Electronic Supplementary Material (ESI) for Dalton Transactions.
This journal is © The Royal Society of Chemistry 2017

Electronic Supplementary Information

# Structurally related hydrazone-based metal complexes with different antitumor activities variably induce apoptotic cell death

Dominik A. Megger,[a] Kristin Rosowski,[a] Christian Radunsky,[b] Jutta Kösters,[b] Barbara Sitek[a] and Jens Müller[b]

[a]Medizinisches Proteom-Center, Ruhr-Universität Bochum, Universitätsstr. 150, 44801 Bochum, Germany
[b]Westfälische Wilhelms-Universität Münster, Institut für Anorganische und Analytische Chemie, Corrensstr. 28/30, 48149 Münster, Germany

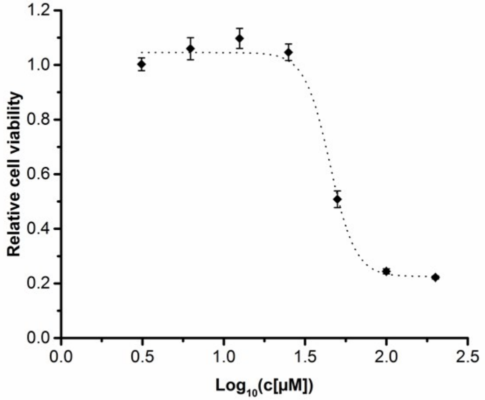

**Figure S1.** Dose-response curve for HepG2 cells treated with the ligand 2-(2-(1-(pyridin-2-yl)ethylidene)hydrazinyl)pyridine (**L**) as determined by the XTT cell viability assay. Data points represent average values of measurements performed in triplicate, error bars indicate the standard deviation and dotted lines are the sigmoidal fits used for the calculation of $EC_{50}$ value.

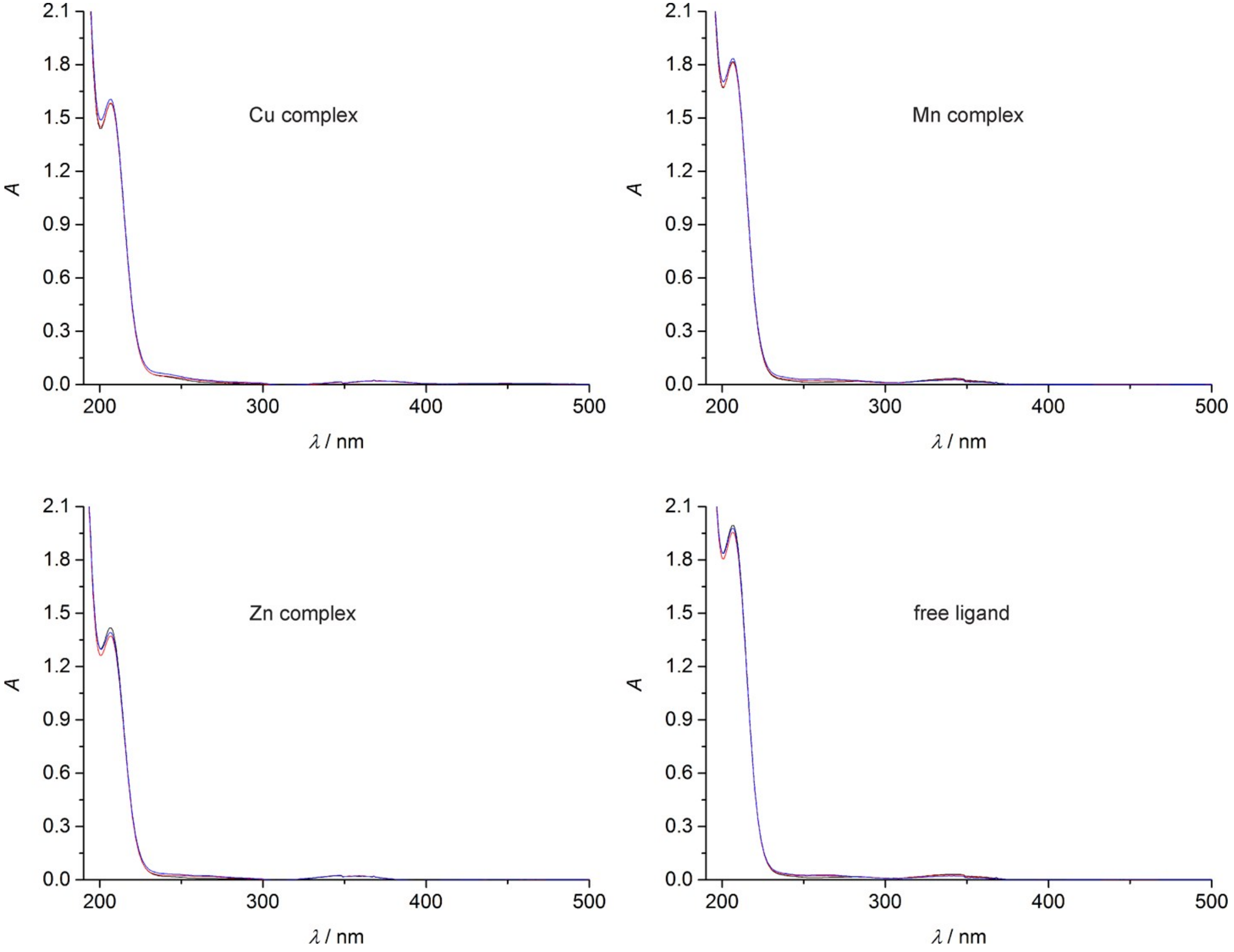

**Figure S2.** Time-dependent UV/Vis spectra of the complexes [CuCl$_2$(**L**)], [CuCl$_2$(**L**)] and [CuCl$_2$(**L**)] as well as the ligand **L**. Each compound was dissolved in DMSO (20 mM) and immediately diluted to a concentration of 2 μM. Spectra were acquired on a Cary 100 Bio instrument at three different time points (black: 0 h, red: 1 d, blue: 2 d).

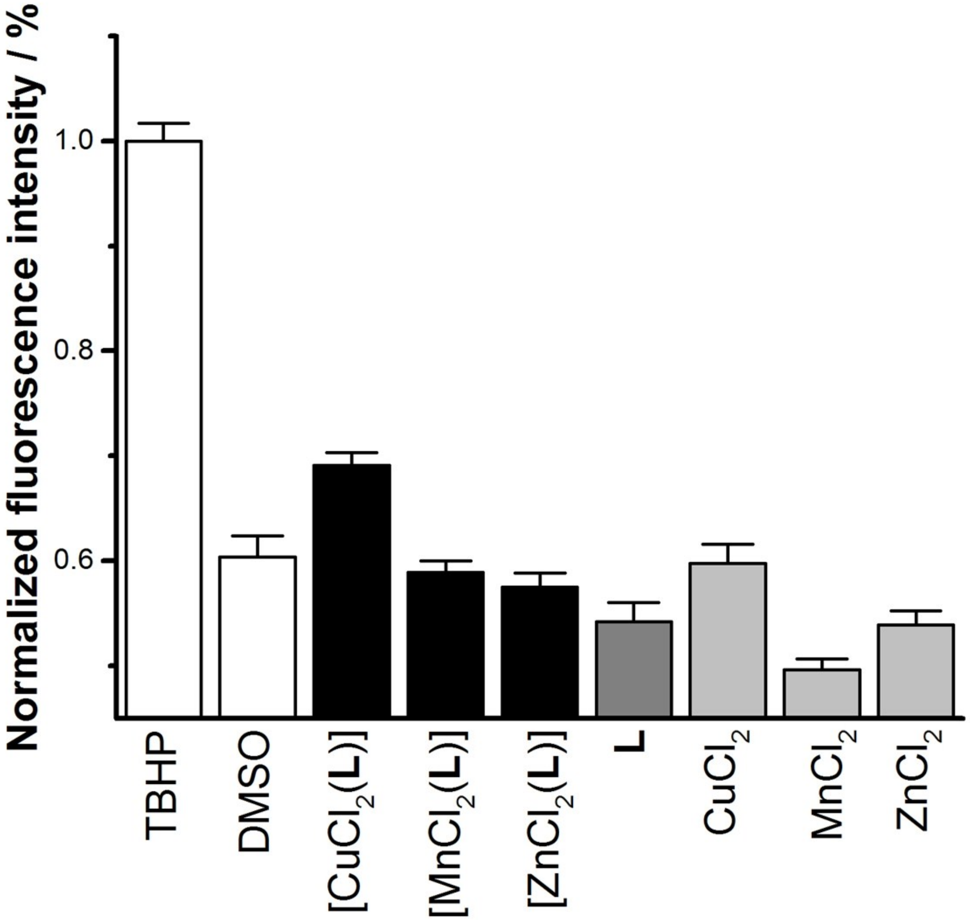

**Figure S3.** Fluorescence-based measurement of ROS generation using CellRox Deep Red assay. Measurements were performed as triplicates after incubation of HepG2 cells with 50 µM of the respective metal complex, the ligand **L** and or the respective metal salt for 90 min. Cells treated with 0.1% DMSO served as negative control. Values (mean values ± standard error of mean) were normalized to the positive control treated with tert-butyl hydroperoxide (TBHP) (200 µM).

