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Mechanism-Guided Design and Synthesis of Mitochondria-targeting Artemisinin Analog with Enhanced Anticancer Activity

Chong-Jing Zhang,^{#[a]} Jigang Wang,^{#[b,c]} Jianbin Zhang,^[d] Yew Mun Lee,^[c] Guangxue Feng,^[a] Teck Kwang Lim,^[c] Han-Ming Shen,^[d] Qingsong Lin,^{*[c]} and Bin Liu^{*[a][e]}

Abstract: Understanding the mechanism of action (MOA) of bioactive natural products will guide the endeavor to improve their cellular activities. Artemisinin and its derivatives are reported to inhibit cancer cell proliferation, yet with much lower efficiencies than their roles in killing malaria parasites. To improve their efficacies on cancer cells, we firstly studied the MOA of artemisinin using chemical proteomics and found that free heme could directly activate artemisinin. We subsequently designed and synthesized a novel derivative of artemisinin, ART-TPP, which is capable of targeting the drug to mitochondria where free heme is synthesized. It was found that ART-TPP exerted remarkably more potent inhibition than its parent compound to cancer cells. In addition, a clickable probe ART-TPP-Alk was employed to prove that the attachment of TPP group could label more mitochondrial proteins than that for the ART derivative without TPP (AP1). This work highlights the importance of MOA study which enables us to optimize the design of natural drug analogs to improve their biological activities.

Artemisinin (ART) is a sesquiterpene lactone endoperoxide compound isolated from an annual wormwood (*Artemisia annua* L.). It potently kills malaria parasites, saving millions of lives.^[1,2] Four decades after its discovery, the ART-based combination therapies (ACTs) remain the first line treatment for malaria as recommended by the World Health Organization (WHO).^[3,4] Interestingly, recent studies suggested that ART may possess anti-cancer properties.^[5–7] Yet, majority of the reported ART analogues showed only limited potency in certain tumor cell lines.^[8] Since understanding the mode of action (MOA) for drugs could contribute greatly towards the improvement of their cellular activities,^[9–12] we seek to elucidate the MOA of ART, with the hope to find an effective strategy to improve the potency of ART against cancer cells.

ART contains a unique endoperoxide bridge (R-O-O-R') which is crucial for its inhibitory activities.^[13–15] It is widely accepted that the activation and breaking of endoperoxide bridge in solution leads to the generation of oxygen radicals, followed by its rearrangement to produce carbon radicals.^[15]

However, there remain debates over the exact mechanism of endoperoxide bridge activation *in vivo*.^[16] Both free ferrous iron^[17,18] and heme^[19] have been proposed to be ART activators.^[20] Very recently, we used a chemical proteomics approach to show that, heme, rather than free ferrous iron, directly activates ART in malaria parasites, which then promiscuously targets various proteins within the parasites.^[21] Based on this discovery, we used alkyne tagged ART probe AP1 in our current study (Figure 1A), and with the help of the chemical proteomics approach, we demonstrate that ART is also activated by heme and it promiscuously targets multiple proteins to kill cancer cells. Moreover, we also find out that modulating the level of heme could greatly affect the anti-cancer activities of ART.

In human cells, fresh free heme is synthesized in the mitochondria.^[22] Therefore, we hypothesize that by directing ART into mitochondria, we could potentially increase its anti-cancer activities. To prove this hypothesis, we synthesized two ART analogs: ART-triphenylphosphoniumbromide (ART-TPP) and ART-TPP-alkyne (ART-TPP-Alk; Figure 1A). TPP is a typical cation, which could direct molecules into mitochondria and this approach is more favorable in cancer cells than normal cells.^[23,24] Indeed, our results demonstrate that ART-TPP could remarkably improve the anti-cancer activities of ART, while ART-TPP-Alk further validates that the TPP group could efficiently direct ART into mitochondria thus increase the activation level of ART and target more protein targets, which is further evidenced by chemical proteomics studies. Our study highlights the importance of MOA study in improving the biological activities of natural products.

Moving into the details of our study, the AP1 probe retains the core structure and activity of ART.^[21] With this probe, we adopted a chemical proteomics approach to study the activation level of AP1 as illustrated in Figure 1B. Briefly, AP1 was incubated with live cells or cell lysate before applying click chemistry to attach a fluorescent dye. This process allowed the fluorescence labelling of AP1 that had attached to their target proteins. The labeled proteins were then resolved with SDS-PAGE. Higher intensity of fluorescent bands in the SDS-PAGE gel indicates a higher activation level of AP1, hence increasing number of target proteins are bound by activated AP1.

To elucidate the activation mechanism of ART *via* this chemical proteomics approach, we first applied AP1 to label the cell lysate of cancer cells. As shown in Figure 1C, the AP1 probe itself without any ART activator, cannot label any proteins. We then used hemin as the source of heme to test for ART activation. Hemin is the oxidized form of heme, and it is stable in air for convenient use. The Fe³⁺ in hemin has no ability to reduce endoperoxide double bond in ART. However, hemin can be easily reduced to heme in the presence of various reducing agents exist in the cells.^[21,25–29] As shown in Figure 1C, the addition of hemin to the cell lysate leads to sufficient protein labelling, which indicates that the source of heme is essential in activation of ART. In contrast, AP1 has negligible binding to any

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protein from the cell lysate in the presence of FeSO_4 , even at a high concentration. Moreover, the addition of deferoxamine (DFO), a free-iron chelator, has no obvious effect on AP1 labeling of proteins in the presence of heme. Therefore, addition or depletion of ferrous iron in cell lysate has no obvious effect on activation of AP1. Subsequently, AP1 was applied to treat the live cells. AP1 labeled large amount of proteins when the cells were treated with hemin, which could be quickly converted to heme in the cellular environment.^[26] Whereas, in FeSO_4 -treated

could modulate endogenous heme level (Figure 2B). As both δ -aminolevulinic acid (ALA) and protoporphyrin IX (PPIX) are intermediates of heme biosynthesis, the addition of these two compounds could increase endogenous heme level. As expected, addition of ALA and PPIX increases the anti-cancer effect of ART (Figure 1F). On the other hand, succinylacetone (SA) is an inhibitor for the synthesis of porphobilinogen from ALA. Addition of SA decreases the anti-cancer activities of ART and even blocks the synergetic effects between ALA and ART,

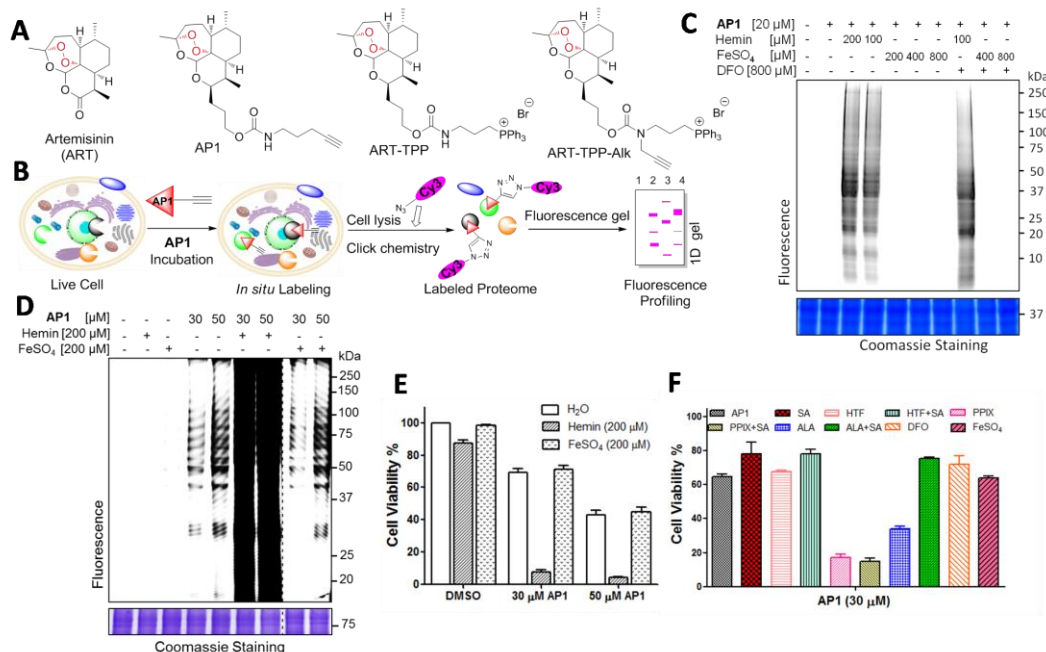


Figure 1 A) structures of artemisinin and probes used in this study; B) General workflow of the chemical proteomics approach with AP1; C) AP1 labeling profile in HCT116 cell lysate in the presence of different mediators; D) AP1 labeling profile in HCT116 live cells treated with or without hemin and FeSO_4 ; E) Cell viability of HCT116 cells treated by AP1 with or without hemin and FeSO_4 ; F) Cell viability of HCT116 cells treated by AP1 alone or AP1 with various mediators in the heme biosynthesis.

cells, AP1 could only label a small amount of proteins, at a level comparable to the cells without treatment (Figure 1D). Collectively, both results from cell lysate and live cells indicate that free heme could effectively activate ART, while free ferrous iron has minimal effects on the activation of ART.

With larger amount of activated ART, more cellular proteins could be targeted by ART, which could lead to enhanced anti-cancer activities. To prove this hypothesis, we went on to examine the viability of HCT116 colorectal cancer cells treated with AP1, with the addition of hemin or FeSO_4 . As shown in Figure 1E, hemin or FeSO_4 alone has little effect on the viability of HCT116, and AP1 alone could only kill ~30% of the cells after 24 hours of incubation. Similar to our AP1 binding results, addition of 200 μM of FeSO_4 did not increase the anti-cancer activities of AP1. Contrastingly, AP1 together with hemin could kill more than 90% of the HCT116 cells. This is positively correlated with the amount of activated ART (Figure 1D). The increased ART activation level leads to the marked decrease of the viability of HCT116 cells (Figure 1E). Our results highlight that the addition of hemin, which is reduced to heme *in vivo*, could dramatically enhance the cell killing effect of AP1 by increasing the amount of activated ART.

After confirming that an external source of heme could increase anticancer activity of the drug, we reasoned that the modulation of endogenous heme could also affect anti-cancer activity of ART. Synthesis of endogenous heme involves multiple steps, and there are a lot of intermediates and mediators that

while PPIX could subvert the inhibitory effects of SA (Figure 1F). Co-administration of ART and DFO can apparently inhibit ART-induced cytotoxicity (Figure 1F). The partial inhibitory effect of DFO might be due to iron chelation that inhibits iron-related oxidative stress and sequesters the iron required for heme synthesis in cancer cells.^[7,15,17,30–34] In addition, co-incubation of ART with human Holo Transferrin (HTF) or FeSO_4 did not have apparent effect on the cytotoxicity of ART (Figure 1F). This can be explained by the fact that the formation of ALA is the rate-limiting step of heme synthesis.^[35] Since ALA is the substrate found upstream of the heme synthesis pathway, the production of the downstream product PPIX in the heme synthesis pathway is dependent on the level of ALA. Therefore, by adding more exogenous iron to cancer cells that already possess a high intracellular iron concentration, it is less likely that the exogenous iron would affect the rates of heme production since the generation of heme involves the incorporation of Fe (II) with PPIX, which in turn is greatly dependent on the amount of ALA.

Taken together, our chemical proteomics and cell viability experiments indicate that heme plays a decisive role on the activation of ART in cancer cells. However, intracellular free heme could promote the generation of reactive oxygen species to cause lipid peroxidation. This would subsequently induce membrane injury and yield cell apoptosis. As a consequence, the intracellular level of free heme is tightly controlled to be less than 100 nM within normal cells and the majority of heme is bound to carrier proteins.^[36] As heme-protein complexes

possess much lower ability to activate ART than free heme,^[15] the intracellular location of free heme accessible to ART is vital for its anti-cancer activities.^[34] Since the final step of heme biosynthesis occurs in mitochondria, we hypothesize that directing ART to the mitochondria could potentially increase the activation level of ART, yielding higher anti-cancer activities.

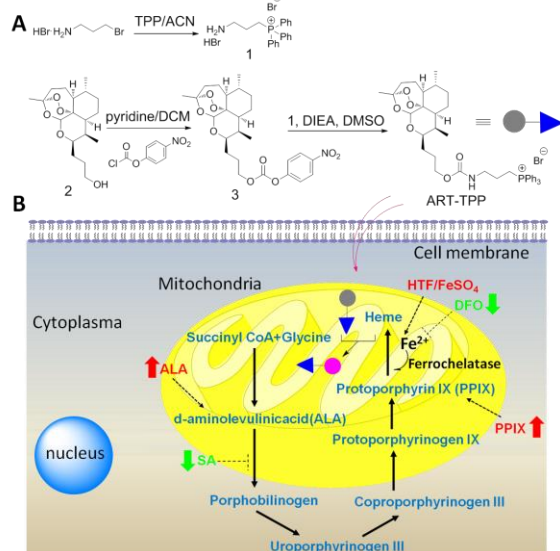


Figure 2 A) Synthetic scheme of ART-TPP; B) Schematic illustration of ART-TPP targeting mitochondria and its activation by heme.

To prove this hypothesis, we went on to synthesize the ART-TPP probe as shown in Figure 2A. In brief, the compound 3-bromopropylamine hydrobromide was reacted with triphenylphosphine to give the key intermediate 1. Subsequently, 1 was reacted with activated ART to generate ART-TPP (Fig. S1-S8) with an overall yield of 10.4%. With ART-TPP at hand, we first compared its cytotoxicity with ART using various cell lines. As shown in Figure 3, ART-TPP is cytotoxic to all tested cancer cells, with the IC₅₀ values of 2.84 μ M for MDA-MB-231 cells, 0.82 μ M for HeLa cells, 6.13 μ M for SKBR3 cells, and 1.73 μ M for HCT116 cells. In comparison, the cytotoxicity of ART-TPP is 26-fold and 94-fold more potent than ART in MDA-MB-231 and HeLa cells, respectively. Moreover, little cytotoxicity in HCT116 cells was observed for compound 1 containing only the TPP group without ART (Figure 3A), which verifies the important synergetic effects between TPP group and ART in enhancing its anti-cancer activities.

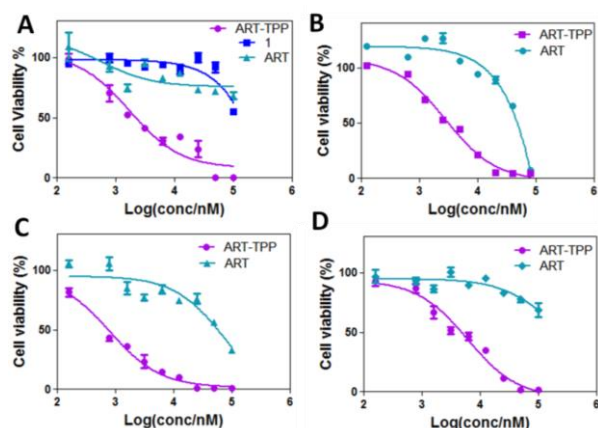


Figure 3 Cell viabilities of HCT116 (A), MDA-MB-231 (B), HeLa (C), SKBR3 (D) treated with ART, ART-TPP or 1.

Next, to confirm that ART-TPP is distributed to the mitochondria, we measured the mitochondrial membrane potential (MMP) using a fluorescent marker of tetramethylrhodamine ethyl ester (TMRE). TMRE is very emissive when MMP is high.^[36,37] As shown in Figure S11, cells treated with DMSO or ART possess high MMP as reflected by the high fluorescent signals. No fluorescence was detected for the cells treated with ART-TPP under the same condition, suggesting that the probe was distributed into the mitochondria, thus reducing the MMP.

Subsequently, to directly visualize the cellular distribution of ART-TPP and perform critical proteomics study, we went on to synthesize a clickable probe (ART-TPP-Alk) to allow for the attachment of a fluorescent molecule and biotin tag through click chemistry. The probe was synthesized according to the scheme shown in Figure 4A. Briefly, the propargyl bromide was reacted with compound 1 to generate compound 4. Compound 4 was then reacted with activated ART to yield the ART-TPP-Alk probe. ART-TPP-Alk possesses similar cytotoxic activity with ART-TPP (Figure S12A), illustrating that the attachment of an alkyne tag has little effect on its overall biological activity while allowing us to visualize and identify the cellular targets of ART-TPP. The images shown in Figures S12B-E reveal that the fluorescent signal from the ART-TPP-Alk overlaps well with that from the mitochondria tracker, demonstrating that majority of the probe indeed localizes well in the mitochondria after cellular uptake.

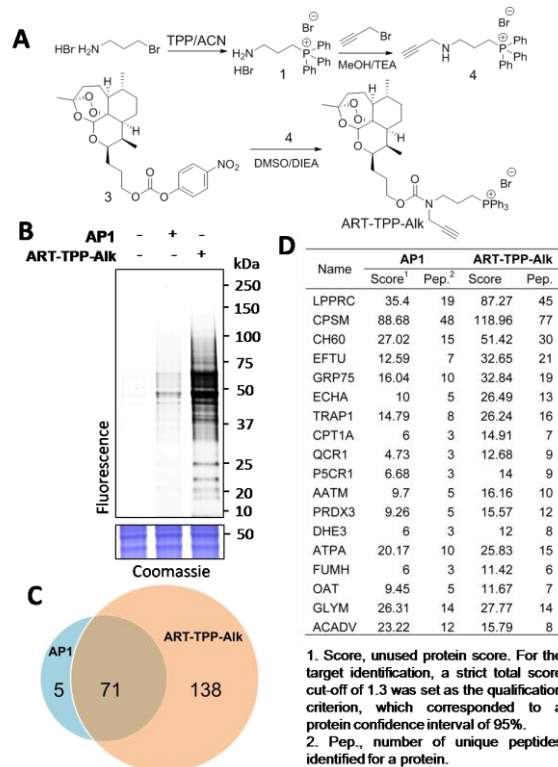


Figure 4 A) Synthetic scheme of ART-TPP-Alk; B) The labeling profile in HeLa live cells treated with AP1 (20 μ M) or ART-TPP-Alk (20 μ M); C) Number of labeled proteins locating in mitochondria for AP1 and ART-TPP-Alk; D) Comparison of selected proteins labeled by both AP1 and ART-TPP-Alk.

Finally, we studied the effects of the TPP group on protein labeling profile. Both AP1 and ART-TPP-Alk were used to treat live cells. The labeled proteins were clicked with rhodamine-azide and resolved by SDS-PAGE. Compared with AP1, ART-

TPP-Alk is able to label more proteins (Figure 4B). In addition, pre-incubation of excess ART or ART-TPP in cell lysate remarkably decreases the protein labeling of both AP1 and ART-TPP-Alk (Figure S13), suggesting that they bind to similar protein targets as their parent. Next, we proceeded to identify the covalent binding targets of AP1 and ART-TPP-Alk in HeLa cells. As shown in the supplementary table 1-4, AP1 and ART-TPP-Alk covalently modified 321 and 860 proteins, respectively, which is consistent with the labeling profile shown in SDS-PAGE (Figure 4B). More importantly, AP1 is able to bind to 76 proteins from the mitochondria, while ART-TPP-Alk is able to bind to 209 proteins from the mitochondria (Figure 4C). In addition, most of the proteins labeled by ART-TPP-Alk have higher scores than those labeled by AP1 (Figure 4D). A protein with a higher score reflects the larger abundance of its unique peptides identified during MS analysis. Therefore, these results suggest that there are more activated ART-TPP-Alk to bind to target proteins. As mitochondria is the powerhouse of the cell, the fact that more mitochondria proteins are covalently modified by ART-TPP-Alk inevitably make it more potent than ART.

In conclusion, we have elucidated the MOA of the natural product ART using chemical proteomics approach in cancer cells. Our results validate that free heme is the main activator in cancer cells. Guided by this unique MOA, we designed and synthesized ART-TPP, where the TPP group could direct ART to the mitochondria. We showed that the incorporation of this mitochondria targeting moiety could remarkably increase the anti-cancer activities of ART. The fluorescence imaging results also proved that the TPP group could efficiently direct ART-TPP into the mitochondria, leading to the reduction of MMP. More importantly, the proteomics results revealed that ART-TPP-Alk could label more proteins in mitochondria than AP1 did. The more protein targets and higher scores identified with ART-TPP-Alk also suggest its greater activation and higher potency than AP1. As such, our results highlight that the activity optimization of natural products could benefit from MOA studies. As cancer cells were reported to possess higher MMP than normal cells, TPP could selectively target the probe to cancer cells to a certain extent.^{[37,38][39]} Moreover, cancer cells are also reported to have higher heme level than normal cells.^[40,41] Taken together, the concentration and activation level of ART-TPP are expected to be higher in cancer cells than in normal cells. Thus, we anticipate that ART-TPP could have good performance in animal cancer models, which is our next goal of study.

Acknowledgements

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Keywords: mitochondria targeting • anti-cancer • fluorescent probe • triphenylphosphonium • drug delivery

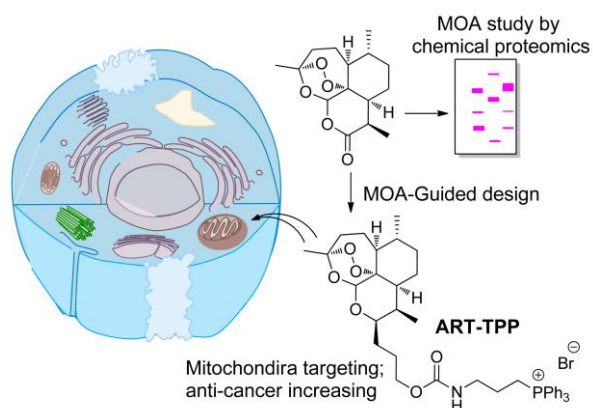
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Entry for the Table of Contents (Please choose one layout)

COMMUNICATION



C. Zhang, J. Wang*, J. Zhang, Y. M. Lee, G. Feng, T. K. Lim, H. M. Shen, Q. Lin*, B. Liu*

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Mechanism Guided Design and Synthesis of Mitochondria-targeting Artemisinin Analog with Enhanced Anticancer Activity

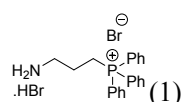
Mechanism of action (MOA) study by chemical proteomics indicates that free heme plays a decisive role in the activation of artemisinin in cancer cells. Guided by this MOA, a mitochondria targeting analog (ART-TPP) was developed and showed remarkable anti-cancer activities.

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Supporting Information

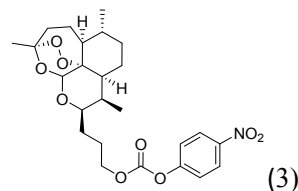
General Information 3-(4,5-Dimethyl-thiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT), and other chemicals were all purchased from commercial vendor and used as received without further purification. Dry dichloromethane was distilled over calcium hydride. All non-aqueous reactions were carried out in oven-dried glassware under nitrogen atmosphere. High-performance liquid chromatography (HPLC) was performed in Agilent technologies (1100 series) with acetonitrile containing trifluoroacetic acid (0.1%) and water containing trifluoroacetic acid (0.1%) as the elution buffer. NMR spectra were recorded on a Bruker ARX 400 NMR spectrometer. Chemical shifts are recorded in parts per million referenced according to residual solvent ($\text{CDCl}_3 = 7.26$ ppm and $(\text{CD}_3)_2\text{SO} = 2.50$ ppm) in ^1H NMR and ($\text{CDCl}_3 = 77.0$ ppm and $(\text{CD}_3)_2\text{SO} = 40.0$ ppm) in ^{13}C NMR. Mass spectra of synthetic small molecules were reported on the AmaZon X LC-MS for ESI. Mass spectra for proteomic study were recorded on a Finnigan LCQ mass spectrometer.

1. Synthesis of 1



Triphenylphosphine (0.84 g, 3.82 mmol) and 3-bromopropylamine hydrobromide (1.0g, 3.82 mmol) were added to acetonitrile (10 mL) and the resulting suspension was refluxed for 12 h. The mixture was cooled down to room temperature. Half of the solvent was removed under reduced pressure and hexane (25 mL) was added. The resulting gel was dissolved in isopropanol (100 mL), diethyl ether (50 mL) was added and the solution was left overnight in arefrigerator (4 °C) to give the product as a white solid (0.50 g, 27.3%). ^1H NMR (400 MHz, $\text{CDCl}_3/\text{CD}_3\text{OD} = 15/1$) δ 7.64-7.79 (m, 15H), 3.69-3.76 (m, 2H), 3.28-3.31 (m, 2H), 2.15-2.21 (m, 2H); ^{13}C NMR (400 MHz, $\text{CDCl}_3/\text{CD}_3\text{OD} = 15/1$) δ 155.2, 155.1, 133.6, 133.5, 130.5, 130.4, 117.8, 117.0, 20.2.

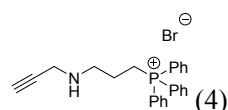
2. Synthesis of 3



To the solution of 2 (81 mg, 0.25 mmol) prepared according to published procedure¹ in DCM (5 mL) was added 4-nitrophenyl chloroformate (60 mg, 0.30 mmol) and pyridine (60 mg, 0.76 mmol) in an ice-water bath. The bath was then removed and solution was stirred at room temperature for 8 h. The reaction was quenched by addition of water (10 mL). The organic phase was collected, washed with ammonium chloride (saturated aqueous solution, 10 mL \times 2) and brine (10 mL). The organic layer was collected, which was further dried with sodium sulfite and purified with chromatography (hexane/EA = 30/1-3/1, v:v) to give the desired product as colorless oil (57 mg,

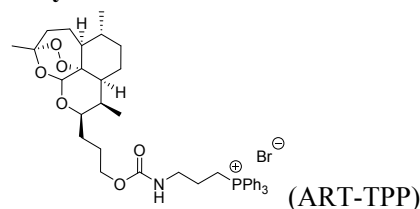
46.7%). ^1H NMR (400 MHz, CDCl_3) δ 8.28 (m, 2H), 7.38 (m, 2H), 5.31 (s, 1H), 4.31-4.41 (m, 2H), 4.23-4.28 (m, 1H), 2.62-2.67 (m, 1H), 2.28-2.35 (m, 1H), 2.01-2.05 (m, 2H), 1.77-1.94 (m, 3H), 1.61-1.68 (m, 3H), 1.53-1.59 (m, 1H), 1.25-1.32 (m, 4H), 0.97 (d, $J = 9.6$ Hz, 3H), 0.89 (d, $J = 7.6$ Hz, 3H); ^{13}C NMR (100 MHz, CDCl_3) δ 155.6, 152.4, 145.3, 126.1, 125.2, 121.7, 115.6, 103.0, 89.4, 81.1, 74.0, 69.4, 52.2, 44.1, 37.5, 36.6, 34.4, 30.3, 26.5, 26.0, 25.8, 24.9, 24.7, 20.1, 12.7; HRMS (ESI) calcd for $[\text{M}+\text{H}]^+$:492.2228, found: 492.2225.

2. Synthesis of 4



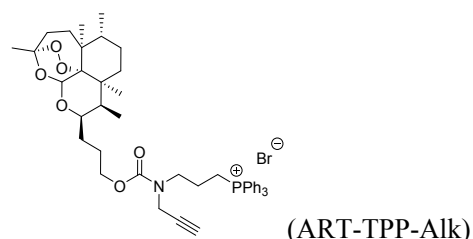
To the suspension of **1** (280 mg, 0.58 mmol) in methyl alcohol (8 mL) was added propargyl bromide (80% (w/w) in hexane, 80 mg, 0.54 mmol) and triethyl amine (58 mg, 0.58 mmol). The mixture was stirred at room temperature for 12 h. Then the solvent was removed under reduced pressure. The resulting residue was purified with high performance liquid chromatography (HPLC) to give the product **4** as colorless oil (20 mg, 6.3%). ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 9.60 (brs, 2H), 7.89-7.94 (m, 3H), 7.76-7.83 (m, 12H), 3.91 (m, 2H), 3.69 (m, 1H), 3.16 (t, $J = 6.8$ Hz, 2H), 1.94 (m, 2H); HRMS (ESI) calcd for $[\text{M}+\text{H}]^+$:358.1719, found: 358.1725.

4. Synthesis of ART-TPP



To the solution of **1** (6.0 mg, 0.011 mmol) in DMSO (0.6 mL) was added **4** (5.2 mg, 0.011) and *N,N*-Diisopropylethylamine (DIPEA) (3.0 mg, 0.023 mmol). The resulting mixture was stirred at room temperature for 24 h. Then the mixture was purified with HPLC to yield **ART-TPP** as colorless oil (6.0 mg, 81.0%). ^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 7.88-7.93 (m, 3H), 7.75-7.81 (m, 12H), 7.22 (t, $J = 5.6$ Hz, 1H), 5.28 (s, 1H), 3.90-4.01 (m, 4H), 3.51-3.58 (m, 2H), 3.11-3.16 (m, 2H), 2.40-2.42 (m, 1H), 2.08-2.17 (dt, $J_1 = 3.6$ Hz, $J_2 = 13.6$ Hz, 1H), 1.95-1.99 (m, 1H), 1.80-1.85 (m, 1H), 1.64-1.72 (m, 4H), 1.48-1.57 (m, 4H), 1.20-1.36 (m, 7H), 1.10-1.17 (m, 1H), 0.89 (d, $J = 6.4$ Hz, 3H), 0.77 (d, $J = 7.6$ Hz, 3H); HRMS (ESI) calcd for $[\text{M}+\text{H}]^+$:672.3449, found: 672.3455.

