 37 kDa	TRUE

124	TRUE	Empty	Cluster of Hei HBB_HUMAN 16 kDa	TRUE
125	TRUE	Empty	Eukaryotic tr IF4H_HUMAN 27 kDa	TRUE
126	TRUE	Empty	40S ribosom RS13_HUMAN 17 kDa	TRUE
127	TRUE	Empty	Glucosidase 2 GLU2B_HUMAN 59 kDa	TRUE
128	TRUE	Empty	Cluster of Hig HMGB2_HUMAN 24 kDa	TRUE
129	TRUE	Empty	Cluster of Eul IF4A1_HUMAN 46 kDa	TRUE
130	TRUE	Empty	60S ribosom RL13_HUMAN 24 kDa	
131	TRUE	Empty	Peptidyl-prol FKBP3_HUMAN 25 kDa	TRUE
132	TRUE	Empty	Myosin regul ML12A_HUMAN 20 kDa	TRUE
133	TRUE	Empty	T-complex pr TCPQ_HUMAN 60 kDa	
134	TRUE	Empty	40S ribosom RS15A_HUMAN 15 kDa	
135	TRUE	Empty	Glycine--trN SYG_HUMAN 83 kDa	TRUE
136	TRUE	Empty	Plasminogen PAIRB_HUMAN 45 kDa	
137	TRUE	Empty	60S ribosom RL7_HUMAN 29 kDa	TRUE
138	TRUE	Empty	Nuclear ubiq NUCKS_HUMAN 27 kDa	
139	TRUE	Empty	ATPase inhibi ATIF1_HUMAN 12 kDa	
140	TRUE	Empty	Procollagen-I PLOD2_HUMAN 85 kDa	
141	TRUE	Empty	40S ribosom RS25_HUMAN 14 kDa	
142	TRUE	Empty	Cluster of 6-p K6PF_HUMAN 85 kDa	TRUE
143	TRUE	Empty	Cluster of Eul IF5A1_HUMAN 17 kDa	TRUE
144	TRUE	Empty	Cluster of Ser 2AAA_HUMAN 65 kDa	TRUE
145	TRUE	Empty	Fatty acid syr FAS_HUMAN 273 kDa	TRUE
146	TRUE	Empty	Lupus La prot LA_HUMAN 47 kDa	
147	TRUE	Empty	Cluster of 60S RL26_HUMAN 17 kDa	TRUE
148	TRUE	Empty	Protein disulf PDIA4_HUMAN 73 kDa	
149	TRUE	Empty	Cluster of Dih DPYL2_HUMAN 62 kDa	TRUE
150	TRUE	Empty	Protein S100-S10AB_HUMAN 12 kDa	
151	TRUE	Empty	Fascin OS=Hc FSCN1_HUMAN 55 kDa	
152	TRUE	Empty	Protein DJ-1 (PARK7_HUMAN 20 kDa	TRUE
153	TRUE	Empty	Cluster of Phc PGAM1_HUMAN 29 kDa	TRUE
154	TRUE	Empty	Heterogeneo HNRPU_HUMAN 91 kDa	
155	TRUE	Empty	60S acidic rib RLA0_HUMAN 34 kDa	
156	TRUE	Empty	60S ribosom RL10_HUMAN 25 kDa	
157	TRUE	Empty	Staphylococc SND1_HUMAN 102 kDa	
158	TRUE	Empty	Cluster of Nu NDKB_HUMAN 17 kDa	TRUE
159	TRUE	Empty	Non-histone HMGN2_HUMAN 9 kDa	TRUE
160	TRUE	Empty	Nuclear mito NUMA1_HUMAN 238 kDa	TRUE
161	TRUE	Empty	Glycogen phc PYGB_HUMAN 97 kDa	TRUE
162	TRUE	Empty	60S ribosom RL31_HUMAN 14 kDa	TRUE
163	TRUE	Empty	Dolichyl-diph RPN1_HUMAN 69 kDa	
164	TRUE	Empty	40S ribosom RS3_HUMAN 27 kDa	
165	TRUE	Empty	Tropomyosin TPM4_HUMAN 29 kDa	TRUE
166	TRUE	Empty	28 kDa heat- HAP28_HUMAN 21 kDa	
167	TRUE	Empty	Programmed PDCD5_HUMAN 14 kDa	TRUE

168	TRUE	Empty	Non-POU domain NONO_HUMAN 54 kDa	TRUE
169	TRUE	Empty	60S ribosomal RL5_HUMAN 34 kDa	
170	TRUE	Empty	Cluster of Sp1 DX39B_HUMAN 49 kDa	TRUE
171	TRUE	Empty	Thioredoxin c TXND5_HUMAN 48 kDa	
172	TRUE	Empty	RNA-binding EWS_HUMAN 68 kDa	TRUE
173	TRUE	Empty	Glutathione S GSTO1_HUMAN 28 kDa	
174	TRUE	Empty	Periplakin OS PEPL_HUMAN 205 kDa	TRUE
175	TRUE	Empty	Epiplakin OS= EPIPL_HUMAN 556 kDa	TRUE
176	TRUE	Empty	Polymerase I PTRF_HUMAN 43 kDa	TRUE
177	TRUE	Empty	Arginine--tRNA SYRC_HUMAN 75 kDa	
178	TRUE	Empty	Exportin-2 OS XPO2_HUMAN 110 kDa	
179	TRUE	Empty	T-complex protein TCPE_HUMAN 60 kDa	
180	TRUE	Empty	Platelet-activating PA1B3_HUMAN 26 kDa	
181	TRUE	Empty	Elongation factor EFTU_HUMAN 50 kDa	TRUE
182	TRUE	Empty	Eukaryotic translation IF4B_HUMAN 69 kDa	
183	TRUE	Empty	Splicing factor SFPO_HUMAN 76 kDa	TRUE
184	TRUE	Empty	Protein disulfide PDIA6_HUMAN 48 kDa	
185	TRUE	Empty	Alpha-2-macroglobulin A2MG_HUMAN 163 kDa	TRUE
186	TRUE	Empty	Inter-alpha-trypsin inhibitor ITIH2_HUMAN 106 kDa	
187	TRUE	Empty	60S acidic ribosomal RLA2_HUMAN 12 kDa	
188	TRUE	Empty	Single-strand binding SSBP_HUMAN 17 kDa	
189	TRUE	Empty	DnaJ homolog DNJC8_HUMAN 30 kDa	
190	TRUE	Empty	40S ribosomal RS2_HUMAN 31 kDa	
191	TRUE	Empty	Elongation factor EF1B_HUMAN 25 kDa	TRUE
192	TRUE	Empty	Caveolin-1 OS CAV1_HUMAN 20 kDa	
193	TRUE	Empty	Non-histone protein HMGN1_HUMAN 11 kDa	TRUE
194	TRUE	Empty	Cluster of T-cell TCPZ_HUMAN 58 kDa	TRUE
195	TRUE	Empty	Peptidyl-prolyl FKBP5_HUMAN 51 kDa	
196	TRUE	Empty	Cluster of ADAR ARF3_HUMAN 21 kDa	TRUE
197	TRUE	Empty	Cluster of Polr PCBP1_HUMAN 37 kDa	TRUE
198	TRUE	Empty	Transaldolase TALDO_HUMAN 38 kDa	TRUE
199	TRUE	Empty	Ubiquitin-associated UBP2L_HUMAN 115 kDa	
200	TRUE	Empty	Small nuclear RUXGL_HUMAN 9 kDa	
201	TRUE	Empty	Serine hydroxylase GLYM_HUMAN 56 kDa	
202	TRUE	Empty	Interleukin receptor ILF2_HUMAN 43 kDa	
203	TRUE	Empty	Caldesmon O CALD1_HUMAN 93 kDa	TRUE
204	TRUE	Empty	Eukaryotic translation EIF3B_HUMAN 92 kDa	
205	TRUE	Empty	D-3-phosphoserine SERA_HUMAN 57 kDa	
206	TRUE	Empty	60S ribosomal RL8_HUMAN 28 kDa	TRUE
207	TRUE	Empty	Cluster of Puro PSA_HUMAN 103 kDa	TRUE
208	TRUE	Empty	Citrate synthase CISO_HUMAN 52 kDa	TRUE
209	TRUE	Empty	ATP-dependent DDX1_HUMAN 82 kDa	
210	TRUE	Empty	Cluster of Ubiquitin UB2V1_HUMAN 16 kDa	TRUE
211	TRUE	Empty	Serine/arginine SRSF3_HUMAN 19 kDa	TRUE

212	TRUE	Empty	LIM and SH3 LASP1_HUMAN 30 kDa	
213	TRUE	Empty	DNA replicati MCM4_HUMAN 97 kDa	TRUE
214	TRUE	Empty	14-3-3 protei 1433E_HUMAN 29 kDa	TRUE
215	TRUE	Empty	Eukaryotic tra EIF3A_HUMAN 167 kDa	TRUE
216	TRUE	Empty	DNA replicati MCM7_HUMAN 81 kDa	
217	TRUE	Empty	Reticulocalbir RCN1_HUMAN 39 kDa	TRUE
218	TRUE	Empty	Ubiquitin-like UBA1_HUMAN 118 kDa	
219	TRUE	Empty	Trifunctional ECHB_HUMAN 51 kDa	
220	TRUE	Empty	Ran-specific C RANG_HUMAN 23 kDa	
221	TRUE	Empty	Flap endonuc FEN1_HUMAN 43 kDa	
222	TRUE	Empty	Rab GDP diss GDIB_HUMAN 51 kDa	
223	TRUE	Empty	Lamin-B2 OS= LMNB2_HUMAN 68 kDa	TRUE
224	TRUE	Empty	DNA replicati MCM5_HUMAN 82 kDa	
225	TRUE	Empty	Aspartate--tr SYDC_HUMAN 57 kDa	
226	TRUE	Empty	14-3-3 protei 1433F_HUMAN 28 kDa	TRUE
227	TRUE	Empty	ADP-ribosyla ARF4_HUMAN 21 kDa	TRUE
228	TRUE	Empty	Extended syn ESYT1_HUMAN 123 kDa	TRUE
229	TRUE	Empty	Kinectin OS= KTN1_HUMAN 156 kDa	TRUE
230	TRUE	Empty	Cluster of UV RD23B_HUMAN 43 kDa	TRUE
231	TRUE	Empty	60S ribosoma RL19_HUMAN 23 kDa	TRUE
232	TRUE	Empty	Serine/argini SRSF7_HUMAN 27 kDa	TRUE
233	TRUE	Empty	40S ribosoma RSSA_HUMAN 33 kDa	TRUE
234	TRUE	Empty	Aspartate am AATM_HUMAN 48 kDa	
235	TRUE	Empty	60S ribosoma RL27_HUMAN 16 kDa	
236	TRUE	Empty	60S ribosoma RL28_HUMAN 16 kDa	
237	TRUE	Empty	Serpin H1 OS= SERPH_HUMAN 46 kDa	TRUE
238	TRUE	Empty	T-complex pr TCPD_HUMAN 58 kDa	
239	TRUE	Empty	Alpha-2-macr AMRP_HUMAN 41 kDa	
240	TRUE	Empty	Catenin delta CTND1_HUMAN 108 kDa	
241	TRUE	Empty	Glutamine--tr SYQ_HUMAN 88 kDa	
242	TRUE	Empty	Annexin A3 CANXA3_HUMAN 36 kDa	TRUE
243	TRUE	Empty	Glucose-6-ph G6PD_HUMAN 59 kDa	
244	TRUE	Empty	Mitochondria IMMT_HUMAN 84 kDa	TRUE
245	TRUE	Empty	Nucleobindin NUCB1_HUMAN 54 kDa	TRUE
246	TRUE	Empty	GTP-binding I RAN_HUMAN 24 kDa	
247	TRUE	Empty	Cluster of DN TOP2B_HUMAN 183 kDa	TRUE
248	TRUE	Empty	Protein CDV3 CDV3_HUMAN 27 kDa	TRUE
249	TRUE	Empty	DNA replicati MCM2_HUMAN 102 kDa	TRUE
250	TRUE	Empty	Proactivator I SAP_HUMAN 58 kDa	
251	TRUE	Empty	T-complex pr T CPA_HUMAN 60 kDa	
252	TRUE	Empty	Dynactin sub DCTN2_HUMAN 44 kDa	TRUE
253	TRUE	Empty	Zyxin OS= Hor ZYX_HUMAN 61 kDa	
254	TRUE	Empty	Proliferating I PCNA_HUMAN 29 kDa	
255	TRUE	Empty	Septin-9 OS= I SEPT9_HUMAN 65 kDa	TRUE