**Table S1.** Overview of apoptosis-related proteins (GO:0006915) quantified by means of label-free proteomics. Proteins that were found to be significantly regulated (sig. reg.) after treatment were marked with "x" in the respective columns. Statistical p values for two-group comparisons refer to the results of Tukey's Honest Significant Difference method (THSD). $Log_2$ ratios were calculated from averaged normalized protein abundances of the different experimental groups.

| Accession | Cu complex (sig. reg.) | Mn complex (sig, reg.) | Peptides (all) | Peptides (unique) | Confidence Socre | Description | p ANOVA | p value Cu/Mn | p value Cu/control | p value Mn/control | $Log_2$ ratio Cu/Mn | $Log_2$ ratio Cu/control | $Log_2$ ratio Mn/control |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| O14737 | x | x | 4 | 4 | 129.28 | Programmed cell death protein 5 OS=Homo sapiens GN=PDCD5 PE=1 SV=3 - [PDCD5_HUMAN] | 5.09E-07 | 1.20E-04 | 6.18E-08 | 4.67E-04 | -1.31 | -2.57 | -1.26 |
| P04179 | x | x | 16 | 15 | 804.9 | Superoxide dismutase [Mn], mitochondrial OS=Homo sapiens GN=SOD2 PE=1 SV=2 - [SODM_HUMAN] | 4.42E-09 | 5.55E-07 | 1.20E-10 | 4.23E-06 | 1.59 | 2.91 | 1.32 |
| P06493 | x | x | 4 | 3 | 197.08 | Cyclin-dependent kinase 1 OS=Homo sapiens GN=CDK1 PE=1 SV=3 - [CDK1_HUMAN] | 4.89E-04 | 1.00E+00 | 7.69E-04 | 7.78E-04 | 0.37 | -1.67 | -2.03 |
| P12235 | x | x | 19 | 2 | 952.93 | ADP/ATP translocase 1 OS=Homo sapiens GN=SLC25A4 PE=1 SV=4 - [ADT1_HUMAN] | 5.82E-09 | 4.09E-03 | 3.24E-10 | 1.78E-08 | 0.94 | 3.67 | 2.74 |
| P12236 | x | x | 18 | 2 | 925.4 | ADP/ATP translocase 3 OS=Homo sapiens GN=SLC25A6 PE=1 SV=4 - [ADT3_HUMAN] | 1.40E-07 | 1.14E-03 | 1.36E-08 | 6.17E-06 | 1.40 | 3.48 | 2.08 |
| P23396 | x | x | 15 | 15 | 688.74 | 40S ribosomal protein S3 OS=Homo sapiens GN=RPS3 PE=1 SV=2 - [RS3_HUMAN] | 2.64E-08 | 3.39E-05 | 4.85E-06 | 1.54E-09 | 1.10 | -1.17 | -2.27 |
| P25788 | x | x | 9 | 9 | 313.98 | Proteasome subunit alpha type-3 OS=Homo sapiens GN=PSMA3 PE=1 SV=2 - [PSA3_HUMAN] | 5.85E-08 | 3.23E-04 | 4.39E-09 | 3.40E-06 | -0.82 | -2.08 | -1.27 |
| P27361 | x | x | 5 | 2 | 250.62 | Mitogen-activated protein kinase 3 OS=Homo sapiens GN=MAPK3 PE=1 SV=4 - [MK03_HUMAN] | 4.88E-07 | 5.56E-01 | 1.98E-07 | 8.58E-07 | -0.29 | -3.13 | -2.84 |
| P28070 | x | x | 5 | 5 | 344.27 | Proteasome subunit beta type-4 OS=Homo sapiens GN=PSMB4 PE=1 SV=4 - [PSB4_HUMAN] | 6.99E-09 | 1.06E-06 | 2.50E-10 | 7.69E-06 | -1.21 | -2.29 | -1.07 |
| P28331 | x | x | 14 | 12 | 718.49 | NADH-ubiquinone oxidoreductase 75 kDa subunit, mitochondrial OS=Homo sapiens GN=NDUFS1 PE=1 SV=3 - [NDUS1_HUMAN] | 1.65E-05 | 7.94E-01 | 1.31E-05 | 4.01E-05 | 0.15 | 1.33 | 1.18 |
| P28482 | x | x | 12 | 9 | 543.78 | Mitogen-activated protein kinase 1 OS=Homo sapiens GN=MAPK1 PE=1 SV=3 - [MK01_HUMAN] | 4.67E-07 | 1.40E-03 | 5.86E-08 | 4.06E-05 | -0.84 | -2.14 | -1.30 |
| P30154 | x | x | 9 | 2 | 597.47 | Serine/threonine-protein phosphatase 2A 65 kDa regulatory subunit A beta isoform OS=Homo sapiens GN=PPP2R1B PE=1 SV=3 - [2AAB_HUMAN] | 2.36E-03 | 7.98E-01 | 7.90E-03 | 2.17E-03 | 1.36 | -1.56 | -2.92 |
| P30419 | x | x | 4 | 4 | 159.16 | Glycylpeptide N-tetradecanoyltransferase 1 OS=Homo sapiens GN=NMT1 PE=1 SV=2 - [NMT1_HUMAN] | 2.53E-08 | 1.66E-05 | 1.42E-09 | 8.36E-06 | -0.96 | -2.03 | -1.06 |
| P51398 | x | x | 3 | 3 | 189.41 | 28S ribosomal protein S29, mitochondrial OS=Homo sapiens GN=DAP3 PE=1 SV=1 - [RT29_HUMAN] | 2.95E-05 | 1.44E-02 | 3.10E-03 | 8.13E-06 | 1.07 | -1.12 | -2.19 |
| P51812 | x | x | 15 | 9 | 712.12 | Ribosomal protein S6 kinase alpha-3 OS=Homo sapiens GN=RPS6KA3 PE=1 SV=1 - [KS6A3_HUMAN] | 4.57E-07 | 9.98E-01 | 3.34E-07 | 3.66E-07 | 0.04 | -1.64 | -1.68 |
| P52701 | x | x | 2 | 2 | 141.66 | DNA mismatch repair protein Msh6 OS=Homo sapiens GN=MSH6 PE=1 SV=2 - [MSH6_HUMAN] | 1.65E-04 | 1.95E-01 | 7.31E-05 | 2.39E-03 | -0.29 | -2.00 | -1.71 |
| P55060 | x | x | 30 | 25 | 1751.95 | Exportin-2 OS=Homo sapiens GN=CSE1L PE=1 SV=3 - [XPO2_HUMAN] | 5.27E-04 | 1.86E-01 | 2.44E-04 | 9.32E-03 | -0.34 | -1.38 | -1.04 |
| P62753 | x | x | 7 | 5 | 445.34 | 40S ribosomal protein S6 OS=Homo sapiens GN=RPS6 PE=1 SV=1 - [RS6_HUMAN] | 4.59E-07 | 6.40E-04 | 7.49E-05 | 5.48E-08 | 1.05 | -1.14 | -2.20 |
| P62979 | x | x | 7 | 3 | 306.76 | Ubiquitin-40S ribosomal protein S27a OS=Homo sapiens GN=RPS27A PE=1 SV=2 - [RS27A_HUMAN] | 7.97E-12 | 6.35E-02 | 1.00E-15 | 1.00E-15 | 0.35 | -3.35 | -3.71 |
| P63244 | x | x | 21 | 19 | 1155.82 | Guanine nucleotide-binding protein subunit beta-2-like 1 OS=Homo sapiens GN=GNB2L1 PE=1 SV=3 - [GBLP_HUMAN] | 2.60E-06 | 6.91E-01 | 5.64E-06 | 1.56E-06 | 0.43 | -1.94 | -2.37 |
| Q06323 | x | x | 16 | 16 | 754.75 | Proteasome activator complex subunit 1 OS=Homo sapiens GN=PSME1 PE=1 SV=1 - [PSME1_HUMAN] | 2.51E-09 | 2.32E-06 | 6.05E-11 | 3.00E-07 | -0.90 | -1.98 | -1.08 |
| Q12904 | x | x | 7 | 7 | 268.52 | Aminoacyl tRNA synthase complex-interacting multifunctional protein 1 OS=Homo sapiens GN=AIMP1 PE=1 SV=2 - [AIMP1_HUMAN] | 2.04E-03 | 1.96E-01 | 1.03E-03 | 3.82E-02 | -0.32 | -1.41 | -1.09 |
| Q13148 | x | x | 7 | 7 | 345.12 | TAR DNA-binding protein 43 OS=Homo sapiens GN=TARDBP PE=1 SV=1 - [TADBP_HUMAN] | 2.00E-03 | 3.25E-01 | 1.12E-03 | 2.17E-02 | -0.11 | -1.64 | -1.53 |
| Q6FI81 | x | x | 4 | 3 | 164.01 | Anamorsin OS=Homo sapiens GN=CIAPIN1 PE=1 SV=2 - [CPIN1_HUMAN] | 2.13E-05 | 1.20E-01 | 7.64E-06 | 3.21E-04 | -0.36 | -1.38 | -1.02 |
| Q86TG7 | x | x | 8 | 8 | 428.14 | Retrotransposon-derived protein PEG10 OS=Homo sapiens GN=PEG10 PE=1 SV=2 - [PEG10_HUMAN] | 3.09E-05 | 7.03E-01 | 9.59E-05 | 2.30E-05 | 0.77 | -2.08 | -2.85 |
| Q92530 | x | x | 2 | 2 | 79.22 | Proteasome inhibitor PI31 subunit OS=Homo sapiens GN=PSMF1 PE=1 SV=2 - [PSMF1_HUMAN] | 1.06E-06 | 9.86E-04 | 1.56E-07 | 2.24E-04 | -1.02 | -2.36 | -1.34 |
| Q969H8 | x | x | 4 | 4 | 218.19 | UPF0556 protein C19orf10 OS=Homo sapiens GN=C19orf10 PE=1 SV=1 - [CS010_HUMAN] | 1.02E-05 | 5.24E-03 | 2.35E-06 | 1.77E-03 | 1.03 | 2.07 | 1.04 |
| Q969N2 | x | x | 3 | 3 | 147.12 | GPI transamidase component PIG-T OS=Homo sapiens GN=PIGT PE=1 SV=1 - [PIGT_HUMAN] | 1.06E-06 | 8.25E-02 | 2.66E-07 | 8.59E-06 | 0.53 | 1.99 | 1.47 |
| Q96A26 | x | x | 3 | 2 | 95.19 | Protein FAM162A OS=Homo sapiens GN=FAM162A PE=1 SV=2 - [F162A_HUMAN] | 1.03E-06 | 2.56E-03 | 1.58E-07 | 9.37E-05 | 1.04 | 2.37 | 1.33 |
| Q96HE7 | x | x | 28 | 24 | 1279 | ERO1-like protein alpha OS=Homo sapiens GN=ERO1L PE=1 SV=2 - [ERO1A_HUMAN] | 1.75E-06 | 4.79E-01 | 8.17E-07 | 4.94E-06 | 0.36 | 2.03 | 1.67 |
| Q9GZU2 | x | x | 7 | 7 | 200.93 | Paternally-expressed gene 3 protein OS=Homo sapiens GN=PEG3 PE=1 SV=1 - [PEG3_HUMAN] | 3.77E-03 | 8.66E-01 | 3.83E-03 | 1.07E-02 | 0.37 | -1.51 | -1.87 |
| Q9NVX2 | x | x | 2 | 2 | 36.52 | Notchless protein homolog 1 OS=Homo sapiens GN=NLE1 PE=1 SV=4 - [NLE1_HUMAN] | 4.35E-07 | 1.87E-02 | 7.13E-08 | 5.93E-06 | 0.49 | 1.69 | 1.20 |
| Q9P0J0 | x | x | 2 | 2 | 66.48 | NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 13 OS=Homo sapiens GN=NDUFA13 PE=1 SV=3 - [NDUAD_HUMAN] | 1.51E-04 | 1.23E-01 | 5.99E-05 | 3.32E-03 | 1.04 | 2.52 | 1.48 |
| Q9UDY2 | x | x | 6 | 6 | 282.71 | Tight junction protein ZO-2 OS=Homo sapiens GN=TJP2 PE=1 SV=2 - [ZO2_HUMAN] | 4.70E-06 | 4.30E-04 | 9.78E-07 | 6.92E-03 | -1.26 | -2.30 | -1.05 |
| Q9Y696 | x | x | 5 | 4 | 296.17 | Chloride intracellular channel protein 4 OS=Homo sapiens GN=CLIC4 PE=1 SV=4 - [CLIC4_HUMAN] | 9.18E-05 | 6.89E-02 | 3.25E-05 | 3.16E-03 | -0.49 | -1.55 | -1.06 |
| O00429 | x |  | 6 | 6 | 252.84 | Dynamin-1-like protein OS=Homo sapiens GN=DNM1L PE=1 SV=2 - [DNM1L_HUMAN] | 8.77E-05 | 5.73E-03 | 2.86E-05 | 3.42E-02 | -0.77 | -1.41 | -0.64 |
| O14818 | x |  | 9 | 5 | 530.17 | Proteasome subunit alpha type-7 OS=Homo sapiens GN=PSMA7 PE=1 SV=1 - [PSA7_HUMAN] | 2.48E-07 | 2.39E-03 | 2.92E-08 | 9.69E-06 | -0.40 | -1.11 | -0.70 |
| O43290 | x |  | 2 | 2 | 52.86 | U4/U6.U5 tri-snRNP-associated protein 1 OS=Homo sapiens GN=SART1 PE=1 SV=1 - [SNUT1_HUMAN] | 4.83E-05 | 2.30E-04 | 2.90E-05 | 5.01E-01 | -1.68 | -2.10 | -0.42 |
| O43464 | x |  | 4 | 2 | 181.86 | Serine protease HTRA2, mitochondrial OS=Homo sapiens GN=HTRA2 PE=1 SV=2 - [HTRA2_HUMAN] | 2.35E-05 | 9.28E-06 | 2.68E-04 | 1.72E-01 | 2.02 | 1.51 | -0.51 |