5. Synthesis of ART-TPP-Alk



To the solution of **4** (5.0 mg, 0.01 mmol) in DMSO (0.6 mL) was added **2** (7.0 mg, 0.012 mmol) and DIPEA (3.0 mg, 0.023 mmol). The resulting mixture was stirred at room temperature for 24 h.

Then the mixture was purified with HPLC to give the product **ART-TPP-Alk** as colorless oil (3.8 mg, 46.9%). ¹H NMR (400 MHz, DMSO-*d*₆) δ 7.88-7.92 (m, 3H), 7.76-7.81 (m, 12H), 5.28 (s, 1H), 4.01 (m, 5H), 3.41 (t, *J* = 7.2 Hz, 2H), 3.15 (t, *J* = 2.4 Hz, 1H), 2.40-2.45 (m, 1H), 2.08-2.16 (m, 1H), 1.94-1.99 (m, 1H), 1.82-1.85 (m, 3H), 1.63-1.66 (m, 1H), 1.47-1.57 (m, 3H), 1.26-1.35 (m, 7H), 1.11-1.17 (m, 1H), 0.85-0.92 (m, 4H), 0.75 (d, *J* = 7.2 Hz, 3H); HRMS (ESI) calcd for [M+H]⁺: 710.3605, found: 710.3609.

6 Cell culture

HeLa human cervix carcinoma cells, MDA-MB-231 human breast cancer cells, NIH-3T3 mouse embryonic fibroblast cells and human colorectal HCT116 cells were provided by American Type Culture Collection (ATCC). The cells were cultured in DMEM (Invitrogen, Carlsbad, CA) containing 10% heat-inactivated FBS (Invitrogen), 100 U mL⁻¹ penicillin, and 100 µg mL⁻¹ streptomycin (Thermo Scientific) and were maintained in a humidified incubator at 37 °C with 5% CO₂. Before experiments, the cells were pre-cultured until confluence was reached.

7 *In vitro* and *in situ* fluorescence labeling of HCT 116 cells lysate or live HCT116 cells by API

7.1 *In situ* 1D gel fluorescence target profiling

HCT116 cells were grown in six well plates until 80 to 90% confluency was reached. The cells were washed twice with PBS (1 ×) after removal of the media. The cells were treated with API or other indicated treatments for 4 hours.

After treatment, medium was removed and the cells were washed once with PBS before trypsin treatment for detachment (harvesting). The cell suspensions were centrifuged at 300 rpm for 5 minutes at 4°C to remove the trypsin solution. The cell pellets were then re-suspended in PBS and centrifuged again at 300 rpm at 4°C for 5 minutes to wash the cells. Next, the cells were lysed in 150 µL of PBS by sonication (25% amplification, one second on and two seconds off for 2 minutes, on ice bath). The resultant cell lysate was centrifuged at 10,000 rpm for 45 minutes at 4°C to remove debris and insoluble fraction from the cell lysate. Protein concentration of the lysates was determined with Bio-Rad protein assay. Equal amount of proteins (100 µg) of different treated samples were clicked with fluorescent tags *via* copper (I) click chemistry (fluorescence labeling). Click reaction was done by adding 10 µM Cy3-azide, 1mM Tris(2-carboxyethyl)phosphine (TCEP), 100 µM Tris [(1-benzyl-1H-1,2,3-triazol-4-yl)methyl] amine (TBTA ligand) and 1mM copper sulphate were added to the lysate and incubated at room temperature for 3 hours with continuous shaking. The fluorescent-labelled proteins were precipitated using acetone and left to air-dried. The clicked protein samples were then solubilized with 35 µL of 1 × Laemmli buffer (SDS loading buffer) and 15 µL of each samples were loaded into wells of 10% polyacrylamide gel and separate through SDS gel electrophoresis. Typhoon 9410 laser scanner (GE Healthcare) was used to visualize the fluorescence-gel images and the images were then analyzed by Image Quant software. The fluorescence contrast was normalized against the DMSO control to eliminate the background effect.

7.2 *In vitro* 1D gel fluorescence target profiling

For the lysate labeling, HCT116 cells were first lysed and then the lysate was treated with API and other indicated treatments. The following labeling steps were same as above mentioned *in situ* fluorescence labeling.

8 Cell cytotoxicity assay

The cytotoxicity of the compounds was evaluated using the MTT assay. The HeLa, MDA-MB-231, NIH-3T3 and HCT116 cells were seeded in 96-well plates at a density of 5000 cells/well. After incubation for 24 h, the medium was replaced with freshly prepared solution of ART-TPP and ART-TPP-Alk at different concentrations and further incubated at 37 °C for 48 h in the dark. After washing the cells with PBS buffer, 100 µL of freshly prepared MTT (0.5 mg mL⁻¹) solution in PBS was added into each well and kept at 37 °C for 3 h. After MTT medium removal, the formazan crystals were dissolved in DMSO and the absorbance was measured at 570 nm using a microplate reader (Genios Tecan). The untreated cells were served as the control and their viability was set as 100%.

9 Intracellular localization of ART-TPP-Alk

MDA-MB-231 cells were cultured in the chambers (LAB-TEK, Chambered Coverglass System) at a density of 5×10⁵ per mL for 18 h. The culture medium was removed, and the cells were rinsed with PBS. MDA-MB-231 cells were incubated with ART-TPP-Alk (10 µM) and mitochondria tracker deep red (400 nm) at 37 °C for 4 h. After the medium was removed, the cells were washed with PBS buffer and then fixed with formic aldehyde solution (3.7%) for 10 minutes at room temperature. The cells were washed with PBS buffer three times and permeabilized with 0.1% Triton X-100 in PBS for 10 min. Cells were then blocked with 2% BSA in PBS for 30 min, washed twice with PBS, and then subsequently treated with a freshly premixed click chemistry reaction solution in a 100 µL volume (final concentrations of reagents: 0.1 mM CuSO₄, 2.5 mM sodium ascorbate, 300 µM TBTA, and 50 µM Azide-fluor in PBS) for 2 h at room temperature. After washing with PBS for 3 times, cells were imaged by confocal laser scanning microscope (CLSM, Zeiss LSM 410, Jena, Germany). For Azide-fluor, the excitation was 543 nm, and the emission filter was 560-620 nm. For mitochondria tracker, the excitation was 633 nm, and the band filter was 650 nm.

10 Fluorescent labeling of live cancer cells and cell lysate with AP1 and ART-TPP-Alk

Briefly, HeLa cells were cultured in 6-well plate till 80% confluence was reached. The medium was removed and washed twice with PBS before treating the cell with AP1 (20 µM), ART-TPP-Alk (20 µM) and DMSO (control) for 6 hours. All three samples contain a final volume of 2 ml and had a final DMSO concentration of 1%. The cells were harvested and lysed prior to Copper (I) click reaction with rhodamine-azide tag. For each biotin click reaction, 10 µM rhodamine-azide, 1 mM TCEP, 100 µM TBTA ligand and 1 mM copper sulphate were added to the lysate and incubated for 3 hours with continuous shaking. Next, tagged proteins were precipitated with acetone and air dried. 1× Laemmli buffer (35 µl) was added to dissolve the pellets, and 15 ml of each sample was separated by SDS-PAGE on 12.5% polyacrylamide gels or 4–20% gradient gels (Bio-Rad). Following one-dimensional gel separation, gels were scanned using a Typhoon 9410 laser scanner (GE Healthcare), and the images were analysed with ImageQuant software. The fluorescence contrast was normalized against the DMSO control to minimize the background.

For competition assays, the HeLa cell lysate was pretreated with excessive artesunate or ART-TPP (25×) for 1 h then together with AP1 or ART-TPP-Alk (20 µM) for 4 h. Probe-

labelled proteins were visualized by click conjugation to the rhodamine-azide followed by SDS-PAGE separation and fluorescence scanning.

11 HeLa cells labeled with AP1 and ART-TPP-Alk for target identification

11.1 Cell labeling

Briefly, HeLa cells were cultured in P150mm culture dish till 80% confluence was reached. The medium was removed and washed twice with PBS before treating the cell with AP1 (30 μ M), ART-TPP-Alk (30 μ M) and DMSO (control) for 6 hours. All three samples contain a final volume of 20ml and had a final DMSO concentration of 1%. The cells were harvested and lysed prior to Copper (I) click reaction with biotin-azide tag. For each biotin click reaction, 10 μ M biotin-azide, 1 mM TCEP, 100 μ M TBTA ligand and 1 mM copper sulphate were added to the lysate and incubated for 3 hours with continuous shaking. The clicked proteins were subjected to precipitation with acetone and air dry. Subsequently, the collected pellet was reconstituted in 5ml of 0.1% SDS in PBS and incubated with 50 μ l of streptavidin beads (Sigma-Aldrich[®], St. Louis, MO, USA) under continuous gentle mixing for 2 hours at room temperature.

11.2 On-beads digestion

The beads were washed three times with 1% SDS, 6 M urea and PBS in order. Next, the beads was re-suspended in 100 μ L triethylammonium bicarbonate (TEAB) and 2 μ L TCEP. The beads were heated up to 65°C for 1 hour. Subsequently, the samples were incubated with 1 μ L methyl methanethiosulfonate (MMTS) for 15min at room temperature. Samples were trypsinized overnight at 37°C to digest the peptide. The digested peptide was separated from the beads with a filter-spin column (GE Healthcare Life Science). Next, 100 μ l diluent made up of 98% water, 2% acetonitrile and 0.05% formic acid was added for re-suspension.

11.3 Liquid chromatography- mass spectrometry/mass spectrometry for proteins identification and quantification

The pooled iTRAQ-labelled pull down sample was separate into fractions using ChiPLC-nanoflex (Eksigent, Dublin, Ca, USA) in Trap-Elute configuration. A volume of sample (5 μ L) was loaded into the column of liquid chromatography (LC). Both trap and analytical columns are made up of 3 μ m ChromXP C18-CL and have a size of 200 μ m X 0.5 mm and 75 μ m X 150mm respectively. The peptides were separated by a gradient formed by mobile phase A (2% ACN, 0.1% FA) and mobile phase B (98%ACN, 0.1% FA) at a flow rate of 300 μ l/min. The following gradients were applied for the peptide separation: 5-12% of mobile phase for 20minutes, 12-30% of mobile phase b for 90 minutes and 30-90% of mobile phase B for 2 minutes. The columns were regenerated with 90% of mobile phase B for 5 min and 90-5% of mobile phase B for 3 min, and equilibrated with 5% of mobile phase B for 13 minutes.

TripleTOF 5600 system (AB SCIEX, Foster City, Ca, USA) was used to obtain mass-spectrometry spectrum in high resolution mode with more than 30000 resolution (250ms accumulation time per spectrum and a mass range of 400-1250 m/z) and mass-spectrometry/mass-spectrometry spectrum in high sensitivity mode with more than 15000 resolution. For each mass-spectrometry spectrum, a maximum of 20 precursors with a charge state between 2 and 4 were chosen for fragmentation. Also, the signals were accumulated for a minimum of 100 ms per

spectrum and dynamic exclusion time was set at 15 seconds.

References

1. J. Wang, C.-J. Zhang, W. N. Chia, C. C. Y. Loh, Z. Li, Y. M. Lee, Y. He, L.-X. Yuan, T. K. Lim, M. Liu, et al., Nat. Commun.2015, 6, 10111

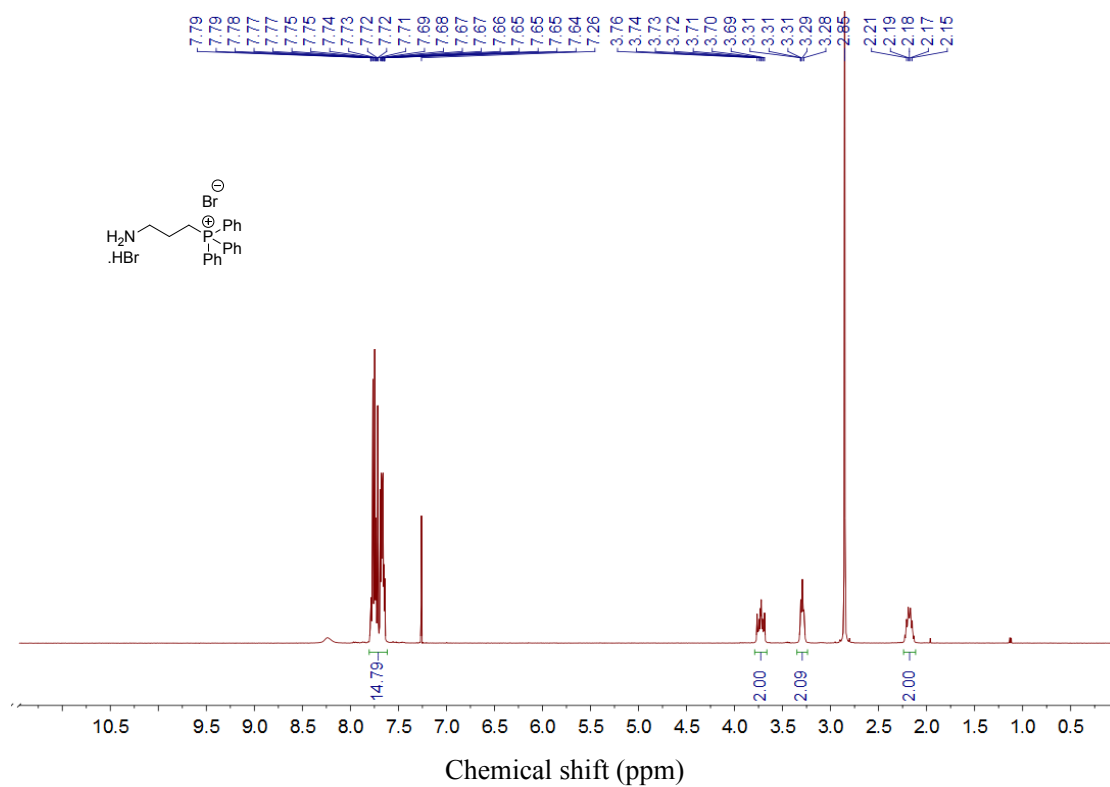


Figure S1 $^1\text{H-NMR}$ of **1**

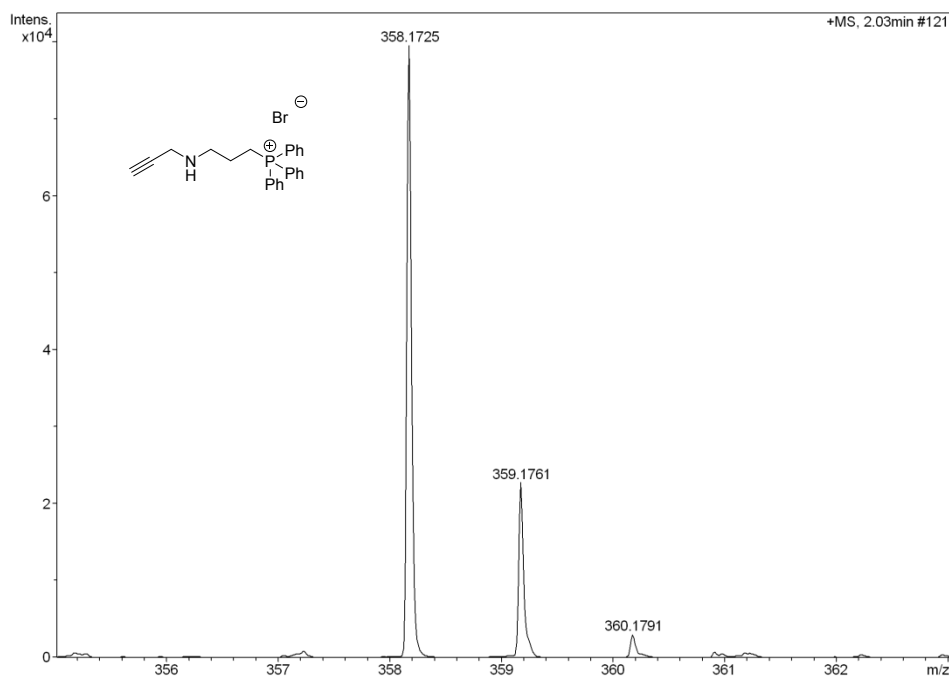
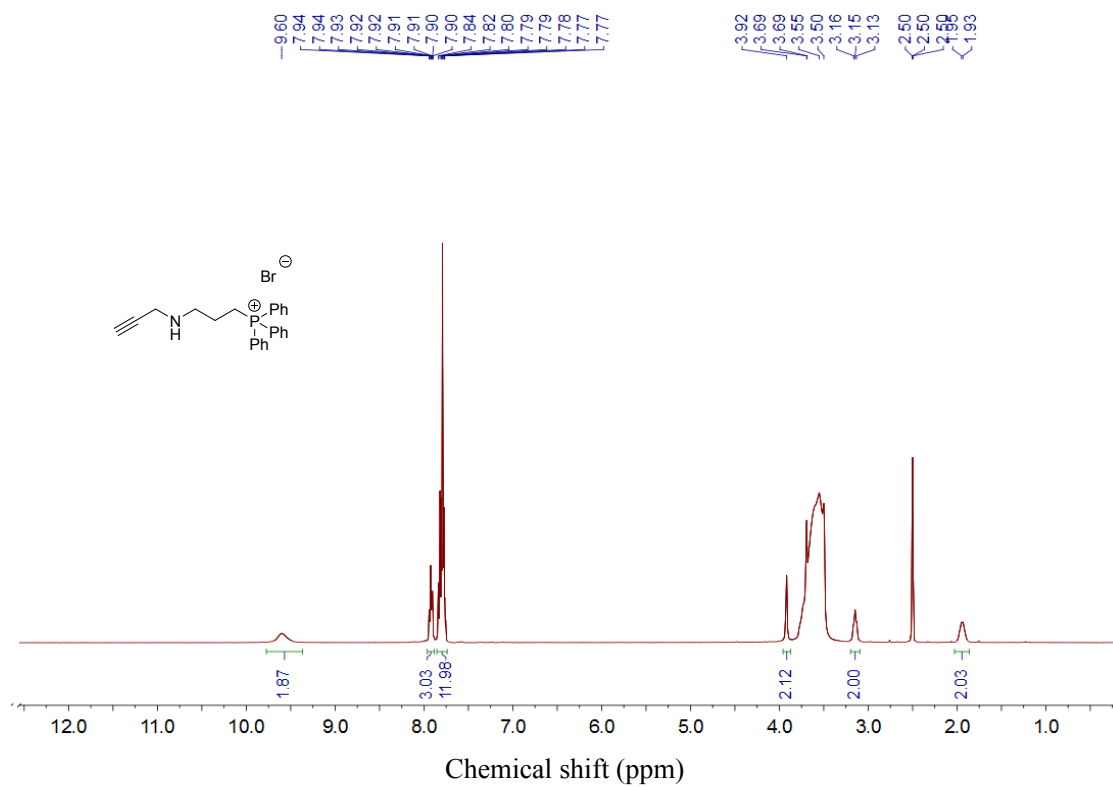
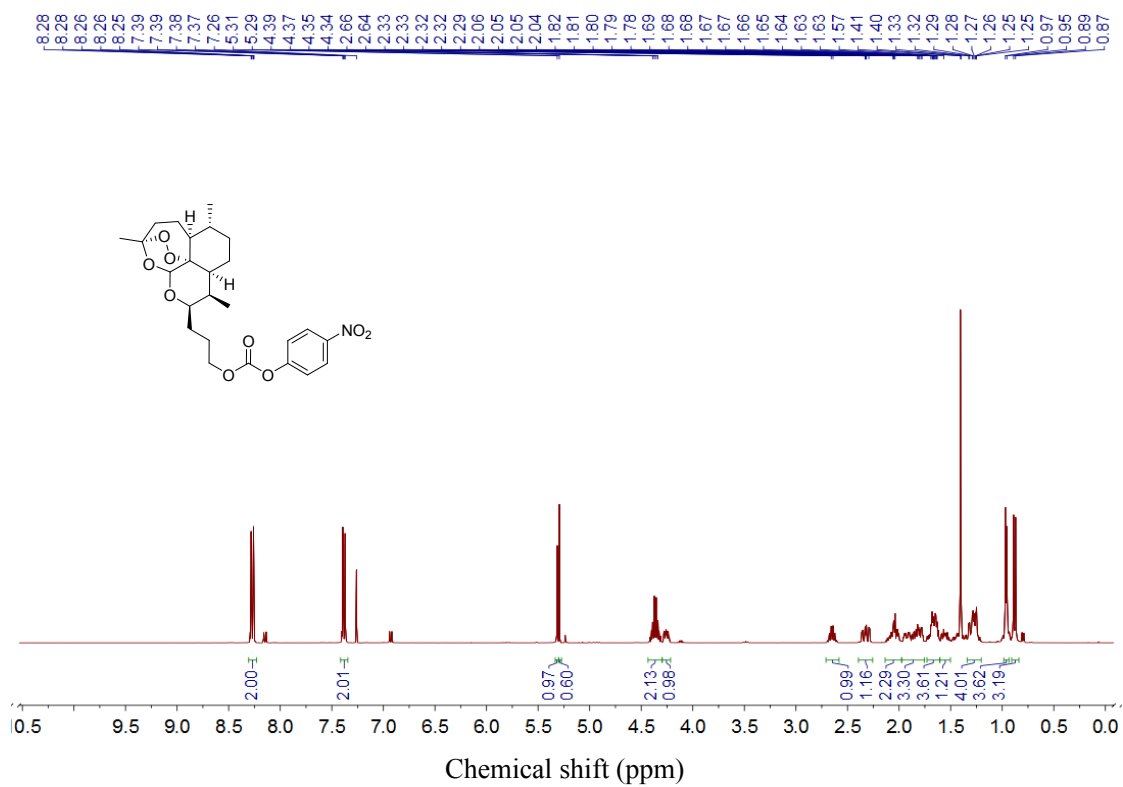
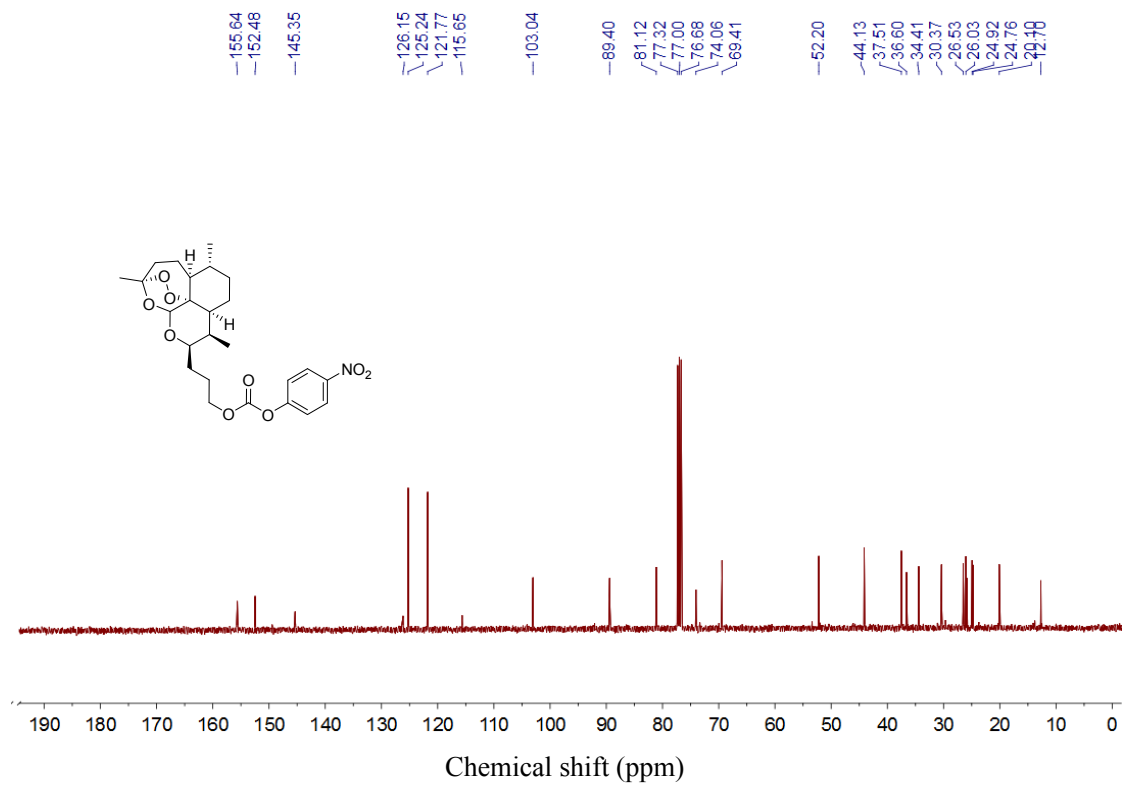


Figure S3 High resolution mass spectrum of **2**

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Figure S4 $^1\text{H-NMR}$ of 4Figure S5 $^{13}\text{C-NMR}$ of 4