256	TRUE	Empty	Thioredoxin c TXD12_HUM/ 19 kDa	
257	TRUE	Empty	Cluster of Ald AK1C2_HUM/ 37 kDa	TRUE
258	TRUE	Empty	Adenylyl cycli CAP1_HUMA 52 kDa	
259	TRUE	Empty	Lamin-B1 OS- LMNB1_HUM 66 kDa	TRUE
260	TRUE	Empty	Voltage-depe VDAC1_HUM 31 kDa	TRUE
261	TRUE	Empty	X-ray repair c XRCC5_HUM/ 83 kDa	TRUE
262	TRUE	Empty	60S ribosomæ RL14_HUMA/ 23 kDa	TRUE
263	TRUE	Empty	Serine protea HTRA1_HUM 51 kDa	
264	TRUE	Empty	Cluster of SW SMCA5_HUM 122 kDa	TRUE
265	TRUE	Empty	Cluster of He: HXK1_HUMA 102 kDa	TRUE
266	TRUE	Empty	Cluster of Ins IF2B3_HUMA 64 kDa	TRUE
267	TRUE	Empty	Peroxiredoxir PRDX2_HUM/ 22 kDa	TRUE
268	TRUE	Empty	Parathymosir PTMS_HUMA 12 kDa	
269	TRUE	Empty	Reticulon-4 CRTN4_HUMA 130 kDa	TRUE
270	TRUE	Empty	Biliverdin red BIEA_HUMA/ 33 kDa	TRUE
271	TRUE	Empty	Chloride intra CLIC1_HUMA 27 kDa	TRUE
272	TRUE	Empty	Cluster of Coi H2AY_HUMA 40 kDa	TRUE
273	TRUE	Empty	DNA replicati MCM3_HUM 91 kDa	TRUE
274	TRUE	Empty	60S ribosomæ RL23_HUMA/ 15 kDa	
275	TRUE	Empty	Adenosylhomr SAHH_HUMA 48 kDa	TRUE
276	TRUE	Empty	Thrombospori TSP1_HUMA/ 129 kDa	TRUE
277	TRUE	Empty	40S ribosomæ RS24_HUMA/ 15 kDa	
278	TRUE	Empty	Cluster of Kin KINH_HUMA/ 110 kDa	TRUE
279	TRUE	Empty	Splicing facto SF3B2_HUM/ 100 kDa	TRUE
280	TRUE	Empty	Cytochrome c CYC_HUMAN 12 kDa	
281	TRUE	Empty	Multifunctioni PUR6_HUMA 47 kDa	
282	TRUE	Empty	Vitronectin O VTNC_HUMA 54 kDa	
283	TRUE	Empty	DNA replicati MCM6_HUM 93 kDa	
284	TRUE	Empty	Desmoplakin DESP_HUMA/ 332 kDa	TRUE
285	TRUE	Empty	Trifunctional PUR2_HUMA 108 kDa	
286	TRUE	Empty	40S ribosomæ RS14_HUMA/ 16 kDa	
287	TRUE	Empty	40S ribosomæ RS12_HUMA/ 15 kDa	
288	TRUE	Empty	Eukaryotic tra EIF3F_HUMA 38 kDa	
289	TRUE	Empty	Beta-2-microi B2MG_HUM/ 14 kDa	
290	TRUE	Empty	UPF0568 proi CN166_HUM/ 28 kDa	
291	TRUE	Empty	rRNA 2'-O-mæ FBRL_HUMA/ 34 kDa	TRUE
292	TRUE	Empty	Heterogeneo HNRPQ_HUM 70 kDa	TRUE
293	TRUE	Empty	Acidic leucine AN32B_HUM 29 kDa	TRUE
294	TRUE	Empty	Small nuclear SMD3_HUM/ 14 kDa	
295	TRUE	Empty	Proteasome c PSME3_HUM 30 kDa	
296	TRUE	Empty	Peroxiredoxir PRDX1_HUM/ 22 kDa	TRUE
297	TRUE	Empty	40S ribosomæ RS6_HUMAN 29 kDa	TRUE
298	TRUE	Empty	Exportin-1 OS XPO1_HUMA 123 kDa	TRUE
299	TRUE	Empty	CD44 antigen CD44_HUMA 82 kDa	

300	TRUE	Empty	Cluster of Integrin ILF3_HUMAN	95 kDa	TRUE
301	TRUE	Empty	Integrin beta ITB1_HUMAN	88 kDa	TRUE
302	TRUE	Empty	Leucine-rich ILPPRC_HUMAN	158 kDa	TRUE
303	TRUE	Empty	Cluster of Ras RAB10_HUMAN	23 kDa	TRUE
304	TRUE	Empty	40S ribosomal RS23_HUMAN	16 kDa	
305	TRUE	Empty	Proliferation- PA2G4_HUMAN	44 kDa	
306	TRUE	Empty	Aldose reductase ALDR_HUMAN	36 kDa	
307	TRUE	Empty	Destrin OS=H DEST_HUMAN	19 kDa	TRUE
308	TRUE	Empty	Cluster of Cyc CD2A1_HUMAN	17 kDa	TRUE
309	TRUE	Empty	Cytochrome c COX5B_HUMAN	14 kDa	
310	TRUE	Empty	Basigin OS=H BASI_HUMAN	42 kDa	
311	TRUE	Empty	Clathrin light CLCA_HUMAN	27 kDa	
312	TRUE	Empty	Polyadenylation PABP3_HUMAN	70 kDa	TRUE
313	TRUE	Empty	Lysophosphatidyl PCAT1_HUMAN	59 kDa	
314	TRUE	Empty	Gelsolin OS=H GELS_HUMAN	86 kDa	
315	TRUE	Empty	TATA-binding RBP56_HUMAN	62 kDa	TRUE
316	TRUE	Empty	Alpha-fetoprotein FETA_HUMAN	69 kDa	TRUE
317	TRUE	Empty	Hepatoma-derived HDGF_HUMAN	27 kDa	TRUE
318	TRUE	Empty	Eukaryotic transcription IF4G1_HUMAN	175 kDa	TRUE
319	TRUE	Empty	Splicing factor SF3B1_HUMAN	146 kDa	TRUE
320	TRUE	Empty	Cluster of Prc PSA7_HUMAN	28 kDa	TRUE
321	TRUE	Empty	Cluster of U1 SNRPA_HUMAN	31 kDa	TRUE
322	TRUE	Empty	Apoptotic chromosome ACINU_HUMAN	152 kDa	
323	TRUE	Empty	Deoxyuridine DUT_HUMAN	27 kDa	
324	TRUE	Empty	Malate dehydrogenase MDHC_HUMAN	36 kDa	
325	TRUE	Empty	Phosphate carrier MPCP_HUMAN	40 kDa	TRUE
326	TRUE	Empty	Prohibitin OS PHB_HUMAN	30 kDa	
327	TRUE	Empty	Cluster of Pol PTBP1_HUMAN	57 kDa	TRUE
328	TRUE	Empty	Glycogen phosphorylase PYGL_HUMAN	97 kDa	TRUE
329	TRUE	Empty	Heterogeneous ROA3_HUMAN	40 kDa	TRUE
330	TRUE	Empty	Serine/arginine SRSF6_HUMAN	40 kDa	TRUE
331	TRUE	Empty	Tight junction ZO2_HUMAN	134 kDa	TRUE
332	TRUE	Empty	Cysteine and CSRP1_HUMAN	21 kDa	
333	TRUE	Empty	Cluster of Put LC7L2_HUMAN	47 kDa	TRUE
334	TRUE	Empty	Coatomer subunit COPD_HUMAN	57 kDa	
335	TRUE	Empty	Sulfide:quinone SQRD_HUMAN	50 kDa	
336	TRUE	Empty	T-complex protein TCPH_HUMAN	59 kDa	TRUE
337	TRUE	Empty	Proteasome subunit PSA1_HUMAN	30 kDa	
338	TRUE	Empty	60S ribosomal RL35A_HUMAN	13 kDa	
339	TRUE	Empty	NAD(P)H dehydrogenase NQO1_HUMAN	31 kDa	
340	TRUE	Empty	Cullin-associated CAND1_HUMAN	136 kDa	TRUE
341	TRUE	Empty	Importin subunit IMB1_HUMAN	97 kDa	
342	TRUE	Empty	Galectin-3 OS LEG3_HUMAN	26 kDa	
343	TRUE	Empty	Leucine-rich repeat LRC59_HUMAN	35 kDa	

344	TRUE	Empty	Nucleobindin NUCB2_HUM	50 kDa	TRUE
345	TRUE	Empty	Protein trans SC23A_HUM	86 kDa	TRUE
346	TRUE	Empty	Vacuolar prot VPS35_HUM	92 kDa	
347	TRUE	Empty	Histone H2A. H2AV_HUMA	14 kDa	TRUE
348	TRUE	Empty	Heterogeneo HNRPD_HUM	38 kDa	TRUE
349	TRUE	Empty	CD166 antigen CD166_HUM	65 kDa	
350	TRUE	Empty	Coatomer sul COPG1_HUM	98 kDa	TRUE
351	TRUE	Empty	Double-stran DSRAD_HUM	136 kDa	
352	TRUE	Empty	Hypoxanthine HPRT_HUMA	25 kDa	TRUE
353	TRUE	Empty	60S ribosome RL10A_HUM	25 kDa	TRUE
354	TRUE	Empty	Tumor protein TPD54_HUM	22 kDa	TRUE
355	TRUE	Empty	Voltage-depe VDAC2_HUM	32 kDa	TRUE
356	TRUE	Empty	Hematologic HN1L_HUMA	20 kDa	
357	TRUE	Empty	AP-1 complex AP1G1_HUM	91 kDa	
358	TRUE	Empty	Complement CO3_HUMAN	187 kDa	TRUE
359	TRUE	Empty	DnaJ homolog DNJB1_HUM	38 kDa	TRUE
360	TRUE	Empty	Dolichyl-diph OST48_HUM	51 kDa	
361	TRUE	Empty	60S ribosome RL38_HUMA	18 kDa	
362	TRUE	Empty	Transferrin re TFR1_HUMA	85 kDa	TRUE
363	TRUE	Empty	WD repeat-co WDR1_HUM	66 kDa	
364	TRUE	Empty	Inorganic pyr IPYR_HUMAN	33 kDa	TRUE
365	TRUE	Empty	Cluster of AP AP2A1_HUM	108 kDa	TRUE
366	TRUE	Empty	E3 ubiquitin-1 TRIPC_HUMA	220 kDa	
367	TRUE	Empty	Flavin reduct BLVRB_HUM	22 kDa	
368	TRUE	Empty	26S protease PSMD2_HUM	100 kDa	
369	TRUE	Empty	Tyrosine-prot PTN1_HUMA	50 kDa	
370	TRUE	Empty	Signal recogn SRP14_HUM	15 kDa	
371	TRUE	Empty	Activated RN TCP4_HUMA	14 kDa	
372	TRUE	Empty	Actin-related ARPC4_HUM	20 kDa	
373	TRUE	Empty	CAD protein (PYR1_HUMA)	243 kDa	TRUE
374	TRUE	Empty	Brain acid sol BASP1_HUM	23 kDa	TRUE
375	TRUE	Empty	ATP-depende DHX9_HUMA	141 kDa	TRUE
376	TRUE	Empty	Hypoxia up-reg HYOU1_HUM	111 kDa	TRUE
377	TRUE	Empty	Phosphoserine SERC_HUMA	40 kDa	TRUE
378	TRUE	Empty	Heterogeneo HNRH3_HUM	37 kDa	
379	TRUE	Empty	Nuclear auto NASP_HUMA	85 kDa	TRUE
380	TRUE	Empty	Glutathione re GSHR_HUMA	56 kDa	
381	TRUE	Empty	Macrophage MIF_HUMAN	12 kDa	
382	TRUE	Empty	Sorting nexin SNX12_HUM	20 kDa	TRUE
383	TRUE	Empty	Cluster of Chi CBX3_HUMA	21 kDa	TRUE
384	TRUE	Empty	T-complex protein TCPB_HUMA	57 kDa	
385	TRUE	Empty	THO complex THOC4_HUM	27 kDa	
386	TRUE	Empty	Peroxiredoxin PRDX5_HUM	22 kDa	
387	TRUE	Empty	Procollagen gamma GT251_HUM	72 kDa	

388	TRUE	Empty	FACT comple:SSRP1_HUM/81 kDa	TRUE
389	TRUE	Empty	Myristoylatec MARCS_HUM 32 kDa	
390	TRUE	Empty	B-cell receptc BAP31_HUM.28 kDa	
391	TRUE	Empty	Glutathione S GSTP1_HUM/23 kDa	
392	TRUE	Empty	Cytoplasmic c ACOC_HUMA98 kDa	TRUE
393	TRUE	Empty	6-phosphofru K6PP_HUMA186 kDa	
394	TRUE	Empty	Nucleoprotei TPR_HUMAN 267 kDa	TRUE
395	TRUE	Empty	Nucleoside diNDKA_HUMA17 kDa	TRUE
396	TRUE	Empty	Insulin-like gr IBP7_HUMAN29 kDa	
397	TRUE	Empty	WW domain- WBP11_HUM 70 kDa	TRUE
398	TRUE	Empty	Tight junctior ZO1_HUMAN195 kDa	TRUE
399	TRUE	Empty	Thyroid horm TR150_HUM/109 kDa	TRUE
400	TRUE	Empty	ATP synthase ATP5J_HUMA13 kDa	
401	TRUE	Empty	Immortalizati IMUP_HUMA11 kDa	TRUE
402	TRUE	Empty	Ataxin-10 OS: ATX10_HUM/53 kDa	
403	TRUE	Empty	Trifunctional ECHA_HUMA83 kDa	
404	TRUE	Empty	Cluster of Ras RB11A_HUM.24 kDa	TRUE
405	TRUE	Empty	40S ribosomæ RS28_HUMA18 kDa	
406	TRUE	Empty	High mobility HMGA1_HUN 12 kDa	TRUE
407	TRUE	Empty	SH3 domain-ISH3L1_HUM/13 kDa	
408	TRUE	Empty	NADH-cytoch NB5R3_HUM 34 kDa	
409	TRUE	Empty	Epidermal grc EGFR_HUMA 134 kDa	
410	TRUE	Empty	Protein SET CSET_HUMAN 33 kDa	
411	TRUE	Empty	Endoplasmic ERP29_HUM/29 kDa	
412	TRUE	Empty	Cathepsin D (CATD_HUMA45 kDa	
413	TRUE	Empty	Prothymosin PTMA_HUMA12 kDa	
414	TRUE	Empty	Acidic leucine AN32A_HUM 29 kDa	TRUE
415	TRUE	Empty	Dihydrolipoyl ODO2_HUM/49 kDa	
416	TRUE	Empty	60S ribosomæ RL12_HUMA118 kDa	
417	TRUE	Empty	Coatomer sul COPB2_HUM 102 kDa	
418	TRUE	Empty	Phenylalanin c SYFA_HUMA158 kDa	
419	TRUE	Empty	Barrier-to-au BAF_HUMAN 10 kDa	
420	TRUE	Empty	Annexin A8 CANXA8_HUM 37 kDa	
421	TRUE	Empty	ATP synthase ATPG_HUMA33 kDa	
422	TRUE	Empty	Heterochrom HP1B3_HUM.61 kDa	
423	TRUE	Empty	Nascent poly NACA_HUMA23 kDa	
424	TRUE	Empty	Polyadenylat PABP4_HUM.71 kDa	TRUE
425	TRUE	Empty	Vesicle-traffic SC22B_HUM/25 kDa	
426	TRUE	Empty	Transmembr c TMM43_HUN45 kDa	
427	TRUE	Empty	Cluster of His SYHC_HUMA 57 kDa	TRUE
428	TRUE	Empty	Protein diaph DIAP1_HUM/141 kDa	TRUE
429	TRUE	Empty	Protein CYR6: CYR61_HUM/42 kDa	
430	TRUE	Empty	Cluster of Se c SEPT7_HUM/51 kDa	TRUE
431	TRUE	Empty	40S ribosomæ RS17L_HUMA16 kDa	TRUE