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| O75915 | x | | 2 | 2 | 84.1 | PRA1 family protein 3 OS=Homo sapiens GN=ARL6IP5 PE=1 SV=1 - [PRAF3_HUMAN] | 1.39E-04 | 8.51E-03 | 4.76E-05 | 4.09E-02 | 0.68 | 1.15 | 0.47 |
| O95831 | x | | 12 | 11 | 693.43 | Apoptosis-inducing factor 1, mitochondrial OS=Homo sapiens GN=AIFM1 PE=1 SV=1 - [AIFM1_HUMAN] | 3.50E-06 | 3.52E-06 | 4.45E-06 | 9.88E-01 | 1.27 | 1.25 | -0.03 |
| P04406 | x | | 25 | 20 | 1487.64 | Glyceraldehyde-3-phosphate dehydrogenase OS=Homo sapiens GN=GAPDH PE=1 SV=3 - [G3P_HUMAN] | 3.92E-09 | 2.64E-05 | 1.15E-10 | 1.15E-07 | -0.60 | -1.54 | -0.95 |
| P06744 | x | | 15 | 14 | 838.22 | Glucose-6-phosphate isomerase OS=Homo sapiens GN=GPI PE=1 SV=4 - [G6PI_HUMAN] | 7.86E-08 | 3.52E-06 | 6.60E-09 | 6.38E-04 | -0.89 | -1.46 | -0.57 |
| P06756 | x | | 6 | 5 | 331.55 | Integrin alpha-V OS=Homo sapiens GN=ITGAV PE=1 SV=2 - [ITAV_HUMAN] | 1.65E-07 | 3.25E-07 | 4.24E-08 | 2.88E-01 | 1.04 | 1.22 | 0.17 |
| P07305 | x | | 5 | 4 | 226.87 | Histone H1.0 OS=Homo sapiens GN=H1F0 PE=1 SV=3 - [H10_HUMAN] | 6.02E-04 | 1.89E-02 | 2.57E-04 | 1.07E-01 | 0.62 | 1.01 | 0.39 |
| P07996 | x | | 2 | 2 | 87.62 | Thrombospondin-1 OS=Homo sapiens GN=THBS1 PE=1 SV=2 - [TSP1_HUMAN] | 6.01E-11 | 9.41E-13 | 8.98E-12 | 3.43E-02 | 2.94 | 2.59 | -0.35 |
| P09327 | x | | 24 | 23 | 1156.98 | Villin-1 OS=Homo sapiens GN=VIL1 PE=1 SV=4 - [VILI_HUMAN] | 9.07E-04 | 2.52E-01 | 4.60E-04 | 1.24E-02 | -0.26 | -1.24 | -0.98 |
| P09429 | x | | 11 | 4 | 551.88 | High mobility group protein B1 OS=Homo sapiens GN=HMGB1 PE=1 SV=3 - [HMGB1_HUMAN] | 1.43E-06 | 5.19E-06 | 5.47E-07 | 3.21E-01 | -1.45 | -1.79 | -0.34 |
| P09601 | x | | 4 | 4 | 230.68 | Heme oxygenase 1 OS=Homo sapiens GN=HMOX1 PE=1 SV=1 - [HMOX1_HUMAN] | 1.15E-07 | 1.39E-08 | 1.17E-06 | 1.02E-02 | 1.56 | 1.12 | -0.44 |
| P10809 | x | | 81 | 81 | 5470.61 | 60 kDa heat shock protein, mitochondrial OS=Homo sapiens GN=HSPD1 PE=1 SV=2 - [CH60_HUMAN] | 6.66E-05 | 1.90E-02 | 2.01E-05 | 6.95E-03 | 0.86 | 1.71 | 0.85 |
| P11279 | x | | 5 | 5 | 318.46 | Lysosome-associated membrane glycoprotein 1 OS=Homo sapiens GN=LAMP1 PE=1 SV=3 - [LAMP1_HUMAN] | 4.60E-07 | 1.57E-04 | 5.39E-08 | 2.87E-04 | 1.07 | 2.03 | 0.96 |
| P17980 | x | | 9 | 9 | 357.89 | 26S protease regulatory subunit 6A OS=Homo sapiens GN=PSMC3 PE=1 SV=3 - [PRS6A_HUMAN] | 1.34E-03 | 8.10E-02 | 6.05E-04 | 6.06E-02 | -0.50 | -1.30 | -0.80 |
| P20618 | x | | 11 | 11 | 596.16 | Proteasome subunit beta type-1 OS=Homo sapiens GN=PSMB1 PE=1 SV=2 - [PSB1_HUMAN] | 9.58E-08 | 4.12E-04 | 8.22E-09 | 6.95E-06 | -0.47 | -1.18 | -0.71 |
| P21796 | x | | 21 | 18 | 1552.41 | Voltage-dependent anion-selective channel protein 1 OS=Homo sapiens GN=VDAC1 PE=1 SV=2 - [VDAC1_HUMAN] | 9.07E-04 | 2.63E-03 | 8.87E-04 | 8.48E-01 | 1.73 | 1.70 | -0.03 |
| P25786 | x | | 11 | 11 | 356.64 | Proteasome subunit alpha type-1 OS=Homo sapiens GN=PSMA1 PE=1 SV=1 - [PSA1_HUMAN] | 7.26E-08 | 2.33E-06 | 6.24E-09 | 9.73E-04 | -0.71 | -1.11 | -0.41 |
| P25787 | x | | 8 | 8 | 582.36 | Proteasome subunit alpha type-2 OS=Homo sapiens GN=PSMA2 PE=1 SV=2 - [PSA2_HUMAN] | 6.91E-10 | 1.36E-08 | 1.24E-11 | 3.85E-06 | -1.13 | -1.87 | -0.74 |
| P25789 | x | | 7 | 7 | 409.16 | Proteasome subunit alpha type-4 OS=Homo sapiens GN=PSMA4 PE=1 SV=1 - [PSA4_HUMAN] | 1.56E-10 | 8.55E-09 | 1.13E-12 | 8.65E-08 | -0.86 | -1.59 | -0.73 |
| P27348 | x | | 14 | 10 | 829.21 | 14-3-3 protein theta OS=Homo sapiens GN=YWHAQ PE=1 SV=1 - [1433T_HUMAN] | 8.74E-10 | 5.39E-08 | 1.60E-11 | 1.14E-06 | -1.07 | -1.92 | -0.86 |
| P28072 | x | | 3 | 3 | 133.42 | Proteasome subunit beta type-6 OS=Homo sapiens GN=PSMB6 PE=1 SV=4 - [PSB6_HUMAN] | 5.27E-10 | 4.36E-09 | 8.92E-12 | 9.38E-06 | -1.11 | -1.74 | -0.62 |
| P28074 | x | | 3 | 3 | 228.95 | Proteasome subunit beta type-5 OS=Homo sapiens GN=PSMB5 PE=1 SV=3 - [PSB5_HUMAN] | 1.91E-08 | 1.08E-06 | 1.07E-09 | 1.03E-04 | -0.90 | -1.52 | -0.62 |
| P30153 | x | | 17 | 10 | 897.64 | Serine/threonine-protein phosphatase 2A 65 kDa regulatory subunit A alpha isoform OS=Homo sapiens GN=PPP2R1A PE=1 SV=4 - [2AAA_HUMAN] | 1.55E-03 | 2.88E-01 | 8.32E-04 | 1.90E-02 | -0.25 | -1.19 | -0.94 |
| P31946 | x | | 13 | 10 | 761.64 | 14-3-3 protein beta/alpha OS=Homo sapiens GN=YWHAB PE=1 SV=3 - [1433B_HUMAN] | 1.85E-07 | 4.06E-06 | 2.16E-08 | 4.24E-03 | -0.89 | -1.35 | -0.47 |