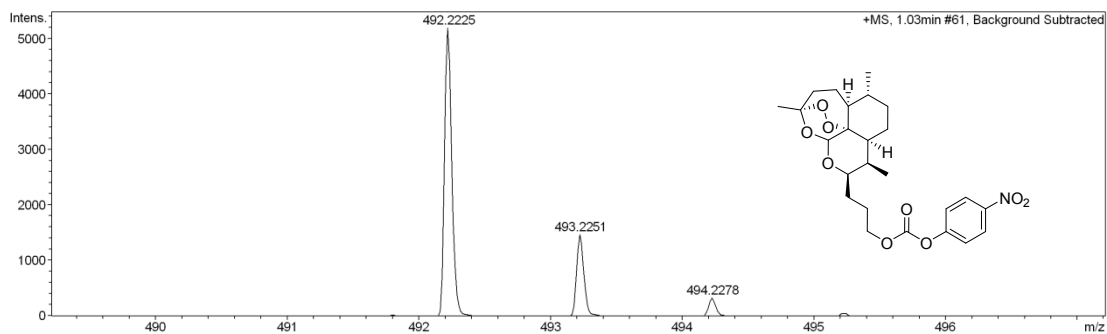


Figure S6 High resolution mass spectrum of 4

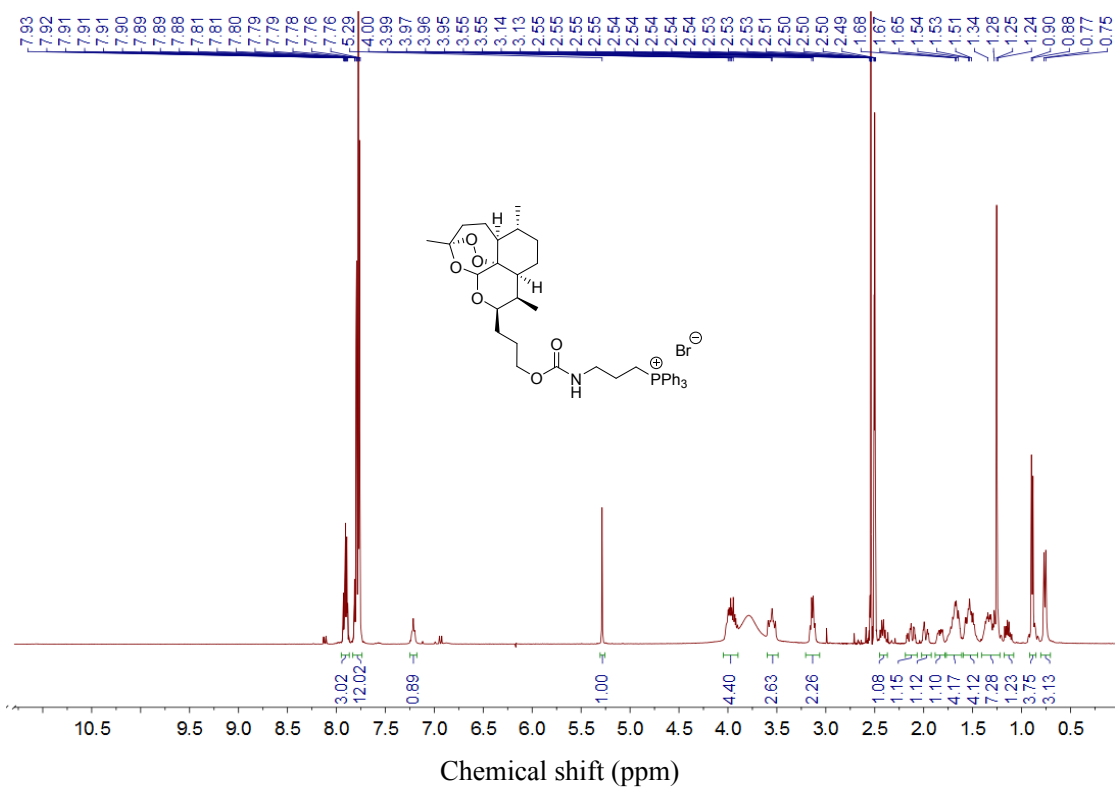


Figure S7 ¹H-NMR of ART-TPP

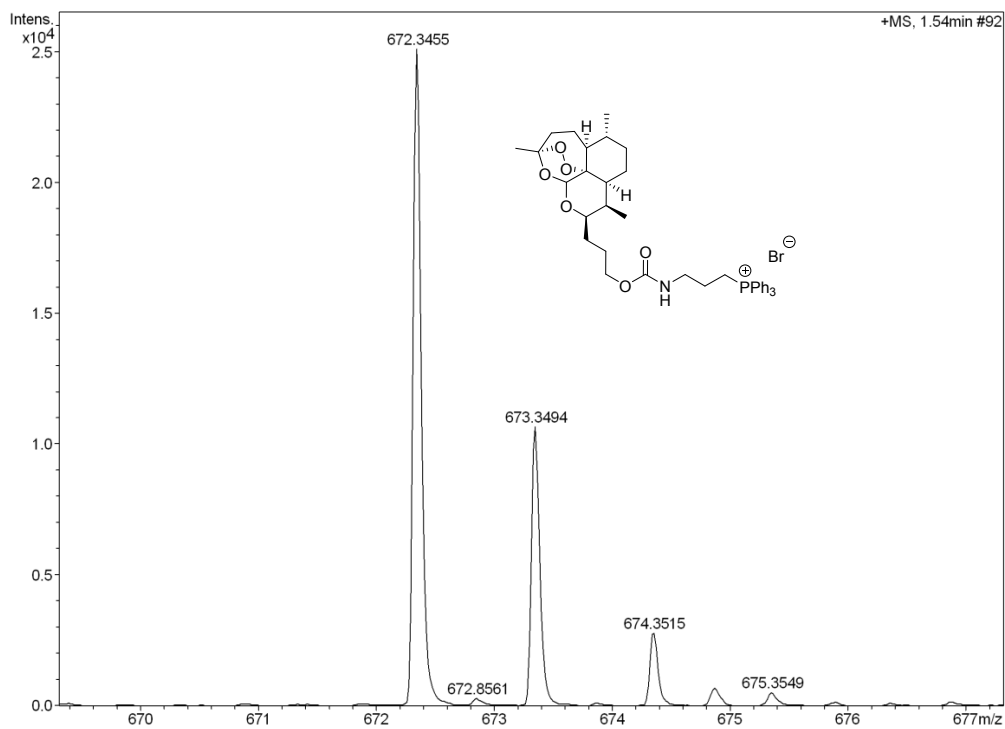


Figure S8 High resolution mass spectrum of ART-TPP

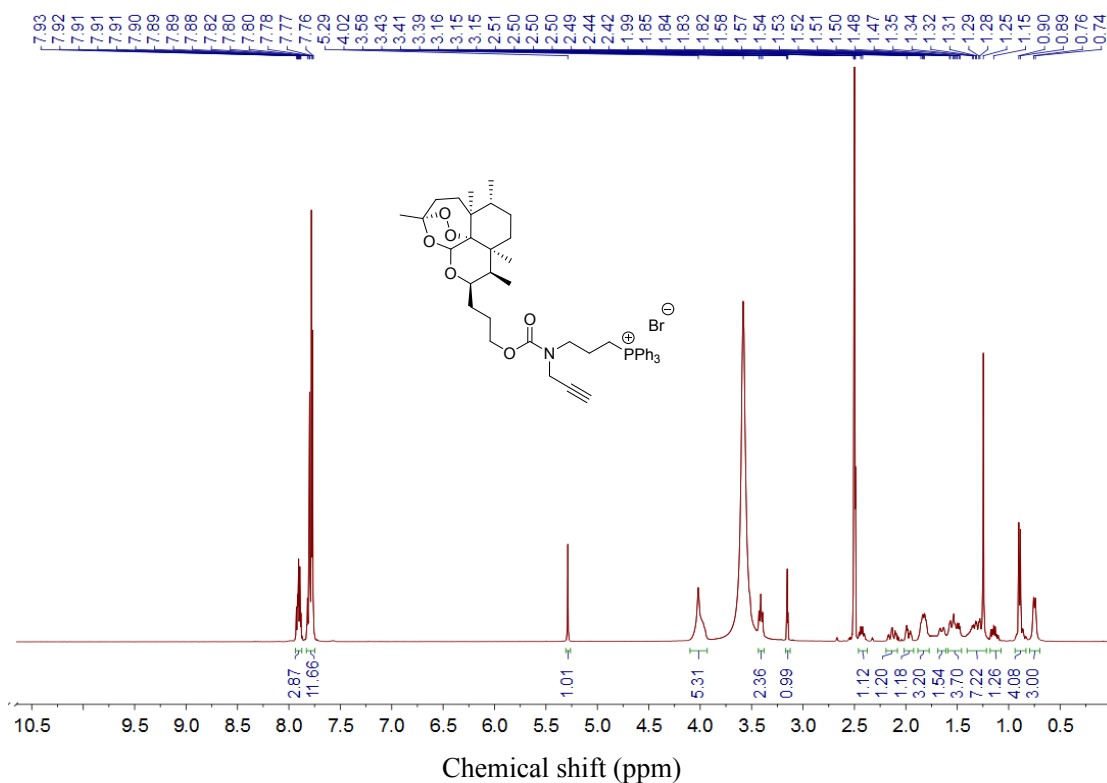


Figure S9 ¹H-NMR of ART-TPP-Alk

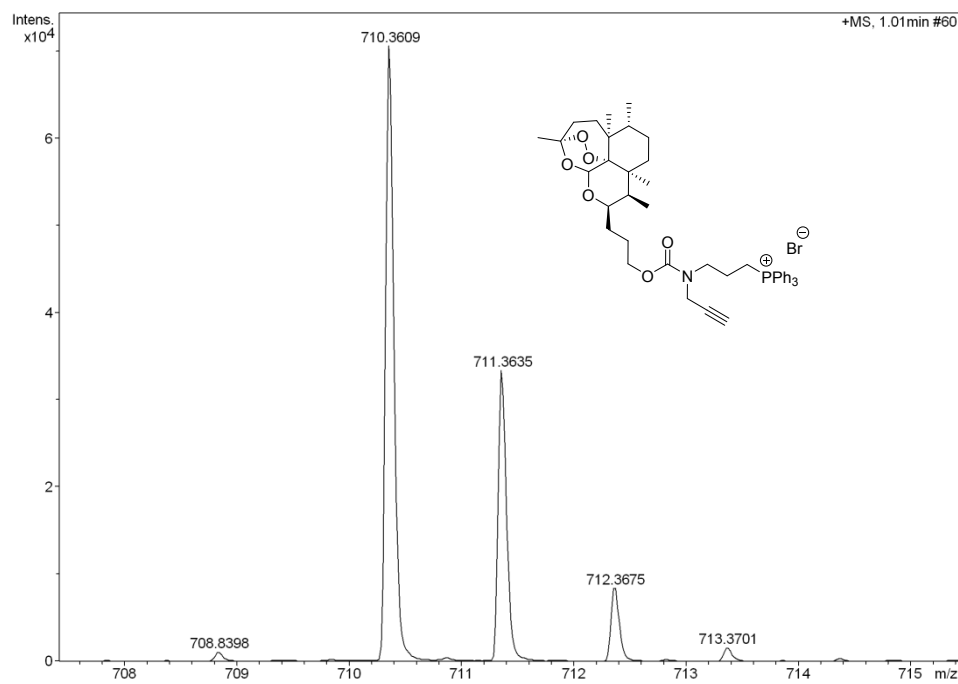


Figure S10 High resolution mass spectrum of ART-TPP-Alk

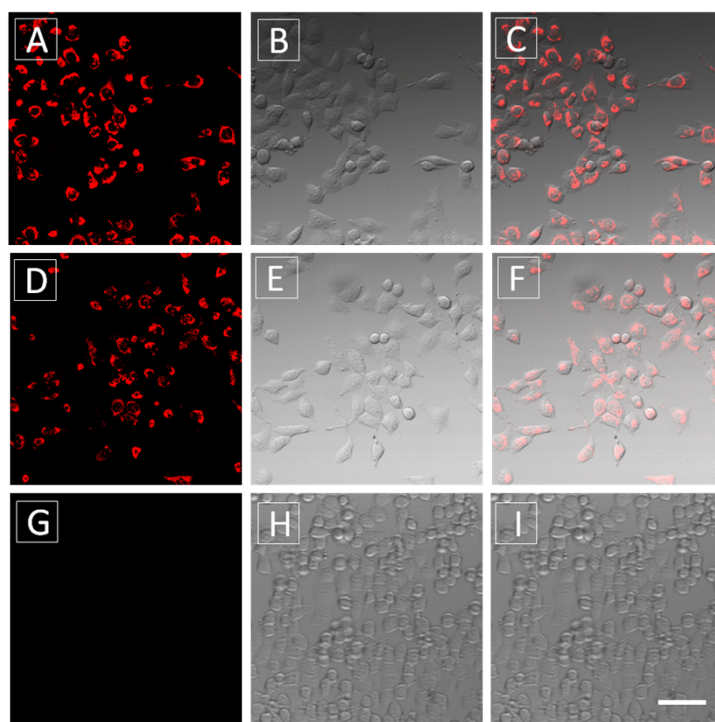


Figure S11 Confocal images of HeLa cells upon incubation with tetramethylrhodamine ethyl ester (TMRE), without (A-C), and with the treatment of 10 μ M ART (D-F) or 10 μ M ART-TPP (G-I) for 2 h. The TMRE was excited at 543 nm and the red fluorescence was detected using a 575–625 nm bandpass filter. All images share the same scale bar of 30 μ m.

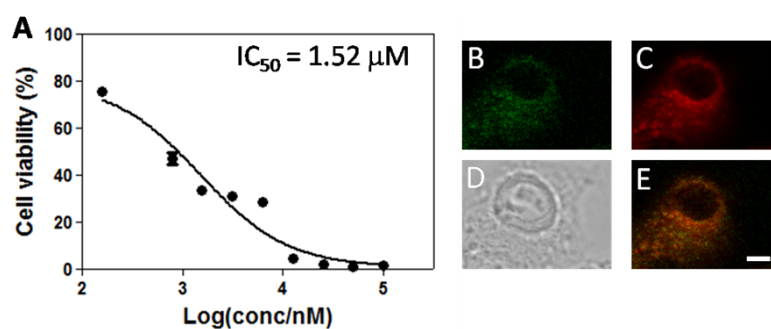


Figure S12 A) Cell viability of MDA-MB-231 by ART-TPP-Alk; B-E) Subcellular location study of clickable ART-TPP-Alk with CuAAC. B) image from Azide-fluor, Ex = 543 nm, Em = 560-620 nm; C) image from mitochondria tracker (deep red); Ex = 633 nm, Em > 650 nm; D) image of bright field; E) overlay of B and C. All figures share the same scale bar (10 μ m).

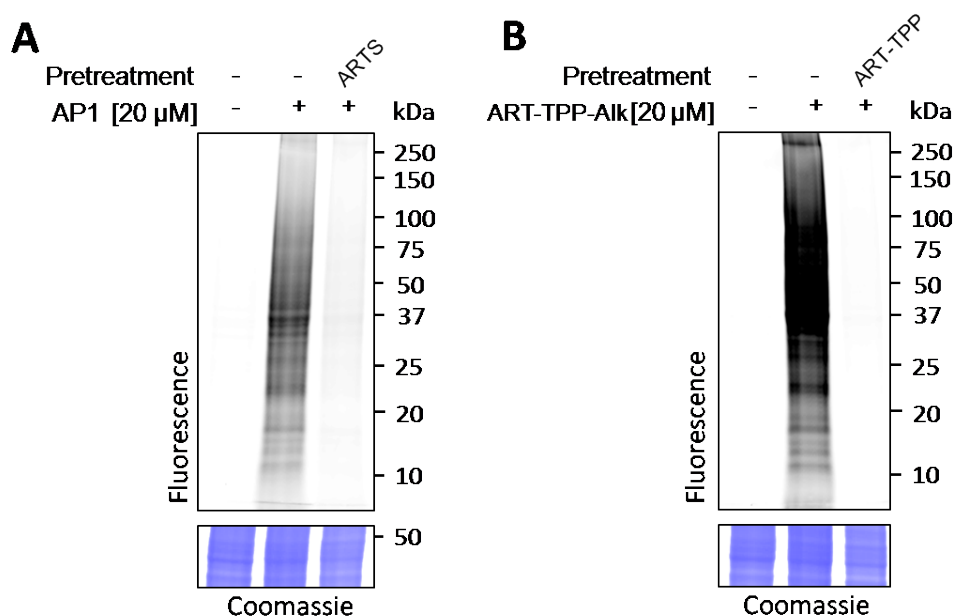


Figure S13. The in vitro competition assay by in-gel fluorescence scanning. (A) The HeLa cell lysates were pretreated with 25 X artesunate for 2 h. Then the lysates were incubated together with AP1 (20 μ M) for another 4 h. A Rhodamine B-azide tag was conjugated to the probe labelled proteins by click chemistry. The protein lysates were then resolved by SDS-PAGE and visualized with fluorescence scanning. (B) The HeLa cell lysates were pretreated with 25 X ART-TPP for 2 h. Then the lysates were incubated together with AP2 (20 μ M) for another 4 h. The following step are same as (A). ARTS, artesunate; Fluo, fluorescence scanning; Coo, Coomassie staining.

Supplementary table 1. List of AP1 targets

No.	Unused Score ¹	% Cov (95) ²	Accession #	Name	Species	Peptide s(95%) ³
1	88.68	40.4	P31327 CPSM	Carbamoyl-phosphate synthase [ammonia], mitochondrial	HUMAN	48
2	63.25	18.7	P49327 FAS	Fatty acid synthase	HUMAN	32
3	52.02	33.6	P13639 EF2	Elongation factor 2	HUMAN	29
4	51.14	22.8	A0A087WVQ6 A0A087WVQ6	Clathrin heavy chain	HUMAN	30
5	48.12	37.6	P08238 HS90B	Heat shock protein HSP 90-beta	HUMAN	29
6	47.37	39	O43707 ACTN4	Alpha-actinin-4	HUMAN	27
7	47.03	55.9	P14618 KPYP	Pyruvate kinase PKM	HUMAN	30
8	46.27	71.9	P07437 TBB5	Tubulin beta chain	HUMAN	39
9	45.25	41.6	P02786 TFR1	Transferrin receptor protein 1	HUMAN	25
10	44.31	47.7	A0A0G2JIW1 A0A0G2JIW1	Heat shock 70 kDa protein 1B	HUMAN	25
11	39.6	14.2	P35579 MYH9	Myosin-9	HUMAN	21
12	38.97	25.5	P53396 ACLY	ATP-citrate synthase	HUMAN	20
13	36.16	40.7	P11142 HSP7C	Heat shock cognate 71 kDa protein	HUMAN	24
14	36	38.3	P50990 TCPQ	T-complex protein 1 subunit theta	HUMAN	18
15	35.4	15.3	P42704 LPPRC	Leucine-rich PPR motif-containing protein, mitochondrial	HUMAN	19
16	34.76	18.9	Q08211 DHX9	ATP-dependent RNA helicase A	HUMAN	18
17	34.36	4.3	Q15149 PLEC	Plectin	HUMAN	16
18	33.29	50.7	P60842 IF4A1	Eukaryotic initiation factor 4A-I	HUMAN	23
19	32.91	16.7	P26640 SYVC	Valine--tRNA ligase	HUMAN	17
20	31.99	10	O75369 FLNB	Filamin-B	HUMAN	19
21	31.52	55.5	P06733 ENOA	Alpha-enolase	HUMAN	23
22	30.66	27.5	J3KTA4 J3KTA4	Probable ATP-dependent RNA helicase DDX5	HUMAN	16
23	29.14	32.3	P49368 TCPG	T-complex protein 1 subunit gamma	HUMAN	15
24	28.52	9.8	P46940 IQGA1	Ras GTPase-activating-like protein IQGAP1	HUMAN	13
25	28.49	31.3	P17987 TCPA	T-complex protein 1 subunit alpha	HUMAN	15
26	28.11	38.3	P68104 EF1A1	Elongation factor 1-alpha 1	HUMAN	20
27	27.88	56.3	P00338 LDHA	L-lactate dehydrogenase A chain	HUMAN	21
28	27.68	18.1	P09874 PARP1	Poly [ADP-ribose] polymerase 1	HUMAN	14
29	27.47	33.2	P12956 XRCC6	X-ray repair cross-complementing protein 6	HUMAN	15
30	27.44	35.2	P08670 VIME	Vimentin	HUMAN	15
31	27.06	20.7	P55072 TERA	Transitional endoplasmic reticulum ATPase	HUMAN	13
32	27.02	37.7	P10809 CH60	60 kDa heat shock protein, mitochondrial	HUMAN	15
33	26.31	39.9	P34897 GLYM	Serine hydroxymethyltransferase, mitochondrial	HUMAN	14
34	26.07	34.6	P78371 TCPB	T-complex protein 1 subunit beta	HUMAN	14
35	25.73	7.8	A0A087WU33 A0A087WU33	Spectrin beta chain, non-erythrocytic 1	HUMAN	14
36	25.06	18.4	P22314 UBA1	Ubiquitin-like modifier-activating enzyme 1	HUMAN	14
37	24.61	37.9	P00558 PGK1	Phosphoglycerate kinase 1	HUMAN	13
38	24.36	21	Q14697 GANAB	Neutral alpha-glucosidase AB	HUMAN	13
39	23.22	21.4	P49748 ACADV	Very long-chain specific acyl-CoA dehydrogenase,	HUMAN	12
40	22.95	26	P11413 G6PD	Glucose-6-phosphate 1-dehydrogenase	HUMAN	12
41	22.91	26	P31939 PUR9	Bifunctional purine biosynthesis protein PURH	HUMAN	11
42	22.89	57.2	P23396 RS3	40S ribosomal protein S3	HUMAN	11
43	22.87	6	Q13813 SPTN1	Spectrin alpha chain, non-erythrocytic 1	HUMAN	12
44	22.76	54.9	P60174 TPIS	Triosephosphate isomerase	HUMAN	12
45	22.65	44.8	P07355 ANXA2	Annexin A2	HUMAN	12
46	22.57	30.3	P11021 GRP78	78 kDa glucose-regulated protein	HUMAN	15
47	22.14	48.9	P63244 RACK1	Receptor of activated protein C kinase 1	HUMAN	12
48	22.01	18	Q14974 IMB1	Importin subunit beta-1	HUMAN	12
49	22	41	J3KPS3 J3KPS3	Fructose-bisphosphate aldolase	HUMAN	16
50	21.91	9.7	P07814 SYEP	Bifunctional glutamate/proline--tRNA ligase	HUMAN	11
51	21.79	18.7	P48643 TCPE	T-complex protein 1 subunit epsilon	HUMAN	11
52	21.78	25.5	J3KPF3 J3KPF3	4F2 cell-surface antigen heavy chain	HUMAN	13
53	21.7	19.1	P02545 LMNA	Prelamin-A/C	HUMAN	11
54	21.64	27.1	P23526 SAHH	Adenosylhomocysteinase	HUMAN	10
55	21.06	31.6	P26641 EF1G	Elongation factor 1-gamma	HUMAN	11
56	20.98	17.1	Q9NR30 DDX21	Nucleolar RNA helicase 2	HUMAN	11
57	20.17	24.1	P25705 ATPA	ATP synthase subunit alpha, mitochondrial	HUMAN	10
58	20.1	20.1	O60506 HNRPQ	Heterogeneous nuclear ribonucleoprotein Q	HUMAN	11
59	20.07	14.9	Q12906 ILF3	Interleukin enhancer-binding factor 3	HUMAN	10
60	19.9	21	Q99832 TCPH	T-complex protein 1 subunit eta	HUMAN	11
61	19.72	29.1	P29401 TKT	Transketolase	HUMAN	11
62	19.64	18.2	P13010 XRCC5	X-ray repair cross-complementing protein 5	HUMAN	11

63	19.54	25.4	P40227 TCPZ	T-complex protein 1 subunit zeta	HUMAN	10
64	19.46	18.7	B4DDN1 B4DDN1	Glutamine--tRNA ligase	HUMAN	10
65	19.01	30.1	P07900 HS90A	Heat shock protein HSP 90-alpha	HUMAN	24
66	18.91	13.8	O00410 IPO5	Importin-5	HUMAN	10
67	18.53	24.3	Q04695 K1C17	Keratin, type I cytoskeletal 17	HUMAN	9
68	18.35	18.8	P31948 STIP1	Stress-induced-phosphoprotein 1	HUMAN	9
69	17.87	16.6	A0A087X0X3 A0A087X0X3	Heterogeneous nuclear ribonucleoprotein M	HUMAN	9
70	17.47	39.4	F8W6I7 F8W6I7	Heterogeneous nuclear ribonucleoprotein A1	HUMAN	11
71	17.04	40.7	P23284 PPIB	Peptidyl-prolyl cis-trans isomerase B	HUMAN	9
72	16.55	14.2	P14625 ENPL	Endoplasmin	HUMAN	9
73	16.3	37.7	P62258 1433E	14-3-3 protein epsilon	HUMAN	10
74	16.27	13.5	E7EQR4 E7EQR4	Ezrin	HUMAN	10
75	16.24	10.4	O95373 IPO7	Importin-7	HUMAN	8
76	16.21	15.3	P11940 PABP1	Polyadenylate-binding protein 1	HUMAN	9
77	16.21	28.5	A0A0A0MTS2 A0A0A0MTS2	Glucose-6-phosphate isomerase (Fragment)	HUMAN	10
78	16.11	21.3	Q13838 DX39B	Spliceosome RNA helicase DDX39B	HUMAN	8
79	16.04	20	P38646 GRP75	Stress-70 protein, mitochondrial	HUMAN	10
80	16	44.7	Q06830 PRDX1	Peroxiredoxin-1	HUMAN	10
81	16	24.3	H0Y4R1 H0Y4R1	Inosine-5'-monophosphate dehydrogenase 2 (Fragment)	HUMAN	8
82	15.97	18.1	P58107 EPIPL	Epiplakin	HUMAN	10
83	15.89	6.4	P11388 TOP2A	DNA topoisomerase 2-alpha	HUMAN	8
84	15.79	9.4	O14980 XPO1	Exportin-1	HUMAN	8
85	15.59	20.4	A0A0D9SG12 A0A0D9SG12	ATP-dependent RNA helicase DDX3X	HUMAN	10
86	15.57	20.3	P52209 6PGD	6-phosphogluconate dehydrogenase, decarboxylating	HUMAN	8
87	15.39	23.5	P61978 HNRPK	Heterogeneous nuclear ribonucleoprotein K	HUMAN	8
88	15.29	46.9	Q32Q12 Q32Q12	Nucleoside diphosphate kinase	HUMAN	9
89	15.01	33.6	P05141 ADT2	ADP/ATP translocase 2	HUMAN	9
90	14.88	8.1	Q15393 SF3B3	Splicing factor 3B subunit 3	HUMAN	7
91	14.81	23.4	P30101 PDIA3	Protein disulfide-isomerase A3	HUMAN	8
92	14.79	16.3	Q12931 TRAP1	Heat shock protein 75 kDa, mitochondrial	HUMAN	8
93	14.61	23.5	P00966 ASSY	Argininosuccinate synthase	HUMAN	9
94	14.49	36.7	P15121 ALDR	Aldose reductase	HUMAN	8
95	14.45	21.1	P50395 GDIB	Rab GDP dissociation inhibitor beta	HUMAN	8
96	14.15	21.8	P07195 LDHB	L-lactate dehydrogenase B chain	HUMAN	10
97	14.15	11.5	P26639 SYTC	Threonine--tRNA ligase, cytoplasmic	HUMAN	7
98	14.06	28.4	B4DY09 B4DY09	Interleukin enhancer-binding factor 2	HUMAN	7
99	14.04	11	P19338 NUCL	Nucleolin	HUMAN	7
100	14	14.8	O43175 SERA	D-3-phosphoglycerate dehydrogenase	HUMAN	7
101	14	43.6	P62937 PPIA	Peptidyl-prolyl cis-trans isomerase A	HUMAN	10
102	13.82	10.4	Q7KZF4 SND1	Staphylococcal nuclease domain-containing protein 1	HUMAN	7
103	13.8	20	H7C2I1 H7C2I1	Protein arginine N-methyltransferase 1	HUMAN	7
104	13.66	18.6	P08729 K2C7	Keratin, type II cytoskeletal 7	HUMAN	7
105	13.54	8.4	O75533 SF3B1	Splicing factor 3B subunit 1	HUMAN	7
106	13.38	20.9	P38919 IF4A3	Eukaryotic initiation factor 4A-III	HUMAN	9
107	13.33	15.1	Q9Y3I0 RTCB	tRNA-splicing ligase RtcB homolog	HUMAN	6
108	13.31	12.1	H0Y8E6 H0Y8E6	DNA helicase (Fragment)	HUMAN	8
109	13.28	31.4	P22626 ROA2	Heterogeneous nuclear ribonucleoproteins A2/B1	HUMAN	9
110	13.26	8.8	Q13200 PSMD2	26S proteasome non-ATPase regulatory subunit 2	HUMAN	6
111	13.2	17.8	Q9Y617 SERC	Phosphoserine aminotransferase	HUMAN	7
112	13.19	7	J3KR24 J3KR24	Isoleucine--tRNA ligase, cytoplasmic	HUMAN	7
113	13.15	15.4	P14868 SYDC	Aspartate--tRNA ligase, cytoplasmic	HUMAN	7
114	13.03	7.3	P55060 XPO2	Exportin-2	HUMAN	7
115	12.95	15.6	F8VS07 F8VS07	LIM domain and actin-binding protein 1	HUMAN	6
116	12.85	10.3	P08133 ANXA6	Annexin A6	HUMAN	6
117	12.75	15	P33993 MCM7	DNA replication licensing factor MCM7	HUMAN	8
118	12.66	7.5	E9PLK3 E9PLK3	Puromycin-sensitive aminopeptidase	HUMAN	6
119	12.59	18.4	P49411 EFTU	Elongation factor Tu, mitochondrial	HUMAN	7
120	12.44	14.7	Q00839 HNRPU	Heterogeneous nuclear ribonucleoprotein U	HUMAN	8
121	12.4	10.3	P17812 PYRG1	CTP synthase 1	HUMAN	6
122	12.19	10	P34932 HSP74	Heat shock 70 kDa protein 4	HUMAN	6
123	12.07	29.2	C9J9K3 C9J9K3	40S ribosomal protein SA (Fragment)	HUMAN	6
124	12.06	9	Q92598 HS105	Heat shock protein 105 kDa	HUMAN	6
125	12.02	9.2	Q01813 PFKAP	ATP-dependent 6-phosphofructokinase, platelet type	HUMAN	6
126	12	37.5	P30041 PRDX6	Peroxiredoxin-6	HUMAN	6
127	12	27.8	P62701 RS4X	40S ribosomal protein S4, X isoform	HUMAN	6
128	12	32.2	B5MDF5 B5MDF5	GTP-binding nuclear protein Ran	HUMAN	6
129	12	30.6	P05388 RLA0	60S acidic ribosomal protein P0	HUMAN	7
130	12	55.7	P07737 PROF1	Profilin-1	HUMAN	7
131	12	36.4	H0YEN5 H0YEN5	40S ribosomal protein S2 (Fragment)	HUMAN	7