432	TRUE	Empty	ATP-binding c ABCF1_HUM/96 kDa	
433	TRUE	Empty	Actin-binding ANLN_HUMA 124 kDa	TRUE
434	TRUE	Empty	Clathrin light CLCB_HUMA/25 kDa	
435	TRUE	Empty	Band 4.1-like E41L1_HUM/99 kDa	TRUE
436	TRUE	Empty	Bifunctional p PUR9_HUMA 65 kDa	TRUE
437	TRUE	Empty	Isoleucine--tF SYIC_HUMAN 145 kDa	TRUE
438	TRUE	Empty	Proteasome s PSB6_HUMA/25 kDa	
439	TRUE	Empty	Atlastin-3 OS: ATLA3_HUM/61 kDa	
440	TRUE	Empty	Coiled-coil dc CC124_HUM/26 kDa	
441	TRUE	Empty	Drebrin OS=F DREB_HUMA 71 kDa	
442	TRUE	Empty	Na(+)/H(+) ex NHRF1_HUM 39 kDa	
443	TRUE	Empty	Methionine a MAT2B_HUM 38 kDa	
444	TRUE	Empty	Endoplasmic ERMP1_HUM 100 kDa	
445	TRUE	Empty	Heterogeneo HNRH2_HUM 49 kDa	TRUE
446	TRUE	Empty	Growth facto GRB2_HUMA 25 kDa	
447	TRUE	Empty	Transcription TCAL3_HUM/23 kDa	
448	TRUE	Empty	CD109 antigen CD109_HUM.162 kDa	TRUE
449	TRUE	Empty	60S ribosome RL24_HUMA/18 kDa	TRUE
450	TRUE	Empty	Nicotinamide NNMT_HUM.30 kDa	
451	TRUE	Empty	Thioredoxin c TXD17_HUM.14 kDa	
452	TRUE	Empty	A-kinase anch AKA12_HUM.191 kDa	
453	TRUE	Empty	Nucleolar RN. DDX21_HUM 87 kDa	TRUE
454	TRUE	Empty	Microtubule- MAP1B_HUM 271 kDa	TRUE
455	TRUE	Empty	Programmed PDC6/1_HUM/96 kDa	
456	TRUE	Empty	Thioredoxin-c PRDX3_HUM.28 kDa	
457	TRUE	Empty	Ubiquitin carl UBP5_HUMA 96 kDa	TRUE
458	TRUE	Empty	Macrophage- CAPG_HUMA 38 kDa	TRUE
459	TRUE	Empty	Protein S100- S10AD_HUM.11 kDa	
460	TRUE	Empty	Very-long-ch: TECR_HUMA/36 kDa	TRUE
461	TRUE	Empty	Nicotinamide NAMPT_HUM 56 kDa	
462	TRUE	Empty	PDZ and LIM PDLI5_HUMA 64 kDa	
463	TRUE	Empty	Eukaryotic pe ERF1_HUMA/49 kDa	TRUE
464	TRUE	Empty	Importin sub IMA1_HUMA 58 kDa	TRUE
465	TRUE	Empty	Coatomer sul COPB_HUMA 107 kDa	
466	TRUE	Empty	26S proteaso PSMD3_HUM 61 kDa	
467	TRUE	Empty	Proteasome s PSA3_HUMA/28 kDa	TRUE
468	TRUE	Empty	Cluster of Fra FXR1_HUMA/70 kDa	TRUE
469	TRUE	Empty	Coatomer sul COPA_HUMA 138 kDa	TRUE
470	TRUE	Empty	Myb-binding MBB1A_HUM 149 kDa	TRUE
471	TRUE	Empty	RNA-binding RBM8A_HUM 20 kDa	
472	TRUE	Empty	60S ribosome RL18A_HUM/21 kDa	
473	TRUE	Empty	60S ribosome RL7A_HUMA/30 kDa	TRUE
474	TRUE	Empty	Translocator TSPOA_HUM.19 kDa	
475	TRUE	Empty	Phenylalanine SYFB_HUMA/66 kDa	

476	TRUE	Empty	RuvB-like 2 O RUVB2_HUM 51 kDa	
477	TRUE	Empty	Calcium-bind SCMC1_HUM 53 kDa	
478	TRUE	Empty	60S ribosomæ RL27A_HUM/ 17 kDa	
479	TRUE	Empty	ATP-depende RECQ1_HUM 73 kDa	
480	TRUE	Empty	Microtubule- MARE1_HUM 30 kDa	TRUE
481	TRUE	Empty	Mesencephal MANF_HUM/ 21 kDa	
482	TRUE	Empty	Ras-related p RAB7A_HUM 23 kDa	TRUE
483	TRUE	Empty	Ubiquitin carl UCHL1_HUM 25 kDa	
484	TRUE	Empty	PC4 and SFRS PSIP1_HUMA 60 kDa	TRUE
485	TRUE	Empty	Phosphatidyl- PEBP1_HUM/ 21 kDa	TRUE
486	TRUE	Empty	EH domain-cç EHD2_HUMA 61 kDa	TRUE
487	TRUE	Empty	Putative pre-i DHX15_HUM 91 kDa	
488	TRUE	Empty	Integrin alphæ ITA3_HUMAN 117 kDa	
489	TRUE	Empty	Major vault p MVP_HUMA/ 99 kDa	
490	TRUE	Empty	PDZ and LIM PDLI1_HUMA 36 kDa	TRUE
491	TRUE	Empty	SAP domain-c SARNP_HUM 24 kDa	TRUE
492	TRUE	Empty	Eukaryotic tra EIF3C_HUMA 105 kDa	
493	TRUE	Empty	26S proteaso PSD11_HUM/ 47 kDa	
494	TRUE	Empty	RNA-binding RBM14_HUM 69 kDa	TRUE
495	TRUE	Empty	60S ribosomæ RL17_HUMA/ 21 kDa	TRUE
496	TRUE	Empty	Latent-transfi LTBP2_HUM/ 195 kDa	
497	TRUE	Empty	Pre-mRNA-pr PRP8_HUMA/ 274 kDa	
498	TRUE	Empty	RuvB-like 1 O RUVB1_HUM 50 kDa	TRUE
499	TRUE	Empty	26S proteaso PSMD8_HUM 40 kDa	
500	TRUE	Empty	Probable ATP DDX17_HUM 80 kDa	TRUE
501	TRUE	Empty	Eukaryotic tra IF5_HUMAN 49 kDa	
502	TRUE	Empty	Testin OS=Ho TES_HUMAN 48 kDa	TRUE
503	TRUE	Empty	Tubulin-speci TBCA_HUMA 13 kDa	
504	TRUE	Empty	Probable ATP DDX5_HUMA 69 kDa	TRUE
505	TRUE	Empty	Ribonucleosic RIR1_HUMAN 90 kDa	TRUE
506	TRUE	Empty	Cytosolic acyl BACH_HUMA 42 kDa	
507	TRUE	Empty	Vesicular inte LMAN2_HUM 40 kDa	
508	TRUE	Empty	SYNE2_HUM/ SYNE2_HUM/ ?	TRUE
509	TRUE	Empty	Cluster of Ser PAK2_HUMA 58 kDa	TRUE
510	TRUE	Empty	Vacuolar proi VPS29_HUM/ 21 kDa	
511	TRUE	Empty	Asparagine--t SYNC_HUMA 63 kDa	TRUE
512	TRUE	Empty	Very long-chæ ACADV_HUM 70 kDa	TRUE
513	TRUE	Empty	26S protease PRS8_HUMA/ 46 kDa	TRUE
514	TRUE	Empty	Sorting nexin SNX1_HUMA 59 kDa	TRUE
515	TRUE	Empty	Protein-L-isoç PIMT_HUMA 25 kDa	
516	TRUE	Empty	Acetyl-CoA ac THIC_HUMA/ 41 kDa	
517	TRUE	Empty	DNA damage DDB1_HUMA 127 kDa	
518	TRUE	Empty	Calponin-3 O: CNN3_HUMA 36 kDa	TRUE
519	TRUE	Empty	U2 small nucl RU2A_HUMA 28 kDa	

520	TRUE	Empty	Actin-related ARP2_HUMA 45 kDa	
521	TRUE	Empty	Ras-related p RAP1B_HUM. 21 kDa	TRUE
522	TRUE	Empty	Transcription TCRG1_HUM. 124 kDa	
523	TRUE	Empty	Ras suppressor RSU1_HUMA 32 kDa	
524	TRUE	Empty	AP-3 complex AP3B1_HUM. 121 kDa	TRUE
525	TRUE	Empty	26S proteasome PSD12_HUM. 53 kDa	
526	TRUE	Empty	Ubiquitin-conjugating UBE2N_HUM 17 kDa	TRUE
527	TRUE	Empty	Septin-2 OS=HSEPT2_HUM. 41 kDa	TRUE
528	TRUE	Empty	Transcription TIF1B_HUMA 89 kDa	
529	TRUE	Empty	Actin-related ARPC2_HUM. 34 kDa	TRUE
530	TRUE	Empty	Ubiquitin thiolase OTUB1_HUM 31 kDa	
531	TRUE	Empty	Eukaryotic translation IF2P_HUMAN 139 kDa	
532	TRUE	Empty	Collagen alpha1(CO) COGA1_HUM 158 kDa	TRUE
533	TRUE	Empty	Small EDRK-related SERF2_HUM. 7 kDa	TRUE
534	TRUE	Empty	Cluster of N-ethylmaleimide-sensitive NAA10_HUM 26 kDa	TRUE
535	TRUE	Empty	Nexilin OS=H1 NEXN_HUMA 81 kDa	TRUE
536	TRUE	Empty	Heterogeneous nuclear HNRL1_HUM. 96 kDa	
537	TRUE	Empty	4F2 cell-surface 4F2_HUMAN 68 kDa	TRUE
538	TRUE	Empty	Adipocyte plasma APMAP_HUM 46 kDa	
539	TRUE	Empty	Ubiquitin carboxyl UBP14_HUM. 56 kDa	
540	TRUE	Empty	26S protease PRS6A_HUM. 49 kDa	
541	TRUE	Empty	Lysosome-associated LAMP2_HUM 45 kDa	
542	TRUE	Empty	Eukaryotic translation IF2A_HUMAN 36 kDa	
543	TRUE	Empty	Trans-Golgi network TGON2_HUM 51 kDa	
544	TRUE	Empty	26S protease PRS7_HUMAN 49 kDa	
545	TRUE	Empty	Unconventional MYO1C_HUM 122 kDa	TRUE
546	TRUE	Empty	Interleukin-1 beta IL18_HUMAN 22 kDa	
547	TRUE	Empty	A-kinase anchoring AKAP2_HUM. 95 kDa	TRUE
548	TRUE	Empty	Lactoylglutathione LGUL_HUMA 21 kDa	
549	TRUE	Empty	Integrin beta-4 ITB4_HUMAN 202 kDa	
550	TRUE	Empty	NSFL1 cofactor NSF1C_HUM. 41 kDa	
551	TRUE	Empty	40S ribosomal protein RS20_HUMAN 13 kDa	
552	TRUE	Empty	Dolichyl-diphosphate RPN2_HUMA 69 kDa	TRUE
553	TRUE	Empty	Peptidyl-prolyl FKBP1A_HUM. 12 kDa	TRUE
554	TRUE	Empty	Twinfilin-1 OS=H1 TWF1_HUMA 40 kDa	
555	TRUE	Empty	Laminin subunit LAMA5_HUM 400 kDa	
556	TRUE	Empty	Nucleolar protein NOP58_HUM 60 kDa	
557	TRUE	Empty	Nuclear migrin NUDC_HUM. 38 kDa	TRUE
558	TRUE	Empty	Dolichyl-diphosphate STT3A_HUM. 81 kDa	TRUE
559	TRUE	Empty	dCTP pyrophosphatase DCTP1_HUM. 19 kDa	
560	TRUE	Empty	Reticulocalbin RCN2_HUMA 37 kDa	
561	TRUE	Empty	Pyridoxal kinase PDXK_HUMA 35 kDa	
562	TRUE	Empty	NADPH-dependent cytochrome NCPR_HUMA 77 kDa	
563	TRUE	Empty	DNA (cytosine) DNMT1_HUM 183 kDa	TRUE

564	TRUE	Empty	S-adenosylmethionine METK2_HUMAN 44 kDa	TRUE
565	TRUE	Empty	Cell division cycle CDC5L_HUMAN 92 kDa	TRUE
566	TRUE	Empty	UTP20_HUMAN, UTP20_HUMAN, ?	TRUE
567	TRUE	Empty	Ribosome maturation SBDS_HUMAN 29 kDa	
568	TRUE	Empty	Cluster of Prickle PSA4_HUMAN 29 kDa	TRUE
569	TRUE	Empty	26S proteasome PSMD6_HUMAN 46 kDa	
570	TRUE	Empty	Electron transport ETFB_HUMAN 28 kDa	
571	TRUE	Empty	U6 snRNA-associated LSM3_HUMAN 12 kDa	
572	TRUE	Empty	Fibrinogen gamma FIBG_HUMAN 52 kDa	
573	TRUE	Empty	Vesicle-fusion NSF_HUMAN 83 kDa	
574	TRUE	Empty	Eukaryotic translation IF6_HUMAN 27 kDa	TRUE
575	TRUE	Empty	Ras GTPase-activator G3BP1_HUMAN 52 kDa	TRUE
576	TRUE	Empty	Alcohol dehydrogenase AK1A1_HUMAN 37 kDa	
577	TRUE	Empty	Secernin-1 Olfactin SCR1_HUMAN 46 kDa	TRUE
578	TRUE	Empty	Cluster of AP-2 AP2B1_HUMAN 105 kDa	TRUE
579	TRUE	Empty	Cluster of Tumor TMOD3_HUMAN 40 kDa	TRUE
580	TRUE	Empty	Drebrin-like protein DBNL_HUMAN 48 kDa	
581	TRUE	Empty	RNA-binding protein FUS_HUMAN 53 kDa	TRUE
582	TRUE	Empty	60S ribosomal protein RL18_HUMAN 22 kDa	
583	TRUE	Empty	Sorting and assembly SAM50_HUMAN 52 kDa	TRUE
584	TRUE	Empty	ERO1-like protein ERO1A_HUMAN 54 kDa	
585	TRUE	Empty	Cytochrome b5 QCR1_HUMAN 53 kDa	
586	TRUE	Empty	Amine oxidase AOFA_HUMAN 60 kDa	
587	TRUE	Empty	Cluster of GTPase SAR1A_HUMAN 22 kDa	TRUE
588	TRUE	Empty	Calponin-2 Olfactin CNN2_HUMAN 34 kDa	TRUE
589	TRUE	Empty	RNA-binding protein RALY_HUMAN 32 kDa	
590	TRUE	Empty	Actin-related ARP3_HUMAN 47 kDa	
591	TRUE	Empty	Insulin-like growth factor IF2B2_HUMAN 66 kDa	TRUE
592	TRUE	Empty	40S ribosomal protein RS11_HUMAN 18 kDa	
593	TRUE	Empty	COP9 signalosome CSN4_HUMAN 46 kDa	
594	TRUE	Empty	UBX domain-containing protein UBXN1_HUMAN 33 kDa	TRUE
595	TRUE	Empty	Hippocalcin-like protein HPCL1_HUMAN 22 kDa	
596	TRUE	Empty	Collagen alpha chain CO4A5_HUMAN 161 kDa	
597	TRUE	Empty	Elongation factor EF1D_HUMAN 31 kDa	TRUE
598	TRUE	Empty	Heterogeneous nuclear protein HNRPR_HUMAN 71 kDa	TRUE
599	TRUE	Empty	Cleavage stimulation factor CSTF2_HUMAN 61 kDa	TRUE
600	TRUE	Empty	Long-chain-fatty acid ACSL1_HUMAN 78 kDa	TRUE
601	TRUE	Empty	ATP synthase ATPD_HUMAN 17 kDa	TRUE
602	TRUE	Empty	DnaJ homologous protein DNJC9_HUMAN 30 kDa	
603	TRUE	Empty	Palladin OS=H PALLD_HUMAN 151 kDa	TRUE
604	TRUE	Empty	Cytoplasmic protein CYFP1_HUMAN 145 kDa	TRUE
605	TRUE	Empty	Cell surface glycoprotein MUC18_HUMAN 72 kDa	
606	TRUE	Empty	Glycerol-3-phosphate GPDM_HUMAN 81 kDa	
607	TRUE	Empty	Nicastrin OS=H NICA_HUMAN 78 kDa	