| P35611 | x | | 2 | 2 | 112.96 | Alpha-adducin OS=Homo sapiens GN=ADD1 PE=1 SV=2 - [ADDA_HUMAN] | 1.41E-04 | 3.05E-03 | 5.60E-05 | 1.24E-01 | -1.39 | -2.30 | -0.90 |
| P35998 | x | | 11 | 11 | 512.82 | 26S protease regulatory subunit 7 OS=Homo sapiens GN=PSMC2 PE=1 SV=3 - [PRS7_HUMAN] | 5.75E-05 | 4.30E-02 | 1.83E-05 | 2.69E-03 | -0.40 | -1.13 | -0.73 |
| P46379 | x | | 6 | 6 | 281.11 | Large proline-rich protein BAG6 OS=Homo sapiens GN=BAG6 PE=1 SV=2 - [BAG6_HUMAN] | 6.31E-03 | 1.40E-01 | 3.48E-03 | 1.67E-01 | -0.44 | -1.28 | -0.84 |
| P49721 | x | | 5 | 5 | 250.73 | Proteasome subunit beta type-2 OS=Homo sapiens GN=PSMB2 PE=1 SV=1 - [PSB2_HUMAN] | 6.85E-07 | 1.89E-05 | 1.11E-07 | 9.18E-03 | -0.67 | -1.02 | -0.35 |
| P49773 | x | | 4 | 4 | 143.09 | Histidine triad nucleotide-binding protein 1 OS=Homo sapiens GN=HINT1 PE=1 SV=2 - [HINT1_HUMAN] | 5.87E-08 | 1.45E-05 | 4.07E-09 | 5.46E-05 | -0.84 | -1.62 | -0.78 |
| P51572 | x | | 2 | 2 | 149.02 | B-cell receptor-associated protein 31 OS=Homo sapiens GN=BCAP31 PE=1 SV=3 - [BAP31_HUMAN] | 4.04E-02 | 5.45E-01 | 2.95E-02 | 2.03E-01 | 0.28 | 1.51 | 1.23 |
| P53634 | x | | 8 | 8 | 373.96 | Dipeptidyl peptidase 1 OS=Homo sapiens GN=CTSC PE=1 SV=2 - [CATC_HUMAN] | 4.74E-03 | 1.22E-01 | 2.52E-03 | 1.46E-01 | 0.59 | 1.05 | 0.46 |
| P54577 | x | | 7 | 6 | 228.26 | Tyrosine--tRNA ligase, cytoplasmic OS=Homo sapiens GN=YARS PE=1 SV=4 - [SYYC_HUMAN] | 9.26E-03 | 1.11E-01 | 5.55E-03 | 2.97E-01 | -0.47 | -1.33 | -0.86 |
| P55072 | x | | 41 | 39 | 2505.63 | Transitional endoplasmic reticulum ATPase OS=Homo sapiens GN=VCP PE=1 SV=4 - [TERA_HUMAN] | 2.98E-08 | 1.80E-06 | 1.92E-09 | 1.59E-04 | -0.59 | -1.01 | -0.41 |
| P60900 | x | | 12 | 12 | 584.34 | Proteasome subunit alpha type-6 OS=Homo sapiens GN=PSMA6 PE=1 SV=1 - [PSA6_HUMAN] | 5.10E-08 | 2.69E-05 | 3.36E-09 | 2.11E-05 | -0.80 | -1.64 | -0.84 |
| P61086 | x | | 8 | 8 | 397.94 | Ubiquitin-conjugating enzyme E2 K OS=Homo sapiens GN=UBE2K PE=1 SV=3 - [UBE2K_HUMAN] | 7.47E-07 | 6.40E-04 | 9.99E-08 | 1.79E-04 | -0.75 | -1.67 | -0.92 |
| P61289 | x | | 8 | 6 | 469.15 | Proteasome activator complex subunit 3 OS=Homo sapiens GN=PSME3 PE=1 SV=1 - [PSME3_HUMAN] | 8.06E-09 | 3.85E-07 | 3.25E-10 | 4.10E-05 | -1.05 | -1.76 | -0.71 |
| P61604 | x | | 8 | 8 | 448.22 | 10 kDa heat shock protein, mitochondrial OS=Homo sapiens GN=HSPE1 PE=1 SV=2 - [CH10_HUMAN] | 1.46E-04 | 1.09E-02 | 4.97E-05 | 3.37E-02 | 1.26 | 2.14 | 0.89 |
| P61981 | x | | 8 | 5 | 503.77 | 14-3-3 protein gamma OS=Homo sapiens GN=YWHAG PE=1 SV=2 - [1433G_HUMAN] | 6.53E-09 | 7.54E-08 | 2.87E-10 | 3.05E-04 | -1.03 | -1.55 | -0.52 |
| P62191 | x | | 7 | 4 | 300.06 | 26S protease regulatory subunit 4 OS=Homo sapiens GN=PSMC1 PE=1 SV=1 - [PRS4_HUMAN] | 1.01E-03 | 2.63E-02 | 4.61E-04 | 1.36E-01 | -0.69 | -1.32 | -0.64 |
| P62333 | x | | 9 | 9 | 455.88 | 26S protease regulatory subunit 10B OS=Homo sapiens GN=PSMC6 PE=1 SV=1 - [PRS10_HUMAN] | 4.56E-04 | 5.35E-02 | 1.79E-04 | 2.74E-02 | -0.49 | -1.24 | -0.75 |
| P63104 | x | | 10 | 7 | 675.31 | 14-3-3 protein zeta/delta OS=Homo sapiens GN=YWHAZ PE=1 SV=1 - [1433Z_HUMAN] | 1.51E-08 | 8.56E-07 | 7.55E-10 | 7.23E-05 | -0.91 | -1.55 | -0.64 |
| Q04917 | x | | 6 | 3 | 364.54 | 14-3-3 protein eta OS=Homo sapiens GN=YWHAH PE=1 SV=4 - [1433F_HUMAN] | 8.80E-08 | 3.36E-06 | 7.91E-09 | 9.36E-04 | -1.23 | -1.99 | -0.76 |
| Q07021 | x | | 9 | 9 | 568.77 | Complement component 1 Q subcomponent-binding protein, mitochondrial OS=Homo sapiens GN=C1QBP PE=1 SV=1 - [C1QBP_HUMAN] | 3.59E-04 | 8.06E-04 | 4.09E-04 | 9.35E-01 | 0.98 | 1.05 | 0.07 |
| Q08752 | x | | 3 | 3 | 119.67 | Peptidyl-prolyl cis-trans isomerase D OS=Homo sapiens GN=PPID PE=1 SV=3 - [PPID_HUMAN] | 6.42E-05 | 1.14E-01 | 2.39E-05 | 1.28E-03 | -0.31 | -1.08 | -0.77 |
| Q13177 | x | | 5 | 3 | 231.24 | Serine/threonine-protein kinase PAK 2 OS=Homo sapiens GN=PAK2 PE=1 SV=3 - [PAK2_HUMAN] | 4.28E-07 | 7.07E-06 | 6.61E-08 | 1.34E-02 | -1.27 | -1.88 | -0.60 |
| Q13200 | x | | 20 | 20 | 1029.3 | 26S proteasome non-ATPase regulatory subunit 2 OS=Homo sapiens GN=PSMD2 PE=1 SV=3 - [PSMD2_HUMAN] | 4.03E-04 | 1.36E-01 | 1.73E-04 | 9.43E-03 | -0.32 | -1.03 | -0.71 |
| Q13564 | x | | 3 | 2 | 110.65 | NEDD8-activating enzyme E1 regulatory subunit OS=Homo sapiens GN=NAE1 PE=1 SV=1 - [ULA1_HUMAN] | 1.18E-06 | 5.00E-05 | 2.03E-07 | 7.54E-03 | -1.45 | -2.29 | -0.84 |