132	11.92	27.8	A0A024R4M0 A0A024R4M0	40S ribosomal protein S9	HUMAN	6
133	11.86	16.3	A0A0U1RRM4 A0A0U1RRM4	Polypyrimidine tract-binding protein 1	HUMAN	6
134	11.84	23.5	Q9Y265 RUVB1	RuvB-like 1	HUMAN	7
135	11.64	18.5	P52292 IMA1	Importin subunit alpha-1	HUMAN	7
136	11.6	50.6	P23528 COF1	Cofilin-1	HUMAN	6
137	11.58	8.2	Q5JQ13 Q5JQ13	Vinculin (Fragment)	HUMAN	6
138	11.37	24.8	Q96AG4 LRC59	Leucine-rich repeat-containing protein 59	HUMAN	6
139	11.31	18.4	G8JLB6 G8JLB6	Heterogeneous nuclear ribonucleoprotein H	HUMAN	7
140	11.3	9.5	P33992 MCM5	DNA replication licensing factor MCM5	HUMAN	6
141	11.08	9.8	A8MXP9 A8MXP9	Matrin-3	HUMAN	6
142	10.85	13.9	P05787 K2C8	Keratin, type II cytoskeletal 8	HUMAN	6
143	10.64	7.6	P23921 RIR1	Ribonucleoside-diphosphate reductase large subunit	HUMAN	5
144	10.36	27.5	P04406 G3P	Glyceraldehyde-3-phosphate dehydrogenase	HUMAN	10
145	10.29	17	P41091 IF2G	Eukaryotic translation initiation factor 2 subunit 3	HUMAN	5
146	10.24	9.1	A0A0A0MSQ0 A0A0A0MSQ0	Plastin-3	HUMAN	5
147	10.18	6	P16615 AT2A2	Sarcoplasmic/endoplasmic reticulum calcium ATPase 2	HUMAN	5
148	10.18	12.6	Q16658 FSCN1	Fascin	HUMAN	6
149	10.17	12	Q16576 RBBP7	Histone-binding protein RBBP7	HUMAN	5
150	10.12	8.3	A0A0C4DGH5 A0A0C4DGH5	Cullin-associated NEDD8-dissociated protein 1 (Fragment)	HUMAN	5
151	10.11	32.7	P37802 TAGL2	Transgelin-2	HUMAN	5
152	10.04	16	P50991 TCPD	T-complex protein 1 subunit delta	HUMAN	6
153	10.03	29.8	Q5T7C4 Q5T7C4	High mobility group protein B1	HUMAN	5
154	10	9	P40939 ECHA	Trifunctional enzyme subunit alpha, mitochondrial	HUMAN	5
155	10	16.4	F8VVM2 F8VVM2	Phosphate carrier protein, mitochondrial	HUMAN	5
156	10	14	Q9UQ80 PA2G4	Proliferation-associated protein 2G4	HUMAN	5
157	10	11.7	A0A087WTP3 A0A087WTP3	Far upstream element-binding protein 2	HUMAN	5
158	10	18.4	D6RD18 D6RD18	Heterogeneous nuclear ribonucleoprotein A/B	HUMAN	5
159	10	25.1	G3V576 G3V576	Heterogeneous nuclear ribonucleoproteins C1/C2	HUMAN	5
160	10	3.8	F8VPD4 F8VPD4	CAD protein	HUMAN	7
161	10	34.2	E7EX29 E7EX29	14-3-3 protein zeta/delta (Fragment)	HUMAN	8
162	9.89	20.2	P12814 ACTN1	Alpha-actinin-1	HUMAN	14
163	9.8	6.3	P56192 SYMC	Methionine--tRNA ligase, cytoplasmic	HUMAN	5
164	9.7	13.5	P00505 AATM	Aspartate aminotransferase, mitochondrial	HUMAN	5
165	9.68	7.7	P54886 P5CS	Delta-1-pyrroline-5-carboxylate synthase	HUMAN	5
166	9.66	25.3	E9PK01 E9PK01	Elongation factor 1-delta (Fragment)	HUMAN	5
167	9.62	5.8	Q99613 EIF3C	Eukaryotic translation initiation factor 3 subunit C	HUMAN	5
168	9.45	14.8	P04181 OAT	Ornithine aminotransferase, mitochondrial	HUMAN	5
169	9.43	7.9	P05023 AT1A1	Sodium/potassium-transporting ATPase subunit alpha-1	HUMAN	6
170	9.38	7	Q15029 U5S1	116 kDa U5 small nuclear ribonucleoprotein component	HUMAN	5
171	9.33	21.3	P05198 IF2A	Eukaryotic translation initiation factor 2 subunit 1	HUMAN	6
172	9.29	24.6	P18124 RL7	60S ribosomal protein L7	HUMAN	5
173	9.26	22.3	P30048 PRDX3	Thioredoxin-dependent peroxide reductase, mitochondrial	HUMAN	5
174	9.16	19.9	A0A0A0MR02 A0A0A0MR02	Voltage-dependent anion-selective channel protein 2	HUMAN	5
175	9.1	7.4	Q09666 AHNK	Neuroblast differentiation-associated protein AHNAK	HUMAN	6
176	9.07	15.6	P05783 K1C18	Keratin, type I cytoskeletal 18	HUMAN	5
177	9.01	18	Q15365 PCBP1	Poly(rC)-binding protein 1	HUMAN	5
178	8.89	11.7	Q15046 SYK	Lysine--tRNA ligase	HUMAN	5
179	8.79	28.1	P62249 RS16	40S ribosomal protein S16	HUMAN	5
180	8.6	21.2	G3XALO G3XALO	Malate dehydrogenase	HUMAN	4
181	8.38	16.4	H3BLZ8 H3BLZ8	Probable ATP-dependent RNA helicase DDX17	HUMAN	11
182	8.37	19.9	I3L504 I3L504	Eukaryotic translation initiation factor 5A-1	HUMAN	4
183	8.25	19.4	O14818 PSA7	Proteasome subunit alpha type-7	HUMAN	4
184	8.22	3.3	Q14152 EIF3A	Eukaryotic translation initiation factor 3 subunit A	HUMAN	4
185	8.19	29.8	J3QQT2 J3QQT2	60S ribosomal protein L17 (Fragment)	HUMAN	5
186	8.11	2.3	Q9Y490 TLN1	Talin-1	HUMAN	4
187	8.05	22.8	P40925 MDHC	Malate dehydrogenase, cytoplasmic	HUMAN	5
188	8	48.2	P08708 RS17	40S ribosomal protein S17	HUMAN	4
189	8	8.5	P09960 LKHA4	Leukotriene A-4 hydrolase	HUMAN	4
190	8	18.4	P39023 RL3	60S ribosomal protein L3	HUMAN	4
191	8	13.1	P46777 RL5	60S ribosomal protein L5	HUMAN	4
192	8	13.4	Q15084 PDIA6	Protein disulfide-isomerase A6	HUMAN	4
193	8	18.3	Q92688 AN32B	Acidic leucine-rich nuclear phosphoprotein 32 family member B	HUMAN	4
194	8	6.7	Q96QK1 VPS35	Vacuolar protein sorting-associated protein 35	HUMAN	4
195	8	6	A0A0A0MR50 A0A0A0MR50	Cullin-4A	HUMAN	4
196	8	30.7	C9JPM4 C9JPM4	ADP-ribosylation factor 4 (Fragment)	HUMAN	4
197	8	9.3	H3BPE7 H3BPE7	RNA-binding protein FUS	HUMAN	4
198	8	15.8	J3QT28 J3QT28	Mitotic checkpoint protein BUB3 (Fragment)	HUMAN	4
199	8	35.8	P30050 RL12	60S ribosomal protein L12	HUMAN	5
200	8	70.6	P68371 TBB4B	Tubulin beta-4B chain	HUMAN	34

201	7.96	6.9	P49915 GUAA	GMP synthase [glutamine-hydrolyzing]	HUMAN	4
202	7.93	3.4	P53621 COPA	Coatomer subunit alpha	HUMAN	4
203	7.85	14.3	Q9Y3F4 STRAP	Serine-threonine kinase receptor-associated protein	HUMAN	4
204	7.82	24.9	P04792 HSPB1	Heat shock protein beta-1	HUMAN	4
205	7.8	26.3	Q9HB71 CYBP	Calcyclin-binding protein	HUMAN	4
206	7.68	34.8	P09382 LEG1	Galectin-1	HUMAN	4
207	7.66	12.7	F8W809 F8W809	Thioredoxin reductase 1, cytoplasmic	HUMAN	5
208	7.63	10.1	O75874 IDHC	Isocitrate dehydrogenase [NADP] cytoplasmic	HUMAN	4
209	7.59	22.7	P21266 GSTM3	Glutathione S-transferase Mu 3	HUMAN	4
210	7.54	8.6	P23246 SFPQ	Splicing factor, proline- and glutamine-rich	HUMAN	4
211	7.52	5.8	E9PPJ0 E9PPJ0	Splicing factor 3B subunit 2	HUMAN	4
212	7.42	10.3	P36578 RL4	60S ribosomal protein L4	HUMAN	4
213	7.23	5.3	P11586 C1TC	C-1-tetrahydrofolate synthase, cytoplasmic	HUMAN	4
214	7.19	10.8	E9PGZ1 E9PGZ1	Caldesmon	HUMAN	4
215	7.05	5.9	Q8N163 CCAR2	Cell cycle and apoptosis regulator protein 2	HUMAN	4
216	7.05	13.7	P37837 TALDO	Transaldolase	HUMAN	4
217	6.87	5.3	Q13263 TIF1B	Transcription intermediary factor 1-beta	HUMAN	4
218	6.85	10.4	B4DJV2 B4DJV2	Citrate synthase	HUMAN	4
219	6.83	5.8	P19367 HKK1	Hexokinase-1	HUMAN	5
220	6.8	1.6	O75643 U520	U5 small nuclear ribonucleoprotein 200 kDa helicase	HUMAN	3
221	6.72	21.6	O00299 CLIC1	Chloride intracellular channel protein 1	HUMAN	4
222	6.68	14.1	P32322 P5CR1	Pyroline-5-carboxylate reductase 1, mitochondrial	HUMAN	3
223	6.61	8.4	Q9P258 RCC2	Protein RCC2	HUMAN	3
224	6.59	4.6	Q14566 MCM6	DNA replication licensing factor MCM6	HUMAN	3
225	6.54	7.5	P22234 PUR6	Multifunctional protein ADE2	HUMAN	3
226	6.53	10.4	P04083 ANXA1	Annexin A1	HUMAN	3
227	6.42	20.4	P24534 EF1B	Elongation factor 1-beta	HUMAN	4
228	6.34	5.5	P54136 SYRC	Arginine--tRNA ligase, cytoplasmic	HUMAN	3
229	6.33	9.8	Q02790 FKBP4	Peptidyl-prolyl cis-trans isomerase FKBP4	HUMAN	4
230	6.3	4.3	P55884 EIF3B	Eukaryotic translation initiation factor 3 subunit B	HUMAN	3
231	6.16	12.6	O43390 HNRPR	Heterogeneous nuclear ribonucleoprotein R	HUMAN	6
232	6.11	11.4	B4DXW1 B4DXW1	Actin-related protein 3	HUMAN	3
233	6.11	24.4	P21291 CSR1	Cysteine and glycine-rich protein 1	HUMAN	3
234	6.1	40.9	P25398 RS12	40S ribosomal protein S12	HUMAN	4
235	6.06	10.3	P21796 VDAC1	Voltage-dependent anion-selective channel protein 1	HUMAN	3
236	6.06	5.4	H0YGW7 H0YGW7	ATP-binding cassette sub-family F member 1 (Fragment)	HUMAN	3
237	6.06	32.6	P30086 PEBP1	Phosphatidylethanolamine-binding protein 1	HUMAN	3
238	6.04	9.3	E9PBF6 E9PBF6	Lamin-B1	HUMAN	3
239	6.01	2.6	K7EIG1 K7EIG1	Clustered mitochondria protein homolog (Fragment)	HUMAN	3
240	6.01	8.1	M0QXS5 M0QXS5	Heterogeneous nuclear ribonucleoprotein L (Fragment)	HUMAN	3
241	6	9.4	P07954 FUMH	Fumarate hydratase, mitochondrial	HUMAN	3
242	6	7.7	P00367 DHE3	Glutamate dehydrogenase 1, mitochondrial	HUMAN	3
243	6	5	P50416 CPT1A	Carnitine O-palmitoyltransferase 1, liver isoform	HUMAN	3
244	6	6.4	P53985 MOT1	Monocarboxylate transporter 1	HUMAN	3
245	6	25.7	P27348 1433T	14-3-3 protein theta	HUMAN	6
246	6	27.6	P31946 1433B	14-3-3 protein beta/alpha	HUMAN	6
247	6	12.6	O00303 EIF3F	Eukaryotic translation initiation factor 3 subunit F	HUMAN	3
248	6	19.3	P00492 HPRT	Hypoxanthine-guanine phosphoribosyltransferase	HUMAN	3
249	6	18.4	P06748 NPM	Nucleophosmin	HUMAN	3
250	6	17.4	P09488 GSTM1	Glutathione S-transferase Mu 1	HUMAN	3
251	6	6.8	P15170 ERF3A	Eukaryotic peptide chain release factor GTP-binding subunit	HUMAN	3
252	6	10.1	P26196 DDX6	Probable ATP-dependent RNA helicase DDX6	HUMAN	3
253	6	22.4	P32969 RL9	60S ribosomal protein L9	HUMAN	3
254	6	4.4	P49588 SYAC	Alanine--tRNA ligase, cytoplasmic	HUMAN	3
255	6	15.7	P62753 RS6	40S ribosomal protein S6	HUMAN	3
256	6	22.4	P62851 RS25	40S ribosomal protein S25	HUMAN	3
257	6	15.9	G3V5Z7 G3V5Z7	Proteasome subunit alpha type	HUMAN	3
258	6	35.3	J3KT29 J3KT29	60S ribosomal protein L23	HUMAN	3
259	6	21	H0YA96 H0YA96	Heterogeneous nuclear ribonucleoprotein D0 (Fragment)	HUMAN	4
260	6	32	I3L3P7 I3L3P7	40S ribosomal protein S15a	HUMAN	4
261	6	23.2	P32119 PRDX2	Peroxiredoxin-2	HUMAN	5
262	6	10.2	P26038 MOES	Moesin	HUMAN	8
263	5.94	9.5	Q9UMS4 PRP19	Pre-mRNA-processing factor 19	HUMAN	3
264	5.8	5.9	P13667 PDIA4	Protein disulfide-isomerase A4	HUMAN	3
265	5.8	15.6	P51991 ROA3	Heterogeneous nuclear ribonucleoprotein A3	HUMAN	5
266	5.77	4.6	P25205 MCM3	DNA replication licensing factor MCM3	HUMAN	3
267	5.74	15.8	G3V5M2 G3V5M2	Purine nucleoside phosphorylase (Fragment)	HUMAN	3
268	5.7	10.8	C9JW69 C9JW69	Regulator of chromosome condensation (Fragment)	HUMAN	3
269	5.66	8.2	O43776 SYNC	Asparagine--tRNA ligase, cytoplasmic	HUMAN	4

270	5.66	18.4	P62906 RL10A	60S ribosomal protein L10a	HUMAN	3
271	5.65	12.3	Q7L2H7 EIF3M	Eukaryotic translation initiation factor 3 subunit M	HUMAN	3
272	5.59	22.9	P10599 THIO	Thioredoxin	HUMAN	3
273	5.59	8.3	H0YIV4 H0YIV4	Nucleosome assembly protein 1-like 1 (Fragment)	HUMAN	3
274	5.54	3.9	O43143 DHX15	Pre-mRNA-splicing factor ATP-dependent RNA helicase DHX15	HUMAN	3
275	5.53	4.4	P63010 AP2B1	AP-2 complex subunit beta	HUMAN	3
276	5.49	12.7	K7ENG2 K7ENG2	Splicing factor U2AF 65 kDa subunit	HUMAN	3
277	5.49	6.9	P48668 K2C6C	Keratin, type II cytoskeletal 6C	HUMAN	3
278	5.48	49.6	P68366 TBA4A	Tubulin alpha-4A chain	HUMAN	18
279	5.41	24.8	P18669 PGAM1	Phosphoglycerate mutase 1	HUMAN	4
280	5.35	23.1	M0R299 M0R299	rRNA 2'-O-methyltransferase fibrillar (Fragment)	HUMAN	4
281	5.34	5.9	F1T0B3 F1T0B3	ATP-dependent RNA helicase DDX1	HUMAN	3
282	5.33	7.6	P27824 CALX	Calnexin	HUMAN	3
283	5.3	10.3	A0A087WT44 A0A087WT44	Heme oxygenase 2	HUMAN	3
284	5.27	14	P61247 RS3A	40S ribosomal protein S3a	HUMAN	3
285	5.22	5.7	Q14166 TTL12	Tubulin--tyrosine ligase-like protein 12	HUMAN	3
286	5.15	24.3	J3KND3 J3KND3	Myosin light polypeptide 6	HUMAN	3
287	5.14	24.8	C9JXB8 C9JXB8	60S ribosomal protein L24	HUMAN	3
288	5.14	14.8	Q13185 CBX3	Chromobox protein homolog 3	HUMAN	3
289	5.06	12.9	O75367 H2AY	Core histone macro-H2A.1	HUMAN	3
290	4.99	18.3	P28066 PSA5	Proteasome subunit alpha type-5	HUMAN	3
291	4.94	9	Q15008 PSMD6	26S proteasome non-ATPase regulatory subunit 6	HUMAN	3
292	4.94	14.4	E9PCW0 E9PCW0	Prohibitin (Fragment)	HUMAN	3
293	4.93	6.6	O43865 SAHH2	Adenosylhomocysteinase 2	HUMAN	3
294	4.88	10.6	Q9Y266 NUDC	Nuclear migration protein nudC	HUMAN	3
295	4.87	9.6	Q9UHD1 CHRD1	Cysteine and histidine-rich domain-containing protein 1	HUMAN	3
296	4.85	32	H0YMV8 H0YMV8	40S ribosomal protein S27	HUMAN	3
297	4.84	25	J3KMX5 J3KMX5	40S ribosomal protein S13	HUMAN	3
298	4.78	2.7	F5GY55 F5GY55	DNA damage-binding protein 1	HUMAN	3
299	4.73	7.1	P31930 QCR1	Cytochrome b-c1 complex subunit 1, mitochondrial	HUMAN	3
300	4.62	12.7	E9PMD7 E9PMD7	Serine/threonine-protein phosphatase (Fragment)	HUMAN	3
301	4.61	4.6	A0A087WW66 A0A087WW66	26S proteasome non-ATPase regulatory subunit 1	HUMAN	3
302	4.24	7.1	Q16401 PSMD5	26S proteasome non-ATPase regulatory subunit 5	HUMAN	3
303	4.1	8.7	Q99536 VAT1	Synaptic vesicle membrane protein VAT-1 homolog	HUMAN	3
304	4.1	1.3	P15924 DESP	Desmoplakin	HUMAN	3
305	4.08	4.3	A0A0A6YYG9 A0A0A6YYG9	Protein ARPC4-TLL3	HUMAN	3
306	4.02	22.4	P09211 GSTP1	Glutathione S-transferase P	HUMAN	3
307	4	19.4	P31947 1433S	14-3-3 protein sigma	HUMAN	5
308	4	19.9	P84077 ARF1	ADP-ribosylation factor 1	HUMAN	3
309	4	10.5	A0A087WUK2 A0A087WUK2	Heterogeneous nuclear ribonucleoprotein D-like	HUMAN	4
310	4	44.7	F5H5D3 F5H5D3	Tubulin alpha-1C chain	HUMAN	23
311	4	43.1	Q13509 TBB3	Tubulin beta-3 chain	HUMAN	26
312	3.09	48.5	Q96C32 Q96C32	Polyubiquitin-C	HUMAN	3
313	2.93	27.5	Q14240 IF4A2	Eukaryotic initiation factor 4A-II	HUMAN	12
314	2.1	13.6	G3V5Q1 G3V5Q1	DNA-(apurinic or apyrimidinic site) lyase (Fragment)	HUMAN	3
315	2.07	10.6	H3BRU6 H3BRU6	Poly(rC)-binding protein 2 (Fragment)	HUMAN	3
316	2	15	P61981 1433G	14-3-3 protein gamma	HUMAN	4
317	2	18.6	H0YN26 H0YN26	Acidic leucine-rich nuclear phosphoprotein 32 family member A	HUMAN	3
318	2	38.1	P42677 RS27	40S ribosomal protein S27	HUMAN	3
319	1.72	62.1	P60709 ACTB	Actin, cytoplasmic 1	HUMAN	39
320	1.52	1.1	Q92616 GCN1	eIF-2-alpha kinase activator GCN1	HUMAN	2
321	1.44	8.1	Q9Y277 VDAC3	Voltage-dependent anion-selective channel protein 3	HUMAN	2

1. Unused Score, unused protein score. For the target identification, a strict total score cut-off of 1.3 was set as the qualification criterion, which corresponded to a protein confidence interval of 95%.
2. % Cov (95), percent protein sequence coverage with the identified peptides.
3. Peptides(95%), number of unique peptides identified for a protein.

Supplementary table 2. List of AP1 targets in mitochondria

No.	Unused Score ¹	% Cov (95) ²	Accession #	Name	Species	Peptides (95%) ³
1	88.68	40.4	P31327 CPSM	Carbamoyl-phosphate synthase [ammonia], mitochondrial	HUMAN	48
2	63.25	18.7	P49327 FAS	Fatty acid synthase	HUMAN	32
3	48.12	37.6	P08238 HS90B	Heat shock protein HSP 90-beta	HUMAN	29
4	47.03	55.9	P14618 KPYM	Pyruvate kinase PKM	HUMAN	30
5	45.25	41.6	P02786 TFR1	Transferrin receptor protein 1	HUMAN	25
6	35.4	15.3	P42704 LPPRC	Leucine-rich PPR motif-containing protein, mitochondrial	HUMAN	19
7	32.91	16.7	P26640 SYVC	Valine--tRNA ligase	HUMAN	17
8	27.68	18.1	P09874 PARP1	Poly [ADP-ribose] polymerase 1	HUMAN	14
9	27.06	20.7	P55072 TERA	Transitional endoplasmic reticulum ATPase	HUMAN	13
10	27.02	37.7	P10809 CH60	60 kDa heat shock protein, mitochondrial	HUMAN	15
11	26.31	39.9	P34897 GLYM	Serine hydroxymethyltransferase, mitochondrial	HUMAN	14
12	25.06	18.4	P22314 UBA1	Ubiquitin-like modifier-activating enzyme 1	HUMAN	14
13	23.22	21.4	P49748 ACADV	Very long-chain specific acyl-CoA dehydrogenase, mitochondrial	HUMAN	12
14	22.91	26	P31939 PUR9	Bifunctional purine biosynthesis protein PURH	HUMAN	11
15	22.89	57.2	P23396 RS3	40S ribosomal protein S3	HUMAN	11
16	22.57	30.3	P11021 GRP78	78 kDa glucose-regulated protein	HUMAN	15
17	22.14	48.9	P63244 RACK1	Receptor of activated protein C kinase 1	HUMAN	12
18	21.7	19.1	P02545 LMNA	Prelamin-A/C	HUMAN	11
19	20.17	24.1	P25705 ATPA	ATP synthase subunit alpha, mitochondrial	HUMAN	10
20	20.07	14.9	Q12906 ILF3	Interleukin enhancer-binding factor 3	HUMAN	10
21	19.9	21	Q99832 TCPH	T-complex protein 1 subunit eta	HUMAN	11
22	19.01	30.1	P07900 HS90A	Heat shock protein HSP 90-alpha	HUMAN	24
23	16.3	37.7	P62258 I433E	14-3-3 protein epsilon	HUMAN	10
24	16.04	20	P38646 GRP75	Stress-70 protein, mitochondrial	HUMAN	10
25	16	44.7	Q06830 PRDX1	Peroxiredoxin-1	HUMAN	10
26	15.39	23.5	P61978 HNRPK	Heterogeneous nuclear ribonucleoprotein K	HUMAN	8
27	15.01	33.6	P05141 ADT2	ADP/ATP translocase 2	HUMAN	9
28	14.79	16.3	Q12931 TRAP1	Heat shock protein 75 kDa, mitochondrial	HUMAN	8
29	14.61	23.5	P00966 ASSY	Argininosuccinate synthase	HUMAN	9
30	14.15	28.1	P07195 LDHB	L-lactate dehydrogenase B chain	HUMAN	10
31	13.82	10.4	Q7KZF4 SND1	Staphylococcal nuclease domain-containing protein 1	HUMAN	7
32	12.85	10.3	P08133 ANXA6	Annexin A6	HUMAN	6
33	12.59	18.4	P49411 EFTU	Elongation factor Tu, mitochondrial	HUMAN	7
34	12.19	10	P34932 HSP74	Heat shock 70 kDa protein 4	HUMAN	6
35	12.06	9	Q92598 HS105	Heat shock protein 105 kDa	HUMAN	6
36	12.02	9.2	Q01813 PFKAP	ATP-dependent 6-phosphofructokinase, platelet type	HUMAN	6
37	11.84	23.5	Q9Y265 RUVB1	RuvB-like 1	HUMAN	7
38	11.37	24.8	Q96AG4 LRC59	Leucine-rich repeat-containing protein 59	HUMAN	6
39	10	9	P40939 ECHA	Trifunctional enzyme subunit alpha, mitochondrial	HUMAN	5
40	10	16.4	F8VVM2 F8VVM2	Phosphate carrier protein, mitochondrial	HUMAN	5
41	9.7	13.5	P00505 AATM	Aspartate aminotransferase, mitochondrial	HUMAN	5
42	9.68	7.7	P54886 P5CS	Delta-1-pyrroline-5-carboxylate synthase	HUMAN	5
43	9.45	14.8	P04181 OAT	Ornithine aminotransferase, mitochondrial	HUMAN	5
44	9.33	21.3	P05198 IF2A	Eukaryotic translation initiation factor 2 subunit 1	HUMAN	6
45	9.26	22.3	P30048 PRDX3	Thioredoxin-dependent peroxide reductase, mitochondrial	HUMAN	5
46	8.89	11.7	Q15046 SYK	Lysine--tRNA ligase	HUMAN	5
47	8.6	21.2	G3XALO G3XALO	Malate dehydrogenase	HUMAN	4
48	8.05	22.8	P40925 MDHC	Malate dehydrogenase, cytoplasmic	HUMAN	5
49	7.63	10.1	O75874 IDHC	Isocitrate dehydrogenase [NADP] cytoplasmic	HUMAN	4

50	7.23	5.3	P11586 C1TC	C-1-tetrahydrofolate synthase, cytoplasmic	HUMAN	4
51	7.05	5.9	Q8N163 CCAR2	Cell cycle and apoptosis regulator protein 2	HUMAN	4
52	6.85	10.4	B4DJV2 B4DJV2	Citrate synthase	HUMAN	4
53	6.83	5.8	P19367 HXK1	Hexokinase-1	HUMAN	5
54	6.72	21.6	O00299 CLIC1	Chloride intracellular channel protein 1	HUMAN	4
55	6.68	14.1	P32322 P5CR1	Pyrroline-5-carboxylate reductase 1, mitochondrial	HUMAN	3
56	6.53	10.4	P04083 ANXA1	Annexin A1	HUMAN	3
57	6.34	5.5	P54136 SYRC	Arginine--tRNA ligase, cytoplasmic	HUMAN	3
58	6.33	9.8	Q02790 FKBP4	Peptidyl-prolyl cis-trans isomerase FKBP4	HUMAN	4
59	6.06	10.3	P21796 VDAC1	Voltage-dependent anion-selective channel protein 1	HUMAN	3
60	6.01	2.6	K7EIG1 K7EIG1	Clustered mitochondria protein homolog (Fragment)	HUMAN	3
61	6	9.4	P07954 FUMH	Fumarate hydratase, mitochondrial	HUMAN	3
62	6	7.7	P00367 DHE3	Glutamate dehydrogenase 1, mitochondrial	HUMAN	3
63	6	5	P50416 CPT1A	Carnitine O-palmitoyltransferase 1, liver isoform	HUMAN	3
64	6	6.4	P53985 MOT1	Monocarboxylate transporter 1	HUMAN	3
65	6	25.7	P27348 1433T	14-3-3 protein theta	HUMAN	6
66	6	27.6	P31946 1433B	14-3-3 protein beta/alpha	HUMAN	6
67	5.66	8.2	O43776 SYNC	Asparagine--tRNA ligase, cytoplasmic	HUMAN	4
68	5.59	22.9	P10599 THIO	Thioredoxin	HUMAN	3
69	5.33	7.6	P27824 CALX	Calnexin	HUMAN	3
70	4.73	7.1	P31930 QCR1	Cytochrome b-c1 complex subunit 1, mitochondrial	HUMAN	3
71	4.1	8.7	Q99536 VAT1	Synaptic vesicle membrane protein VAT-1 homolog	HUMAN	3
72	4.02	22.4	P09211 GSTP1	Glutathione S-transferase P	HUMAN	3
73	4	19.4	P31947 1433S	14-3-3 protein sigma	HUMAN	5
74	2.1	13.6	G3V5Q1 G3V5Q1	DNA-(apurinic or apyrimidinic site) lyase (Fragment)	HUMAN	3
75	2	15	P61981 1433G	14-3-3 protein gamma	HUMAN	4
76	1.44	8.1	Q9Y277 VDAC3	Voltage-dependent anion-selective channel protein 3	HUMAN	2

1. Unused Score, unused protein score. For the target identification, a strict total score cut-off of 1.3 was set as the qualification criterion, which corresponded to a protein confidence interval of 95%.
2. % Cov (95), percent protein sequence coverage with the identified peptides.
3. Peptides(95%), number of unique peptides identified for a protein.