608	TRUE	Empty	39S ribosomal RPS38_HUMAN 45 kDa	
609	TRUE	Empty	RNA-binding RBM12_HUMAN 97 kDa	TRUE
610	TRUE	Empty	Cluster of sperm MRCKG_HUMAN ?	TRUE
611	TRUE	Empty	Double-strand STAU1_HUMAN 63 kDa	TRUE
612	TRUE	Empty	Protein PRRC PRC2A_HUMAN 229 kDa	
613	TRUE	Empty	Transgelin OSGTAGL_HUMAN 23 kDa	
614	TRUE	Empty	Cluster of EHD EHD1_HUMAN 61 kDa	TRUE
615	TRUE	Empty	Actin-binding ABLM1_HUMAN 88 kDa	
616	TRUE	Empty	ATP synthase ATP5L_HUMAN 11 kDa	TRUE
617	TRUE	Empty	Splicing factor U2AF2_HUMAN 54 kDa	
618	TRUE	Empty	Isocitrate dehydrogenase IDHP_HUMAN 51 kDa	TRUE
619	TRUE	Empty	Sortilin OS=H SORT_HUMAN 92 kDa	TRUE
620	TRUE	Empty	Leukotriene 4-LKHA4_HUMAN 69 kDa	
621	TRUE	Empty	Polyadenylation PABP2_HUMAN 33 kDa	
622	TRUE	Empty	Cluster of Trans RHOA_HUMAN 22 kDa	TRUE
623	TRUE	Empty	Isovaleryl-CoA IVD_HUMAN 46 kDa	
624	TRUE	Empty	Cluster of E3 RBP2_HUMAN 358 kDa	TRUE
625	TRUE	Empty	Eukaryotic translation EIF3J_HUMAN 29 kDa	
626	TRUE	Empty	Gem-associated GEMI5_HUMAN 169 kDa	
627	TRUE	Empty	5'-nucleotidase 5NTD_HUMAN 63 kDa	TRUE
628	TRUE	Empty	Transcription ELOB_HUMAN 13 kDa	
629	TRUE	Empty	Thioredoxin-related TMX1_HUMAN 32 kDa	
630	TRUE	Empty	PEST proteolysis PCNP_HUMAN 19 kDa	
631	TRUE	Empty	Alpha/beta helix ABHEB_HUMAN 22 kDa	
632	TRUE	Empty	Cluster of Dyx DYN2_HUMAN 98 kDa	TRUE
633	TRUE	Empty	Protein FAM1F136A_HUMAN 16 kDa	
634	TRUE	Empty	DnaJ homolog DJB11_HUMAN 41 kDa	
635	TRUE	Empty	Probable helicase SETX_HUMAN 303 kDa	
636	TRUE	Empty	Lysosomal alpha MA2B1_HUMAN 114 kDa	TRUE
637	TRUE	Empty	Tryptophan-- SYWC_HUMAN 53 kDa	
638	TRUE	Empty	Serpin B6 OS= SPB6_HUMAN 43 kDa	TRUE
639	TRUE	Empty	Coactosin-like COTL1_HUMAN 16 kDa	
640	TRUE	Empty	Plakophilin-2 PKP2_HUMAN 97 kDa	
641	TRUE	Empty	Heterogeneous HNRPF_HUMAN 46 kDa	TRUE
642	TRUE	Empty	Purine nucleoside PNPH_HUMAN 32 kDa	
643	TRUE	Empty	Probable ATPase DDX6_HUMAN 54 kDa	
644	TRUE	Empty	Tubulin-foldin TBCB_HUMAN 27 kDa	
645	TRUE	Empty	PRKC apoptotic PAWR_HUMAN 37 kDa	TRUE
646	TRUE	Empty	Enoyl-CoA hydratase ECHM_HUMAN 31 kDa	
647	TRUE	Empty	RNA-binding RNPS1_HUMAN 34 kDa	
648	TRUE	Empty	26S protease PRS6B_HUMAN 47 kDa	TRUE
649	TRUE	Empty	Regulator of transcription RMD1_HUMAN 36 kDa	TRUE
650	TRUE	Empty	Prefoldin subunit PFD2_HUMAN 17 kDa	
651	TRUE	Empty	Phosphoserine SERB_HUMAN 25 kDa	

652	TRUE	Empty	Signal peptid: SC11A_HUM/ 21 kDa	
653	TRUE	Empty	N(G),N(G)-dir DDAH1_HUM 31 kDa	TRUE
654	TRUE	Empty	Serine--tRNA SYSC_HUMA/ 59 kDa	
655	TRUE	Empty	Interferon-in: IFIT2_HUMA/ 55 kDa	TRUE
656	TRUE	Empty	Structural ma SMC4_HUMA 147 kDa	TRUE
657	TRUE	Empty	Copine-1 OS= CPNE1_HUM. 59 kDa	
658	TRUE	Empty	Integrin-link: ILK_HUMAN 51 kDa	
659	TRUE	Empty	Procollagen-I PLOD3_HUM. 85 kDa	
660	TRUE	Empty	Mannosyl-oli: MOGS_HUM/ 92 kDa	
661	TRUE	Empty	Melanoma-a: MAGD2_HUM 65 kDa	
662	TRUE	Empty	Aminopeptid: AMPN_HUM/ 110 kDa	
663	TRUE	Empty	Methionine-- SYMC_HUMA 101 kDa	
664	TRUE	Empty	Nucleosome : NP1L1_HUM/ 45 kDa	TRUE
665	TRUE	Empty	GDP-L-fucose FCL_HUMAN 36 kDa	
666	TRUE	Empty	Far upstream FUBP1_HUM. 68 kDa	TRUE
667	TRUE	Empty	Acylamino-ac ACPH_HUMA 81 kDa	
668	TRUE	Empty	Proteasomal ADRM1_HUM 42 kDa	
669	TRUE	Empty	sp P02461 C CO3A1_HUM ?	
670	TRUE	Empty	Annexin A4 CANXA4_HUM 36 kDa	TRUE
671	TRUE	Empty	Collagen alph CO6A1_HUM 109 kDa	
672	TRUE	Empty	Electron tran: ETFA_HUMA/ 35 kDa	
673	TRUE	Empty	SPEG_HUMA/ SPEG_HUMA ?	
674	TRUE	Empty	Tyrosine--tRNA SYYC_HUMA/ 59 kDa	
675	TRUE	Empty	39S ribosoma RM12_HUM/ 21 kDa	
676	TRUE	Empty	Serine/argini: SRSF9_HUM/ 26 kDa	TRUE
677	TRUE	Empty	Collagen alph CO2A1_HUM 142 kDa	TRUE
678	TRUE	Empty	Profilin-2 OS= PROF2_HUM. 15 kDa	
679	TRUE	Empty	AH receptor-i AIP_HUMAN 38 kDa	
680	TRUE	Empty	Adenylate kir KAD1_HUMA 22 kDa	
681	TRUE	Empty	Heterogeneo HNRPL_HUM 64 kDa	TRUE
682	TRUE	Empty	Sideroflexin-1 SFXN1_HUM/ 36 kDa	
683	TRUE	Empty	Probable rRNA EBP2_HUMA/ 35 kDa	
684	TRUE	Empty	Selenide, wat SPS1_HUMA/ 43 kDa	
685	TRUE	Empty	Peptidyl-pro: FKBP2_HUM/ 16 kDa	
686	TRUE	Empty	Collagen alph CO7A1_HUM 295 kDa	
687	TRUE	Empty	Collagen alph CO5A3_HUM 172 kDa	
688	TRUE	Empty	Threonine--t: SYTC_HUMA/ 83 kDa	TRUE
689	TRUE	Empty	Phosphatidyl: PIPNB_HUM/ 32 kDa	
690	TRUE	Empty	EMILIN-2 OS= EMIL2_HUM/ 116 kDa	
691	TRUE	Empty	Protein phos: PP1R7_HUM/ 42 kDa	
692	TRUE	Empty	sp P08572 C CO4A2_HUM ?	
693	TRUE	Empty	Glutathione S GSTK1_HUM/ 25 kDa	
694	TRUE	Empty	DMWD_HUM DMWD_HUM ?	TRUE
695	TRUE	Empty	Serine/threor PPP6_HUMA/ 35 kDa	TRUE

696	TRUE	Empty	F-actin-cappi CAZA1_HUM, 33 kDa	TRUE
697	TRUE	Empty	14-3-3 protei 1433S_HUM/ 28 kDa	TRUE
698	TRUE	Empty	Polyglutamin PQBP1_HUM 30 kDa	
699	TRUE	Empty	Phosphopant COAC_HUMA 22 kDa	
700	TRUE	Empty	Rho guanine ARHG7_HUM 90 kDa	
701	TRUE	Empty	Cluster of Pu1 RS26L_HUM/ 13 kDa	TRUE
702	TRUE	Empty	Alpha-centrai ACTZ_HUMA/ 43 kDa	TRUE
703	TRUE	Empty	Zinc finger pr ZN207_HUM, 51 kDa	
704	TRUE	Empty	sp Q32P51 FRA1L2_HUM/ ?	
705	TRUE	Empty	Huntingtin-in HYPK_HUMA 15 kDa	

END OF FILE

incubation with exosomes from *Opisthorchis viverrini* . Scaffold-generated report of the iTRAQ

atabase

opic)
:)
plex)
tion), +57 on C (Carbamidomethyl), +304 on Y (iTRAQ8plex)
ase (selected for Homo sapiens, 2013_09, 20272 entries)

xosomes_A): LFDR Model, Classifier data: Bayes, Good (50%) m:44.4/s:12.7 m:31.8/s:0.995 m:N
xosomes_B): LFDR Model, Classifier data: Bayes, Good (50%) m:45.3/s:12.8 m:31.8/s:0.983 m:N

opic)
:)
plex)
yro-Glu), -17 on n (Ammonia-loss), -17 on n (Gln->pyro-Glu), +16 on M (Oxidation), +57 on C (Ca

3_09 database

xosomes_A): LFDR Model, Classifier data: Bayes, Good (50%) m:41.4/s:6.69 m:3.25/s:1.08 m:0.3

xosomes_B): LFDR Model, Classifier data: Bayes, Good (50%) m:41.0/s:6.78 m:3.17/s:1.12 m:0.3

meters\unimod.xml

with protein cluster analysis

inimum

00220]; [0.000,0.00940,0.930,0.0590,0.00160]; [0.000,0.0188,0.931,0.0490,0.001000]; [0.000,0.

.72,0.794]

Kruskal-Wallis Taxonomy	Control	0.5h	3h	16h	
95% (< 0.000 unknown	0	0.8	-1.5	-2.2	
95% (< 0.000 unknown	0	-0.6	0.6	0.5	
95% (< 0.000 unknown	0.2	-0.1	0.6	0.5	
95% (< 0.000 unknown	0	0.5	0.3	0.6	
95% (< 0.000 unknown	0	1	-0.3	-0.1	
95% (< 0.000 unknown	0	0.3	0.5	0.7	
95% (< 0.000 unknown	-0.1	-0.5	0.8	0.7	
95% (< 0.000 unknown	-0.1	-0.6	0.3	0.4	
95% (< 0.000 unknown	0.1	-0.8	0.6	0.5	
95% (< 0.000 unknown	-0.1	-0.5	0.6	0.4	
95% (< 0.000 unknown	-0.1	-0.4	0.4	0.6	
95% (< 0.000 unknown	0.1	0.4	0.3	0.6	
95% (< 0.000 unknown	0	0	0.3	0.5	
95% (< 0.000 unknown	-0.1	-0.4	0.4	0.3	
95% (< 0.000 unknown	0.1	-0.4	0.7	0.6	
95% (< 0.000 unknown	0	0.3	0.2	0.4	
95% (< 0.000 unknown	0	0.5	-0.6	-0.6	
95% (< 0.000 unknown	0	-0.6	0.8	0.8	
95% (< 0.000 unknown	-0.2	0.6	-0.2	0	
95% (< 0.000 unknown	0	1	0	0.2	
95% (< 0.000 unknown	0	-0.1	0.3	0.2	
95% (< 0.000 unknown	0	-0.3	0.7	0.8	
95% (< 0.000 unknown	0.1	-0.1	0	0.1	
95% (< 0.000 unknown	0	-0.1	0.2	0.2	
95% (< 0.000 unknown	0	0.6	-1.1	-1.1	
95% (< 0.000 unknown	0	0.4	0.2	0.5	
95% (< 0.000 unknown	0	-0.5	0.7	0.5	
95% (< 0.000 unknown	0	-0.2	0.3	0.4	
95% (< 0.000 unknown	0	0.4	0	0.1	
95% (< 0.000 unknown	0	-0.4	-0.3	-0.5	
95% (< 0.000 unknown	0	-0.1	0.3	0.2	
95% (< 0.000 unknown	0	-0.6	0.8	0.6	
95% (< 0.000 unknown	0.1	0.4	0.1	0.1	
95% (< 0.000 unknown	0	-0.5	0.7	0.5	
95% (< 0.000 unknown	0	0.1	-0.1	-0.2	