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Q14974 | x | | 28 | 28 | 1607.35 | Importin subunit beta-1 OS=Homo sapiens GN=KPNB1 PE=1 SV=2 - [IMB1_HUMAN] | 1.94E-05 | 2.29E-04 | 7.32E-06 | 1.55E-01 | -1.03 | -1.44 | -0.41 |
| Q3ZCQ8 | x | | 5 | 4 | 354.07 | Mitochondrial import inner membrane translocase subunit TIM50 OS=Homo sapiens GN=TIMM50 PE=1 SV=2 - [TIM50_HUMAN] | 1.73E-06 | 1.06E-06 | 3.18E-06 | 7.52E-01 | 1.25 | 1.14 | -0.11 |
| Q8IXB1 | x | | 4 | 4 | 186.59 | DnaJ homolog subfamily C member 10 OS=Homo sapiens GN=DNAJC10 PE=1 SV=2 - [DJC10_HUMAN] | 1.17E-05 | 6.65E-03 | 2.79E-06 | 1.74E-03 | 0.78 | 1.63 | 0.85 |
| Q8N163 | x | | 13 | 13 | 534.42 | DBIRD complex subunit KIAA1967 OS=Homo sapiens GN=KIAA1967 PE=1 SV=2 - [K1967_HUMAN] | 3.03E-03 | 1.29E-02 | 2.45E-03 | 6.90E-01 | -0.89 | -1.21 | -0.32 |
| Q8WUM4 | x | | 10 | 10 | 570.24 | Programmed cell death 6-interacting protein OS=Homo sapiens GN=PDCD6IP PE=1 SV=1 - [PDC6I_HUMAN] | 4.83E-04 | 7.18E-03 | 2.30E-04 | 2.19E-01 | -0.67 | -1.07 | -0.40 |
| Q8WYA6 | x | | 2 | 2 | 61.44 | Beta-catenin-like protein 1 OS=Homo sapiens GN=CTNNBL1 PE=1 SV=1 - [CTBL1_HUMAN] | 5.67E-03 | 7.27E-02 | 3.25E-03 | 2.83E-01 | -0.60 | -1.16 | -0.56 |
| Q92542 | x | | 3 | 3 | 147.61 | Nicastrin OS=Homo sapiens GN=NCSTN PE=1 SV=2 - [NICA_HUMAN] | 9.15E-06 | 1.64E-04 | 2.80E-06 | 7.31E-02 | 1.23 | 1.71 | 0.48 |
| Q99523 | x | | 2 | 2 | 173.78 | Sortilin OS=Homo sapiens GN=SORT1 PE=1 SV=3 - [SORT_HUMAN] | 1.37E-06 | 1.37E-04 | 2.24E-07 | 2.86E-03 | 0.88 | 1.49 | 0.61 |
| Q9BZZ5 | x | | 6 | 6 | 346.82 | Apoptosis inhibitor 5 OS=Homo sapiens GN=API5 PE=1 SV=3 - [API5_HUMAN] | 2.36E-08 | 6.16E-08 | 2.86E-09 | 4.14E-02 | -1.28 | -1.61 | -0.33 |
| Q9NQ88 | x | | 2 | 2 | 152.54 | Fructose-2,6-bisphosphatase TIGAR OS=Homo sapiens GN=TIGAR PE=1 SV=1 - [TIGAR_HUMAN] | 3.38E-03 | 3.72E-02 | 1.96E-03 | 3.27E-01 | -0.74 | -1.30 | -0.56 |
| Q9NQC3 | x | | 11 | 11 | 655.84 | Reticulon-4 OS=Homo sapiens GN=RTN4 PE=1 SV=2 - [RTN4_HUMAN] | 1.02E-05 | 5.20E-03 | 2.36E-06 | 1.79E-03 | 0.98 | 1.97 | 0.99 |
| Q9NR28 | x | | 3 | 2 | 171.57 | Diablo homolog, mitochondrial OS=Homo sapiens GN=DIABLO PE=1 SV=1 - [DBLOH_HUMAN] | 2.63E-04 | 9.46E-05 | 2.73E-02 | 2.76E-02 | 1.90 | 1.04 | -0.86 |
| Q9NYF8 | x | | 4 | 3 | 158.95 | Bcl-2-associated transcription factor 1 OS=Homo sapiens GN=BCLAF1 PE=1 SV=2 - [BCLF1_HUMAN] | 7.71E-07 | 4.18E-06 | 2.03E-07 | 1.28E-01 | -1.30 | -1.66 | -0.36 |
| Q9UHX1 | x | | 4 | 4 | 238.15 | Poly(U)-binding-splicing factor PUF60 OS=Homo sapiens GN=PUF60 PE=1 SV=1 - [PUF60_HUMAN] | 1.13E-06 | 3.50E-05 | 2.05E-07 | 1.14E-02 | -1.41 | -2.22 | -0.81 |
| Q9UKV3 | x | | 4 | 3 | 104.07 | Apoptotic chromatin condensation inducer in the nucleus OS=Homo sapiens GN=ACIN1 PE=1 SV=2 - [ACINU_HUMAN] | 1.26E-04 | 1.01E-03 | 6.63E-05 | 3.43E-01 | -1.14 | -1.56 | -0.43 |
| Q9UL46 | x | | 17 | 17 | 1110.98 | Proteasome activator complex subunit 2 OS=Homo sapiens GN=PSME2 PE=1 SV=4 - [PSME2_HUMAN] | 7.30E-09 | 1.27E-06 | 2.64E-10 | 6.91E-06 | -1.12 | -2.09 | -0.98 |
| Q9Y6C9 | x | | 4 | 4 | 179.69 | Mitochondrial carrier homolog 2 OS=Homo sapiens GN=MTCH2 PE=1 SV=1 - [MTCH2_HUMAN] | 3.96E-02 | 1.41E-01 | 3.22E-02 | 7.05E-01 | 1.37 | 1.38 | 0.00 |
| P02545 | | x | 26 | 26 | 1520.18 | Prelamin-A/C OS=Homo sapiens GN=LMNA PE=1 SV=1 - [LMNA_HUMAN] | 1.98E-03 | 1.22E-01 | 6.03E-02 | 9.43E-04 | -0.59 | 0.57 | 1.16 |
| P30405 | | x | 4 | 4 | 257.81 | Peptidyl-prolyl cis-trans isomerase F, mitochondrial OS=Homo sapiens GN=PPIF PE=1 SV=1 - [PPIF_HUMAN] | 7.55E-05 | 9.53E-03 | 1.64E-02 | 2.32E-05 | 0.64 | -0.47 | -1.11 |
| Q71UM5 | | x | 3 | 2 | 116.58 | 40S ribosomal protein S27-like OS=Homo sapiens GN=RPS27L PE=1 SV=3 - [RS27L_HUMAN] | 5.22E-08 | 1.95E-06 | 5.44E-04 | 3.99E-09 | 0.97 | -0.58 | -1.55 |
| O00231 | | | 13 | 10 | 655.74 | 26S proteasome non-ATPase regulatory subunit 11 OS=Homo sapiens GN=PSMD11 PE=1 SV=3 - [PSD11_HUMAN] | 2.90E-04 | 1.44E-02 | 1.09E-04 | 5.94E-02 | -0.52 | -0.98 | -0.46 |
| O00232 | | | 4 | 4 | 197.69 | 26S proteasome non-ATPase regulatory subunit 12 OS=Homo sapiens GN=PSMD12 PE=1 SV=3 - [PSD12_HUMAN] | 4.35E-03 | 7.23E-02 | 2.37E-03 | 2.23E-01 | -0.43 | -0.83 | -0.40 |
| O00487 | | | 3 | 3 | 110.71 | 26S proteasome non-ATPase regulatory subunit 14 OS=Homo sapiens GN=PSMD14 PE=1 SV=1 - [PSDE_HUMAN] | 7.30E-02 | 5.40E-02 | 4.01E-01 | 4.57E-01 | 0.32 | 0.17 | -0.15 |
| O00571 | | | 13 | 2 | 668.84 | ATP-dependent RNA helicase DDX3X OS=Homo sapiens GN=DDX3X PE=1 SV=3 - [DDX3X_HUMAN] | 1.75E-05 | 6.64E-06 | 1.89E-04 | 1.67E-01 | 0.86 | 0.64 | -0.22 |
| O43242 | | | 10 | 9 | 545.36 | 26S proteasome non-ATPase regulatory subunit 3 OS=Homo sapiens GN=PSMD3 PE=1 SV=2 - [PSMD3_HUMAN] | 1.14E-01 | 2.26E-01 | 1.11E-01 | 9.06E-01 | 0.29 | 0.34 | 0.05 |
| O75223 | | | 4 | 4 | 142.46 | Gamma-glutamylcyclotransferase OS=Homo sapiens GN=GGCT PE=1 SV=1 - [GGCT_HUMAN] | 5.06E-02 | 4.25E-02 | 1.63E-01 | 7.40E-01 | 0.48 | 0.34 | -0.14 |
| O75340 | | | 4 | 3 | 139.89 | Programmed cell death protein 6 OS=Homo sapiens GN=PDCD6 PE=1 SV=1 - [PDCD6_HUMAN] | 3.34E-02 | 3.23E-01 | 2.24E-02 | 3.09E-01 | 0.25 | 0.48 | 0.22 |
| O95470 | | | 4 | 4 | 164.37 | Sphingosine-1-phosphate lyase 1 OS=Homo sapiens GN=SGPL1 PE=1 SV=3 - [SGPL1_HUMAN] | 3.07E-04 | 4.36E-01 | 2.10E-03 | 1.82E-04 | -0.15 | 0.63 | 0.79 |
| P05783 | | | 44 | 38 | 2572.07 | Keratin, type I cytoskeletal 18 OS=Homo sapiens GN=KRT18 PE=1 SV=2 - [K1C18_HUMAN] | 7.24E-03 | 7.32E-01 | 6.11E-03 | 2.77E-02 | 0.14 | 0.54 | 0.40 |
| P05787 | | | 40 | 36 | 2465.78 | Keratin, type II cytoskeletal 8 OS=Homo sapiens GN=KRT8 PE=1 SV=7 - [K2C8_HUMAN] | 2.09E-03 | 9.78E-01 | 4.16E-03 | 2.78E-03 | 0.02 | 0.64 | 0.62 |
| P06396 | | | 5 | 5 | 202.56 | Gelsolin OS=Homo sapiens GN=GSN PE=1 SV=1 - [GELS_HUMAN] | 5.07E-06 | 5.77E-05 | 1.60E-06 | 1.06E-01 | 0.47 | 0.64 | 0.17 |
| P07148 | | | 5 | 5 | 349.95 | Fatty acid-binding protein, liver OS=Homo sapiens GN=FABP1 PE=1 SV=1 - [FABPL_HUMAN] | 4.88E-01 | 9.50E-01 | 6.56E-01 | 4.74E-01 | 0.18 | -0.58 | -0.76 |
| P08133 | | | 22 | 20 | 1050.94 | Annexin A6 OS=Homo sapiens GN=ANXA6 PE=1 SV=3 - [ANXA6_HUMAN] | 2.63E-03 | 1.14E-01 | 1.30E-03 | 8.77E-02 | 0.42 | 0.78 | 0.36 |
| P09382 | | | 8 | 8 | 418.37 | Galectin-1 OS=Homo sapiens GN=LGALS1 PE=1 SV=2 - [LEG1_HUMAN] | 8.61E-02 | 1.19E-01 | 1.16E-01 | 1.00E+00 | -0.39 | -0.40 | -0.01 |
| P09668 | | | 5 | 3 | 213.56 | Pro-cathepsin H OS=Homo sapiens GN=CTSH PE=1 SV=4 - [CATH_HUMAN] | 3.05E-02 | 2.59E-01 | 3.55E-01 | 2.03E-02 | 0.36 | -0.24 | -0.60 |
| P11388 | | | 9 | 8 | 489.4 | DNA topoisomerase 2-alpha OS=Homo sapiens GN=TOP2A PE=1 SV=3 - [TOP2A_HUMAN] | 7.26E-01 | 9.78E-01 | 7.16E-01 | 8.29E-01 | 0.67 | -0.03 | -0.70 |
| P15924 | | | 19 | 18 | 1011.97 | Desmoplakin OS=Homo sapiens GN=DSP PE=1 SV=3 - [DESP_HUMAN] | 3.36E-02 | 4.77E-01 | 2.35E-02 | 2.03E-01 | -0.13 | -0.66 | -0.53 |
| P16435 | | | 26 | 26 | 1444.24 | NADPH--cytochrome P450 reductase OS=Homo sapiens GN=POR PE=1 SV=2 - [NCPR_HUMAN] | 5.14E-02 | 2.40E-01 | 3.85E-02 | 5.63E-01 | 0.36 | 0.52 | 0.16 |
| P17844 | | | 14 | 10 | 573.61 | Probable ATP-dependent RNA helicase DDX5 OS=Homo sapiens GN=DDX5 PE=1 SV=1 - [DDX5_HUMAN] | 6.70E-03 | 8.25E-01 | 6.34E-03 | 2.07E-02 | 0.05 | -0.86 | -0.91 |
| P19784 | | | 5 | 5 | 277.16 | Casein kinase II subunit alpha' OS=Homo sapiens GN=CSNK2A2 PE=1 SV=1 - [CSK22_HUMAN] | 9.26E-03 | 4.13E-02 | 6.60E-01 | 7.25E-03 | 0.38 | -0.10 | -0.47 |
| P20700 | | | 10 | 8 | 553.64 | Lamin-B1 OS=Homo sapiens GN=LMNB1 PE=1 SV=2 - [LMNB1_HUMAN] | 1.87E-01 | 9.84E-01 | 2.07E-01 | 2.70E-01 | 0.11 | 0.37 | 0.25 |
| P26583 | | | 9 | 5 | 488.67 | High mobility group protein B2 OS=Homo sapiens GN=HMGB2 PE=1 SV=2 - [HMGB2_HUMAN] | 1.89E-02 | 1.46E-02 | 8.21E-02 | 6.49E-01 | -0.98 | -0.86 | 0.12 |
| P28066 | | | 4 | 4 | 270.77 | Proteasome subunit alpha type-5 OS=Homo sapiens GN=PSMA5 PE=1 SV=3 - [PSA5_HUMAN] | 2.63E-06 | 1.30E-01 | 8.19E-07 | 2.13E-05 | -0.21 | -0.91 | -0.70 |
| P30044 | | | 13 | 13 | 761.78 | Peroxiredoxin-5, mitochondrial OS=Homo sapiens GN=PRDX5 PE=1 SV=4 - [PRDX5_HUMAN] | 1.29E-06 | 6.65E-01 | 6.88E-07 | 2.51E-06 | -0.05 | -0.60 | -0.54 |