Supplementary table 3. List of AP2 targets

No.	Unused Score ¹	% Cov (95) ²	Accession #	Name	Species	Peptide s(95%) ³
1	155.96	45.9	P21333 FLNA	Filamin-A	HUMAN	87
2	118.96	55.8	P31327 CPSM	Carbamoyl-phosphate synthase [ammonia], mitochondrial	HUMAN	77
3	116.68	17.9	Q15149 PLEC	Plectin	HUMAN	59
4	111.58	33.7	P49327 FAS	Fatty acid synthase	HUMAN	59
5	96.37	27.4	Q13813 SPTN1	Spectrin alpha chain, non-erythrocytic 1	HUMAN	50
6	90.35	39	Q00610 CLH1	Clathrin heavy chain 1	HUMAN	48
7	87.27	38.7	P42704 LPPRC	Leucine-rich PPR motif-containing protein, mitochondrial	HUMAN	45
8	83.15	25.5	Q01082 SPTB2	Spectrin beta chain, non-erythrocytic 1	HUMAN	42
9	81.53	26	O75369 FLNB	Filamin-B	HUMAN	49
10	81.23	63.8	P08238 HS90B	Heat shock protein HSP 90-beta	HUMAN	53
11	80.05	61.5	P13639 EF2	Elongation factor 2	HUMAN	46
12	77.54	29.2	P35579 MYH9	Myosin-9	HUMAN	42
13	71.61	11.5	P78527 PRKDC	DNA-dependent protein kinase catalytic subunit	HUMAN	36
14	70.76	54.3	O43707 ACTN4	Alpha-actinin-4	HUMAN	38
15	67.08	28.7	P46940 IQGA1	Ras GTPase-activating-like protein IQGAP1	HUMAN	36
16	63.69	33.1	Q08211 DHX9	ATP-dependent RNA helicase A	HUMAN	33
17	63.48	65.9	P14618 KPYM	Pyruvate kinase PKM	HUMAN	46
18	59.25	36.2	P53396 ACLY	ATP-citrate synthase	HUMAN	30
19	57.49	53.7	P02786 TFR1	Transferrin receptor protein 1	HUMAN	44
20	55.82	26.7	P07814 SYEP	Bifunctional glutamate/proline--tRNA ligase	HUMAN	30
21	55.51	19.3	O75643 U520	U5 small nuclear ribonucleoprotein 200 kDa helicase	HUMAN	27
22	55.44	53.4	P11142 HSP7C	Heat shock cognate 71 kDa protein	HUMAN	42
23	54.56	8.3	Q14204 DYHC1	Cytoplasmic dynein 1 heavy chain 1	HUMAN	27
24	53.64	24.4	P11388 TOP2A	DNA topoisomerase 2-alpha	HUMAN	28
25	53.46	50	P55072 TERA	Transitional endoplasmic reticulum ATPase	HUMAN	29
26	51.42	57.9	P10809 CH60	60 kDa heat shock protein, mitochondrial	HUMAN	30
27	51.26	71.2	P68104 EF1A1	Elongation factor 1-alpha 1	HUMAN	45
28	50.45	31.3	P58107 EPIPL	Epiplakin	HUMAN	25
29	48.99	74.3	P07437 TBB5	Tubulin beta chain	HUMAN	47
30	48.54	62.5	P08670 VIME	Vimentin	HUMAN	31
31	47.7	25.9	P26640 SYVC	Valine--tRNA ligase	HUMAN	24
32	47.08	42.2	P02545 LMNA	Prelamin-A/C	HUMAN	26
33	46.08	62.6	P0DMV9 HS71B	Heat shock 70 kDa protein 1B	HUMAN	32
34	45.68	56.8	P48643 TCPE	T-complex protein 1 subunit epsilon	HUMAN	24
35	44.64	41.1	Q14974 IMB1	Importin subunit beta-1	HUMAN	27
36	44.3	38	Q12906 ILF3	Interleukin enhancer-binding factor 3	HUMAN	24
37	43.89	47.9	P49368 TCPG	T-complex protein 1 subunit gamma	HUMAN	23
38	43.57	25.8	P09874 PARP1	Poly [ADP-ribose] polymerase 1	HUMAN	22
39	42.96	31.5	P14625 ENPL	Endoplasmic	HUMAN	23
40	42.84	31.7	O00410 IPO5	Importin-5	HUMAN	24
41	42.8	53.1	P17987 TCPA	T-complex protein 1 subunit alpha	HUMAN	23
42	42.72	52.1	Q04695 K1C17	Keratin, type I cytoskeletal 17	HUMAN	26
43	42.7	36.2	Q14697 GANAB	Neutral alpha-glucosidase AB	HUMAN	22
44	42.63	42.7	P12956 XRCC6	X-ray repair cross-complementing protein 6	HUMAN	23
45	42.51	53.3	P50395 GDIB	Rab GDP dissociation inhibitor beta	HUMAN	22
46	42.23	43.1	P11021 GRP78	78 kDa glucose-regulated protein	HUMAN	26
47	42.13	36.3	Q92598 HS105	Heat shock protein 105 kDa	HUMAN	21
48	41.95	31.4	P22314 UBA1	Ubiquitin-like modifier-activating enzyme 1	HUMAN	25
49	41.57	64.5	P06733 ENOA	Alpha-enolase	HUMAN	31
50	41	25.8	O75533 SF3B1	Splicing factor 3B subunit 1	HUMAN	22

51	40.27	52.2	P07900 HS90A	Heat shock protein HSP 90-alpha	HUMAN	47
52	40.09	37.8	P27824 CALX	Calnexin	HUMAN	23
53	38.87	51.8	P78371 TCPB	T-complex protein 1 subunit beta	HUMAN	24
54	38.15	51.9	P29401 TKT	Transketolase	HUMAN	23
55	37.93	46	P50990 TCPQ	T-complex protein 1 subunit theta	HUMAN	23
56	37.76	22.3	Q15393 SF3B3	Splicing factor 3B subunit 3	HUMAN	20
57	37.1	42.5	P52272 HNRPM	Heterogeneous nuclear ribonucleoprotein M	HUMAN	23
58	37.08	28.5	P55060 XPO2	Exportin-2	HUMAN	20
59	36.93	34	Q92841 DDX17	Probable ATP-dependent RNA helicase DDX17	HUMAN	19
60	36.8	28.1	Q15029 U5S1	116 kDa U5 small nuclear ribonucleoprotein component	HUMAN	20
61	36.68	48.3	P60842 IF4A1	Eukaryotic initiation factor 4A-I	HUMAN	24
62	35.69	29.5	Q13200 PSMD2	26S proteasome non-ATPase regulatory subunit 2	HUMAN	18
63	34.91	12.6	Q9Y490 TLN1	Talin-1	HUMAN	18
64	34.76	9.5	Q09666 AHNK	Neuroblast differentiation-associated protein AHNK	HUMAN	17
65	34.68	63.9	P00338 LDHA	L-lactate dehydrogenase A chain	HUMAN	24
66	34.43	54.2	P00558 PGK1	Phosphoglycerate kinase 1	HUMAN	22
67	34.33	37.7	Q92945 FUBP2	Far upstream element-binding protein 2	HUMAN	17
68	33.87	39.6	P13010 XRCC5	X-ray repair cross-complementing protein 5	HUMAN	18
69	33.77	45.9	Q99832 TCPH	T-complex protein 1 subunit eta	HUMAN	18
70	33.68	54.9	P07355 ANXA2	Annexin A2	HUMAN	17
71	33.66	23	P18206 VINC	Vinculin	HUMAN	19
72	33.55	30.8	Q9NR30 DDX21	Nucleolar RNA helicase 2	HUMAN	19
73	33.54	31.3	Q00839 HNRPU	Heterogeneous nuclear ribonucleoprotein U	HUMAN	24
74	33.25	7.3	P15924 DESP	Desmoplakin	HUMAN	17
75	33.18	10.8	Q92616 GCN1	eIF-2-alpha kinase activator GCN1	HUMAN	17
76	33	18.9	Q86VP6 CAND1	Cullin-associated NEDD8-dissociated protein 1	HUMAN	16
77	32.95	59.3	P04075 ALDOA	Fructose-bisphosphate aldolase A	HUMAN	24
78	32.84	33.9	P38646 GRP75	Stress-70 protein, mitochondrial	HUMAN	19
79	32.65	48.5	P49411 EFTU	Elongation factor Tu, mitochondrial	HUMAN	21
80	32.17	41	P11413 G6PD	Glucose-6-phosphate 1-dehydrogenase	HUMAN	18
81	31.88	45.4	P52292 IMA1	Importin subunit alpha-1	HUMAN	17
82	31.84	30.2	P15311 EZRI	Ezrin	HUMAN	18
83	31.72	21.2	P16615 AT2A2	Sarcoplasmic/endoplasmic reticulum calcium ATPase 2	HUMAN	17
84	31.68	38.6	P08729 K2C7	Keratin, type II cytoskeletal 7	HUMAN	17
85	31.67	31.4	P34932 HSP74	Heat shock 70 kDa protein 4	HUMAN	17
86	31.27	34.4	O60506 HNRPQ	Heterogeneous nuclear ribonucleoprotein Q	HUMAN	17
87	31.25	11.5	P27708 PYR1	CAD protein	HUMAN	18
88	31.2	27.9	P47897 SYQ	Glutamine--tRNA ligase	HUMAN	16
89	31.12	34.3	P08195 4F2	4F2 cell-surface antigen heavy chain	HUMAN	18
90	31.03	20.6	P49736 MCM2	DNA replication licensing factor MCM2	HUMAN	16
91	30.83	42.3	P26641 EF1G	Elongation factor 1-gamma	HUMAN	16
92	30.75	36.2	P04843 RPN1	subunit 1	HUMAN	19
93	30.59	20	P05023 AT1A1	Sodium/potassium-transporting ATPase subunit alpha-1	HUMAN	16
94	30.29	52.2	P09651 ROA1	Heterogeneous nuclear ribonucleoprotein A1	HUMAN	23
95	30.08	22.6	P55786 PSA	Puromycin-sensitive aminopeptidase	HUMAN	15
96	30	21.8	P54886 P5CS	Delta-1-pyrroline-5-carboxylate synthase	HUMAN	15
97	29.93	29.6	P33992 MCM5	DNA replication licensing factor MCM5	HUMAN	15
98	29.67	64.3	P60174 TPIS	Triosephosphate isomerase	HUMAN	17
99	29.44	43.2	P50991 TCPD	T-complex protein 1 subunit delta	HUMAN	17
100	29.21	64.2	P23396 RS3	40S ribosomal protein S3	HUMAN	15
101	29.15	23.9	P25205 MCM3	DNA replication licensing factor MCM3	HUMAN	16
102	29.12	41.9	P07237 PDIA1	Protein disulfide-isomerase	HUMAN	15
103	29.08	24.7	Q8NE71 ABCF1	ATP-binding cassette sub-family F member 1	HUMAN	15
104	28.75	27.5	P33993 MCM7	DNA replication licensing factor MCM7	HUMAN	16
105	28.71	17.7	O14980 XPO1	Exportin-1	HUMAN	15
106	28.55	60.3	P08865 RSSA	40S ribosomal protein SA	HUMAN	17

107	28.47	26.4	P26639 SYTC	Threonine--tRNA ligase, cytoplasmic	HUMAN	16
108	28.43	13.4	P41252 SYIC	Isoleucine--tRNA ligase, cytoplasmic	HUMAN	14
109	28.2	64.5	P04406 G3P	Glyceraldehyde-3-phosphate dehydrogenase	HUMAN	30
110	28.09	28.9	P13797 PLST	Plastin-3	HUMAN	14
111	27.88	41.1	P40227 TCPZ	T-complex protein 1 subunit zeta	HUMAN	14
112	27.8	23.3	Q7KZF4 SND1	Staphylococcal nuclease domain-containing protein 1	HUMAN	14
113	27.77	43.3	P34897 GLYM	Serine hydroxymethyltransferase, mitochondrial	HUMAN	14
114	27.76	11.3	Q04637 IF4G1	Eukaryotic translation initiation factor 4 gamma 1	HUMAN	14
115	27.7	23.2	P55884 EIF3B	Eukaryotic translation initiation factor 3 subunit B	HUMAN	14
116	27.67	45.3	P06744 G6PI	Glucose-6-phosphate isomerase	HUMAN	20
117	27.57	42.3	Q13838 DX39B	Spliceosome RNA helicase DDX39B	HUMAN	14
118	27.45	41.9	P61978 HNRPK	Heterogeneous nuclear ribonucleoprotein K	HUMAN	16
119	27.34	36	P31939 PUR9	Bifunctional purine biosynthesis protein PURH	HUMAN	14
120	27.33	11.5	Q14839 CHD4	Chromodomain-helicase-DNA-binding protein 4	HUMAN	14
121	27	21.3	Q99460 PSMD1	26S proteasome non-ATPase regulatory subunit 1	HUMAN	14
122	26.93	29.8	P09960 LKHA4	Leukotriene A-4 hydrolase	HUMAN	13
123	26.89	16.9	O75153 CLU	Clustered mitochondria protein homolog	HUMAN	14
124	26.7	55.6	Q15365 PCBP1	Poly(rC)-binding protein 1	HUMAN	18
125	26.52	25.5	P11940 PABP1	Polyadenylate-binding protein 1	HUMAN	17
126	26.49	27.7	P40939 ECHA	Trifunctional enzyme subunit alpha, mitochondrial	HUMAN	13
127	26.27	43.5	P05787 K2C8	Keratin, type II cytoskeletal 8	HUMAN	17
128	26.24	29.8	Q12931 TRAP1	Heat shock protein 75 kDa, mitochondrial	HUMAN	16
129	26.23	39	P30101 PDIA3	Protein disulfide-isomerase A3	HUMAN	15
130	26	33.7	P14868 SYDC	Aspartate--tRNA ligase, cytoplasmic	HUMAN	13
131	25.83	35.6	P25705 ATPA	ATP synthase subunit alpha, mitochondrial	HUMAN	15
132	25.65	36.8	O43175 SERA	D-3-phosphoglycerate dehydrogenase	HUMAN	14
133	25.55	47.6	P07195 LDHB	L-lactate dehydrogenase B chain	HUMAN	16
134	25.53	52.1	P40926 MDHM	Malate dehydrogenase, mitochondrial	HUMAN	14
135	25.15	64	P63244 RACK1	Receptor of activated protein C kinase 1	HUMAN	15
136	25.15	7.6	Q6P2Q9 PRP8	Pre-mRNA-processing-splicing factor 8	HUMAN	14
137	25.07	17.7	O95373 IPO7	Importin-7	HUMAN	14
138	24.92	30.6	P17812 PYRG1	CTP synthase 1	HUMAN	13
139	24.84	35.8	P36578 RL4	60S ribosomal protein L4	HUMAN	13
140	24.6	45.2	Q9UQ80 PA2G4	Proliferation-associated protein 2G4	HUMAN	15
141	24.35	19.7	P22102 PUR2	Trifunctional purine biosynthetic protein adenosine-3	HUMAN	14
142	24.13	35.3	Q9UMS4 PRP19	Pre-mRNA-processing factor 19	HUMAN	14
143	23.99	35.9	P31943 HNRH1	Heterogeneous nuclear ribonucleoprotein H	HUMAN	13
144	23.99	22.7	P43243 MATR3	Matrin-3	HUMAN	13
145	23.93	38.4	P17844 DDX5	Probable ATP-dependent RNA helicase DDX5	HUMAN	18
146	23.93	21.2	Q96RP9 EFGM	Elongation factor G, mitochondrial	HUMAN	12
147	23.77	46	P26599 PTBP1	Polypyrimidine tract-binding protein 1	HUMAN	14
148	23.53	18.4	P36776 LONM	Lon protease homolog, mitochondrial	HUMAN	12
149	23.28	34.9	Q16658 FSCN1	Fascin	HUMAN	12
150	22.97	29.1	Q9Y2X3 NOP58	Nucleolar protein 58	HUMAN	12
151	22.93	18	Q96QK1 VPS35	Vacuolar protein sorting-associated protein 35	HUMAN	12
152	22.71	35.2	Q9Y230 RUVB2	RuvB-like 2	HUMAN	13
153	22.67	18.6	P11586 C1TC	C-1-tetrahydrofolate synthase, cytoplasmic	HUMAN	11
154	22.59	31.5	P23526 SAHH	Adenosylhomocysteinase	HUMAN	11
155	22.5	24.6	P23246 SFPQ	Splicing factor, proline- and glutamine-rich	HUMAN	15
156	22.45	56.1	P62258 1433E	14-3-3 protein epsilon	HUMAN	14
157	22.42	36.7	P05783 K1C18	Keratin, type I cytoskeletal 18	HUMAN	13
158	22.12	26.7	P30153 2AAA	subunit A alpha isoform	HUMAN	11
159	22.11	51.7	P05141 ADT2	ADP/ATP translocase 2	HUMAN	18
160	21.99	19.6	P54136 SYRC	Arginine--tRNA ligase, cytoplasmic	HUMAN	12
161	21.92	19.6	Q92499 DDX1	ATP-dependent RNA helicase DDX1	HUMAN	11
162	21.81	20.2	Q8N163 CCAR2	Cell cycle and apoptosis regulator protein 2	HUMAN	11

163	21.75	22.8	P43304 GPDM	Glycerol-3-phosphate dehydrogenase, mitochondrial	HUMAN	11
164	21.72	41	P00966 ASSY	Argininosuccinate synthase	HUMAN	13
165	21.61	27	P12268 IMDH2	Inosine-5'-monophosphate dehydrogenase 2	HUMAN	11
166	21.55	18.1	P33991 MCM4	DNA replication licensing factor MCM4	HUMAN	12
167	21.49	16.1	Q13619 CUL4A	Cullin-4A	HUMAN	10
168	21.36	22.1	Q9NVP1 DDX18	ATP-dependent RNA helicase DDX18	HUMAN	11
169	21.19	13.9	Q9H0A0 NAT10	RNA cytidine acetyltransferase	HUMAN	10
170	21.13	25.7	Q00571 DDX3X	ATP-dependent RNA helicase DDX3X	HUMAN	12
171	20.88	22.3	Q15046 SYK	Lysine--tRNA ligase	HUMAN	11
172	20.84	38.1	P27797 CALR	Calreticulin	HUMAN	10
173	20.64	49.4	P15121 ALDR	Aldose reductase	HUMAN	11
174	20.58	42	P52209 6PGD	6-phosphogluconate dehydrogenase, decarboxylating	HUMAN	13
175	20.45	22.4	Q13263 TIF1B	Transcription intermediary factor 1-beta	HUMAN	11
176	20.32	21.9	Q9UHB6 LIMA1	LIM domain and actin-binding protein 1	HUMAN	11
177	20.14	11.4	P53621 COPA	Coatomer subunit alpha	HUMAN	10
178	20.12	15.8	Q01813 PFKAP	ATP-dependent 6-phosphofructokinase, platelet type	HUMAN	10
179	20.09	17.5	P19338 NUCL	Nucleolin	HUMAN	11
180	20.06	35.8	P12814 ACTN1	Alpha-actinin-1	HUMAN	25
181	20.05	49.1	Q15181 IPYR	Inorganic pyrophosphatase	HUMAN	10
182	20.03	9.9	Q9BQGO MBB1A	Myb-binding protein 1A	HUMAN	10
183	20	21.2	P13667 PDIA4	Protein disulfide-isomerase A4	HUMAN	13
184	20	62.5	P30041 PRDX6	Peroxiredoxin-6	HUMAN	10
185	19.74	23.2	P20700 LMNB1	Lamin-B1	HUMAN	10
186	19.66	10.9	Q14152 EIF3A	Eukaryotic translation initiation factor 3 subunit A	HUMAN	12
187	19.64	12.8	Q9Y5B9 SP16H	FACT complex subunit SPT16	HUMAN	10
188	19.62	37.2	P15880 RS2	40S ribosomal protein S2	HUMAN	11
189	19.59	47.1	P00491 PNPH	Purine nucleoside phosphorylase	HUMAN	10
190	19.55	10	Q00341 VIGLN	Vigilin	HUMAN	10
191	19.41	19.8	P08133 ANXA6	Annexin A6	HUMAN	11
192	19.34	48	P16152 CBR1	Carbonyl reductase [NADPH] 1	HUMAN	10
193	19.24	21.5	P36871 PGM1	Phosphoglucomutase-1	HUMAN	10
194	19.19	46.7	Q12905 ILF2	Interleukin enhancer-binding factor 2	HUMAN	11
195	18.99	43.1	Q16576 RBBP7	Histone-binding protein RBBP7	HUMAN	12
196	18.92	31.8	Q02790 FKBP4	Peptidyl-prolyl cis-trans isomerase FKBP4	HUMAN	10
197	18.91	18.2	P49915 GUAA	GMP synthase [glutamine-hydrolyzing]	HUMAN	9
198	18.9	42.8	P08574 CY1	Cytochrome c1, heme protein, mitochondrial	HUMAN	13
199	18.64	13.7	P63010 AP2B1	AP-2 complex subunit beta	HUMAN	10
200	18.59	32.1	P38919 IF4A3	Eukaryotic initiation factor 4A-III	HUMAN	11
201	18.55	12.2	P55265 DSRAD	Double-stranded RNA-specific adenosine deaminase	HUMAN	11
202	18.48	71.8	O00299 CLIC1	Chloride intracellular channel protein 1	HUMAN	12
203	18.45	15.6	Q99613 EIF3C	Eukaryotic translation initiation factor 3 subunit C	HUMAN	9
204	18.45	13.5	Q9Y4L1 HYOU1	Hypoxia up-regulated protein 1	HUMAN	9
205	18.34	60.6	P62937 PPIA	Peptidyl-prolyl cis-trans isomerase A	HUMAN	19
206	18.33	30.6	O00231 PSD11	26S proteasome non-ATPase regulatory subunit 11	HUMAN	10
207	18.28	31.6	P14866 HNRPL	Heterogeneous nuclear ribonucleoprotein L	HUMAN	12
208	18.26	13.1	Q15459 SF3A1	Splicing factor 3A subunit 1	HUMAN	9
209	18.22	25.2	Q9Y3I0 RTCB	tRNA-splicing ligase RtcB homolog	HUMAN	9
210	18.18	47	P21796 VDAC1	Voltage-dependent anion-selective channel protein 1	HUMAN	10
211	18.08	45.7	P13804 ETFA	Electron transfer flavoprotein subunit alpha, mitochondrial	HUMAN	9
212	18.06	7.3	Q5VYK3 ECM29	Proteasome-associated protein ECM29 homolog	HUMAN	9
213	18	34.7	P04083 ANXA1	Annexin A1	HUMAN	9
214	18	61.5	P32969 RL9	60S ribosomal protein L9	HUMAN	10
215	18	14.2	P49588 SYAC	Alanine--tRNA ligase, cytoplasmic	HUMAN	11
216	17.97	31.8	P22234 PUR6	Multifunctional protein ADE2	HUMAN	10
217	17.9	14.3	Q14566 MCM6	DNA replication licensing factor MCM6	HUMAN	9
218	17.8	32.8	P08758 ANXA5	Annexin A5	HUMAN	9

219	17.78	10.7	Q12965 MYO1E	Unconventional myosin-le	HUMAN	9
220	17.77	67.8	P04792 HSPB1	Heat shock protein beta-1	HUMAN	9
221	17.72	40.7	Q9UHD1 CHRD1	Cysteine and histidine-rich domain-containing protein 1	HUMAN	9
222	17.7	33.8	P35232 PHB	Prohibitin	HUMAN	9
223	17.69	24.7	Q16881 TRXR1	Thioredoxin reductase 1, cytoplasmic	HUMAN	11
224	17.67	49.8	Q06830 PRDX1	Peroxiredoxin-1	HUMAN	10
225	17.67	8.5	Q9H2M9 RBGPR	Rab3 GTPase-activating protein non-catalytic subunit	HUMAN	9
226	17.52	15.2	P35606 COPB2	Coatomer subunit beta'	HUMAN	10
227	17.49	33.7	P41091 IF2G	Eukaryotic translation initiation factor 2 subunit 3	HUMAN	11
228	17.37	44.4	P62826 RAN	GTP-binding nuclear protein Ran	HUMAN	9
229	17.33	48.2	P00492 HPRT	Hypoxanthine-guanine phosphoribosyltransferase	HUMAN	9
230	17.23	20.6	O43776 SYNC	Asparagine--tRNA ligase, cytoplasmic	HUMAN	9
231	17.19	38.7	P27695 APEX1	DNA-(apurinic or apyrimidinic site) lyase	HUMAN	9
232	17.18	31	P12277 KCRB	Creatine kinase B-type	HUMAN	10
233	16.99	21.6	O00116 ADAS	Alkylidihydroxyacetonephosphate synthase, peroxisomal	HUMAN	9
234	16.89	63.9	P23528 COF1	Cofilin-1	HUMAN	10
235	16.77	12.7	P78347 GTF2I	General transcription factor II-I	HUMAN	11
236	16.72	55.2	Q9BUF5 TBB6	Tubulin beta-6 chain	HUMAN	30
237	16.67	9.1	Q8TEQ6 GEMI5	Gem-associated protein 5	HUMAN	10
238	16.64	13.3	P56192 SYMC	Methionine--tRNA ligase, cytoplasmic	HUMAN	9
239	16.48	19.5	Q9Y262 EIF3L	Eukaryotic translation initiation factor 3 subunit L	HUMAN	8
240	16.46	11	P19367 HXK1	Hexokinase-1	HUMAN	9
241	16.45	30	P62140 PP1B	Serine/threonine-protein phosphatase PP1-beta catalytic subunit	HUMAN	8
242	16.44	40.2	P30519 HMOX2	Heme oxygenase 2	HUMAN	11
243	16.44	36.8	P40925 MDHC	Malate dehydrogenase, cytoplasmic	HUMAN	9
244	16.4	32.7	P46777 RL5	60S ribosomal protein L5	HUMAN	12
245	16.39	19.5	P31948 STIP1	Stress-induced-phosphoprotein 1	HUMAN	8
246	16.37	48.9	P21266 GSTM3	Glutathione S-transferase Mu 3	HUMAN	10
247	16.36	31.1	Q9Y3F4 STRAP	Serine-threonine kinase receptor-associated protein	HUMAN	9
248	16.32	10.9	Q7L014 DDX46	Probable ATP-dependent RNA helicase DDX46	HUMAN	10
249	16.2	32.6	P09429 HMGB1	High mobility group protein B1	HUMAN	12
250	16.19	12.7	P53618 COPB	Coatomer subunit beta	HUMAN	8
251	16.18	52	P18669 PGAM1	Phosphoglycerate mutase 1	HUMAN	9
252	16.16	29.5	P00505 AATM	Aspartate aminotransferase, mitochondrial	HUMAN	10
253	16.14	57.8	P37802 TAGL2	Transgelin-2	HUMAN	10
254	16.08	8.7	O94906 PRP6	Pre-mRNA-processing factor 6	HUMAN	7
255	16.08	14.5	Q92973 TNPO1	Transportin-1	HUMAN	11
256	16.06	15.3	Q9Y678 COPG1	Coatomer subunit gamma-1	HUMAN	8
257	16.05	17.3	P40763 STAT3	Signal transducer and activator of transcription 3	HUMAN	8
258	16.04	36.9	P05388 RLA0	60S acidic ribosomal protein P0	HUMAN	8
259	16.02	17.7	P46060 RAGP1	Ran GTPase-activating protein 1	HUMAN	8
260	16.01	37.1	P61247 RS3A	40S ribosomal protein S3a	HUMAN	8
261	16	31.6	P45880 VDAC2	Voltage-dependent anion-selective channel protein 2	HUMAN	10
262	15.94	23.8	P38606 VATA	V-type proton ATPase catalytic subunit A	HUMAN	9
263	15.92	15.6	Q9UG63 ABCF2	ATP-binding cassette sub-family F member 2	HUMAN	8
264	15.79	15.7	P49748 ACADV	Very long-chain specific acyl-CoA dehydrogenase, mitochondrial	HUMAN	8
265	15.66	40.7	P23284 PPIB	Peptidyl-prolyl cis-trans isomerase B	HUMAN	8
266	15.58	40.8	P22626 ROA2	Heterogeneous nuclear ribonucleoproteins A2/B1	HUMAN	16
267	15.57	40.6	P30048 PRDX3	Thioredoxin-dependent peroxide reductase, mitochondrial	HUMAN	12
268	15.46	19.9	P31040 SDHA	mitochondrial	HUMAN	8
269	15.46	20.4	Q9UHX1 PUF60	Poly(U)-binding-splicing factor PUF60	HUMAN	8
270	15.38	26.9	Q8NBS9 TXND5	Thioredoxin domain-containing protein 5	HUMAN	9
271	15.36	7.3	Q8TEM1 PO210	Nuclear pore membrane glycoprotein 210	HUMAN	8
272	15.33	17	Q9BZE4 NOG1	Nucleolar GTP-binding protein 1	HUMAN	8
273	15.29	19	P04040 CATA	Catalase	HUMAN	7
274	15.28	26.1	P39023 RL3	60S ribosomal protein L3	HUMAN	14