95% (< 0.000 unknown	0	-0.2	0.8	0.7
95% (< 0.000 unknown	0	0.3	-0.1	-0.2
95% (< 0.000 unknown	0	0	0	0
95% (< 0.000 unknown	0	0.8	-1.2	-1.2
95% (< 0.000 unknown	0	-0.1	-0.4	-0.4
95% (< 0.000 unknown	0	-0.2	0.4	0.4
95% (< 0.000 unknown	0	0	0.1	0
95% (< 0.000 unknown	0	0.4	-0.4	-0.5
95% (< 0.000 unknown	0	0.7	-0.6	-0.4
95% (< 0.000 unknown	0	-0.5	0.2	0.1
95% (< 0.000 unknown	0	0.6	-1.7	-1.8
95% (< 0.000 unknown	0	0.7	-0.3	-0.3
95% (< 0.000 unknown	0	0.6	-0.4	-0.3
95% (< 0.000 unknown	0	0.8	0.1	0
95% (< 0.000 unknown	0	0.1	0.5	0.4
95% (< 0.000 unknown	0	1.2	-0.2	-0.2
95% (< 0.000 unknown	0	0.1	-0.9	-0.7
95% (< 0.000 unknown	0	0.8	-2.9	-2.8
95% (< 0.000 unknown	0	0	0.4	0.6
95% (< 0.000 unknown	0	0.3	0.3	0.2
95% (< 0.000 unknown	0	0.4	-0.5	-0.4
95% (< 0.000 unknown	0	0.5	-1	-1.2
95% (< 0.000 unknown	-0.1	0.6	-0.4	-0.2
95% (0.0013] unknown	0.1	0.3	0.3	0.3
95% (< 0.000 unknown	0.1	0.3	-0.8	-0.9
95% (< 0.000 unknown	0	-0.1	0.2	0.3
95% (< 0.000 unknown	0	-0.6	0.1	-0.1
95% (< 0.000 unknown	0	0.2	0	0.1
95% (< 0.000 unknown	0	0	-0.5	-0.6
95% (< 0.000 unknown	-0.1	0	0.3	0.3
95% (< 0.000 unknown	0	-0.2	0.6	0.6
95% (< 0.000 unknown	0	0	0.4	0.4
95% (< 0.000 unknown	0	0.6	0.1	0.1
95% (< 0.000 unknown	0	0.6	-1.3	-1.7
95% (< 0.000 unknown	0	-0.3	0.7	0.5
95% (< 0.000 unknown	0	0.1	-0.7	-0.9
95% (< 0.000 unknown	-0.1	-0.2	0.5	0.5
95% (< 0.000 unknown	0	0	0.5	0.7
95% (< 0.000 unknown	0	0.5	-1.5	-1.1
95% (< 0.000 unknown	-0.2	-0.5	0.6	0.5
95% (< 0.000 unknown	0	-0.2	0.5	0.5
95% (< 0.000 unknown	0	-0.5	0.6	0.5
95% (< 0.000 unknown	0	-0.1	0.6	0.6
95% (< 0.000 unknown	-0.1	-0.1	0.5	0.3

95% (< 0.000 unknown	0	-0.3	0.7	0.5
95% (< 0.000 unknown	0	0	-1.4	-1.4
95% (0.0011) unknown	0	0.3	-0.6	-0.6
95% (< 0.000 unknown	0.1	0.2	0.5	0.4
95% (< 0.000 unknown	0	0.2	0.3	0.3
95% (< 0.000 unknown	-0.1	0	0.7	0.7
95% (< 0.000 unknown	0	-0.1	0.1	-0.6
95% (< 0.000 unknown	0	0.4	-0.5	-0.3
95% (< 0.000 unknown	0	-0.5	0.6	0.6
95% (< 0.000 unknown	0	0	-0.4	-0.2
95% (< 0.000 unknown	0	-0.2	0.5	0.5
95% (< 0.000 unknown	0	-0.6	0.7	0.6
95% (< 0.000 unknown	0	-0.5	0.2	0
95% (< 0.000 unknown	0	0.2	0.4	0.4
95% (< 0.000 unknown	0	1.3	1	0.3
95% (0.040) unknown	0	0.5	0.6	0.4
95% (< 0.000 unknown	0	0.2	-1.8	-1.9
95% (< 0.000 unknown	0	0	0.7	0.6
95% (< 0.000 unknown	0	0.6	-1.6	-1.6
95% (< 0.000 unknown	0	0.8	-1.9	-2
95% (< 0.000 unknown	0	0.2	0.6	0.7
95% (< 0.000 unknown	0	-0.2	0.9	0.8
95% (< 0.000 unknown	0	0.2	-2.2	-2.3
95% (< 0.000 unknown	0	0.9	-1.2	-1
95% (< 0.000 unknown	0	0.1	0.2	0.3
95% (< 0.000 unknown	0	0.3	-1.1	-1
95% (< 0.000 unknown	0	0.5	-1.3	-1.3
95% (< 0.000 unknown	0	0.7	-1.5	-1.4
95% (< 0.000 unknown	0	0.3	0.6	0.4
95% (< 0.000 unknown	0	-0.4	0.7	0.5
95% (< 0.000 unknown	0	0.3	-0.5	-0.6
95% (< 0.000 unknown	0	-0.4	0.8	0.5
75% (0.14) unknown	0.2	0	0.2	0.2
95% (< 0.000 unknown	0	0	0.6	0.7
95% (< 0.000 unknown	-0.1	0.3	0.1	0.1
95% (< 0.000 unknown	0	0.6	0	-0.1
95% (< 0.000 unknown	0.1	0.4	-0.2	0
95% (< 0.000 unknown	0	0.4	-0.7	-0.9
95% (< 0.000 unknown	0	0.3	0	0
95% (< 0.000 unknown	0	0	0.5	0.7
95% (< 0.000 unknown	0	0.4	0.3	0.3
95% (< 0.000 unknown	0	-0.1	0.5	0.4
95% (< 0.000 unknown	0	-0.3	0.6	0.6
95% (< 0.000 unknown	0	0.4	-2.6	-2.6

95% (< 0.000 unknown	0	0.1	-0.1	-0.5
95% (< 0.000 unknown	0	0.4	-0.6	-0.6
95% (< 0.000 unknown	0	0	0.6	0.6
95% (< 0.000 unknown	0	0.4	-1.2	-1.2
95% (< 0.000 unknown	0	0.2	-1.6	-1.7
95% (< 0.000 unknown	0	0	0.6	0.5
95% (< 0.000 unknown	0	0	0.6	0.5
95% (< 0.000 unknown	0	0.5	-1.2	-1.2
95% (< 0.000 unknown	0	0.5	-1.3	-1.2
95% (< 0.000 unknown	0	-0.1	0.4	0.5
95% (< 0.000 unknown	0	0.1	0.5	0.4
95% (< 0.000 unknown	0	-0.4	0.7	0.6
95% (< 0.000 unknown	0	0.5	-0.8	-0.9
95% (< 0.000 unknown	0	0.2	0.2	0.1
95% (< 0.000 unknown	0	0	-1.3	-1.4
95% (< 0.000 unknown	0	0.4	-1.3	-1.1
95% (< 0.000 unknown	0	-0.4	0.7	0.5
95% (< 0.000 unknown	0.2	0.1	0.6	0.4
75% (0.065) unknown	0	-0.1	0.3	0.4
95% (< 0.000 unknown	0	0.4	-0.6	-0.7
95% (< 0.000 unknown	0	-0.3	0.3	0.2
95% (< 0.000 unknown	-0.1	0.1	0.6	0.7
95% (< 0.000 unknown	0	0.2	-0.4	-0.6
95% (< 0.000 unknown	0	0.5	0.3	0.2
95% (< 0.000 unknown	0	0.1	-0.2	-0.2
95% (< 0.000 unknown	0	0.1	0.4	0.4
95% (< 0.000 unknown	0	0.5	-2.1	-1.8
95% (< 0.000 unknown	0	0.6	0.3	0.4
95% (< 0.000 unknown	0	0	-0.1	-0.1
95% (< 0.000 unknown	0	-0.4	0.5	0.5
95% (< 0.000 unknown	0.1	-0.1	0.7	0.8
95% (< 0.000 unknown	0	-0.4	0.7	0.6
95% (< 0.000 unknown	0	0.4	0.6	0.6
95% (< 0.000 unknown	0	0.3	0.3	0.3
95% (0.023) unknown	0	-0.2	0.1	0.1
95% (< 0.000 unknown	0	0.2	-2.2	-2
95% (< 0.000 unknown	0	1.2	0.5	0.5
95% (< 0.000 unknown	0	0.4	0.4	0.6
95% (< 0.000 unknown	0	-0.1	-0.5	-0.6
95% (< 0.000 unknown	0	0.1	0.5	0.5
95% (< 0.000 unknown	0	0	0.5	0.3
95% (< 0.000 unknown	0	0.5	-2	-2
95% (< 0.000 unknown	0	0.8	-1.1	-1.3
95% (< 0.000 unknown	0	0.5	-1.1	-1.1

95% (0.0001(unknown	0	0.2	0.3	0.3
95% (< 0.000 unknown	0	-0.1	0.6	0.5
95% (< 0.000 unknown	-0.1	-0.2	0.4	0.6
95% (< 0.000 unknown	0	0	-0.3	-0.3
95% (< 0.000 unknown	0	0.5	-1	-0.9
95% (< 0.000 unknown	0	0.2	0.4	0.3
95% (< 0.000 unknown	-0.1	0.7	0.2	0.4
0% (NaN) unknown	No Values	No Values	No Values	No Values
95% (< 0.000 unknown	0	0.2	-0.3	-0.3
95% (< 0.000 unknown	0	-0.1	0.7	0.8
95% (0.0001!unknown	0	-0.2	0.5	0.6
95% (< 0.000 unknown	0	0.1	0.9	0.7
75% (0.092) unknown	-0.1	0.1	0.1	0.2
95% (< 0.000 unknown	0	0.1	0.5	0.4
95% (< 0.000 unknown	0	0.7	-0.6	-0.6
95% (< 0.000 unknown	0	0.5	0.1	0.2
95% (< 0.000 unknown	0	-0.1	0.2	0.2
95% (< 0.000 unknown	0	-0.8	0.9	0.2
95% (< 0.000 unknown	0	0.2	0.6	0
95% (< 0.000 unknown	0	0.3	-1.4	-1.8
95% (< 0.000 unknown	0	0.8	-0.4	-0.4
95% (< 0.000 unknown	0	0.7	-0.8	-0.9
95% (< 0.000 unknown	0	-0.3	0.8	0.7
95% (< 0.000 unknown	0	0.3	-0.7	-0.8
95% (< 0.000 unknown	0	-0.6	0.6	0.8
95% (< 0.000 unknown	0	0.4	-1.5	-1.7
95% (< 0.000 unknown	0	-0.4	0.6	0.5
95% (0.0009!unknown	0	0.1	0.3	-0.1
95% (< 0.000 unknown	0	-0.1	0.4	0.4
95% (< 0.000 unknown	0	-0.3	0.5	0.4
95% (< 0.000 unknown	0	-0.2	0.3	0.2
95% (< 0.000 unknown	0	0.8	-0.4	-0.6
95% (< 0.000 unknown	0	0.5	0	0
95% (< 0.000 unknown	0	-0.1	0.5	0.7
95% (< 0.000 unknown	0	0	0.5	0.7
95% (< 0.000 unknown	0	0.8	-1	-0.9
95% (< 0.000 unknown	0	0.1	0.5	0.5
95% (< 0.000 unknown	0.1	0	0.6	0.6
95% (< 0.000 unknown	0	-0.1	0.8	0.8
95% (0.0082)unknown	-0.1	0.3	0.4	0.5
95% (< 0.000 unknown	0	-0.5	0.9	0.8
95% (< 0.000 unknown	0	0.3	0.5	0.4
95% (< 0.000 unknown	0	0.2	0	0.1
95% (< 0.000 unknown	0	-0.6	-0.2	0.2

95% (< 0.000 unknown	0	0.7	-0.5	-0.5
95% (< 0.000 unknown	0.1	0.3	0.6	0.6
95% (< 0.000 unknown	0	0.2	-0.5	-0.6
0% (0.28) unknown	0	0.2	0.2	0.2
95% (0.0091) unknown	0	0.4	0.1	0.2
95% (< 0.000 unknown	0	0.4	-2	-2.1
95% (< 0.000 unknown	0	-0.3	0.2	0.3
95% (< 0.000 unknown	0	-0.1	0.5	0.5
95% (< 0.000 unknown	0	0.5	-0.7	-1.2
0% (0.11) unknown	0	0.3	0.3	0.3
95% (< 0.000 unknown	0	-0.5	0.6	0.4
95% (< 0.000 unknown	0	0.7	-0.1	-0.1
95% (< 0.000 unknown	-0.1	0.1	0.4	0.5
95% (< 0.000 unknown	0	-0.1	0.6	0.7
95% (< 0.000 unknown	-0.1	0	0.1	0.3
95% (< 0.000 unknown	0	-0.2	0.4	0
95% (< 0.000 unknown	0	-0.3	0.8	0.9
95% (< 0.000 unknown	0	0.1	0.5	0.6
95% (< 0.000 unknown	0	0.4	-0.9	-1
95% (< 0.000 unknown	0	0	0.9	1
95% (< 0.000 unknown	0	-0.6	-0.6	-0.3
95% (0.0012) unknown	0	0.5	0.4	0.3
95% (< 0.000 unknown	0	0.1	0.4	0.4
95% (< 0.000 unknown	0	1	0.9	0.8
95% (< 0.000 unknown	0	-0.6	0.8	0.6
95% (< 0.000 unknown	0	0	0.1	0
95% (< 0.000 unknown	0	-0.3	1	0.9
95% (< 0.000 unknown	0	0.1	-1.4	-1.6
95% (< 0.000 unknown	0.1	-0.1	0.3	0.6
95% (< 0.000 unknown	0	0.4	0.3	0.6
95% (0.021) unknown	0	-0.1	0	0.2
95% (0.0061) unknown	0	0	0.1	-0.2
95% (0.012) unknown	0	0.6	0.5	0.7
95% (< 0.000 unknown	0	0.4	-1.2	-1.3
95% (< 0.000 unknown	0	-0.3	0.4	0.4
95% (0.0019) unknown	0	0	0.5	0.4
95% (< 0.000 unknown	0	0.5	-1.2	-1.3
95% (< 0.000 unknown	0	-0.2	0.6	0.6
95% (< 0.000 unknown	0	0.8	-2.4	-2.4
95% (0.0086) unknown	0	0.1	0.3	0.2
95% (< 0.000 unknown	0	0.3	-0.5	-0.6
95% (< 0.000 unknown	0	0.9	0.2	0.2
95% (< 0.000 unknown	0	-0.2	0.4	0.3
95% (< 0.000 unknown	0	0	0.7	0.7