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| P30048 | | | 10 | 10 | 525.51 | Thioredoxin-dependent peroxide reductase, mitochondrial OS=Homo sapiens GN=PRDX3 PE=1 SV=3 - [PRDX3_HUMAN] | 1.91E-02 | 1.81E-02 | 5.44E-02 | 8.39E-01 | 0.86 | 0.72 | -0.13 |
| P31947 | | | 7 | 4 | 306.43 | 14-3-3 protein sigma OS=Homo sapiens GN=SFN PE=1 SV=1 - [1433S_HUMAN] | 1.04E-02 | 3.05E-02 | 1.01E-02 | 8.42E-01 | -0.63 | -0.77 | -0.14 |
| P35222 | | | 11 | 11 | 592.22 | Catenin beta-1 OS=Homo sapiens GN=CTNNB1 PE=1 SV=1 - [CTNB1_HUMAN] | 1.09E-04 | 9.82E-01 | 1.95E-04 | 1.39E-04 | 0.04 | -0.54 | -0.58 |
| P42224 | | | 8 | 8 | 289.92 | Signal transducer and activator of transcription 1-alpha/beta OS=Homo sapiens GN=STAT1 PE=1 SV=2 - [STAT1_HUMAN] | 2.49E-03 | 6.75E-01 | 1.98E-03 | 1.10E-02 | -0.07 | -0.90 | -0.83 |
| P42765 | | | 20 | 20 | 1107.57 | 3-ketoacyl-CoA thiolase, mitochondrial OS=Homo sapiens GN=ACAA2 PE=1 SV=2 - [THIM_HUMAN] | 1.89E-01 | 3.80E-01 | 1.72E-01 | 8.57E-01 | 0.39 | 0.50 | 0.11 |
| P43246 | | | 6 | 6 | 222.53 | DNA mismatch repair protein Msh2 OS=Homo sapiens GN=MSH2 PE=1 SV=1 - [MSH2_HUMAN] | 9.42E-02 | 1.20E-01 | 1.35E-01 | 9.97E-01 | 0.55 | 0.52 | -0.02 |
| P43686 | | | 12 | 12 | 520.95 | 26S protease regulatory subunit 6B OS=Homo sapiens GN=PSMC4 PE=1 SV=2 - [PRS6B_HUMAN] | 1.83E-05 | 1.08E-01 | 6.29E-06 | 2.87E-04 | -0.25 | -0.95 | -0.69 |
| P48506 | | | 2 | 2 | 112.66 | Glutamate--cysteine ligase catalytic subunit OS=Homo sapiens GN=GCLC PE=1 SV=2 - [GSH1_HUMAN] | 2.74E-02 | 6.82E-02 | 2.71E-02 | 8.79E-01 | -0.68 | -0.89 | -0.21 |
| P48556 | | | 8 | 8 | 282.67 | 26S proteasome non-ATPase regulatory subunit 8 OS=Homo sapiens GN=PSMD8 PE=1 SV=2 - [PSMD8_HUMAN] | 1.82E-01 | 7.59E-01 | 1.55E-01 | 4.43E-01 | 0.14 | 0.34 | 0.20 |
| P49720 | | | 6 | 6 | 404.78 | Proteasome subunit beta type-3 OS=Homo sapiens GN=PSMB3 PE=1 SV=2 - [PSB3_HUMAN] | 2.30E-03 | 1.77E-01 | 1.16E-03 | 4.85E-02 | -0.18 | -0.46 | -0.28 |
| P51665 | | | 13 | 13 | 531.29 | 26S proteasome non-ATPase regulatory subunit 7 OS=Homo sapiens GN=PSMD7 PE=1 SV=2 - [PSD7_HUMAN] | 2.89E-03 | 5.34E-03 | 4.12E-03 | 9.91E-01 | 0.56 | 0.58 | 0.02 |
| P52789 | | | 13 | 12 | 530.85 | Hexokinase-2 OS=Homo sapiens GN=HK2 PE=1 SV=2 - [HXK2_HUMAN] | 7.64E-01 | 9.06E-01 | 9.45E-01 | 7.40E-01 | 0.00 | 0.14 | 0.14 |
| P55036 | | | 6 | 4 | 318.13 | 26S proteasome non-ATPase regulatory subunit 4 OS=Homo sapiens GN=PSMD4 PE=1 SV=1 - [PSMD4_HUMAN] | 7.10E-08 | 9.00E-07 | 7.19E-09 | 4.47E-03 | -0.64 | -0.93 | -0.28 |
| P62195 | | | 12 | 9 | 530.09 | 26S protease regulatory subunit 8 OS=Homo sapiens GN=PSMC5 PE=1 SV=1 - [PRS8_HUMAN] | 1.80E-04 | 3.68E-02 | 6.26E-05 | 1.29E-02 | -0.37 | -0.86 | -0.50 |
| P62258 | | | 14 | 9 | 705.49 | 14-3-3 protein epsilon OS=Homo sapiens GN=YWHAE PE=1 SV=1 - [1433E_HUMAN] | 4.06E-01 | 4.54E-01 | 4.74E-01 | 9.99E-01 | -0.15 | -0.15 | 0.00 |
| P62330 | | | 4 | 2 | 78.31 | ADP-ribosylation factor 6 OS=Homo sapiens GN=ARF6 PE=1 SV=2 - [ARF6_HUMAN] | 2.26E-01 | 3.81E-01 | 2.18E-01 | 9.22E-01 | 0.09 | -0.64 | -0.73 |
| P62873 | | | 6 | 3 | 251.58 | Guanine nucleotide-binding protein G(I)/G(S)/G(T) subunit beta-1 OS=Homo sapiens GN=GNB1 PE=1 SV=3 - [GBB1_HUMAN] | 3.60E-01 | 9.48E-01 | 5.21E-01 | 3.53E-01 | 0.05 | -0.15 | -0.20 |
| P63000 | | | 4 | 2 | 168.84 | Ras-related C3 botulinum toxin substrate 1 OS=Homo sapiens GN=RAC1 PE=1 SV=1 - [RAC1_HUMAN] | 1.62E-02 | 7.44E-01 | 1.38E-02 | 5.81E-02 | -0.12 | -0.61 | -0.49 |
| P63241 | | | 13 | 7 | 600.47 | Eukaryotic translation initiation factor 5A-1 OS=Homo sapiens GN=EIF5A PE=1 SV=2 - [IF5A1_HUMAN] | 7.85E-03 | 6.50E-01 | 6.08E-03 | 3.59E-02 | -0.05 | -0.84 | -0.79 |
| P68400 | | | 9 | 3 | 438.91 | Casein kinase II subunit alpha OS=Homo sapiens GN=CSNK2A1 PE=1 SV=1 - [CSK21_HUMAN] | 5.79E-01 | 6.13E-01 | 6.46E-01 | 9.98E-01 | -0.07 | -0.07 | 0.01 |
| P78527 | | | 61 | 58 | 3011.96 | DNA-dependent protein kinase catalytic subunit OS=Homo sapiens GN=PRKDC PE=1 SV=3 - [PRKDC_HUMAN] | 5.13E-03 | 4.52E-02 | 3.17E-03 | 3.95E-01 | -0.53 | -0.89 | -0.36 |
| P99999 | | | 3 | 3 | 106.85 | Cytochrome c OS=Homo sapiens GN=CYCS PE=1 SV=2 - [CYC_HUMAN] | 7.38E-06 | 2.24E-06 | 7.60E-02 | 1.21E-04 | 1.36 | 0.44 | -0.92 |
| Q07812 | | | 3 | 2 | 195.09 | Apoptosis regulator BAX OS=Homo sapiens GN=BAX PE=1 SV=1 - [BAX_HUMAN] | 2.08E-05 | 1.64E-05 | 7.79E-01 | 5.34E-05 | -0.76 | -0.06 | 0.70 |
| Q13155 | | | 5 | 5 | 233.36 | Aminoacyl tRNA synthase complex-interacting multifunctional protein 2 OS=Homo sapiens GN=AIMP2 PE=1 SV=2 - [AIMP2_HUMAN] | 7.03E-03 | 3.80E-01 | 4.35E-03 | 6.42E-02 | -0.18 | -0.90 | -0.72 |
| Q13618 | | | 2 | 2 | 93.21 | Cullin-3 OS=Homo sapiens GN=CUL3 PE=1 SV=2 - [CUL3_HUMAN] | 1.12E-03 | 5.22E-01 | 7.50E-04 | 6.82E-03 | -0.16 | -0.93 | -0.78 |
| Q13813 | | | 71 | 64 | 3543.72 | Spectrin alpha chain, non-erythrocytic 1 OS=Homo sapiens GN=SPTAN1 PE=1 SV=3 - [SPTN1_HUMAN] | 4.39E-04 | 5.77E-03 | 2.15E-04 | 2.44E-01 | -0.52 | -0.79 | -0.27 |
| Q15008 | | | 12 | 12 | 479.32 | 26S proteasome non-ATPase regulatory subunit 6 OS=Homo sapiens GN=PSMD6 PE=1 SV=1 - [PSMD6_HUMAN] | 1.48E-01 | 4.44E-01 | 1.21E-01 | 6.71E-01 | 0.33 | 0.49 | 0.16 |
| Q15149 | | | 28 | 24 | 1008.41 | Plectin OS=Homo sapiens GN=PLEC PE=1 SV=3 - [PLEC_HUMAN] | 2.84E-02 | 2.64E-02 | 7.84E-02 | 8.35E-01 | -0.66 | -0.48 | 0.17 |
| Q15392 | | | 7 | 7 | 346.47 | Delta(24)-sterol reductase OS=Homo sapiens GN=DHCR24 PE=1 SV=2 - [DHC24_HUMAN] | 7.34E-02 | 1.54E-01 | 7.31E-02 | 9.06E-01 | 0.24 | 0.29 | 0.04 |
| Q6NUQ4 | | | 5 | 5 | 306.18 | Transmembrane protein 214 OS=Homo sapiens GN=TMEM214 PE=1 SV=2 - [TM214_HUMAN] | 9.51E-04 | 1.14E-02 | 2.86E-01 | 5.01E-04 | 0.45 | -0.19 | -0.64 |
| Q86W42 | | | 2 | 2 | 49.81 | THO complex subunit 6 homolog OS=Homo sapiens GN=THOC6 PE=1 SV=1 - [THOC6_HUMAN] | 5.29E-02 | 7.11E-02 | 8.02E-02 | 9.98E-01 | -0.67 | -0.67 | -0.01 |
| Q96JB5 | | | 2 | 2 | 80.76 | CDK5 regulatory subunit-associated protein 3 OS=Homo sapiens GN=CDK5RAP3 PE=1 SV=2 - [CK5P3_HUMAN] | 2.11E-01 | 2.03E-01 | 3.69E-01 | 9.12E-01 | -0.47 | -0.21 | 0.26 |
| Q99436 | | | 2 | 2 | 57.87 | Proteasome subunit beta type-7 OS=Homo sapiens GN=PSMB7 PE=1 SV=1 - [PSB7_HUMAN] | 7.42E-05 | 5.33E-01 | 4.71E-05 | 3.51E-04 | -0.13 | -0.92 | -0.79 |
| Q99460 | | | 19 | 19 | 813.59 | 26S proteasome non-ATPase regulatory subunit 1 OS=Homo sapiens GN=PSMD1 PE=1 SV=2 - [PSMD1_HUMAN] | 2.93E-01 | 2.57E-01 | 7.79E-01 | 6.07E-01 | 0.29 | 0.14 | -0.15 |
| Q99497 | | | 7 | 7 | 369.33 | Protein DJ-1 OS=Homo sapiens GN=PARK7 PE=1 SV=2 - [PARK7_HUMAN] | 2.10E-05 | 2.11E-01 | 8.68E-06 | 1.95E-04 | -0.17 | -0.69 | -0.53 |
| Q9BQG0 | | | 9 | 8 | 527.01 | Myb-binding protein 1A OS=Homo sapiens GN=MYBBP1A PE=1 SV=2 - [MBB1A_HUMAN] | 1.34E-02 | 3.46E-02 | 1.38E-02 | 8.87E-01 | -0.54 | -0.66 | -0.12 |
| Q9BRQ8 | | | 4 | 4 | 193.62 | Apoptosis-inducing factor 2 OS=Homo sapiens GN=AIFM2 PE=1 SV=1 - [AIFM2_HUMAN] | 6.68E-05 | 6.99E-01 | 2.25E-04 | 5.07E-05 | 0.15 | -0.72 | -0.87 |
| Q9BX68 | | | 2 | 2 | 83.42 | Histidine triad nucleotide-binding protein 2, mitochondrial OS=Homo sapiens GN=HINT2 PE=1 SV=1 - [HINT2_HUMAN] | 5.47E-03 | 4.19E-03 | 2.57E-02 | 6.42E-01 | 0.82 | 0.64 | -0.19 |
| Q9BY67 | | | 2 | 2 | 104.07 | Cell adhesion molecule 1 OS=Homo sapiens GN=CADM1 PE=1 SV=2 - [CADM1_HUMAN] | 9.16E-01 | 9.41E-01 | 9.17E-01 | 9.98E-01 | 0.22 | -0.11 | -0.33 |
| Q9H0S4 | | | 2 | 2 | 125.7 | Probable ATP-dependent RNA helicase DDX47 OS=Homo sapiens GN=DDX47 PE=1 SV=1 - [DDX47_HUMAN] | 3.00E-02 | 1.09E-01 | 2.44E-02 | 7.10E-01 | -0.51 | -0.95 | -0.44 |
| Q9NY61 | | | 2 | 2 | 45.19 | Protein AATF OS=Homo sapiens GN=AATF PE=1 SV=1 - [AATF_HUMAN] | 7.16E-03 | 7.22E-03 | 2.00E-02 | 8.67E-01 | -1.06 | -0.90 | 0.16 |