275	15.26	12.6	P43246 MSH2	DNA mismatch repair protein Msh2	HUMAN	9
276	15.12	8.1	O75694 NU155	Nuclear pore complex protein Nup155	HUMAN	9
277	15.04	16.6	P51659 DHB4	Peroxisomal multifunctional enzyme type 2	HUMAN	8
278	15	5.2	Q9NZM1 MYOF	Myoferlin	HUMAN	8
279	14.91	19.9	P07910 HNRPC	Heterogeneous nuclear ribonucleoproteins C1/C2	HUMAN	7
280	14.91	11.1	P50416 CPT1A	Carnitine O-palmitoyltransferase 1, liver isoform	HUMAN	7
281	14.88	6.2	Q14980 NUMA1	Nuclear mitotic apparatus protein 1	HUMAN	8
282	14.86	27.2	O00303 EIF3F	Eukaryotic translation initiation factor 3 subunit F	HUMAN	7
283	14.82	58.4	P63241 IF5A1	Eukaryotic translation initiation factor 5A-1	HUMAN	10
284	14.73	16.6	Q9H4A4 AMPB	Aminopeptidase B	HUMAN	9
285	14.71	28.7	Q9Y265 RUVB1	RuvB-like 1	HUMAN	8
286	14.63	14.2	P35221 CTNA1	Catenin alpha-1	HUMAN	8
287	14.62	22.5	Q92769 HDAC2	Histone deacetylase 2	HUMAN	8
288	14.58	22.3	O43390 HNRPR	Heterogeneous nuclear ribonucleoprotein R	HUMAN	11
289	14.56	16.5	O00232 PSD12	26S proteasome non-ATPase regulatory subunit 12	HUMAN	8
290	14.42	36.1	P06748 NPM	Nucleophosmin	HUMAN	7
291	14.41	59.9	P15531 NDKA	Nucleoside diphosphate kinase A	HUMAN	10
292	14.35	64.2	P30086 PEBP1	Phosphatidylethanolamine-binding protein 1	HUMAN	8
293	14.27	21.3	P61158 ARP3	Actin-related protein 3	HUMAN	7
294	14.24	29.1	Q15233 NONO	Non-POU domain-containing octamer-binding protein	HUMAN	11
295	14.2	12.5	Q13435 SF3B2	Splicing factor 3B subunit 2	HUMAN	8
296	14.19	17.9	P49591 SYSC	Serine--tRNA ligase, cytoplasmic	HUMAN	7
297	14.16	17.6	P49419 AL7A1	Alpha-aminoadipic semialdehyde dehydrogenase	HUMAN	7
298	14.15	57	P60660 MYL6	Myosin light polypeptide 6	HUMAN	8
299	14.12	9	Q93009 UBP7	Ubiquitin carboxyl-terminal hydrolase 7	HUMAN	7
300	14.1	9.2	P42285 SK2L2	Superkiller viralicidic activity 2-like 2	HUMAN	7
301	14.07	24	P28074 PSB5	Proteasome subunit beta type-5	HUMAN	7
302	14.04	73.6	P07737 PROF1	Profilin-1	HUMAN	11
303	14.03	22.6	P18754 RCC1	Regulator of chromosome condensation	HUMAN	8
304	14	26.4	P20042 IF2B	Eukaryotic translation initiation factor 2 subunit 2	HUMAN	7
305	14	36.1	P32322 P5CR1	Pyrroline-5-carboxylate reductase 1, mitochondrial	HUMAN	9
306	14	42	P51149 RAB7A	Ras-related protein Rab-7a	HUMAN	7
307	14	38.5	P52907 CAZA1	F-actin-capping protein subunit alpha-1	HUMAN	7
308	14	35.8	P60900 PSA6	Proteasome subunit alpha type-6	HUMAN	7
309	14	25.2	Q15084 PDIA6	Protein disulfide-isomerase A6	HUMAN	7
310	14	27.5	Q96D17 SNR40	U5 small nuclear ribonucleoprotein 40 kDa protein	HUMAN	7
311	13.98	25.2	O94826 TOM70	Mitochondrial import receptor subunit TOM70	HUMAN	8
312	13.88	20.7	P16435 NCPR	NADPH--cytochrome P450 reductase	HUMAN	8
313	13.83	22.4	P35998 PRS7	26S protease regulatory subunit 7	HUMAN	7
314	13.82	29.8	Q99536 VAT1	Synaptic vesicle membrane protein VAT-1 homolog	HUMAN	7
315	13.7	18	O43242 PSMD3	26S proteasome non-ATPase regulatory subunit 3	HUMAN	7
316	13.7	14.6	Q16891 MIC60	MICOS complex subunit MIC60	HUMAN	7
317	13.66	46.9	Q15366 PCBP2	Poly(rC)-binding protein 2	HUMAN	13
318	13.63	22.1	Q00325 MPCP	Phosphate carrier protein, mitochondrial	HUMAN	9
319	13.63	27.7	Q9UNM6 PSD13	26S proteasome non-ATPase regulatory subunit 13	HUMAN	8
320	13.62	20.6	P09622 DLDH	Dihydrolipoyl dehydrogenase, mitochondrial	HUMAN	7
321	13.62	41.4	P54819 KAD2	Adenylate kinase 2, mitochondrial	HUMAN	7
322	13.57	21.6	P60228 EIF3E	Eukaryotic translation initiation factor 3 subunit E	HUMAN	7
323	13.54	53.6	P84077 ARF1	ADP-ribosylation factor 1	HUMAN	7
324	13.52	17.6	Q14166 TTL12	Tubulin--tyrosine ligase-like protein 12	HUMAN	8
325	13.51	30.5	Q92597 NDRG1	Protein NDRG1	HUMAN	8
326	13.49	37.5	P51858 HDGF	Hepatoma-derived growth factor	HUMAN	7
327	13.35	20.8	P05455 LA	Lupus La protein	HUMAN	7
328	13.32	31.8	P22087 FBRL	rRNA 2'-O-methyltransferase fibrillar	HUMAN	7
329	13.17	32.1	P60891 PRPS1	Ribose-phosphate pyrophosphokinase 1	HUMAN	8
330	13.17	23.6	Q02978 M2OM	Mitochondrial 2-oxoglutarate/malate carrier protein	HUMAN	7

331	13.08	49 Q99714 HCD2	3-hydroxyacyl-CoA dehydrogenase type-2	HUMAN	8
332	13.07	27.6 P11177 ODPB	mitochondrial	HUMAN	9
333	13.02	23.8 Q7L2H7 EIF3M	Eukaryotic translation initiation factor 3 subunit M	HUMAN	7
334	13	11.7 Q09161 NCBP1	Nuclear cap-binding protein subunit 1	HUMAN	7
335	12.96	30.7 O75367 H2AY	Core histone macro-H2A.1	HUMAN	7
336	12.89	40.4 P62241 RS8	40S ribosomal protein S8	HUMAN	8
337	12.88	24.7 Q99873 ANM1	Protein arginine N-methyltransferase 1	HUMAN	8
338	12.78	11 Q05682 CALD1	Caldesmon	HUMAN	8
339	12.75	25.5 Q13347 EIF3I	Eukaryotic translation initiation factor 3 subunit I	HUMAN	7
340	12.71	11.9 P11387 TOP1	DNA topoisomerase 1	HUMAN	8
341	12.68	25 P31930 QCR1	Cytochrome b-c1 complex subunit 1, mitochondrial	HUMAN	9
342	12.61	25.3 P26038 MOES	Moesin	HUMAN	14
343	12.59	22.2 P30740 ILEU	Leukocyte elastase inhibitor	HUMAN	6
344	12.59	25.9 P31689 DNJA1	DnaJ homolog subfamily A member 1	HUMAN	6
345	12.51	16.2 Q9BVP2 GNL3	Guanine nucleotide-binding protein-like 3	HUMAN	6
346	12.47	29 Q9Y266 NUDC	Nuclear migration protein nudC	HUMAN	8
347	12.44	20.3 P62333 PRS10	26S protease regulatory subunit 10B	HUMAN	6
348	12.43	8.9 O00159 MYO1C	Unconventional myosin-1c	HUMAN	7
349	12.42	28.2 P62191 PRS4	26S protease regulatory subunit 4	HUMAN	7
350	12.32	29 O75390 CISY	Citrate synthase, mitochondrial	HUMAN	7
351	12.3	10 Q14683 SMC1A	Structural maintenance of chromosomes protein 1A	HUMAN	8
352	12.27	12.1 Q8TCS8 PNPT1	Polyribonucleotide nucleotidyltransferase 1, mitochondrial	HUMAN	6
353	12.18	27.5 P51991 ROA3	Heterogeneous nuclear ribonucleoprotein A3	HUMAN	10
354	12.14	10.6 Q96PK6 RBM14	RNA-binding protein 14	HUMAN	6
355	12.12	27.8 Q07955 SRSF1	Serine/arginine-rich splicing factor 1	HUMAN	6
356	12.11	25.4 P61160 ARP2	Actin-related protein 2	HUMAN	7
357	12.09	6.4 P49790 NU153	Nuclear pore complex protein Nup153	HUMAN	6
358	12.09	28.3 Q96AG4 LRC59	Leucine-rich repeat-containing protein 59	HUMAN	6
359	12.05	21.2 P22695 QCR2	Cytochrome b-c1 complex subunit 2, mitochondrial	HUMAN	6
360	12.02	17.1 Q9P258 RCC2	Protein RCC2	HUMAN	6
361	12	17.4 O14979 HNRDL	Heterogeneous nuclear ribonucleoprotein D-like	HUMAN	6
362	12	17 P00367 DHE3	Glutamate dehydrogenase 1, mitochondrial	HUMAN	8
363	12	26.6 P06493 CDK1	Cyclin-dependent kinase 1	HUMAN	6
364	12	22.3 P26368 U2AF2	Splicing factor U2AF 65 kDa subunit	HUMAN	6
365	12	21.1 P50502 F10A1	Hsc70-interacting protein	HUMAN	7
366	12	16.9 P51648 AL3A2	Fatty aldehyde dehydrogenase	HUMAN	6
367	12	52.4 Q99497 PARK7	Protein deglycase DJ-1	HUMAN	6
368	12	31.7 Q9Y5M8 SRPRB	Signal recognition particle receptor subunit beta	HUMAN	6
369	11.92	28.1 O43684 BUB3	Mitotic checkpoint protein BUB3	HUMAN	7
370	11.92	20.7 P0CW18 PRS56	Serine protease 56	HUMAN	8
371	11.87	6.4 Q9P2J5 SYLC	Leucine--tRNA ligase, cytoplasmic	HUMAN	6
372	11.83	31 P29692 EF1D	Elongation factor 1-delta	HUMAN	6
373	11.81	12.3 P23921 RIR1	Ribonucleoside-diphosphate reductase large subunit	HUMAN	7
374	11.75	35.8 Q13162 PRDX4	Peroxiredoxin-4	HUMAN	7
375	11.72	27.2 O76003 GLRX3	Glutaredoxin-3	HUMAN	6
376	11.67	21.2 P04181 OAT	Ornithine aminotransferase, mitochondrial	HUMAN	7
377	11.66	15.7 O14744 ANM5	Protein arginine N-methyltransferase 5	HUMAN	8
378	11.66	12.5 Q06210 GFPT1	Glutamine--fructose-6-phosphate aminotransferase [isomerizing] 1	HUMAN	6
379	11.66	45 Q15185 TEBP	Prostaglandin E synthase 3	HUMAN	6
380	11.65	45.2 P09211 GSTP1	Glutathione S-transferase P	HUMAN	8
381	11.65	14.6 P42166 LAP2A	Lamina-associated polypeptide 2, isoform alpha	HUMAN	6
382	11.64	19.4 P30419 NMT1	Glycylpeptide N-tetradecanoyltransferase 1	HUMAN	6
383	11.56	21.7 P23381 SYWC	Tryptophan--tRNA ligase, cytoplasmic	HUMAN	7
384	11.48	26 O95433 AHSA1	Activator of 90 kDa heat shock protein ATPase homolog 1	HUMAN	7
385	11.47	10.6 Q1KMD3 HNRL2	Heterogeneous nuclear ribonucleoprotein U-like protein 2	HUMAN	6
386	11.46	8.6 P46379 BAG6	Large proline-rich protein BAG6	HUMAN	6

387	11.42	19.8	P07954 FUMH	Fumarate hydratase, mitochondrial	HUMAN	6
388	11.39	22	P24752 THIL	Acetyl-CoA acetyltransferase, mitochondrial	HUMAN	6
389	11.36	24.2	P46781 RS9	40S ribosomal protein S9	HUMAN	6
390	11.3	19.5	P62195 PRS8	26S protease regulatory subunit 8	HUMAN	6
391	11.29	22.7	O00567 NOP56	Nucleolar protein 56	HUMAN	8
392	11.28	12.9	Q9NSD9 SYFB	Phenylalanine--tRNA ligase beta subunit	HUMAN	6
393	11.18	6	Q9HAV4 XPO5	Exportin-5	HUMAN	6
394	11.17	21.7	Q8IZV5 RDH10	Retinol dehydrogenase 10	HUMAN	6
395	11.17	11.5	Q9BQ52 RNZ2	Zinc phosphodiesterase ELAC protein 2	HUMAN	6
396	11.12	36.9	P30084 ECHM	Enoyl-CoA hydratase, mitochondrial	HUMAN	7
397	11.02	30.7	P18124 RL7	60S ribosomal protein L7	HUMAN	6
398	10.95	23.1	P35237 SPB6	Serpin B6	HUMAN	6
399	10.91	32.7	O14818 PSA7	Proteasome subunit alpha type-7	HUMAN	7
400	10.9	13.1	O95573 ACSL3	Long-chain-fatty-acid--CoA ligase 3	HUMAN	6
401	10.9	20.4	P62495 ERF1	Eukaryotic peptide chain release factor subunit 1	HUMAN	7
402	10.85	13.2	P06576 ATPB	ATP synthase subunit beta, mitochondrial	HUMAN	5
403	10.79	18	P54578 UBP14	Ubiquitin carboxyl-terminal hydrolase 14	HUMAN	6
404	10.77	35.5	P27348 1433T	14-3-3 protein theta	HUMAN	8
405	10.77	9.4	Q8IY81 SPB1	pre-rRNA processing protein FTSJ3	HUMAN	5
406	10.76	18.1	Q2TAY7 SMU1	WD40 repeat-containing protein SMU1	HUMAN	6
407	10.73	6.4	O95347 SMC2	Structural maintenance of chromosomes protein 2	HUMAN	5
408	10.72	18.5	P08559 ODPA	form, mitochondrial	HUMAN	7
409	10.68	11.4	O75874 IDHC	Isocitrate dehydrogenase [NADP] cytoplasmic	HUMAN	5
410	10.66	15.6	Q07065 CKAP4	Cytoskeleton-associated protein 4	HUMAN	6
411	10.61	21.1	P50454 SERPH	Serpin H1	HUMAN	5
412	10.57	36.4	Q9HB71 CYBP	Calcyclin-binding protein	HUMAN	6
413	10.53	20.3	P35659 DEK	Protein DEK	HUMAN	5
414	10.44	19.7	P26196 DDX6	Probable ATP-dependent RNA helicase DDX6	HUMAN	6
415	10.37	37	P62249 RS16	40S ribosomal protein S16	HUMAN	6
416	10.35	14	O95831 AIFM1	Apoptosis-inducing factor 1, mitochondrial	HUMAN	6
417	10.32	17.8	P17980 PRS6A	26S protease regulatory subunit 6A	HUMAN	5
418	10.32	12.3	Q9UHD8 SEPT9	Septin-9	HUMAN	5
419	10.31	9.6	Q9NQC3 RTN4	Reticulon-4	HUMAN	6
420	10.29	15.6	Q12874 SF3A3	Splicing factor 3A subunit 3	HUMAN	6
421	10.27	6.3	Q9UQE7 SMC3	Structural maintenance of chromosomes protein 3	HUMAN	6
422	10.2	9.8	P54577 SYYC	Tyrosine--tRNA ligase, cytoplasmic	HUMAN	5
423	10.16	6	Q9BSJ8 ESYT1	Extended synaptotagmin-1	HUMAN	6
424	10.15	54.6	P25398 RS12	40S ribosomal protein S12	HUMAN	6
425	10.11	13.7	P05091 ALDH2	Aldehyde dehydrogenase, mitochondrial	HUMAN	6
426	10.11	3.5	P46013 KI67	Antigen KI-67	HUMAN	6
427	10.1	14.3	O76021 RL1D1	Ribosomal L1 domain-containing protein 1	HUMAN	5
428	10.09	31.1	P28066 PSA5	Proteasome subunit alpha type-5	HUMAN	6
429	10.09	17	Q9Y617 SERC	Phosphoserine aminotransferase	HUMAN	5
430	10.04	4.9	O60264 SMCA5	chromatin subfamily A member 5	HUMAN	5
431	10.04	18.1	Q9Y2Z0 SGT1	Protein SGT1 homolog	HUMAN	5
432	10.03	30.6	P63104 1433Z	14-3-3 protein zeta/delta	HUMAN	8
433	10.02	7.2	Q6PKG0 LARP1	La-related protein 1	HUMAN	5
434	10	27.1	O00151 PDLI1	PDZ and LIM domain protein 1	HUMAN	5
435	10	14.6	O15371 EIF3D	Eukaryotic translation initiation factor 3 subunit D	HUMAN	5
436	10	14.4	P00390 GSHR	Glutathione reductase, mitochondrial	HUMAN	5
437	10	22.8	P31942 HNRH3	Heterogeneous nuclear ribonucleoprotein H3	HUMAN	5
438	10	23.5	P47756 CAPZB	F-actin-capping protein subunit beta	HUMAN	5
439	10	20.3	P54920 SNAA	Alpha-soluble NSF attachment protein	HUMAN	5
440	10	22.1	P62701 RS4X	40S ribosomal protein S4, X isoform	HUMAN	5
441	10	20.6	Q15717 ELAV1	ELAV-like protein 1	HUMAN	5
442	9.96	10.6	Q13724 MOGS	Mannosyl-oligosaccharide glucosidase	HUMAN	6

443	9.95	17.7	Q01518 CAP1	Adenylyl cyclase-associated protein 1	HUMAN	5
444	9.9	13.7	Q08J23 NSUN2	tRNA (cytosine(34)-C(5))-methyltransferase	HUMAN	7
445	9.89	16.9	Q8NCS1 PAIRB	Plasminogen activator inhibitor 1 RNA-binding protein	HUMAN	5
446	9.85	18.8	O96008 TOM40	Mitochondrial import receptor subunit TOM40 homolog	HUMAN	5
447	9.85	35.5	P30044 PRDX5	Peroxiredoxin-5, mitochondrial	HUMAN	5
448	9.81	8.3	O43143 DHX15	Pre-mRNA-splicing factor ATP-dependent RNA helicase DHX15	HUMAN	5
449	9.75	15.6	P43034 LIS1	Platelet-activating factor acetylhydrolase IB subunit alpha	HUMAN	5
450	9.74	29.5	P62906 RL10A	60S ribosomal protein L10a	HUMAN	5
451	9.73	18.6	P04899 GNAI2	Guanine nucleotide-binding protein G(i) subunit alpha-2	HUMAN	5
452	9.66	32.7	O15173 PGRC2	Membrane-associated progesterone receptor component 2	HUMAN	5
453	9.65	11.9	Q7LOY3 MRRP1	Mitochondrial ribonuclease P protein 1	HUMAN	5
454	9.64	7.7	O60841 IF2P	Eukaryotic translation initiation factor 5B	HUMAN	5
455	9.62	21.2	Q02878 RL6	60S ribosomal protein L6	HUMAN	6
456	9.62	20.2	Q9NTK5 OLA1	Obg-like ATPase 1	HUMAN	6
457	9.59	7.8	P46087 NOP2	Probable 28S rRNA (cytosine(4447)-C(5))-methyltransferase	HUMAN	5
458	9.53	7.9	P05556 ITB1	Integrin beta-1	HUMAN	5
459	9.51	7	Q9BUJ2 HNRL1	Heterogeneous nuclear ribonucleoprotein U-like protein 1	HUMAN	5
460	9.49	16.6	P37837 TALDO	Transaldolase	HUMAN	5
461	9.49	14.2	Q02809 PLOD1	Procollagen-lysine,2-oxoglutarate 5-dioxygenase 1	HUMAN	6
462	9.48	46.9	P62244 RS15A	40S ribosomal protein S15a	HUMAN	6
463	9.46	31.8	P63000 RAC1	Ras-related C3 botulinum toxin substrate 1	HUMAN	5
464	9.36	6.8	Q13423 NNTM	NAD(P) transhydrogenase, mitochondrial	HUMAN	5
465	9.35	15.1	P30520 PURA2	Adenylosuccinate synthetase isozyme 2	HUMAN	5
466	9.35	8.5	Q5JRX3 PREP	Presequence protease, mitochondrial	HUMAN	5
467	9.26	16.6	Q9BY44 EIF2A	Eukaryotic translation initiation factor 2A	HUMAN	6
468	9.25	2	P49792 RBP2	E3 SUMO-protein ligase RanBP2	HUMAN	5
469	9.25	7.7	Q6UB35 C1TM	Monofunctional C1-tetrahydrofolate synthase, mitochondrial	HUMAN	6
470	9.24	14.9	O43865 SAHH2	Adenosylhomocysteinase 2	HUMAN	5
471	9.22	10.9	Q14247 SRC8	Src substrate cortactin	HUMAN	5
472	9.17	26	P52597 HNRPF	Heterogeneous nuclear ribonucleoprotein F	HUMAN	9
473	9.11	40.6	P60981 DEST	Destrin	HUMAN	5
474	9.08	17.9	P11172 UMPS	Uridine 5'-monophosphate synthase	HUMAN	5
475	9.07	13.3	Q16181 SEPT7	Septin-7	HUMAN	5
476	9.02	4.8	P52701 MSH6	DNA mismatch repair protein Msh6	HUMAN	6
477	9.01	12.6	Q14498 RBM39	RNA-binding protein 39	HUMAN	5
478	8.98	12.3	P14314 GLU2B	Glucosidase 2 subunit beta	HUMAN	5
479	8.96	58.5	P09382 LEG1	Galectin-1	HUMAN	7
480	8.96	15.4	Q15008 PSMD6	26S proteasome non-ATPase regulatory subunit 6	HUMAN	5
481	8.95	42.7	P24534 EF1B	Elongation factor 1-beta	HUMAN	7
482	8.95	14.5	P63151 2ABA	subunit B alpha isoform	HUMAN	5
483	8.94	34.8	P18621 RL17	60S ribosomal protein L17	HUMAN	5
484	8.94	10.9	Q10471 GALT2	Polypeptide N-acetylgalactosaminyltransferase 2	HUMAN	5
485	8.93	33.5	O75947 ATP5H	ATP synthase subunit d, mitochondrial	HUMAN	5
486	8.85	24.4	P05198 IF2A	Eukaryotic translation initiation factor 2 subunit 1	HUMAN	5
487	8.84	28.3	P32119 PRDX2	Peroxiredoxin-2	HUMAN	7
488	8.81	30.7	Q13126 MTAP	S-methyl-5'-thioadenosine phosphorylase	HUMAN	5
489	8.75	8.1	P35580 MYH10	Myosin-10	HUMAN	13
490	8.74	37.4	P62888 RL30	60S ribosomal protein L30	HUMAN	4
491	8.74	10.1	Q99829 CPNE1	Copine-1	HUMAN	5
492	8.69	4.1	Q14690 RRP5	Protein RRP5 homolog	HUMAN	5
493	8.66	27.7	Q13011 ECH1	Delta(3,5)-Delta(2,4)-dienoyl-CoA isomerase, mitochondrial	HUMAN	5
494	8.62	10.1	Q10713 MPPA	Mitochondrial-processing peptidase subunit alpha	HUMAN	4
495	8.61	3.4	Q9NYU2 UGGG1	UDP-glucose:glycoprotein glucosyltransferase 1	HUMAN	4
496	8.61	6.8	Q9UJS0 CMC2	Calcium-binding mitochondrial carrier protein Aralar2	HUMAN	4
497	8.57	16.3	O96019 ACL6A	Actin-like protein 6A	HUMAN	5
498	8.55	8.9	Q8WUM4 PDC6I	Programmed cell death 6-interacting protein	HUMAN	4

499	8.52	10.5	O00429 DNM1L	Dynamin-1-like protein	HUMAN	5
500	8.51	9.8	P53985 MOT1	Monocarboxylate transporter 1	HUMAN	5
501	8.51	22.4	P61289 PSME3	Proteasome activator complex subunit 3	HUMAN	5
502	8.5	5.2	Q12769 NU160	Nuclear pore complex protein Nup160	HUMAN	5
503	8.43	12.1	Q9NZI8 IF2B1	Insulin-like growth factor 2 mRNA-binding protein 1	HUMAN	5
504	8.42	15.2	O60832 DKC1	H/ACA ribonucleoprotein complex subunit 4	HUMAN	4
505	8.4	25.5	O00487 PSDE	26S proteasome non-ATPase regulatory subunit 14	HUMAN	4
506	8.4	18	Q96KB5 TOPK	Lymphokine-activated killer T-cell-originated protein kinase	HUMAN	5
507	8.39	23.2	P20618 PSB1	Proteasome subunit beta type-1	HUMAN	4
508	8.37	18.6	Q13501 SQSTM	Sequestosome-1	HUMAN	6
509	8.34	6.2	Q92922 SMRC1	SWI/SNF complex subunit SMARCC1	HUMAN	5
510	8.33	74.2	P68371 TBB4B	Tubulin beta-4B chain	HUMAN	46
511	8.32	9.7	P27694 RFA1	Replication protein A 70 kDa DNA-binding subunit	HUMAN	4
512	8.31	4.8	Q16531 DDB1	DNA damage-binding protein 1	HUMAN	5
513	8.26	10.2	Q15436 SC23A	Protein transport protein Sec23A	HUMAN	6
514	8.25	14.5	O15355 PPM1G	Protein phosphatase 1G	HUMAN	4
515	8.25	14.3	P55209 NP1L1	Nucleosome assembly protein 1-like 1	HUMAN	4
516	8.24	5.4	P14735 IDE	Insulin-degrading enzyme	HUMAN	5
517	8.22	9.7	P46459 NSF	Vesicle-fusing ATPase	HUMAN	6
518	8.19	11.8	Q9NVI7 ATD3A	ATPase family AAA domain-containing protein 3A	HUMAN	5
519	8.18	6.2	O94979 SC31A	Protein transport protein Sec31A	HUMAN	4
520	8.14	8.6	P13798 ACPH	Acylamino-acid-releasing enzyme	HUMAN	4
521	8.1	39.4	P30050 RL12	60S ribosomal protein L12	HUMAN	4
522	8.08	7.1	P51116 FXR2	Fragile X mental retardation syndrome-related protein 2	HUMAN	4
523	8.08	14.7	Q13867 BLMH	Bleomycin hydrolase	HUMAN	5
524	8.08	28.1	Q15631 TSN	Translin	HUMAN	4
525	8.08	25.5	Q9H9B4 SFXN1	Sideroflexin-1	HUMAN	4
526	8.07	17	Q9GZL7 WDR12	Ribosome biogenesis protein WDR12	HUMAN	4
527	8.06	5.9	P53992 SC24C	Protein transport protein Sec24C	HUMAN	4
528	8.05	6.2	Q15269 PWP2	Periodic tryptophan protein 2 homolog	HUMAN	4
529	8.03	21.6	Q07021 C1QBP	mitochondrial	HUMAN	5
530	8.02	19.7	P39687 AN32A	Acidic leucine-rich nuclear phosphoprotein 32 family member A	HUMAN	4
531	8.02	20.6	P61313 RL15	60S ribosomal protein L15	HUMAN	4
532	8.01	15.9	Q16543 CDC37	Hsp90 co-chaperone Cdc37	HUMAN	4
533	8.01	11	Q96AE4 FUBP1	Far upstream element-binding protein 1	HUMAN	5
534	8	50.7	O43169 CYB5B	Cytochrome b5 type B	HUMAN	5
535	8	11.2	O75844 FACE1	CAAX prenyl protease 1 homolog	HUMAN	4
536	8	14.9	O95218 ZRAB2	Zinc finger Ran-binding domain-containing protein 2	HUMAN	4
537	8	17.5	P04632 CPNS1	Calpain small subunit 1	HUMAN	4
538	8	27.7	P10768 ESTD	S-formylglutathione hydrolase	HUMAN	4
539	8	36.8	P21291 CSRP1	Cysteine and glycine-rich protein 1	HUMAN	4
540	8	19.4	P26373 RL13	60S ribosomal protein L13	HUMAN	4
541	8	23	P33316 DUT	Deoxyuridine 5'-triphosphate nucleotidohydrolase, mitochondrial	HUMAN	5
542	8	14.6	P35637 FUS	RNA-binding protein FUS	HUMAN	5
543	8	26.5	P46782 RS5	40S ribosomal protein S5	HUMAN	4
544	8	9	P48444 COPD	Coatomer subunit delta	HUMAN	4
545	8	22.5	P61026 RAB10	Ras-related protein Rab-10	HUMAN	4
546	8	13.2	P62424 RL7A	60S ribosomal protein L7a	HUMAN	5
547	8	40.8	P62805 H4	Histone H4	HUMAN	5
548	8	11.2	Q01650 LAT1	Large neutral amino acids transporter small subunit 1	HUMAN	4
549	8	14.8	Q13283 G3BP1	Ras GTPase-activating protein-binding protein 1	HUMAN	4
550	8	12.1	Q15637 SF01	Splicing factor 1	HUMAN	4
551	8	11.6	Q16643 DREB	Drebrin	HUMAN	4
552	8	14.6	Q6YN16 HSDL2	Hydroxysteroid dehydrogenase-like protein 2	HUMAN	4
553	8	22.7	Q8TDN6 BRX1	Ribosome biogenesis protein BRX1 homolog	HUMAN	4
554	8	17.2	Q99729 ROAA	Heterogeneous nuclear ribonucleoprotein A/B	HUMAN	5