95% (< 0.000 unknown	0	0.3	-1.1	-1.1
95% (< 0.000 unknown	0	-0.5	0.3	0.1
95% (< 0.000 unknown	0	0	0.5	0.5
95% (< 0.000 unknown	0	0.4	0.2	0.4
95% (< 0.000 unknown	0	-0.1	0.6	0.5
95% (< 0.000 unknown	0	-0.2	0.6	0.7
95% (< 0.000 unknown	0	-0.3	0.8	0.7
95% (0.015) unknown	0	-0.2	-0.2	0
75% (0.047) unknown	0	-0.1	0	0.1
0% (0.076) unknown	0	0.5	0.3	0.1
95% (< 0.000 unknown	0	0	0.5	0.5
95% (< 0.000 unknown	0	0.1	-0.1	-0.1
95% (< 0.000 unknown	0	0.6	-2	-2
95% (0.0001) unknown	0	0.2	0.2	0.3
95% (< 0.000 unknown	0	0	0	0.1
95% (< 0.000 unknown	0	0	0.8	0.7
95% (< 0.000 unknown	-0.1	0.2	0.6	0.6
75% (0.12) unknown	0.1	0.4	0.6	0.4
95% (< 0.000 unknown	0	0	0.7	0.7
95% (< 0.000 unknown	0	0.1	0.6	0.5
95% (0.0035) unknown	-0.2	0.1	0.2	0.1
95% (< 0.000 unknown	0	-0.2	0.5	0.2
95% (0.0002) unknown	0	0.1	0.4	0.4
95% (0.0009) unknown	0	0.3	0.2	0.4
95% (< 0.000 unknown	0	0.2	-0.5	-0.5
95% (< 0.000 unknown	0	-0.2	1	0.7
95% (0.0004) unknown	0	-0.1	0.3	-0.1
95% (< 0.000 unknown	0	0	0.3	0.3
0% (0.75) unknown	0	1.1	0.4	0.5
95% (0.0001) unknown	0	0	0.6	0.6
95% (0.011) unknown	0	0.2	0.2	0.2
95% (< 0.000 unknown	0	0.1	-0.2	-0.1
95% (< 0.000 unknown	0	0	0.4	0.3
95% (< 0.000 unknown	0	0.2	-1.5	-1.3
95% (< 0.000 unknown	0	0.4	-0.4	-0.5
95% (< 0.000 unknown	-0.1	0.5	0.4	0.4
95% (< 0.000 unknown	0	0.2	0.1	0.1
95% (< 0.000 unknown	0	0.1	-0.4	-0.6
95% (< 0.000 unknown	0	0.2	0.6	0.7
95% (0.0005) unknown	0.1	0.6	0.5	0.2
95% (0.0001) unknown	0	0.2	0.1	0.2
95% (0.022) unknown	0	0.3	0.5	0.2
95% (< 0.000 unknown	0	-0.3	0.6	0.3
95% (< 0.000 unknown	0	0.1	-0.2	-0.2

95% (< 0.000 unknown	0	0.4	0.2	0.4
95% (< 0.000 unknown	0	-0.4	-0.1	-0.2
95% (0.040) unknown	0	0.2	0.6	0.4
95% (0.0013) unknown	0	0.2	0.5	0.4
95% (< 0.000 unknown	0	0.1	0.7	0.6
95% (< 0.000 unknown	0	0.3	0.5	0.4
95% (0.028) unknown	0	0.3	0.7	0.8
95% (< 0.000 unknown	0	-0.2	0	0
95% (< 0.000 unknown	0	1.2	-0.6	-0.4
95% (< 0.000 unknown	0	0.3	-1.6	-1.4
95% (0.0042) unknown	0	-0.1	-0.3	-0.2
95% (< 0.000 unknown	0	0.8	-1.1	-0.8
95% (< 0.000 unknown	0	0.6	0.2	0.4
95% (< 0.000 unknown	0	0.1	0.4	0.5
95% (0.0040) unknown	0	0.7	0.4	0.4
95% (< 0.000 unknown	0	0.8	-1.2	-0.9
95% (< 0.000 unknown	0	0.8	-0.9	-1.3
95% (< 0.000 unknown	0	0.9	-1	-1.2
75% (0.0054) unknown	0	0.3	0.4	0.2
95% (< 0.000 unknown	0	0.5	0.3	0.4
0% (0.15) unknown	0	0	-0.2	-0.1
95% (0.0089) unknown	0	-0.1	-0.3	-0.4
75% (0.069) unknown	0	1.1	0.9	0.9
95% (< 0.000 unknown	0	0.2	-0.4	-0.5
95% (< 0.000 unknown	0	-0.2	0.3	0.4
95% (< 0.000 unknown	-0.1	-0.3	0.6	0.7
95% (0.0041) unknown	0	0.2	0.2	0.2
95% (< 0.000 unknown	0.1	0.2	0.5	0.4
95% (< 0.000 unknown	0	-0.3	0.5	0.5
95% (< 0.000 unknown	0	0.5	0	0
95% (< 0.000 unknown	0	-0.2	0.1	0.1
95% (0.011) unknown	0	0.1	0.5	0.6
95% (< 0.000 unknown	0	0	-0.8	-0.5
95% (< 0.000 unknown	0	-0.1	0.4	0.6
95% (< 0.000 unknown	0	-0.1	0.3	0.3
95% (< 0.000 unknown	0	0.3	0.6	0.4
95% (0.0002) unknown	0	-0.1	0.4	0.4
95% (< 0.000 unknown	0	-0.1	0.8	0.8
95% (< 0.000 unknown	0	-0.2	0.9	0.8
95% (< 0.000 unknown	0	0.2	0.6	0.6
95% (< 0.000 unknown	0	0.3	0.3	0.1
95% (< 0.000 unknown	0	-0.3	0.3	0.1
95% (< 0.000 unknown	0	0.1	-0.2	0
95% (< 0.000 unknown	0	-0.4	0.5	0.5

95% (< 0.000 unknown	0	0.5	-1.8	-1.8
0% (0.11) unknown	0	0.1	0.1	0.1
0% (0.053) unknown	0	0.1	0.3	0.3
95% (< 0.000 unknown	0	0	0.5	0.6
95% (< 0.000 unknown	0	0.3	-0.6	-0.6
95% (< 0.000 unknown	0	-0.5	-1.1	-1.2
95% (< 0.000 unknown	0	-0.5	0.7	0.6
95% (< 0.000 unknown	0	0.3	0.6	0.5
95% (0.0001: unknown	0	-0.1	0.2	0.4
95% (< 0.000 unknown	0	-0.1	0.6	0.4
95% (< 0.000 unknown	0	0.1	-0.7	-0.6
95% (< 0.000 unknown	0	0.4	0.7	0.6
95% (< 0.000 unknown	0	0.7	-1.2	-1
75% (0.29) unknown	-0.1	0.2	0.5	0.5
95% (0.0004: unknown	0	0.1	0.9	0.2
95% (0.0013: unknown	0	0.5	0.3	0.3
95% (< 0.000 unknown	0	0.3	0.3	0.5
95% (0.0001: unknown	0	0.5	-0.5	-0.5
95% (< 0.000 unknown	0	-0.4	0.8	0.6
95% (< 0.000 unknown	0	0	0.3	-0.1
95% (< 0.000 unknown	0	0.7	0.5	-0.5
95% (< 0.000 unknown	0	0	0.5	0.6
0% (0.92) unknown	0	0	0	0
0% (0.17) unknown	0	0	-0.1	-0.1
95% (< 0.000 unknown	0	-0.3	0.6	0.5
95% (0.024) unknown	0	0	0.2	0.2
95% (< 0.000 unknown	0	-0.1	-0.1	0
95% (< 0.000 unknown	0	0.2	0	0.2
95% (< 0.000 unknown	0	-0.2	0.4	0.5
0% (0.12) unknown	-0.6	3.7	3.9	3.6
95% (< 0.000 unknown	0.1	0.5	-1.8	-2.1
95% (0.0026: unknown	0	0.1	0.4	0.5
0% (0.36) unknown	0	0.2	0	0
95% (< 0.000 unknown	-0.1	0.3	0.5	0.5
95% (< 0.000 unknown	0	0.3	-0.5	-0.3
95% (0.0002: unknown	0	0.2	-0.4	-0.5
95% (0.0023: unknown	0.1	0.2	0.6	0.5
95% (< 0.000 unknown	0	-0.4	0.3	0.2
0% (0.18) unknown	0	-0.2	0.1	0.2
95% (< 0.000 unknown	0	0.2	-0.7	-0.9
95% (< 0.000 unknown	0	0	0.4	0.2
95% (< 0.000 unknown	0	0.7	-0.7	-0.8
95% (< 0.000 unknown	0	0	0.1	0.2
95% (0.021) unknown	0	0	0.1	0.5

95% (< 0.000 unknown	0	0.1	0.5	0.6
95% (0.0054) unknown	0	0	-1.3	-1.2
0% (0.54) unknown	0	0.3	0.2	0
95% (< 0.000 unknown	0	-0.9	0.1	0.2
95% (< 0.000 unknown	0	0	0.5	0.5
95% (< 0.000 unknown	0	0.3	0.6	0.6
95% (0.0007) unknown	0	0.6	-0.2	0.1
95% (< 0.000 unknown	0	-0.2	0.2	0
95% (< 0.000 unknown	0	0.4	-1.2	-1.2
95% (< 0.000 unknown	0	-0.6	-0.3	-0.4
0% (0.12) unknown	-0.4	3.4	1.5	2.4
95% (0.0002) unknown	0	0.2	-0.1	0.3
95% (< 0.000 unknown	0	0.5	-2.1	-2
95% (< 0.000 unknown	0	-0.1	-0.6	-0.1
95% (< 0.000 unknown	-0.1	-0.1	0.4	0.3
95% (0.0017) unknown	0	-0.2	0.7	0.5
95% (0.026) unknown	0	-0.2	0.2	0.3
95% (< 0.000 unknown	0	0.9	-0.6	-0.6
95% (< 0.000 unknown	0	0.9	-1.2	-1.1
95% (0.0001) unknown	0	0.6	-1.2	-1.4
95% (< 0.000 unknown	0	-0.4	0.3	0.3
95% (< 0.000 unknown	0	0	0.5	0.5
95% (< 0.000 unknown	0	0.6	-1.3	-1.5
95% (< 0.000 unknown	0	0.2	-0.8	-0.8
95% (< 0.000 unknown	0	-0.5	-0.1	0
95% (< 0.000 unknown	0	0.8	-1.9	-2.2
95% (< 0.000 unknown	0	0.4	-0.9	-1
95% (0.019) unknown	0	0.2	0.8	0.8
95% (< 0.000 unknown	0	-0.5	0.4	0.3
0% (0.59) unknown	0	0.4	0.2	0.1
95% (0.048) unknown	0	-0.1	0.2	0.3
95% (< 0.000 unknown	0	0.3	-0.8	-1
0% (0.36) unknown	0.2	0	-0.1	0.2
95% (< 0.000 unknown	0	-0.1	0.4	0.6
95% (< 0.000 unknown	0	0.7	0.3	0.7
95% (< 0.000 unknown	0	0.4	-0.7	-0.6
0% (0.32) unknown	0	0.3	0.4	0.3
95% (< 0.000 unknown	0	-0.9	0.5	0.5
95% (0.0046) unknown	0	0.1	0.3	0.2
95% (0.0052) unknown	0	0.4	0	0.4
0% (0.28) unknown	0	0.3	0.2	0.2
95% (< 0.000 unknown	0	0.6	0	0.2
95% (< 0.000 unknown	0	-0.6	0.6	0.5
95% (< 0.000 unknown	0	0	0.6	0.4

95% (< 0.000 unknown	0	0.1	0.7	0.8
95% (< 0.000 unknown	0	-0.1	0.5	0.4
95% (< 0.000 unknown	0	0.6	-1	-1
95% (< 0.000 unknown	0.1	0.8	0.3	0.4
95% (< 0.000 unknown	-0.1	-0.2	0.5	0.4
95% (< 0.000 unknown	0	0.3	1	0.8
75% (0.026) unknown	0	0.3	0	-0.2
95% (< 0.000 unknown	0	0.1	0.4	0.8
95% (< 0.000 unknown	0	0.7	-0.8	-0.9
95% (< 0.000 unknown	0	-0.3	-0.4	-0.3
95% (< 0.000 unknown	0	0.2	-0.3	-0.2
75% (0.031) unknown	0	0.2	0.3	0.2
0% (0.21) unknown	0.1	2.7	1.9	2.4
95% (0.0048) unknown	0	-0.3	0.4	0.4
95% (< 0.000 unknown	0	0.6	-0.6	-0.7
95% (< 0.000 unknown	0	0.7	-0.9	-0.7
95% (0.0059) unknown	0	-0.4	0.1	0.1
95% (< 0.000 unknown	0	-0.7	0.6	0.5
95% (0.0002) unknown	0	0.2	-0.3	-0.2
95% (< 0.000 unknown	0	0.2	-0.1	-0.1
95% (0.014) unknown	0	0.8	-0.1	-0.3
95% (< 0.000 unknown	0	-0.6	1	0.7
95% (< 0.000 unknown	0	0.4	0	0
95% (0.015) unknown	0	0.3	0.4	0.2
95% (0.042) unknown	0	0.2	0	0
0% (0.58) unknown	0	0.2	0	0.2
95% (0.0011) unknown	0	0.2	-0.2	-0.2
95% (< 0.000 unknown	0	0.3	-1.7	-1.6
0% (0.12) unknown	0	0	0.2	0.2
0% (0.18) unknown	0	-0.7	-0.1	0.2
95% (< 0.000 unknown	0	0.7	-0.1	0.2
95% (< 0.000 unknown	0	-0.2	0.7	0.6
75% (0.057) unknown	0	-0.3	0.5	0.4
75% (0.072) unknown	0	0.4	0.2	0.2
95% (0.035) unknown	0	1	0.9	0.9
95% (< 0.000 unknown	0	0.2	0.2	0.2
0% (0.12) unknown	0	-0.1	0.3	0.3
95% (< 0.000 unknown	0	-0.5	0.7	0.4
95% (0.0001) unknown	0	0.4	0.7	0.5
95% (< 0.000 unknown	0	0.6	-0.8	-0.7
95% (< 0.000 unknown	0	0.1	0.8	0.6
95% (< 0.000 unknown	0	-0.1	0.6	0.5
95% (< 0.000 unknown	0	0	0.5	0.5
95% (< 0.000 unknown	0	-0.1	0.3	0.2