555	8	16.1	Q9P0L0 VAPA	Vesicle-associated membrane protein-associated protein A	HUMAN	4
556	8	21.9	Q9Y3U8 RL36	60S ribosomal protein L36	HUMAN	4
557	7.93	21.7	Q13310 PABP4	Polyadenylate-binding protein 4	HUMAN	14
558	7.92	15.9	Q13148 TADBP	TAR DNA-binding protein 43	HUMAN	4
559	7.9	7.6	Q8N1F7 NUP93	Nuclear pore complex protein Nup93	HUMAN	5
560	7.89	12.2	O75821 EIF3G	Eukaryotic translation initiation factor 3 subunit G	HUMAN	4
561	7.89	12.1	P08621 RU17	U1 small nuclear ribonucleoprotein 70 kDa	HUMAN	4
562	7.87	6.9	P33176 KINH	Kinesin-1 heavy chain	HUMAN	6
563	7.86	42.9	P31949 S10AB	Protein S100-A11	HUMAN	4
564	7.82	21.9	P62913 RL11	60S ribosomal protein L11	HUMAN	4
565	7.74	22.3	O43399 TPD54	Tumor protein D54	HUMAN	4
566	7.68	7.6	Q2NL82 TSR1	Pre-rRNA-processing protein TSR1 homolog	HUMAN	5
567	7.63	3.5	Q7KZ85 SPT6H	Transcription elongation factor SPT6	HUMAN	4
568	7.62	15.9	P19623 SPEE	Spermidine synthase	HUMAN	5
569	7.62	25.5	P61019 RAB2A	Ras-related protein Rab-2A	HUMAN	4
570	7.59	36.4	P62829 RL23	60S ribosomal protein L23	HUMAN	4
571	7.56	12.9	P49257 LMAN1	Protein ERGIC-53	HUMAN	4
572	7.51	28	P61086 UBE2K	Ubiquitin-conjugating enzyme E2 K	HUMAN	4
573	7.51	9.7	Q16850 CP51A	Lanosterol 14-alpha demethylase	HUMAN	4
574	7.49	14.1	Q9UBB4 ATX10	Ataxin-10	HUMAN	5
575	7.45	13.6	O15372 EIF3H	Eukaryotic translation initiation factor 3 subunit H	HUMAN	4
576	7.45	13.9	Q10567 AP1B1	AP-1 complex subunit beta-1	HUMAN	9
577	7.42	9.4	P18031 PTN1	Tyrosine-protein phosphatase non-receptor type 1	HUMAN	4
578	7.4	5.2	Q14203 DCTN1	Dynactin subunit 1	HUMAN	5
579	7.39	10.1	O75083 WDR1	WD repeat-containing protein 1	HUMAN	4
580	7.36	6	Q03701 CEBPZ	CCAAT/enhancer-binding protein zeta	HUMAN	4
581	7.35	13.2	O75521 ECI2	Enoyl-CoA delta isomerase 2, mitochondrial	HUMAN	4
582	7.34	8.2	Q08945 SSRP1	FACT complex subunit SSRP1	HUMAN	4
583	7.31	22.2	P51148 RAB5C	Ras-related protein Rab-5C	HUMAN	4
584	7.31	9.3	Q16851 UGPA	UTP--glucose-1-phosphate uridylyltransferase	HUMAN	4
585	7.3	17.7	P25788 PSA3	Proteasome subunit alpha type-3	HUMAN	5
586	7.27	23.4	P30040 ERP29	Endoplasmic reticulum resident protein 29	HUMAN	4
587	7.26	9.2	P42892 ECE1	Endothelin-converting enzyme 1	HUMAN	4
588	7.25	40.6	P62987 RL40	Ubiquitin-60S ribosomal protein L40	HUMAN	7
589	7.21	11.2	O75131 CPNE3	Copine-3	HUMAN	5
590	7.21	10.6	Q9Y285 SYFA	Phenylalanine--tRNA ligase alpha subunit	HUMAN	4
591	7.19	19.4	P67775 PP2AA	isoform	HUMAN	4
592	7.18	8.5	P11166 GTR1	Solute carrier family 2, facilitated glucose transporter member 1	HUMAN	4
593	7.16	23.8	P27635 RL10	60S ribosomal protein L10	HUMAN	5
594	7.1	7.9	P45974 UBP5	Ubiquitin carboxyl-terminal hydrolase 5	HUMAN	4
595	7.1	24.4	P49721 PSB2	Proteasome subunit beta type-2	HUMAN	4
596	7.08	8.5	P10515 ODP2	pyruvate dehydrogenase complex, mitochondrial	HUMAN	4
597	7.07	9	P12081 SYHC	Histidine--tRNA ligase, cytoplasmic	HUMAN	4
598	7.04	13.4	P31153 METK2	S-adenosylmethionine synthase isoform type-2	HUMAN	4
599	7.03	18.8	P38117 ETFB	Electron transfer flavoprotein subunit beta	HUMAN	4
600	7	2.3	P12270 TPR	Nucleoprotein TPR	HUMAN	4
601	6.98	46.7	P99999 CYC	Cytochrome c	HUMAN	4
602	6.96	10.2	P37198 NUP62	Nuclear pore glycoprotein p62	HUMAN	4
603	6.95	6.1	O75534 CSDE1	Cold shock domain-containing protein E1	HUMAN	5
604	6.91	5	Q15061 WDR43	WD repeat-containing protein 43	HUMAN	3
605	6.91	13.5	Q9HAV0 GGB4	Guanine nucleotide-binding protein subunit beta-4	HUMAN	4
606	6.9	6	Q99459 CDC5L	Cell division cycle 5-like protein	HUMAN	4
607	6.88	2.3	Q9H583 HEAT1	HEAT repeat-containing protein 1	HUMAN	3
608	6.87	27.7	P48047 ATPO	ATP synthase subunit O, mitochondrial	HUMAN	4
609	6.85	27.4	P31947 1433S	14-3-3 protein sigma	HUMAN	7
610	6.77	5	Q92900 RENT1	Regulator of nonsense transcripts 1	HUMAN	4

611	6.75	10 Q6DD88 ATLA3	Atlastin-3	HUMAN	4
612	6.73	9.8 Q9Y6E2 BZW2	Basic leucine zipper and W2 domain-containing protein 2	HUMAN	4
613	6.65	8.1 O94776 MTA2	Metastasis-associated protein MTA2	HUMAN	4
614	6.6	10.1 Q6NUK1 SCMC1	Calcium-binding mitochondrial carrier protein SCaMC-1	HUMAN	4
615	6.56	7.4 P55084 ECHB	Trifunctional enzyme subunit beta, mitochondrial	HUMAN	3
616	6.55	10 P43490 NAMPT	Nicotinamide phosphoribosyltransferase	HUMAN	4
617	6.51	3.3 O95163 ELP1	Elongator complex protein 1	HUMAN	3
618	6.44	8.4 Q9H0S4 DDX47	Probable ATP-dependent RNA helicase DDX47	HUMAN	3
619	6.4	39.8 P30046 DOPD	D-dopachrome decarboxylase	HUMAN	5
620	6.4	28.8 P61224 RAP1B	Ras-related protein Rap-1b	HUMAN	4
621	6.34	32.9 P31946 1433B	14-3-3 protein beta/alpha	HUMAN	7
622	6.34	13.7 P61619 S61A1	Protein transport protein Sec61 subunit alpha isoform 1	HUMAN	5
623	6.32	13.9 O94905 ERLN2	Erlin-2	HUMAN	4
624	6.32	11 Q14444 CAPR1	Caprin-1	HUMAN	4
625	6.3	13.8 P55263 ADK	Adenosine kinase	HUMAN	3
626	6.3	10 Q16630 CPSF6	Cleavage and polyadenylation specificity factor subunit 6	HUMAN	3
627	6.29	50 P06703 S10A6	Protein S100-A6	HUMAN	4
628	6.29	7.7 P41250 SYG	Glycine--tRNA ligase	HUMAN	4
629	6.26	5.3 Q15020 SART3	Squamous cell carcinoma antigen recognized by T-cells 3	HUMAN	3
630	6.26	12.2 Q3ZCQ8 TIM50	Mitochondrial import inner membrane translocase subunit TIM50	HUMAN	3
631	6.25	20.9 O95816 BAG2	BAG family molecular chaperone regulator 2	HUMAN	3
632	6.25	12.4 P39748 FEN1	Flap endonuclease 1	HUMAN	3
633	6.23	9.7 O43719 HTSF1	HIV Tat-specific factor 1	HUMAN	4
634	6.23	14.7 Q13155 AIMP2	protein 2	HUMAN	3
635	6.19	15.7 P62753 RS6	40S ribosomal protein S6	HUMAN	3
636	6.18	46.1 P18085 ARF4	ADP-ribosylation factor 4	HUMAN	6
637	6.17	31.4 P52565 GDIR1	Rho GDP-dissociation inhibitor 1	HUMAN	4
638	6.15	9.9 Q9UN52 CSN3	COP9 signalosome complex subunit 3	HUMAN	3
639	6.12	11.4 O60488 ACSL4	Long-chain-fatty-acid--CoA ligase 4	HUMAN	5
640	6.12	8.4 P52789 HXK2	Hexokinase-2	HUMAN	7
641	6.12	1.4 Q5T4S7 UBR4	E3 ubiquitin-protein ligase UBR4	HUMAN	3
642	6.12	8.7 Q99805 TM9S2	Transmembrane 9 superfamily member 2	HUMAN	5
643	6.1	40.4 P62263 RS14	40S ribosomal protein S14	HUMAN	4
644	6.1	8.1 Q15758 AAAT	Neutral amino acid transporter B(0)	HUMAN	3
645	6.07	7.6 Q8WYA6 CTBL1	Beta-catenin-like protein 1	HUMAN	3
646	6.06	4.3 P50570 DYN2	Dynamin-2	HUMAN	3
647	6.06	22.1 Q15819 UB2V2	Ubiquitin-conjugating enzyme E2 variant 2	HUMAN	3
648	6.05	23.1 P25787 PSA2	Proteasome subunit alpha type-2	HUMAN	3
649	6.04	78.1 P05386 RLA1	60S acidic ribosomal protein P1	HUMAN	5
650	6.04	21.6 P22061 PIMT	Protein-L-isoaspartate(D-aspartate) O-methyltransferase	HUMAN	4
651	6.03	27.7 O00264 PGRC1	Membrane-associated progesterone receptor component 1	HUMAN	3
652	6.03	12 Q00796 DHSO	Sorbitol dehydrogenase	HUMAN	3
653	6.03	30.2 Q14240 IF4A2	Eukaryotic initiation factor 4A-II	HUMAN	11
654	6.03	5.9 Q14258 TRI25	E3 ubiquitin/ISG15 ligase TRIM25	HUMAN	3
655	6.03	16.9 Q9UL25 RAB21	Ras-related protein Rab-21	HUMAN	3
656	6.02	32.4 P04179 SODM	Superoxide dismutase [Mn], mitochondrial	HUMAN	4
657	6.02	6.6 Q15424 SAFB1	Scaffold attachment factor B1	HUMAN	4
658	6.01	2.2 P26358 DNMT1	DNA (cytosine-5)-methyltransferase 1	HUMAN	3
659	6.01	9.7 P51114 FXR1	Fragile X mental retardation syndrome-related protein 1	HUMAN	4
660	6.01	8 Q9BZZ5 API5	Apoptosis inhibitor 5	HUMAN	3
661	6	10 O00629 IMA3	Importin subunit alpha-3	HUMAN	3
662	6	17.5 O15260 SURF4	Surfeit locus protein 4	HUMAN	3
663	6	25.6 O43809 CPSF5	Cleavage and polyadenylation specificity factor subunit 5	HUMAN	3
664	6	11.6 O75436 VP26A	Vacuolar protein sorting-associated protein 26A	HUMAN	3
665	6	10.7 O75794 CD123	Cell division cycle protein 123 homolog	HUMAN	3
666	6	6.9 O94925 GLSK	Glutaminase kidney isoform, mitochondrial	HUMAN	3

667	6	9.3	O95747 OXSR1	Serine/threonine-protein kinase OSR1	HUMAN	3
668	6	11.7	O95817 BAG3	BAG family molecular chaperone regulator 3	HUMAN	3
669	6	45.9	P04080 CYTB	Cystatin-B	HUMAN	3
670	6	11.2	P06753 TPM3	Tropomyosin alpha-3 chain	HUMAN	3
671	6	41.5	P08708 RS17	40S ribosomal protein S17	HUMAN	3
672	6	15.8	P08754 GNAI3	Guanine nucleotide-binding protein G(k) subunit alpha	HUMAN	4
673	6	16.5	P12004 PCNA	Proliferating cell nuclear antigen	HUMAN	4
674	6	54	P22392 NDKB	Nucleoside diphosphate kinase B	HUMAN	9
675	6	21.6	P28070 PSB4	Proteasome subunit beta type-4	HUMAN	3
676	6	39.1	P35268 RL22	60S ribosomal protein L22	HUMAN	4
677	6	22.4	P43487 RANG	Ran-specific GTPase-activating protein	HUMAN	3
678	6	24.1	P45973 CBX5	Chromobox protein homolog 5	HUMAN	3
679	6	22.3	P46776 RL27A	60S ribosomal protein L27a	HUMAN	3
680	6	22.7	P51153 RAB13	Ras-related protein Rab-13	HUMAN	4
681	6	6.2	P52888 THOP1	Thimet oligopeptidase	HUMAN	3
682	6	17.9	P59998 ARPC4	Actin-related protein 2/3 complex subunit 4	HUMAN	3
683	6	33.9	P62854 RS26	40S ribosomal protein S26	HUMAN	3
684	6	35.7	P68036 UB2L3	Ubiquitin-conjugating enzyme E2 L3	HUMAN	3
685	6	28.2	P69905 HBA	Hemoglobin subunit alpha	HUMAN	4
686	6	20.4	P83731 RL24	60S ribosomal protein L24	HUMAN	3
687	6	16.5	Q02543 RL18A	60S ribosomal protein L18a	HUMAN	3
688	6	23.5	Q13185 CBX3	Chromobox protein homolog 3	HUMAN	3
689	6	17.8	Q14103 HNRPD	Heterogeneous nuclear ribonucleoprotein D0	HUMAN	5
690	6	3.5	Q14157 UBP2L	Ubiquitin-associated protein 2-like	HUMAN	3
691	6	13.1	Q14914 PTGR1	Prostaglandin reductase 1	HUMAN	3
692	6	7.5	Q16401 PSMD5	26S proteasome non-ATPase regulatory subunit 5	HUMAN	3
693	6	19.8	Q16836 HCDH	Hydroxyacyl-coenzyme A dehydrogenase, mitochondrial	HUMAN	3
694	6	3.5	Q5JPE7 NOMO2	Nodal modulator 2	HUMAN	3
695	6	5.6	Q8TDB8 GTR14	Solute carrier family 2, facilitated glucose transporter member 14	HUMAN	3
696	6	30.4	Q96A72 MGN2	Protein mago nashi homolog 2	HUMAN	3
697	6	51.2	Q9H3K6 BOLA2	BoLA-like protein 2	HUMAN	3
698	6	10	Q9H3P7 GCP60	Golgi resident protein GCP60	HUMAN	3
699	6	15.6	Q9NQR4 NIT2	Omega-amidase NIT2	HUMAN	3
700	6	11.7	Q9NUQ9 FA49B	Protein FAM49B	HUMAN	3
701	6	11.4	Q9NZL9 MAT2B	Methionine adenosyltransferase 2 subunit beta	HUMAN	3
702	6	2.8	Q9P2E9 RRBP1	Ribosome-binding protein 1	HUMAN	3
703	6	32.8	Q9UI30 TR112	Multifunctional methyltransferase subunit TRM112-like protein	HUMAN	4
704	6	31.3	Q9Y3E5 PTH2	Peptidyl-tRNA hydrolase 2, mitochondrial	HUMAN	3
705	6	17.8	Q9Y6C9 MTCH2	Mitochondrial carrier homolog 2	HUMAN	3
706	5.96	15	Q9H3N1 TMX1	Thioredoxin-related transmembrane protein 1	HUMAN	4
707	5.94	12.4	O00154 BACH	Cytosolic acyl coenzyme A thioester hydrolase	HUMAN	3
708	5.9	25.7	P19105 ML12A	Myosin regulatory light chain 12A	HUMAN	4
709	5.89	7.2	P28331 NDUS1	NADH-ubiquinone oxidoreductase 75 kDa subunit, mitochondrial	HUMAN	3
710	5.89	12.3	P42765 THIM	3-ketoacyl-CoA thiolase, mitochondrial	HUMAN	4
711	5.86	25.6	O75396 SC22B	Vesicle-trafficking protein SEC22b	HUMAN	4
712	5.86	32.2	P62316 SMD2	Small nuclear ribonucleoprotein Sm D2	HUMAN	3
713	5.81	8	O75955 FLOT1	Flotillin-1	HUMAN	3
714	5.81	18.7	Q07666 KHDR1	associated protein 1	HUMAN	4
715	5.8	10	O95232 LC7L3	Luc7-like protein 3	HUMAN	3
716	5.8	30.6	P51571 SSRD	Translocon-associated protein subunit delta	HUMAN	4
717	5.78	1.1	Q7Z6Z7 HUWE1	E3 ubiquitin-protein ligase HUWE1	HUMAN	3
718	5.77	13.6	P30566 PUR8	Adenylosuccinate lyase	HUMAN	3
719	5.77	26.9	P56537 IF6	Eukaryotic translation initiation factor 6	HUMAN	5
720	5.77	18.4	Q03013 GSTM4	Glutathione S-transferase Mu 4	HUMAN	3
721	5.77	8.8	Q14738 2A5D	subunit delta isoform	HUMAN	3
722	5.77	32.2	Q5R115 COX20	Cytochrome c oxidase protein 20 homolog	HUMAN	3

723	5.75	22.9	P82979 SARNP	SAP domain-containing ribonucleoprotein	HUMAN	4
724	5.74	6.6	P08240 SRPRA	Signal recognition particle receptor subunit alpha	HUMAN	4
725	5.74	8.3	Q9UBT2 SAE2	SUMO-activating enzyme subunit 2	HUMAN	3
726	5.71	10.4	Q9HB07 MYG1	UPF0160 protein MYG1, mitochondrial	HUMAN	3
727	5.7	15	P49841 GSK3B	Glycogen synthase kinase-3 beta	HUMAN	3
728	5.7	10.8	Q9NR50 EI2BG	Translation initiation factor eIF-2B subunit gamma	HUMAN	3
729	5.66	14.9	O75494 SRS10	Serine/arginine-rich splicing factor 10	HUMAN	3
730	5.66	17.1	P68400 CSK21	Casein kinase II subunit alpha	HUMAN	4
731	5.64	14.9	Q13242 SRSF9	Serine/arginine-rich splicing factor 9	HUMAN	3
732	5.61	19.8	Q99880 H2B1L	Histone H2B type 1-L	HUMAN	5
733	5.6	9.6	Q12849 GRSF1	G-rich sequence factor 1	HUMAN	3
734	5.59	5.6	Q9BUQ8 DDX23	Probable ATP-dependent RNA helicase DDX23	HUMAN	4
735	5.56	22.2	Q6UW68 TM205	Transmembrane protein 205	HUMAN	3
736	5.55	14.3	P21912 SDHB	mitochondrial	HUMAN	3
737	5.54	21.6	P67809 YBOX1	Nuclease-sensitive element-binding protein 1	HUMAN	3
738	5.51	4.2	Q8NBJ5 GT251	Procollagen galactosyltransferase 1	HUMAN	3
739	5.44	4.5	A0FGR8 ESYT2	Extended synaptotagmin-2	HUMAN	3
740	5.44	10.3	P53007 TXTP	Tricarboxylate transport protein, mitochondrial	HUMAN	3
741	5.44	35.3	Q71D13 H32	Histone H3.2	HUMAN	5
742	5.42	2.1	P51610 HCFC1	Host cell factor 1	HUMAN	3
743	5.42	13.2	Q9BWF3 RBM4	RNA-binding protein 4	HUMAN	3
744	5.41	38.1	P42677 RS27	40S ribosomal protein S27	HUMAN	3
745	5.39	4.8	P46977 STT3A	subunit STT3A	HUMAN	3
746	5.38	4.2	P27816 MAP4	Microtubule-associated protein 4	HUMAN	3
747	5.35	9.8	Q13895 BYST	Bystin	HUMAN	3
748	5.34	11.9	O15160 RPAC1	DNA-directed RNA polymerases I and III subunit RPAC1	HUMAN	3
749	5.34	21.6	P55795 HNRH2	Heterogeneous nuclear ribonucleoprotein H2	HUMAN	7
750	5.34	13.9	Q9BQ67 GRWD1	Glutamate-rich WD repeat-containing protein 1	HUMAN	3
751	5.29	13.8	P14324 FPPS	Farnesyl pyrophosphate synthase	HUMAN	7
752	5.27	35.1	P60903 S10AA	Protein S100-A10	HUMAN	3
753	5.26	10.5	O00425 IF2B3	Insulin-like growth factor 2 mRNA-binding protein 3	HUMAN	4
754	5.24	19.2	Q04323 UBXN1	UBX domain-containing protein 1	HUMAN	3
755	5.22	5.4	Q8TEX9 IPO4	Importin-4	HUMAN	4
756	5.2	24.7	P61981 1433G	14-3-3 protein gamma	HUMAN	6
757	5.2	11.4	Q15942 ZYX	Zyxin	HUMAN	3
758	5.2	31.7	Q9Y221 NIP7	60S ribosome subunit biogenesis protein NIP7 homolog	HUMAN	4
759	5.19	26	P24666 PPAC	Low molecular weight phosphotyrosine protein phosphatase	HUMAN	3
760	5.19	31.7	P26447 S10A4	Protein S100-A4	HUMAN	4
761	5.16	3.7	O95782 AP2A1	AP-2 complex subunit alpha-1	HUMAN	3
762	5.15	4.5	Q9H8H0 NOL11	Nucleolar protein 11	HUMAN	3
763	5.14	6.5	Q71RC2 LARP4	La-related protein 4	HUMAN	3
764	5.12	6.3	O00541 PESC	Pescadillo homolog	HUMAN	3
765	5.11	17.2	Q9Y5S9 RBM8A	RNA-binding protein 8A	HUMAN	4
766	5.09	14.1	P04818 TYSY	Thymidylate synthase	HUMAN	3
767	5.08	8.1	Q96555 WRIP1	ATPase WRNIP1	HUMAN	3
768	5.07	5.1	Q9UGP8 SEC63	Translocation protein SEC63 homolog	HUMAN	3
769	5.06	4.2	Q8WXF1 PSPC1	Paraspeckle component 1	HUMAN	3
770	5.05	5.4	O15042 SR140	U2 snRNP-associated SURP motif-containing protein	HUMAN	3
771	5.05	9.5	Q9Y295 DRG1	Developmentally-regulated GTP-binding protein 1	HUMAN	3
772	5.02	16	Q99733 NP1L4	Nucleosome assembly protein 1-like 4	HUMAN	4
773	5.01	4.8	Q96R06 SPAG5	Sperm-associated antigen 5	HUMAN	3
774	4.97	12.2	P25786 PSA1	Proteasome subunit alpha type-1	HUMAN	3
775	4.93	5	Q9UHI6 DDX20	Probable ATP-dependent RNA helicase DDX20	HUMAN	3
776	4.92	21.5	P62280 RS11	40S ribosomal protein S11	HUMAN	3
777	4.92	12.6	Q16629 SRSF7	Serine/arginine-rich splicing factor 7	HUMAN	3
778	4.9	22.9	P10599 THIO	Thioredoxin	HUMAN	3

779	4.9	7.7	Q99615 DNJC7	DnaJ homolog subfamily C member 7	HUMAN	3
780	4.89	34.4	P55769 NH2L1	NHP2-like protein 1	HUMAN	4
781	4.82	10.8	P39656 OST48	kDa subunit	HUMAN	3
782	4.82	15	P52788 SPSY	Spermine synthase	HUMAN	3
783	4.8	7.2	P15170 ERF3A	Eukaryotic peptide chain release factor GTP-binding subunit ERF3A	HUMAN	3
784	4.78	13.8	P35250 RFC2	Replication factor C subunit 2	HUMAN	3
785	4.76	10	P48556 PSMD8	26S proteasome non-ATPase regulatory subunit 8	HUMAN	3
786	4.71	10.5	Q14929 HAT1	Histone acetyltransferase type B catalytic subunit	HUMAN	3
787	4.66	9.2	P13807 GYS1	Glycogen [starch] synthase, muscle	HUMAN	5
788	4.65	20.6	P62917 RL8	60S ribosomal protein L8	HUMAN	4
789	4.64	16.3	P50914 RL14	60S ribosomal protein L14	HUMAN	3
790	4.59	9.4	P25685 DNJB1	DnaJ homolog subfamily B member 1	HUMAN	3
791	4.59	17	Q9UBQ5 EIF3K	Eukaryotic translation initiation factor 3 subunit K	HUMAN	3
792	4.56	6.8	P46063 RECQ1	ATP-dependent DNA helicase Q1	HUMAN	3
793	4.54	13.5	Q9BQA1 MEP50	Methylosome protein 50	HUMAN	3
794	4.47	5.9	Q96124 FUBP3	Far upstream element-binding protein 3	HUMAN	3
795	4.46	13.3	P78417 GSTO1	Glutathione S-transferase omega-1	HUMAN	3
796	4.45	12.5	Q13151 ROA0	Heterogeneous nuclear ribonucleoprotein A0	HUMAN	3
797	4.44	13.1	P36952 SPB5	Serpin B5	HUMAN	3
798	4.33	5.2	Q13616 CUL1	Cullin-1	HUMAN	3
799	4.29	5.8	Q9BYT8 NEUL	Neurolysin, mitochondrial	HUMAN	3
800	4.25	4.4	Q15042 RB3GP	Rab3 GTPase-activating protein catalytic subunit	HUMAN	3
801	4.24	10.8	Q99436 PSB7	Proteasome subunit beta type-7	HUMAN	3
802	4.19	14.8	P24539 AT5F1	ATP synthase F(0) complex subunit B1, mitochondrial	HUMAN	3
803	4.15	8.8	P11766 ADHX	Alcohol dehydrogenase class-3	HUMAN	3
804	4.11	6.5	P08237 PFKAM	ATP-dependent 6-phosphofructokinase, muscle type	HUMAN	4
805	4.1	27.7	P63220 RS21	40S ribosomal protein S21	HUMAN	3
806	4.09	19.6	P15374 UCHL3	Ubiquitin carboxyl-terminal hydrolase isozyme L3	HUMAN	3
807	4.07	3.2	P28340 DPOD1	DNA polymerase delta catalytic subunit	HUMAN	3
808	4.05	25.4	P14678 RSMB	Small nuclear ribonucleoprotein-associated proteins B and B'	HUMAN	3
809	4.05	24.2	P61106 RAB14	Ras-related protein Rab-14	HUMAN	3
810	4.03	3.9	Q5JWF2 GNAS1	XLas	HUMAN	3
811	4.03	15.2	Q9Y277 VDAC3	Voltage-dependent anion-selective channel protein 3	HUMAN	3
812	4.02	12.9	P35241 RADI	Radixin	HUMAN	10
813	4.02	14.7	Q04760 LGUL	Lactoylglutathione lyase	HUMAN	3
814	4	31.9	O00148 DX39A	ATP-dependent RNA helicase DDX39A	HUMAN	10
815	4	7.2	O75475 PSIP1	PC4 and SFRS1-interacting protein	HUMAN	3
816	4	53.9	P05387 RLA2	60S acidic ribosomal protein P2	HUMAN	3
817	4	20.7	P42167 LAP2B	Lamina-associated polypeptide 2, isoforms beta/gamma	HUMAN	5
818	4	23.2	P61006 RAB8A	Ras-related protein Rab-8A	HUMAN	4
819	4	6.6	Q14684 RRP1B	Ribosomal RNA processing protein 1 homolog B	HUMAN	3
820	4	9.3	Q5T9A4 ATD3B	ATPase family AAA domain-containing protein 3B	HUMAN	4
821	4	77.7	Q9BQE3 TBA1C	Tubulin alpha-1C chain	HUMAN	38
822	4	5.7	Q9H078 CLPB	Caseinolytic peptidase B protein homolog	HUMAN	3
823	3.93	7.1	P35520 CBS	Cystathionine beta-synthase	HUMAN	3
824	3.91	1.8	Q92621 NU205	Nuclear pore complex protein Nup205	HUMAN	3
825	3.74	5.4	P18858 DNLI1	DNA ligase 1	HUMAN	4
826	3.68	9.7	P50995 ANX11	Annexin A11	HUMAN	4
827	3.64	27	P13929 ENOB	Beta-enolase	HUMAN	9
828	3.59	11.9	Q01844 EWS	RNA-binding protein EWS	HUMAN	5
829	3.57	12.5	Q01081 U2AF1	Splicing factor U2AF 35 kDa subunit	HUMAN	3
830	3.42	26	P63279 UBC9	SUMO-conjugating enzyme UBC9	HUMAN	3
831	3.29	32.9	P10620 MGST1	Microsomal glutathione S-transferase 1	HUMAN	4
832	3.14	32.9	P12236 ADT3	ADP/ATP translocase 3	HUMAN	13
833	2.96	5.6	P49756 RBM25	RNA-binding protein 25	HUMAN	3
834	2.93	24.2	P31150 GDIA	Rab GDP dissociation inhibitor alpha	HUMAN	12