95% (< 0.000 unknown	0	0.2	0.6	0.4
95% (< 0.000 unknown	0	-0.1	0.2	0.2
95% (0.0003] unknown	0	0.1	0.5	0.1
0% (0.29) unknown	0	0.2	0.2	0.1
95% (< 0.000 unknown	0	0.6	0	0
95% (< 0.000 unknown	0	0	-1.4	-1.5
75% (< 0.000 unknown	0	-0.3	0	-0.1
95% (0.0043] unknown	0	0.3	0	0.1
95% (< 0.000 unknown	0	0.3	-0.5	-0.2
95% (< 0.000 unknown	0	0.2	-0.2	-0.1
95% (0.0001] unknown	0	0.5	-0.1	0.1
95% (< 0.000 unknown	0	0.2	0.7	0.7
95% (0.0011] unknown	0	-0.5	0.3	0.4
95% (< 0.000 unknown	0	0	0.9	0.7
95% (< 0.000 unknown	0	-0.2	-0.5	-0.3
95% (< 0.000 unknown	0	0.3	-0.7	-0.6
95% (0.0073] unknown	0	0.3	0.4	0.4
0% (0.93) unknown	0	0.1	0	0.1
0% (0.51) unknown	0	0.2	0.1	-0.4
95% (< 0.000 unknown	0	-0.5	1	0.5
95% (< 0.000 unknown	0	0.9	-0.1	-0.2
0% (0.59) unknown	0	0.1	0.2	0.5
95% (0.011) unknown	0	-0.1	0.5	0.5
0% (0.095) unknown	0	0.6	-0.1	-0.1
95% (< 0.000 unknown	0	-0.3	0.7	0.7
0% (0.39) unknown	0	-0.1	0.2	0
95% (< 0.000 unknown	0	0.1	0.3	0.5
95% (< 0.000 unknown	0	0.6	-1.3	-1.3
0% (0.27) unknown	0	0.1	0.1	0.3
95% (< 0.000 unknown	0	-0.3	0.7	0.7
95% (< 0.000 unknown	0	0.9	-0.1	-0.1
95% (0.0005] unknown	0	0	0.4	0.4
75% (0.12) unknown	0	0.9	-1.6	-2.3
95% (< 0.000 unknown	0	0.9	0.5	0.6
95% (0.0023] unknown	-0.1	0.1	0.5	0.6
75% (0.034) unknown	0	0.7	0.8	0.2
0% (0.32) unknown	0.1	0.4	0.4	0.3
95% (0.0049] unknown	0	0	0.4	0.1
95% (< 0.000 unknown	-0.1	1.4	1.2	0.8
0% (0.11) unknown	0	0	0	0.1
0% (0.27) unknown	0	0.1	0.4	0.7
95% (0.016) unknown	0	-0.4	0.7	0.4
95% (0.0028] unknown	0	0.2	-0.4	0
95% (0.025) unknown	0	0.3	0.1	0.2

95% (< 0.000 unknown	0	0.3	0.4	0.4
95% (< 0.000 unknown	0	0.1	0.4	0.4
95% (0.048) unknown	0.1	0.6	0.7	0.2
0% (0.96) unknown	0	0.1	0	0.1
0% (0.79) unknown	0	-0.4	0	0.1
95% (< 0.000 unknown	0	-0.5	0.7	0.4
0% (0.45) unknown	0	0.2	0	-0.1
95% (< 0.000 unknown	0	-0.1	0.4	0.4
0% (0.71) unknown	0	0.1	0.2	0.4
95% (0.0026) unknown	0	0.5	0.5	0.4
95% (0.0009) unknown	0	0.4	-0.2	0
75% (0.052) unknown	0	-0.3	0	0.1
95% (< 0.000 unknown	0	0.9	-0.3	-0.1
95% (< 0.000 unknown	0	0.6	-1.4	-1.3
95% (< 0.000 unknown	0	-0.2	0.8	0.4
95% (< 0.000 unknown	0	0.7	-0.5	-0.9
95% (0.045) unknown	0	0.7	0.3	0.6
95% (< 0.000 unknown	0	1.1	0.1	0
95% (0.0008) unknown	0	-0.4	0	-0.3
95% (< 0.000 unknown	0	0.2	0.6	0.5
95% (0.0088) unknown	0	0.3	0.5	0.3
95% (< 0.000 unknown	0	0.1	-1	-1
0% (0.19) unknown	0	1	1.4	1.5
95% (< 0.000 unknown	0	0.2	-0.6	-0.9
0% (0.49) unknown	0	0.5	0.1	0.2
0% (0.91) unknown	0	-0.1	-0.2	0
95% (0.0085) unknown	0	-0.3	-1.1	-0.9
0% (0.47) unknown	0	0.6	-0.1	-0.1
95% (0.0005) unknown	0	1.3	-1	-0.8
0% (0.17) unknown	0	0	0.5	0.4
95% (< 0.000 unknown	0	0.4	-0.8	-0.8
95% (0.0019) unknown	0	0.3	0	-0.1
95% (< 0.000 unknown	0	-0.5	0.4	0.3
95% (< 0.000 unknown	0	0.5	-0.6	-0.5
0% (0.061) unknown	0	0.7	0	0.1
0% (0.23) unknown	0	0.6	0.7	0.5
95% (0.0004) unknown	0	-0.1	0.8	0.7
95% (0.0011) unknown	0	0.8	0	0.2
0% (0.13) unknown	0	-0.4	0.5	0.4
95% (0.0026) unknown	0	0.3	-0.3	-0.1
95% (0.0001) unknown	0	0.3	-0.8	-0.8
75% (0.026) unknown	0	-0.2	0.1	-0.3
95% (0.045) unknown	0	-0.1	0.9	0.7
0% (0.40) unknown	0	1.6	0.9	0.8

95% (0.0056] unknown	0	0.3	0.5	0.4
95% (0.0035] unknown	0	0	0.1	0.4
0% (0.70) unknown	0	0.4	-0.6	-1
0% (0.052) unknown	0	0.4	0.2	0.1
95% (< 0.000 unknown	0	-0.3	0.7	0.7
0% (0.26) unknown	0	0.2	0.4	0
95% (0.0052] unknown	0	0.5	0.3	0.3
95% (0.0007] unknown	0	0.3	-0.7	-0.7
75% (0.093) unknown	0	-0.2	0.3	-0.3
0% (0.25) unknown	0	0.2	0.4	0.8
95% (< 0.000 unknown	0	0.9	0.3	0.4
95% (0.0005] unknown	0	0.5	-0.2	-0.4
0% (0.058) unknown	0	0.4	0.3	0.3
0% (0.35) unknown	0	0.2	-0.1	-0.2
95% (0.014) unknown	0	0.7	0.7	0.5
0% (0.13) unknown	0	0.3	-0.2	-0.2
95% (< 0.000 unknown	-0.1	1.1	-0.1	-0.2
95% (0.0001] unknown	0	0.6	-0.5	-0.5
95% (< 0.000 unknown	0	-0.1	0.6	0.5
75% (0.25) unknown	0	1	0.3	-0.1
0% (0.44) unknown	0	0.4	0.3	0.3
0% (0.19) unknown	0	0.3	0.2	0.4
0% (0.47) unknown	0	0.1	0.5	0.3
95% (< 0.000 unknown	0	-0.4	0.4	0.2
0% (0.20) unknown	0	0.2	-0.2	-0.2
95% (0.0001] unknown	0	0.2	0.4	0.7
0% (0.056) unknown	0	0.4	0.6	0.6
0% (0.12) unknown	0	0.3	-0.1	0.5
95% (< 0.000 unknown	0	0.2	0.5	0.5
0% (0.25) unknown	0	0.2	-0.2	-0.1
95% (< 0.000 unknown	0	0.6	-0.3	-0.6
95% (0.013) unknown	0	0.7	-0.5	-0.8
95% (0.029) unknown	0	-0.1	0.6	0.6
95% (< 0.000 unknown	0	0.4	-0.4	-0.4
0% (0.69) unknown	0	0.1	0.3	0.6
0% (0.30) unknown	0	0.8	0.6	0.4
95% (0.0098] unknown	0	0	0.2	0.1
95% (< 0.000 unknown	0	0.2	-1.1	-0.9
95% (< 0.000 unknown	0	0.3	-0.1	0.1
95% (0.0080] unknown	0	0.3	-0.5	0.1
0% (0.48) unknown	0	0.5	0.9	0.5
95% (0.016) unknown	0	-0.5	-0.5	-0.4
95% (0.034) unknown	0	-0.4	0.6	0.6
95% (0.0082] unknown	0	0.1	-0.5	-0.5

0% (0.47)	unknown	0	0.4	-0.2	-0.1
0% (0.81)	unknown	0	0.3	0.1	0.2
95% (0.0023)	unknown	0	0.1	-0.2	-0.1
95% (0.0003)	unknown	0	0.5	0.1	-0.3
0% (0.19)	unknown	-0.1	0.8	0	-0.1
95% (0.020)	unknown	0	-0.1	0.2	0.4
95% (< 0.000	unknown	0	-0.2	0.2	0
95% (0.046)	unknown	0	0.7	-0.1	-0.1
0% (0.46)	unknown	0	0.4	0.2	0.1
0% (0.58)	unknown	0	0.2	0	-0.1
95% (0.0003)	unknown	0	0.1	0.6	0.9
95% (0.039)	unknown	0	-0.6	-0.2	-0.5
0% (0.72)	unknown	0	0.4	0.1	0.1
95% (< 0.000	unknown	0	0.5	-0.1	-0.4
95% (0.018)	unknown	0	0.2	0.4	0.5
95% (0.042)	unknown	0	0.4	0.6	0.3
0% (0.18)	unknown	0	0.8	-0.8	-1.2
95% (< 0.000	unknown	0	0.6	-0.5	-0.7
0% (0.46)	unknown	0	0.5	0.3	0.4
95% (0.0007)	unknown	0	0.2	0.5	0.5
75% (0.066)	unknown	0	0.7	0.3	-0.3
0% (0.89)	unknown	0	0.1	-0.2	-0.3
95% (0.0069)	unknown	0	0.6	-1.4	-1
75% (0.29)	unknown	0.1	0.9	0.6	0.7
95% (0.045)	unknown	0	0.1	0.8	0.4
95% (0.031)	unknown	0	0.6	-0.2	-0.3
95% (0.019)	unknown	0	0.6	-0.7	-0.7
95% (0.020)	unknown	0	0.2	-0.9	-1.4
75% (0.0022)	unknown	0.1	0.7	-0.2	-0.1
75% (0.0012)	unknown	-0.1	0.2	0.3	0.3
75% (0.0071)	unknown	-0.1	0.2	0.3	0.4
0% (0.30)	unknown	0	0.9	0.4	0.5
75% (0.061)	unknown	0	0.2	0.8	0.9
75% (0.068)	unknown	0	-0.2	0.1	0.3
95% (0.0005)	unknown	0	-0.3	0.3	0.6
0% (0.86)	unknown	0	0.2	0.3	0.2
0% (0.079)	unknown	0	0.7	0.2	0.2
95% (< 0.000	unknown	0	1	-0.3	-0.3
0% (0.22)	unknown	0	0	0.3	0.3
75% (0.087)	unknown	0	0	-0.4	-0.3
95% (< 0.000	unknown	0	-0.3	0.4	0.4
0% (0.36)	unknown	0	0.3	0.1	-0.2
95% (0.0047)	unknown	0	0.5	-1.2	-0.8
0% (0.79)	unknown	0	0.1	0.1	0.2

75% (0.059) unknown	0	-0.1	0	0.2
75% (0.055) unknown	0	0.4	0.1	0
95% (0.018) unknown	0	-0.1	0.4	0.4
0% (0.97) unknown	0	0.1	-0.1	0
0% (0.13) unknown	0	0	0.4	0.4
0% (0.30) unknown	0	0.6	0.3	0.1
0% (0.60) unknown	0	0.2	0.3	0.5
95% (0.037) unknown	0	0	-0.1	-0.3
0% (0.85) unknown	0	0.1	0	-0.1
0% (0.18) unknown	0	-0.2	-0.8	-1.2
0% (0.48) unknown	0	-0.1	0.2	0.2
0% (0.30) unknown	0	0.6	0	0.2
95% (< 0.000) unknown	0	0.2	-0.1	-0.1
95% (0.046) unknown	0	0.7	0.3	0.4
95% (< 0.000) unknown	0	0.4	-0.7	-0.7
0% (0.92) unknown	0	-0.1	-0.2	-0.1
95% (0.013) unknown	0	0.6	-0.4	-0.3
0% (0.064) unknown	0	0.8	0.1	-0.2
0% (0.25) unknown	0	0.6	0.4	0.5
95% (0.046) unknown	0	0.7	0	-0.2
0% (0.19) unknown	0	0.4	0.6	0.8
0% (0.25) unknown	0	0.1	-0.3	-0.3
0% (0.28) unknown	0	0.1	-0.4	-0.1
95% (0.0016) unknown	0	0.7	-0.9	-1.3
0% (0.42) unknown	0	0	0.3	-0.2
0% (0.24) unknown	0	0	0.5	0.5
75% (0.079) unknown	0	0.4	0	-0.5
75% (0.097) unknown	0	-0.1	-0.6	-0.1
0% (0.33) unknown	0	-0.1	0.3	0.2
0% (0.54) unknown	0	0.4	0	0.3
0% (0.13) unknown	0	0.7	0.2	0.5
0% (0.085) unknown	0	0	-0.9	-0.9
95% (0.012) unknown	0	-0.1	0.4	0.1
0% (0.094) unknown	0	0.4	0.1	-0.3
0% (0.42) unknown	0	0.7	-0.4	0.1
0% (0.76) unknown	0	0.8	0.8	0.5
0% (0.061) unknown	-0.2	0.9	2.3	1.7
0% (0.70) unknown	0	0.3	-0.2	-0.1
0% (0.16) unknown	0	0.7	0	0.5
0% (0.72) unknown	0	0.2	0.1	0
0% (0.31) unknown	0	-0.4	0.2	0.5
95% (0.021) unknown	0	0.3	0.1	0.1
0% (0.83) unknown	0	0.5	0.2	0.4
0% (0.30) unknown	0	-0.2	0	0

0% (0.24)	unknown	0	0.3	0.6	-0.1
0% (0.56)	unknown	0	1.3	-0.2	No Values
75% (0.043)	unknown	0	0.4	-0.9	-0.4
0% (0.20)	unknown	0	-0.2	0.4	0.2
0% (0.25)	unknown	0	0.2	-0.3	-0.1
0% (0.18)	unknown	0	0.4	0.3	0.2
0% (0.84)	unknown	0	-0.4	0.2	0
0% (0.20)	unknown	0	0.1	-0.3	-0.5
0% (0.40)	unknown	0	0.7	-0.9	-1.2
75% (0.081)	unknown	0	0.6	-0.6	-1.1

results showing the proteins identified by MASCOT and X! Tandem and peptides matching each

A m:37.0/s:14.6, Bad (50%) m:11.6/s:4.32 m:30.3/s:2.00 m:NA m:5.12/s:4.29 [all charge states]
A m:38.0/s:14.6, Bad (50%) m:11.6/s:4.56 m:30.1/s:2.10 m:NA m:5.22/s:4.44 [all charge states]

rbamidomethyl), +304 on Y (iTRAQ8plex)

14/s:0.0809 m:0.617/s:0.0898, Bad (50%) m:27.4/s:4.17 m:0.0671/s:0.508 m:0.0714/s:0.0514 r
12/s:0.0844 m:0.611/s:0.0901, Bad (50%) m:26.8/s:4.20 m:-0.104/s:0.515 m:0.0613/s:0.0482 m

.0282,0.932,0.0390,0.000700]; [0.000600,0.0377,0.933,0.0288,0.000]; [0.000900,0.0471,0.933,0

protein.

r:0.431/s:0.118 [all charge states]

:0.415/s:0.113 [all charge states]

l.0188,0.000]; [0.00140,0.0566,0.933,0.00870,0.000]; [0.000,0.000,0.000,0.000,0.000]; [0.00270,

,0.0744,0.921,0.00180,0.000]

Table S3. Reactome pathway. Human cholangiocyte proteins associated with Reactome pathway

Category	Term	Count	%	PValue
REACTOME_PATHWAY\	REACT_6167:Influenza Infection	50	15.15	3.03E-28
REACTOME_PATHWAY\	REACT_71:Gene Expression	67	20.30	2.00E-24
REACTOME_PATHWAY\	REACT_1762:3' -UTR-mediated	38	11.52	8.20E-23
REACTOME_PATHWAY\	REACT_17015:Metabolism of pi	50	15.15	2.94E-21
REACTOME_PATHWAY\	REACT_125:Processing of Cappel	17	5.15	8.60E-05
REACTOME_PATHWAY\	REACT_6185:HIV Infection	22	6.67	2.51E-04
REACTOME_PATHWAY\	REACT_578:Apoptosis	17	5.15	5.68E-04
REACTOME_PATHWAY\	REACT_13635:Regulation of act	8	2.42	0.00552566
REACTOME_PATHWAY\	REACT_1698:Metablism of nucl	10	3.03	0.01359661
REACTOME_PATHWAY\	REACT_9035:APC/C:Cdh1-medi	8	2.42	0.03090836
REACTOME_PATHWAY\	REACT_11045:Signaling by Wnt	8	2.42	0.03090836
REACTOME_PATHWAY\	REACT_474:Metabolism of carb	10	3.03	0.04352214
REACTOME_PATHWAY\	REACT_6850:Cdc20:Phospho-Al	8	2.42	0.04485484
REACTOME_PATHWAY\	REACT_383:DNA Replication	10	3.03	0.05151479

ys after incubation with *Opisthorchis viverrini* exosomes.

Proteins	List Total	Pop Hits	Pop Total	old Enrichment
P36578, P62750, P62277, Q07020, P2763	171	157	3398	6.32845383
P36578, P62750, P47897, Q07020, P6227	171	350	3398	3.80394319
P36578, P46777, P62750, P46779, P6227	171	108	3398	6.99176955
P36578, P62750, P62277, Q07020, P6070	171	217	3398	4.57865093
P84103, O75937, P22626, Q07955, P0793	171	110	3398	3.07102605
Q13200, O43242, P25789, P25786, O755	171	184	3398	2.37592169
Q13200, O43242, P25789, P25786, Q063	171	129	3398	2.61870438
P62987, O43242, Q13200, P25789, P6128	171	44	3398	3.61297182
P05141, P23921, P22234, P00491, P2210	171	77	3398	2.58069416
P62987, O43242, Q13200, P25789, P6128	171	61	3398	2.60607804
P62987, O43242, Q13200, P25789, P6128	171	61	3398	2.60607804
P04406, P00558, P00338, P06733, P0407	171	94	3398	2.11397288
P62987, O43242, Q13200, P25789, P6128	171	66	3398	2.40864788
P62987, O43242, P33991, Q13200, P2578	171	97	3398	2.04859227

Bonferroni	Benjamini	FDR
1.58E-26	1.58E-26	2.95E-25
1.04E-22	5.19E-23	1.94E-21
4.26E-21	1.42E-21	7.97E-20
1.53E-19	3.83E-20	2.86E-18
0.0044614	8.94E-04	0.08350818
0.01299322	0.00217736	0.24405723
0.02909015	0.0042085	0.55006245
0.25033666	0.03537551	5.2410823
0.50927638	0.07604983	12.4540283
0.80457868	0.15062946	26.2901322
0.80457868	0.15062946	26.2901322
0.90112283	0.18970139	35.1000501
0.90803813	0.18033954	35.9733001
0.93608698	0.19067631	40.1812903

Table S4. Phagosome pathway. Human cholangiocyte proteins involved in the Phagosome patl

#Query_ID	KEGG_description	ko_description
sp P60709 ACTB_HUMAN	actin beta/gamma 1	Phagosome
sp P27797 CALR_HUMAN	calreticulin	Phagosome
sp P01024 CO3_HUMAN	complement component 3	Phagosome
sp P13473 LAMP2_HUMAN	lysosomal-associated membrane protein 1/2	Phagosome
sp P02786 TFR1_HUMAN	transferrin receptor	Phagosome
sp P07437 TBB5_HUMAN	tubulin beta	Phagosome
sp O75396 SC22B_HUMAN	vesicle transport protein SEC22	Phagosome

hway after incubation with *Opisthorchis viverrini* exosomes.

#Query_ID	Control	0.5 h	3 h	16 h
ACTB_HUMAN	0	-0.6	0.6	0.5
CALR_HUMAN	-0.1	0.4	-1.1	-1.2
CO3_HUMAN	0	0.1	0.9	0.2
LAMP2_HUMAN	-0.1	0	-1.1	-1.1
TFR1_HUMAN	-0.1	-0.5	0.7	0.5
TBB5_HUMAN	0.1	-0.6	0.4	0.4
SC22B_HUMAN	0	-0.8	0.6	0.6

Table S5. Proteins related to wound healing and cancer pathways that were differentia

Pathway	Iniprot-Accessio	Access name	Protein name	Control
Adherens junction	O60716	CTND1_HUM	Catenin delta-1	0.1
Adherens junction	P60709	ACTB_HUMA	Actin, cytoplasmic	0
Bladder cancer	P42771	CD2A1_HUM	Cyclin-dependent	0
Cell adhesion	Q13740	CD166_HUM	CD166 antigen	0
Chemical carcinogene	P09211	GSTP1_HUM	Glutathione S-trar	0
Endometrial cancer	P62993	GRB2_HUMA	Growth factor rece	0
Focal adhesion	P19105	ML12A_HUM	Myosin regulatory	0
Focal adhesion	P29400	CO4A5_HUM	Collagen alpha-5(0
Focal adhesion	P12109	CO6A1_HUM	Collagen alpha-1(0
Focal adhesion	P62993	GRB2_HUMA	Growth factor rece	0
Focal adhesion	Q13177	PAK2_HUMA	Serine/threonine-p	0
Focal adhesion	P60709	ACTB_HUMA	Actin, cytoplasmic	0
Focal adhesion	Q15942	ZYX_HUMAN	Zyxin	0
Focal adhesion	Q03135	CAV1_HUMA	Caveolin-1	0
Gap junction	P07437	TBB5_HUMA	Tubulin beta chair	-0.1
Gap junction	P62993	GRB2_HUMA	Growth factor rece	0
MicroRNAs in cancer	P42771	CD2A1_HUM	Cyclin-dependent	0
MicroRNAs in cancer	P62993	GRB2_HUMA	Growth factor rece	0
MicroRNAs in cancer	P61978	HNRPK_HUM	Heterogeneous nu	0
MicroRNAs in cancer	P16949	STMN1_HUM	Stathmin	0
MicroRNAs in cancer	P29966	MARCS_HUM	Myristoylated alan	0
MicroRNAs in cancer	Q16658	FSCN1_HUM	Fascin	0
MicroRNAs in cancer	P09493	TPM1_HUMA	Tropomyosin alph	0
MicroRNAs in cancer	P08670	VIME_HUMA	Vimentin	0
Non-small cell lung ca	P42771	CD2A1_HUM	Cyclin-dependent	0
Non-small cell lung ca	P62993	GRB2_HUMA	Growth factor rece	0
Pancreatic cancer	P42771	CD2A1_HUM	Cyclin-dependent	0
Pathways in cancer	P42771	CD2A1_HUM	Cyclin-dependent	0
Pathways in cancer	P29400	CO4A5_HUM	Collagen alpha-5(0
Pathways in cancer	P62993	GRB2_HUMA	Growth factor rece	0
Pathways in cancer	P09211	GSTP1_HUM	Glutathione S-trar	0
Pathways in cancer	P08238	HS90B_HUM	Heat shock protei	-0.1
Pathways in cancer	P06753	TPM3_HUMA	Tropomyosin alph	0
Pathways in cancer	P12270	TPR_HUMAN	Nucleoprotein TPI	0
Prostate cancer	P62993	GRB2_HUMA	Growth factor rece	0
Prostate cancer	P09211	GSTP1_HUM	Glutathione S-trar	0
Prostate cancer	P08238	HS90B_HUM	Heat shock protei	-0.1
Proteoglycans in canci	P23588	IF4B_HUMAN	Eukaryotic transla	0
Proteoglycans in canci	P60709	ACTB_HUMA	Actin, cytoplasmic	0
Proteoglycans in canci	Q03135	CAV1_HUMA	Caveolin-1	0
renal cell carcinoma	P62993	GRB2_HUMA	Growth factor rece	0

renal cell carcinoma	Q13177	PAK2_HUMA Serine/threonine-p	0
Small cell lung cancer	P29400	CO4A5_HUM Collagen alpha-5(0
Thyroid cancer	P06753	TPM3_HUMA Tropomyosin alph	0
Thyroid cancer	P12270	TPR_HUMAN Nucleoprotein TPI	0
Tight junction	P19105	ML12A_HUM Myosin regulatory	0
Tight junction	Q9H4G0	E41L1_HUM/ Band 4.1-like prot	0.1
Tight junction	P35579	MYH9_HUMA Myosin-9	0
Tight junction	P60709	ACTB_HUMA Actin, cytoplasmic	0
Tight junction	Q9UDY2	ZO2_HUMAN Tight junction prot	0
Trans. misreg. in canc	Q01844	EWS_HUMA RNA-binding prote	0
Trans. misreg. in canc	P35637	FUS_HUMAN RNA-binding prote	0
Trans. misreg. in canc	Q92804	RBP56_HUM TATA-binding pro	0
Trans. misreg. in canc	Q16695	H31T_HUMA Histone H3.1t	0
Viral carcinogenesis	P42771	CD2A1_HUM Cyclin-dependent	0
Viral carcinogenesis	Q16531	DDB1_HUMA DNA damage-bind	0
Viral carcinogenesis	P62993	GRB2_HUMA Growth factor rec	0
Viral carcinogenesis	P06396	GELS_HUMA Gelsolin	0
Viral carcinogenesis	P61978	HNRPK_HUM Heterogeneous n	0
Viral carcinogenesis	P14618	KPYM_HUMA Pyruvate kinase F	0
Viral carcinogenesis	P43487	RANG_HUM/ Ran-specific GTP	0
Viral carcinogenesis	P01024	CO3_HUMAN Complement C3	0
Viral carcinogenesis	P62258	1433E_HUM/ 14-3-3 protein eps	0
Viral carcinogenesis	Q99879	H2B1M_HUM Histone H2B type	0.2
Viral carcinogenesis	P62805	H4_HUMAN Histone H4	0.1

lly regulated in human cholangiocytes after co-culture with exosomes from *Opisthorchis vi*

0.5h	3h	16h
-0.1	0.3	0.6
-0.6	0.6	0.5
1.2	-0.6	-0.4
-0.5	-1.1	-1.2
-0.9	0.1	0.2
0.6	-0.6	-0.7
0.5	-1.3	-1.2
-0.1	0.6	0.6
0.7	0	-0.2
0.6	-0.6	-0.7
0.9	0.5	0.6
-0.6	0.6	0.5
0.9	0.2	0.2
-0.6	0.6	0.8
-0.6	0.3	0.4
0.6	-0.6	-0.7
1.2	-0.6	-0.4
0.6	-0.6	-0.7
0.8	0.1	0
0.6	-1.7	-1.8
0	-1.3	-1.2
0.6	0.3	0.4
0.2	-2.2	-2.3
0.3	0.5	0.7
1.2	-0.6	-0.4
0.6	-0.6	-0.7
1.2	-0.6	-0.4
1.2	-0.6	-0.4
-0.1	0.6	0.6
0.6	-0.6	-0.7
-0.9	0.1	0.2
-0.5	0.6	0.4
0.6	-1.6	-1.6
0.6	-0.2	0.1
0.6	-0.6	-0.7
-0.9	0.1	0.2
-0.5	0.6	0.4
0.7	-0.6	-0.6
-0.6	0.6	0.5
-0.6	0.6	0.8
0.6	-0.6	-0.7

0.9	0.5	0.6
-0.1	0.6	0.6
0.6	-1.6	-1.6
0.6	-0.2	0.1
0.5	-1.3	-1.2
0.8	0.3	0.4
0.5	0.3	0.6
-0.6	0.6	0.5
0.1	0.5	0.6
0.5	-1	-0.9
0.6	-0.5	-0.5
0.8	-1.2	-0.9
-0.6	0.8	0.8
1.2	-0.6	-0.4
-0.4	0.7	0.4
0.6	-0.6	-0.7
0.7	0.4	0.4
0.8	0.1	0
-0.3	0.7	0.8
0.5	-0.7	-1.2
0.1	0.9	0.2
0.2	-0.5	-0.6
-0.1	0.6	0.5
-0.8	0.6	0.5

verrini . Proteins significantly up- or downregulated in cholangiocytes after incubation with exosc

omes were subjected to functional enrichment analysis using the Kyoto Encyclopedia of Genes and

1 Genomes (KEGG). A $\log_2=0.6$ corresponding to a 1.5-fold change in proteins with P -value <0.0

.05 was considered to be significant.

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