835	2.92	9.8	P12532 KCRU	Creatine kinase U-type, mitochondrial	HUMAN	4
836	2.83	17.4	P15927 RFA2	Replication protein A 32 kDa subunit	HUMAN	3
837	2.76	11.5	P54709 AT1B3	Sodium/potassium-transporting ATPase subunit beta-3	HUMAN	3
838	2.65	8.2	Q9P2R7 SUCB1	Succinyl-CoA ligase [ADP-forming] subunit beta, mitochondrial	HUMAN	3
839	2.62	17.6	Q13547 HDAC1	Histone deacetylase 1	HUMAN	6
840	2.59	9.5	P54727 RD23B	UV excision repair protein RAD23 homolog B	HUMAN	3
841	2.59	14.8	Q09028 RBBP4	Histone-binding protein RBBP4	HUMAN	6
842	2.47	9.1	Q9NVA2 SEP11	Septin-11	HUMAN	3
843	2.46	4.8	Q8TBC4 UBA3	NEDD8-activating enzyme E1 catalytic subunit	HUMAN	3
844	2.44	8.1	Q13620 CUL4B	Cullin-4B	HUMAN	7
845	2.33	2.7	Q9UKV3 ACINU	Apoptotic chromatin condensation inducer in the nucleus	HUMAN	3
846	2.28	15	P08779 K1C16	Keratin, type I cytoskeletal 16	HUMAN	8
847	2.21	42.6	P14174 MIF	Macrophage migration inhibitory factor	HUMAN	4
848	2.06	22.5	P60953 CDC42	Cell division control protein 42 homolog	HUMAN	3
849	2.03	13	Q04917 1433F	14-3-3 protein eta	HUMAN	4
850	2.02	10.1	P67936 TPM4	Tropomyosin alpha-4 chain	HUMAN	4
851	2.01	18	P02533 K1C14	Keratin, type I cytoskeletal 14	HUMAN	9
852	2.01	17	P09972 ALDOC	Fructose-bisphosphate aldolase C	HUMAN	8
853	2.01	4.4	P17858 PFKAL	ATP-dependent 6-phosphofructokinase, liver type	HUMAN	3
854	2	74.1	P60709 ACTB	Actin, cytoplasmic 1	HUMAN	74
855	2	29.4	P62136 PP1A	Serine/threonine-protein phosphatase PP1-alpha catalytic subunit	HUMAN	8
856	2	66.5	P68366 TBA4A	Tubulin alpha-4A chain	HUMAN	38
857	2	41.7	P84085 ARF5	ADP-ribosylation factor 5	HUMAN	5
858	2	3.4	Q13733 AT1A4	Sodium/potassium-transporting ATPase subunit alpha-4	HUMAN	3
859	2	35.4	Q6F113 H2A2A	Histone H2A type 2-A	HUMAN	3
860	2	19.5	Q92688 AN32B	Acidic leucine-rich nuclear phosphoprotein 32 family member B	HUMAN	4

1. Unused Score, unused protein score. For the target identification, a strict total score cut-off of 1.3 was set as the qualification criterion, which corresponded to a protein confidence interval of 95%.
2. % Cov (95), percent protein sequence coverage with the identified peptides.
3. Peptides(95%)., number of unique peptides identified for a protein.

Supplementary table 4. List of AP2 targets in mitochondria

No.	Unused Score ¹	% Cov (95) ²	Accession #	Name	Species	Peptides(95%) ³
1	118.96	55.8	P31327 CPSM	Carbamoyl-phosphate synthase [ammonia], mitochondrial	HUMAN	77
2	111.58	33.7	P49327 FAS	Fatty acid synthase	HUMAN	59
3	87.27	38.7	P42704 LPPRC	Leucine-rich PPR motif-containing protein, mitochondrial	HUMAN	45
4	81.23	63.8	P08238 HS90B	Heat shock protein HSP 90-beta	HUMAN	53
5	63.48	65.9	P14618 KPYM	Pyruvate kinase PKM	HUMAN	46
6	57.49	53.7	P02786 TFR1	Transferrin receptor protein 1	HUMAN	44
7	53.46	50	P55072 TERA	Transitional endoplasmic reticulum ATPase	HUMAN	29
8	51.42	57.9	P10809 CH60	60 kDa heat shock protein, mitochondrial	HUMAN	30
9	47.7	25.9	P26640 SYVC	Valine--tRNA ligase	HUMAN	24
10	47.08	42.2	P02545 LMNA	Prelamin-A/C	HUMAN	26
11	44.3	38	Q12906 ILF3	Interleukin enhancer-binding factor 3	HUMAN	24
12	43.57	25.8	P09874 PARP1	Poly [ADP-ribose] polymerase 1	HUMAN	22
13	42.23	43.1	P11021 GRP78	78 kDa glucose-regulated protein	HUMAN	26
14	42.13	36.3	Q92598 HS105	Heat shock protein 105 kDa	HUMAN	21
15	41.95	31.4	P22314 UBA1	Ubiquitin-like modifier-activating enzyme 1	HUMAN	25
16	40.27	52.2	P07900 HS90A	Heat shock protein HSP 90-alpha	HUMAN	47
17	40.09	37.8	P27824 CALX	Calnexin	HUMAN	23
18	33.77	45.9	Q99832 TCPH	T-complex protein 1 subunit eta	HUMAN	18
19	32.84	33.9	P38646 GRP75	Stress-70 protein, mitochondrial	HUMAN	19
20	32.65	48.5	P49411 EFTU	Elongation factor Tu, mitochondrial	HUMAN	21
21	31.67	31.4	P34932 HSP74	Heat shock 70 kDa protein 4	HUMAN	17
22	31.2	27.9	P47897 SYQ	Glutamine--tRNA ligase	HUMAN	16
23	30.08	22.6	P55786 PSA	Puromycin-sensitive aminopeptidase	HUMAN	15
24	30	21.8	P54886 P5CS	Delta-1-pyrroline-5-carboxylate synthase	HUMAN	15
25	29.21	64.2	P23396 RS3	40S ribosomal protein S3	HUMAN	15
26	27.8	23.3	Q7KZF4 SND1	Staphylococcal nuclease domain-containing protein 1	HUMAN	14
27	27.77	43.3	P34897 GLYM	Serine hydroxymethyltransferase, mitochondrial	HUMAN	14
28	27.45	41.9	P61978 HNRPK	Heterogeneous nuclear ribonucleoprotein K	HUMAN	16
29	27.34	36	P31939 PUR9	Bifunctional purine biosynthesis protein PURH	HUMAN	14
30	26.89	16.9	O75153 CLU	Clustered mitochondria protein homolog	HUMAN	14
31	26.49	27.7	P40939 ECHA	Trifunctional enzyme subunit alpha, mitochondrial	HUMAN	13
32	26.24	29.8	Q12931 TRAP1	Heat shock protein 75 kDa, mitochondrial	HUMAN	16
33	25.83	35.6	P25705 ATPA	ATP synthase subunit alpha, mitochondrial	HUMAN	15
34	25.55	47.6	P07195 LDHB	L-lactate dehydrogenase B chain	HUMAN	16
35	25.53	52.1	P40926 MDHM	Malate dehydrogenase, mitochondrial	HUMAN	14
36	25.15	64	P63244 RACK1	Receptor of activated protein C kinase 1	HUMAN	15
37	23.93	21.2	Q96RP9 EFGM	Elongation factor G, mitochondrial	HUMAN	12
38	23.53	18.4	P36776 LONM	Lon protease homolog, mitochondrial	HUMAN	12
39	22.67	18.6	P11586 C1TC	C-1-tetrahydrofolate synthase, cytoplasmic	HUMAN	11
40	22.45	56.1	P62258 1433E	14-3-3 protein epsilon	HUMAN	14
41	22.12	26.7	P30153 2AAA	alpha isoform	HUMAN	11
42	22.11	51.7	P05141 ADT2	ADP/ATP translocase 2	HUMAN	18
43	21.99	19.6	P54136 SYRC	Arginine--tRNA ligase, cytoplasmic	HUMAN	12
44	21.81	20.2	Q8N163 CCAR2	Cell cycle and apoptosis regulator protein 2	HUMAN	11
45	21.75	22.8	P43304 GPDM	Glycerol-3-phosphate dehydrogenase, mitochondrial	HUMAN	11
46	21.72	41	P00966 ASSY	Argininosuccinate synthase	HUMAN	13
47	21.13	25.7	O00571 DDX3X	ATP-dependent RNA helicase DDX3X	HUMAN	12
48	20.88	22.3	Q15046 SYK	Lysine--tRNA ligase	HUMAN	11
49	20.12	15.8	Q01813 PFKAP	ATP-dependent 6-phosphofructokinase, platelet type	HUMAN	10
50	19.41	19.8	P08133 ANXA6	Annexin A6	HUMAN	11

51	18.92	31.8	Q02790 FKBP4	Peptidyl-prolyl cis-trans isomerase FKBP4	HUMAN	10
52	18.9	42.8	P08574 CY1	Cytochrome c1, heme protein, mitochondrial	HUMAN	13
53	18.48	71.8	O00299 CLIC1	Chloride intracellular channel protein 1	HUMAN	12
54	18.18	47	P21796 VDAC1	Voltage-dependent anion-selective channel protein 1	HUMAN	10
55	18.08	45.7	P13804 ETFA	Electron transfer flavoprotein subunit alpha, mitochondrial	HUMAN	9
56	18	34.7	P04083 ANXA1	Annexin A1	HUMAN	9
57	17.8	32.8	P08758 ANXA5	Annexin A5	HUMAN	9
58	17.7	33.8	P35232 PHB	Prohibitin	HUMAN	9
59	17.69	24.7	Q16881 TRXR1	Thioredoxin reductase 1, cytoplasmic	HUMAN	11
60	17.67	49.8	Q06830 PRDX1	Peroxiredoxin-1	HUMAN	10
61	17.23	20.6	O43776 SYNC	Asparagine--tRNA ligase, cytoplasmic	HUMAN	9
62	17.19	38.7	P27695 APEX1	DNA-(apurinic or apyrimidinic site) lyase	HUMAN	9
63	17.18	31	P12277 KCRB	Creatine kinase B-type	HUMAN	10
64	16.99	21.6	O00116 ADAS	Alkyldihydroxyacetonephosphate synthase, peroxisomal	HUMAN	9
65	16.46	11	P19367 HKK1	Hexokinase-1	HUMAN	9
66	16.44	36.8	P40925 MDHC	Malate dehydrogenase, cytoplasmic	HUMAN	9
67	16.16	29.5	P00505 AATM	Aspartate aminotransferase, mitochondrial	HUMAN	10
68	16.05	17.3	P40763 STAT3	Signal transducer and activator of transcription 3	HUMAN	8
69	16	31.6	P45880 VDAC2	Voltage-dependent anion-selective channel protein 2	HUMAN	10
70	15.94	23.8	P38606 VATA	V-type proton ATPase catalytic subunit A	HUMAN	9
71	15.92	15.6	Q9UG63 ABCF2	ATP-binding cassette sub-family F member 2	HUMAN	8
72	15.79	15.7	P49748 ACADV	Very long-chain specific acyl-CoA dehydrogenase, mitochondrial	HUMAN	8
73	15.57	40.6	P30048 PRDX3	Thioredoxin-dependent peroxide reductase, mitochondrial	HUMAN	12
74	15.46	19.9	P31040 SDHA	mitochondrial	HUMAN	8
75	15.29	19	P04040 CATA	Catalase	HUMAN	7
76	15.04	16.6	P51659 DHB4	Peroxisomal multifunctional enzyme type 2	HUMAN	8
77	14.91	11.1	P50416 CPT1A	Carnitine O-palmitoyltransferase 1, liver isoform	HUMAN	7
78	14.71	28.7	Q9Y265 RUVB1	RuvB-like 1	HUMAN	8
79	14.41	59.9	P15531 NDKA	Nucleoside diphosphate kinase A	HUMAN	10
80	14.16	17.6	P49419 AL7A1	Alpha-aminoadipic semialdehyde dehydrogenase	HUMAN	7
81	14	36.1	P32322 P5CR1	Pyrroline-5-carboxylate reductase 1, mitochondrial	HUMAN	9
82	13.98	25.2	O94826 TOM70	Mitochondrial import receptor subunit TOM70	HUMAN	8
83	13.88	20.7	P16435 NCPR	NADPH--cytochrome P450 reductase	HUMAN	8
84	13.82	29.8	Q99536 VAT1	Synaptic vesicle membrane protein VAT-1 homolog	HUMAN	7
85	13.7	14.6	Q16891 MIC60	MICOS complex subunit MIC60	HUMAN	7
86	13.63	22.1	Q00325 MPCP	Phosphate carrier protein, mitochondrial	HUMAN	9
87	13.62	20.6	P09622 DLDH	Dihydrolipoyl dehydrogenase, mitochondrial	HUMAN	7
88	13.62	41.4	P54819 KAD2	Adenylate kinase 2, mitochondrial	HUMAN	7
89	13.17	23.6	Q02978 M2OM	Mitochondrial 2-oxoglutarate/malate carrier protein	HUMAN	7
90	13.08	49	Q99714 HCD2	3-hydroxyacyl-CoA dehydrogenase type-2	HUMAN	8
91	13.07	27.6	P11177 ODPB	Pyruvate dehydrogenase E1 component subunit beta, mitochondrial	HUMAN	9
92	13	11.7	Q09161 NCBP1	Nuclear cap-binding protein subunit 1	HUMAN	7
93	12.68	25	P31930 QCR1	Cytochrome b-c1 complex subunit 1, mitochondrial	HUMAN	9
94	12.59	25.9	P31689 DNJA1	DnaJ homolog subfamily A member 1	HUMAN	6
95	12.32	29	O75390 CISY	Citrate synthase, mitochondrial	HUMAN	7
96	12.27	12.1	Q8TCS8 PNPT1	Polyribonucleotide nucleotidyltransferase 1, mitochondrial	HUMAN	6
97	12.09	28.3	Q96AG4 LRC59	Leucine-rich repeat-containing protein 59	HUMAN	6
98	12.05	21.2	P22695 QCR2	Cytochrome b-c1 complex subunit 2, mitochondrial	HUMAN	6
99	12	17	P00367 DHE3	Glutamate dehydrogenase 1, mitochondrial	HUMAN	8
100	12	26.6	P06493 CDK1	Cyclin-dependent kinase 1	HUMAN	6
101	12	22.3	P26368 U2AF2	Splicing factor U2AF 65 kDa subunit	HUMAN	6
102	12	16.9	P51648 AL3A2	Fatty aldehyde dehydrogenase	HUMAN	6
103	12	52.4	Q99497 PARK7	Protein deglycase DJ-1	HUMAN	6
104	11.75	35.8	Q13162 PRDX4	Peroxiredoxin-4	HUMAN	7
105	11.67	21.2	P04181 OAT	Ornithine aminotransferase, mitochondrial	HUMAN	7
106	11.65	45.2	P09211 GSTP1	Glutathione S-transferase P	HUMAN	8

107	11.64	19.4	P30419 NMT1	Glycylpeptide N-tetradecanoyltransferase 1	HUMAN	6
108	11.42	19.8	P07954 FUMH	Fumarate hydratase, mitochondrial	HUMAN	6
109	11.39	22	P24752 THIL	Acetyl-CoA acetyltransferase, mitochondrial	HUMAN	6
110	11.17	11.5	Q9BQ52 RNZ2	Zinc phosphodiesterase ELAC protein 2	HUMAN	6
111	11.12	36.9	P30084 ECHM	Enoyl-CoA hydratase, mitochondrial	HUMAN	7
112	10.9	13.1	O95573 ACSL3	Long-chain-fatty-acid--CoA ligase 3	HUMAN	6
113	10.85	13.2	P06576 ATPB	ATP synthase subunit beta, mitochondrial	HUMAN	5
114	10.77	35.5	P27348 1433T	14-3-3 protein theta	HUMAN	8
115	10.72	18.5	P08559 ODPA	mitochondrial	HUMAN	7
116	10.68	11.4	O75874 IDHC	Isocitrate dehydrogenase [NADP] cytoplasmic	HUMAN	5
117	10.35	14	O95831 AIFM1	Apoptosis-inducing factor 1, mitochondrial	HUMAN	6
118	10.11	13.7	P05091 ALDH2	Aldehyde dehydrogenase, mitochondrial	HUMAN	6
119	10.03	30.6	P63104 1433Z	14-3-3 protein zeta/delta	HUMAN	8
120	10	14.4	P00390 GSHR	Glutathione reductase, mitochondrial	HUMAN	5
121	9.85	18.8	O96008 TOM40	Mitochondrial import receptor subunit TOM40 homolog	HUMAN	5
122	9.85	35.5	P30044 PRDX5	Peroxioredoxin-5, mitochondrial	HUMAN	5
123	9.65	11.9	Q7L0Y3 MRRP1	Mitochondrial ribonuclease P protein 1	HUMAN	5
124	9.36	6.8	Q13423 NNTM	NAD(P) transhydrogenase, mitochondrial	HUMAN	5
125	9.35	8.5	Q5JRX3 PREP	Presequence protease, mitochondrial	HUMAN	5
126	9.25	7.7	Q6UB35 C1TM	Monofunctional C1-tetrahydrofolate synthase, mitochondrial	HUMAN	6
127	9.25	2	P49792 RBP2	E3 SUMO-protein ligase RanBP2	HUMAN	5
128	8.93	33.5	O75947 ATP5H	ATP synthase subunit d, mitochondrial	HUMAN	5
129	8.85	24.4	P05198 IF2A	Eukaryotic translation initiation factor 2 subunit 1	HUMAN	5
130	8.75	8.1	P35580 MYH10	Myosin-10	HUMAN	13
131	8.66	27.7	Q13011 ECH1	Delta(3,5)-Delta(2,4)-dienoyl-CoA isomerase, mitochondrial	HUMAN	5
132	8.62	10.1	Q10713 MPPA	Mitochondrial-processing peptidase subunit alpha	HUMAN	4
133	8.61	6.8	Q9UJS0 CMC2	Calcium-binding mitochondrial carrier protein Aralar2	HUMAN	4
134	8.57	16.3	O96019 ACL6A	Actin-like protein 6A	HUMAN	5
135	8.52	10.5	O00429 DNM1L	Dynamin-1-like protein	HUMAN	5
136	8.51	9.8	P53985 MOT1	Monocarboxylate transporter 1	HUMAN	5
137	8.37	18.6	Q13501 SQSTM	Sequestosome-1	HUMAN	6
138	8.24	5.4	P14735 IDE	Insulin-degrading enzyme	HUMAN	5
139	8.19	11.8	Q9NVI7 ATD3A	ATPase family AAA domain-containing protein 3A	HUMAN	5
140	8.08	25.5	Q9H9B4 SFXN1	Sideroflexin-1	HUMAN	4
141	8.03	21.6	Q07021 C1QBP	mitochondrial	HUMAN	5
142	8.01	15.9	Q16543 CDC37	Hsp90 co-chaperone Cdc37	HUMAN	4
143	8	23	P33316 DUT	Deoxyuridine 5'-triphosphate nucleotidohydrolase, mitochondrial	HUMAN	5
144	8	50.7	O43169 CYB5B	Cytochrome b5 type B	HUMAN	5
145	8	14.6	Q6YN16 HSDL2	Hydroxysteroid dehydrogenase-like protein 2	HUMAN	4
146	7.9	7.6	Q8N1F7 NUP93	Nuclear pore complex protein Nup93	HUMAN	5
147	7.35	13.2	O75521 ECI2	Enoyl-CoA delta isomerase 2, mitochondrial	HUMAN	4
148	7.19	19.4	P67775 PP2AA	isoform	HUMAN	4
149	7.08	8.5	P10515 ODP2	dehydrogenase complex, mitochondrial	HUMAN	4
150	7.07	9	P12081 SYHC	Histidine--tRNA ligase, cytoplasmic	HUMAN	4
151	7.03	18.8	P38117 ETFB	Electron transfer flavoprotein subunit beta	HUMAN	4
152	6.98	46.7	P99999 CYC	Cytochrome c	HUMAN	4
153	6.95	6.1	O75534 CSDE1	Cold shock domain-containing protein E1	HUMAN	5
154	6.88	2.3	Q9H583 HEAT1	HEAT repeat-containing protein 1	HUMAN	3
155	6.87	27.7	P48047 ATPO	ATP synthase subunit O, mitochondrial	HUMAN	4
156	6.85	27.4	P31947 1433S	14-3-3 protein sigma	HUMAN	7
157	6.6	10.1	Q6NUK1 SCMC1	Calcium-binding mitochondrial carrier protein SCaMC-1	HUMAN	4
158	6.56	7.4	P55084 ECHB	Trifunctional enzyme subunit beta, mitochondrial	HUMAN	3
159	6.34	32.9	P31946 1433B	14-3-3 protein beta/alpha	HUMAN	7
160	6.29	7.7	P41250 SYG	Glycine--tRNA ligase	HUMAN	4
161	6.26	12.2	Q3ZCQ8 TIM50	Mitochondrial import inner membrane translocase subunit TIM50	HUMAN	3
162	6.25	12.4	P39748 FEN1	Flap endonuclease 1	HUMAN	3

163	6.12	11.4	O60488 ACSL4	Long-chain-fatty-acid--CoA ligase 4	HUMAN	5
164	6.12	8.4	P52789 HXK2	Hexokinase-2	HUMAN	7
165	6.1	40.4	P62263 RS14	40S ribosomal protein S14	HUMAN	4
166	6.03	12	Q00796 DHSO	Sorbitol dehydrogenase	HUMAN	3
167	6.02	32.4	P04179 SODM	Superoxide dismutase [Mn], mitochondrial	HUMAN	4
168	6	6.9	O94925 GLSK	Glutaminase kidney isoform, mitochondrial	HUMAN	3
169	6	19.8	Q16836 HCDH	Hydroxyacyl-coenzyme A dehydrogenase, mitochondrial	HUMAN	3
170	6	31.3	Q9Y3E5 PTH2	Peptidyl-tRNA hydrolase 2, mitochondrial	HUMAN	3
171	6	17.8	Q9Y6C9 MTCH2	Mitochondrial carrier homolog 2	HUMAN	3
172	6	54	P22392 NDKB	Nucleoside diphosphate kinase B	HUMAN	9
173	6	6.2	P52888 THOP1	Thimet oligopeptidase	HUMAN	3
174	6	35.7	P68036 UB2L3	Ubiquitin-conjugating enzyme E2 L3	HUMAN	3
175	6	10	Q9H3P7 GCP60	Golgi resident protein GCP60	HUMAN	3
176	6	15.6	Q9NQR4 NIT2	Omega-amidase NIT2	HUMAN	3
177	6	11.4	Q9NZL9 MAT2B	Methionine adenosyltransferase 2 subunit beta	HUMAN	3
178	5.94	12.4	O00154 BACH	Cytosolic acyl coenzyme A thioester hydrolase	HUMAN	3
179	5.89	7.2	P28331 NDUS1	NADH-ubiquinone oxidoreductase 75 kDa subunit, mitochondrial	HUMAN	3
180	5.89	12.3	P42765 THIM	3-ketoacyl-CoA thiolase, mitochondrial	HUMAN	4
181	5.78	1.1	Q7Z6Z7 HUWE1	E3 ubiquitin-protein ligase HUWE1	HUMAN	3
182	5.77	32.2	Q5RI15 COX20	Cytochrome c oxidase protein 20 homolog	HUMAN	3
183	5.71	10.4	Q9HB07 MYG1	UPF0160 protein MYG1, mitochondrial	HUMAN	3
184	5.7	15	P49841 GSK3B	Glycogen synthase kinase-3 beta	HUMAN	3
185	5.6	9.6	Q12849 GRSF1	G-rich sequence factor 1	HUMAN	3
186	5.55	14.3	P21912 SDHB	mitochondrial	HUMAN	3
187	5.44	10.3	P53007 TXTP	Tricarboxylate transport protein, mitochondrial	HUMAN	3
188	5.42	2.1	P51610 HCFC1	Host cell factor 1	HUMAN	3
189	5.2	24.7	P61981 1433G	14-3-3 protein gamma	HUMAN	6
190	5.09	14.1	P04818 TYSY	Thymidylate synthase	HUMAN	3
191	4.9	22.9	P10599 THIO	Thioredoxin	HUMAN	3
192	4.76	10	P48556 PSMD8	26S proteasome non-ATPase regulatory subunit 8	HUMAN	3
193	4.29	5.8	Q9BYT8 NEUL	Neurolysin, mitochondrial	HUMAN	3
194	4.24	10.8	Q99436 PSB7	Proteasome subunit beta type-7	HUMAN	3
195	4.19	14.8	P24539 AT5F1	ATP synthase F(0) complex subunit B1, mitochondrial	HUMAN	3
196	4.15	8.8	P11766 ADHX	Alcohol dehydrogenase class-3	HUMAN	3
197	4.05	25.4	P14678 RSMB	Small nuclear ribonucleoprotein-associated proteins B and B'	HUMAN	3
198	4.03	15.2	Q9Y277 VDAC3	Voltage-dependent anion-selective channel protein 3	HUMAN	3
199	4	9.3	Q5T9A4 ATD3B	ATPase family AAA domain-containing protein 3B	HUMAN	4
200	4	5.7	Q9H078 CLPB	Caseinolytic peptidase B protein homolog	HUMAN	3
201	3.74	5.4	P18858 DNLI1	DNA ligase 1	HUMAN	4
202	3.57	12.5	Q01081 U2AF1	Splicing factor U2AF 35 kDa subunit	HUMAN	3
203	3.29	32.9	P10620 MGST1	Microsomal glutathione S-transferase 1	HUMAN	4
204	3.14	32.9	P12236 ADT3	ADP/ATP translocase 3	HUMAN	13
205	2.92	9.8	P12532 KCRU	Creatine kinase U-type, mitochondrial	HUMAN	4
206	2.65	8.2	Q9P2R7 SUCB1	Succinyl-CoA ligase [ADP-forming] subunit beta, mitochondrial	HUMAN	3
207	2.33	2.7	Q9UKV3 ACINU	Apoptotic chromatin condensation inducer in the nucleus	HUMAN	3
208	2.03	13	Q04917 1433F	14-3-3 protein eta	HUMAN	4
209	2.01	17	P09972 ALDOC	Fructose-bisphosphate aldolase C	HUMAN	8

1. Unused Score, unused protein score. For the target identification, a strict total score cut-off of 1.3 was set as the qualification criterion, which corresponded to a protein confidence interval of 95%.

2. % Cov (95), percent protein sequence coverage with the identified peptides.

3. Peptides(95%), number of unique peptides identified for a protein.