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Q9UNM6 | | | 9 | 9 | 498.58 | 26S proteasome non-ATPase regulatory subunit 13 OS=Homo sapiens GN=PSMD13 PE=1 SV=2 - [PSD13_HUMAN] | 6.32E-07 | 1.50E-02 | 1.07E-07 | 1.19E-05 | -0.24 | -0.79 | -0.55 |
| Q9Y3E5 | | | 4 | 4 | 202.43 | Peptidyl-tRNA hydrolase 2, mitochondrial OS=Homo sapiens GN=PTRH2 PE=1 SV=1 - [PTH2_HUMAN] | 2.33E-01 | 5.96E-01 | 6.91E-01 | 1.98E-01 | -0.14 | 0.45 | 0.58 |

**Table S2.** Overview of proteins responsive to oxidative stress (GO:0006979) quantified by means of label-free proteomics. Proteins that were found to be significantly regulated (sig. reg.) after treatment were marked with "x" in the respective columns. Statistical p values for two-group comparisons refer to the results of Tukey's Honest Significant Difference method (THSD). $Log_2$ ratios were calculated from averaged normalized protein abundances of the different experimental groups.

| Accession | Cu complex (sig. reg.) | Mn complex (sig, reg.) | Peptides (all) | Peptides (unique) | Confidence Socre | Description | p ANOVA | p value Cu/Mn | p value Cu/control | p value Mn/control | $Log_2$ ratio Cu/Mn | $Log_2$ ratio Cu/control | $Log_2$ ratio Mn/control |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| P69905 | x | x | 10 | 7 | 403.11 | Hemoglobin subunit alpha OS=Homo sapiens GN=HBA1 PE=1 SV=2 - [HBA_HUMAN] | 6.01E-11 | 3.06E-07 | 1.00E-15 | 4.33E-10 | 2.02 | 5.15 | 3.14 |
| P39210 | x | x | 2 | 2 | 117.52 | Protein Mpv17 OS=Homo sapiens GN=MPV17 PE=1 SV=1 - [MPV17_HUMAN] | 3.36E-06 | 2.78E-03 | 6.35E-07 | 5.81E-04 | 1.64 | 3.31 | 1.67 |
| Q6NUK1 | x | x | 3 | 3 | 167.98 | Calcium-binding mitochondrial carrier protein SCaMC-1 OS=Homo sapiens GN=SLC25A24 PE=1 SV=2 - [SCMC1_HUMAN] | 9.38E-07 | 2.55E-03 | 1.41E-07 | 8.00E-05 | 1.27 | 2.97 | 1.69 |
| P04179 | x | x | 16 | 15 | 804.9 | Superoxide dismutase [Mn], mitochondrial OS=Homo sapiens GN=SOD2 PE=1 SV=2 - [SODM_HUMAN] | 4.42E-09 | 5.55E-07 | 1.20E-10 | 4.23E-06 | 1.59 | 2.91 | 1.32 |
| P03915 | x | x | 3 | 3 | 119.22 | NADH-ubiquinone oxidoreductase chain 5 OS=Homo sapiens GN=MT-ND5 PE=1 SV=2 - [NU5M_HUMAN] | 7.02E-05 | 1.22E-01 | 2.68E-05 | 1.35E-03 | 1.02 | 2.74 | 1.72 |
| P10620 | x | x | 5 | 5 | 288.29 | Microsomal glutathione S-transferase 1 OS=Homo sapiens GN=MGST1 PE=1 SV=1 - [MGST1_HUMAN] | 7.45E-07 | 2.50E-02 | 1.41E-07 | 1.11E-05 | 0.68 | 2.12 | 1.44 |
| Q96HE7 | x | x | 28 | 24 | 1279 | ERO1-like protein alpha OS=Homo sapiens GN=ERO1L PE=1 SV=2 - [ERO1A_HUMAN] | 1.75E-06 | 4.79E-01 | 8.17E-07 | 4.94E-06 | 0.36 | 2.03 | 1.67 |
| P07237 | x | x | 51 | 45 | 2691.97 | Protein disulfide-isomerase OS=Homo sapiens GN=P4HB PE=1 SV=3 - [PDIA1_HUMAN] | 4.84E-06 | 7.82E-03 | 1.02E-06 | 4.06E-04 | 0.89 | 2.01 | 1.11 |
| Q92887 | x | x | 2 | 2 | 87.03 | Canalicular multispecific organic anion transporter 1 OS=Homo sapiens GN=ABCC2 PE=1 SV=3 - [MRP2_HUMAN] | 2.27E-03 | 9.14E-01 | 2.53E-03 | 5.67E-03 | 0.41 | 1.84 | 1.43 |
| Q16595 | x |  | 3 | 3 | 178.84 | Frataxin, mitochondrial OS=Homo sapiens GN=FXN PE=1 SV=2 - [FRDA_HUMAN] | 3.45E-04 | 2.56E-03 | 2.00E-04 | 4.09E-01 | 1.32 | 1.68 | 0.36 |
| Q9UI09 | x | x | 2 | 2 | 96.89 | NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 12 OS=Homo sapiens GN=NDUFA12 PE=1 SV=1 - [NDUAC_HUMAN] | 4.56E-03 | 6.00E-01 | 3.35E-03 | 2.37E-02 | 0.58 | 1.64 | 1.06 |
| O75306 | x |  | 4 | 3 | 141.49 | NADH dehydrogenase [ubiquinone] iron-sulfur protein 2, mitochondrial OS=Homo sapiens GN=NDUFS2 PE=1 SV=2 - [NDUS2_HUMAN] | 3.40E-04 | 4.55E-03 | 1.62E-04 | 2.33E-01 | 1.23 | 1.62 | 0.39 |
| P04040 | x |  | 33 | 32 | 1600.58 | Catalase OS=Homo sapiens GN=CAT PE=1 SV=3 - [CATA_HUMAN] | 1.56E-04 | 2.34E-02 | 5.30E-05 | 1.71E-02 | 0.84 | 1.59 | 0.75 |
| Q9NNW7 | x |  | 4 | 4 | 187.46 | Thioredoxin reductase 2, mitochondrial OS=Homo sapiens GN=TXNRD2 PE=1 SV=3 - [TRXR2_HUMAN] | 2.86E-03 | 1.93E-02 | 1.90E-03 | 4.94E-01 | 1.18 | 1.56 | 0.37 |
| O43464 | x |  | 4 | 2 | 181.86 | Serine protease HTRA2, mitochondrial OS=Homo sapiens GN=HTRA2 PE=1 SV=2 - [HTRA2_HUMAN] | 2.35E-05 | 9.28E-06 | 2.68E-04 | 1.72E-01 | 2.02 | 1.51 | -0.51 |
| Q15165 | x |  | 11 | 11 | 349.79 | Serum paraoxonase/arylesterase 2 OS=Homo sapiens GN=PON2 PE=1 SV=3 - [PON2_HUMAN] | 4.46E-08 | 9.50E-05 | 2.94E-09 | 5.27E-06 | 0.63 | 1.41 | 0.78 |
| O95831 | x |  | 12 | 11 | 693.43 | Apoptosis-inducing factor 1, mitochondrial OS=Homo sapiens GN=AIFM1 PE=1 SV=1 - [AIFM1_HUMAN] | 3.50E-06 | 3.52E-06 | 4.45E-06 | 9.88E-01 | 1.27 | 1.25 | -0.03 |
| P09601 | x |  | 4 | 4 | 230.68 | Heme oxygenase 1 OS=Homo sapiens GN=HMOX1 PE=1 SV=1 - [HMOX1_HUMAN] | 1.15E-07 | 1.39E-08 | 1.17E-06 | 1.02E-02 | 1.56 | 1.12 | -0.44 |
| P02649 |  | x | 11 | 10 | 622.81 | Apolipoprotein E OS=Homo sapiens GN=APOE PE=1 SV=1 - [APOE_HUMAN] | 1.57E-07 | 1.43E-08 | 2.99E-04 | 2.09E-05 | 2.18 | 0.99 | -1.19 |
| O00217 |  |  | 2 | 2 | 107.32 | NADH dehydrogenase [ubiquinone] iron-sulfur protein 8, mitochondrial OS=Homo sapiens GN=NDUFS8 PE=1 SV=1 - [NDUS8_HUMAN] | 4.69E-02 | 9.29E-02 | 5.15E-02 | 9.45E-01 | 1.11 | 0.97 | -0.14 |
| Q99757 |  |  | 2 | 2 | 60.63 | Thioredoxin, mitochondrial OS=Homo sapiens GN=TXN2 PE=1 SV=2 - [THIOM_HUMAN] | 1.88E-02 | 1.19E-02 | 2.87E-01 | 2.16E-01 | 1.32 | 0.74 | -0.59 |
| P30048 |  |  | 10 | 10 | 525.51 | Thioredoxin-dependent peroxide reductase, mitochondrial OS=Homo sapiens GN=PRDX3 PE=1 SV=3 - [PRDX3_HUMAN] | 1.91E-02 | 1.81E-02 | 5.44E-02 | 8.39E-01 | 0.86 | 0.72 | -0.13 |
| P56556 |  |  | 4 | 4 | 143.62 | NADH dehydrogenase [ubiquinone] 1 alpha subcomplex subunit 6 OS=Homo sapiens GN=NDUFA6 PE=1 SV=3 - [NDUA6_HUMAN] | 6.52E-03 | 4.47E-03 | 4.07E-02 | 5.19E-01 | 0.78 | 0.51 | -0.27 |
| P99999 |  |  | 3 | 3 | 106.85 | Cytochrome c OS=Homo sapiens GN=CYCS PE=1 SV=2 - [CYC_HUMAN] | 7.38E-06 | 2.24E-06 | 7.60E-02 | 1.21E-04 | 1.36 | 0.44 | -0.92 |
| Q8TCS8 |  |  | 18 | 17 | 751.32 | Polyribonucleotide nucleotidyltransferase 1, mitochondrial OS=Homo sapiens GN=PNPT1 PE=1 SV=2 - [PNPT1_HUMAN] | 8.87E-03 | 6.18E-03 | 5.27E-01 | 5.39E-02 | 1.01 | 0.39 | -0.63 |
| P16615 |  |  | 17 | 10 | 846.26 | Sarcoplasmic/endoplasmic reticulum calcium ATPase 2 OS=Homo sapiens GN=ATP2A2 PE=1 SV=1 - [AT2A2_HUMAN] | 1.10E-01 | 4.99E-01 | 4.96E-01 | 8.55E-02 | -0.17 | 0.31 | 0.48 |
| Q15392 |  |  | 7 | 7 | 346.47 | Delta(24)-sterol reductase OS=Homo sapiens GN=DHCR24 PE=1 SV=2 - [DHC24_HUMAN] | 7.34E-02 | 1.54E-01 | 7.31E-02 | 9.06E-01 | 0.24 | 0.29 | 0.04 |
| P09874 |  |  | 13 | 12 | 604.06 | Poly [ADP-ribose] polymerase 1 OS=Homo sapiens GN=PARP1 PE=1 SV=4 - [PARP1_HUMAN] | 7.36E-02 | 1.23E-01 | 9.78E-01 | 8.62E-02 | -0.40 | 0.05 | 0.45 |
| P04264 |  |  | 4 | 3 | 251.26 | Keratin, type II cytoskeletal 1 OS=Homo sapiens GN=KRT1 PE=1 SV=6 - [K2C1_HUMAN] | 3.44E-01 | 3.64E-01 | 9.86E-01 | 4.47E-01 | 0.92 | 0.01 | -0.90 |
| P30405 |  | x | 4 | 4 | 257.81 | Peptidyl-prolyl cis-trans isomerase F, mitochondrial OS=Homo sapiens GN=PPIF PE=1 SV=1 - [PPIF_HUMAN] | 7.55E-05 | 9.53E-03 | 1.64E-02 | 2.32E-05 | 0.64 | -0.47 | -1.11 |
| Q13268 |  |  | 21 | 21 | 1322.14 | Dehydrogenase/reductase SDR family member 2, mitochondrial OS=Homo sapiens GN=DHRS2 PE=1 SV=4 - [DHRS2_HUMAN] | 2.33E-03 | 9.99E-01 | 3.60E-03 | 3.96E-03 | 0.03 | -0.49 | -0.53 |
| P07148 |  |  | 5 | 5 | 349.95 | Fatty acid-binding protein, liver OS=Homo sapiens GN=FABP1 PE=1 SV=1 - [FABPL_HUMAN] | 4.88E-01 | 9.50E-01 | 6.56E-01 | 4.74E-01 | 0.18 | -0.58 | -0.76 |
| P30044 |  |  | 13 | 13 | 761.78 | Peroxiredoxin-5, mitochondrial OS=Homo sapiens GN=PRDX5 PE=1 SV=4 - [PRDX5_HUMAN] | 1.29E-06 | 6.65E-01 | 6.88E-07 | 2.51E-06 | -0.05 | -0.60 | -0.54 |
| P00390 |  |  | 13 | 13 | 679.05 | Glutathione reductase, mitochondrial OS=Homo sapiens GN=GSR PE=1 SV=2 - [GSHR_HUMAN] | 4.35E-04 | 2.12E-01 | 2.05E-04 | 6.61E-03 | -0.20 | -0.67 | -0.47 |
| Q99497 |  |  | 7 | 7 | 369.33 | Protein DJ-1 OS=Homo sapiens GN=PARK7 PE=1 SV=2 - [PARK7_HUMAN] | 2.10E-05 | 2.11E-01 | 8.68E-06 | 1.95E-04 | -0.17 | -0.69 | -0.53 |

| | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| P48506 | | | 2 | 2 | 112.66 | Glutamate--cysteine ligase catalytic subunit OS=Homo sapiens GN=GCLC PE=1 SV=2 - [GSH1_HUMAN] | 2.74E-02 | 6.82E-02 | 2.71E-02 | 8.79E-01 | -0.68 | -0.89 | -0.21 |
| O00151 | | x | 18 | 18 | 870.23 | PDZ and LIM domain protein 1 OS=Homo sapiens GN=PDLIM1 PE=1 SV=4 - [PDLI1_HUMAN] | 2.08E-05 | 5.88E-01 | 7.52E-05 | 1.32E-05 | 0.17 | -0.89 | -1.06 |
| P00338 | | | 21 | 21 | 1173.53 | L-lactate dehydrogenase A chain OS=Homo sapiens GN=LDHA PE=1 SV=2 - [LDHA_HUMAN] | 5.43E-06 | 1.04E-04 | 1.50E-06 | 5.36E-02 | -0.64 | -0.95 | -0.30 |
| P18827 | x | x | 2 | 2 | 110.02 | Syndecan-1 OS=Homo sapiens GN=SDC1 PE=1 SV=3 - [SDC1_HUMAN] | 2.31E-05 | 4.86E-02 | 7.55E-04 | 7.03E-06 | 0.65 | -1.03 | -1.68 |
| Q16881 | x | | 7 | 7 | 379.95 | Thioredoxin reductase 1, cytoplasmic OS=Homo sapiens GN=TXNRD1 PE=1 SV=3 - [TRXR1_HUMAN] | 2.55E-04 | 1.98E-03 | 1.42E-04 | 3.81E-01 | -0.76 | -1.03 | -0.28 |
| P23396 | x | x | 15 | 15 | 688.74 | 40S ribosomal protein S3 OS=Homo sapiens GN=RPS3 PE=1 SV=2 - [RS3_HUMAN] | 2.64E-08 | 3.39E-05 | 4.85E-06 | 1.54E-09 | 1.10 | -1.17 | -2.27 |
| P12004 | x | | 14 | 14 | 892.71 | Proliferating cell nuclear antigen OS=Homo sapiens GN=PCNA PE=1 SV=1 - [PCNA_HUMAN] | 1.83E-05 | 2.94E-01 | 8.37E-06 | 1.25E-04 | -0.20 | -1.18 | -0.97 |
| Q14103 | x | | 7 | 3 | 396.47 | Heterogeneous nuclear ribonucleoprotein D0 OS=Homo sapiens GN=HNRNPD PE=1 SV=1 - [HNRPD_HUMAN] | 6.44E-05 | 2.31E-03 | 2.15E-05 | 5.92E-02 | -0.71 | -1.19 | -0.48 |
| P50570 | x | | 7 | 4 | 255.77 | Dynamin-2 OS=Homo sapiens GN=DNM2 PE=1 SV=2 - [DYN2_HUMAN] | 3.06E-03 | 2.70E-02 | 1.87E-03 | 3.97E-01 | -0.76 | -1.32 | -0.55 |
| P27695 | x | | 15 | 15 | 740.48 | DNA-(apurinic or apyrimidinic site) lyase OS=Homo sapiens GN=APEX1 PE=1 SV=2 - [APEX1_HUMAN] | 1.12E-06 | 9.23E-06 | 2.81E-07 | 8.18E-02 | -1.01 | -1.37 | -0.36 |
| O95793 | x | | 6 | 6 | 180.04 | Double-stranded RNA-binding protein Staufen homolog 1 OS=Homo sapiens GN=STAU1 PE=1 SV=2 - [STAU1_HUMAN] | 2.81E-04 | 7.08E-02 | 1.07E-04 | 1.17E-02 | -0.49 | -1.42 | -0.93 |
| P28074 | x | | 3 | 3 | 228.95 | Proteasome subunit beta type-5 OS=Homo sapiens GN=PSMB5 PE=1 SV=3 - [PSB5_HUMAN] | 1.91E-08 | 1.08E-06 | 1.07E-09 | 1.03E-04 | -0.90 | -1.52 | -0.62 |
| P10599 | x | | 12 | 12 | 675.5 | Thioredoxin OS=Homo sapiens GN=TXN PE=1 SV=3 - [THIO_HUMAN] | 2.70E-08 | 2.06E-05 | 1.57E-09 | 7.96E-06 | -0.72 | -1.53 | -0.81 |
| P00441 | x | | 6 | 6 | 350.19 | Superoxide dismutase [Cu-Zn] OS=Homo sapiens GN=SOD1 PE=1 SV=2 - [SODC_HUMAN] | 1.21E-08 | 1.14E-04 | 5.66E-10 | 3.94E-07 | -0.59 | -1.56 | -0.98 |
| P32119 | x | | 13 | 12 | 664.19 | Peroxiredoxin-2 OS=Homo sapiens GN=PRDX2 PE=1 SV=5 - [PRDX2_HUMAN] | 8.54E-08 | 7.09E-06 | 7.04E-09 | 3.08E-04 | -0.94 | -1.63 | -0.69 |
| P30041 | x | x | 16 | 15 | 784.95 | Peroxiredoxin-6 OS=Homo sapiens GN=PRDX6 PE=1 SV=3 - [PRDX6_HUMAN] | 1.36E-06 | 1.33E-02 | 2.59E-07 | 4.15E-05 | -0.52 | -1.65 | -1.12 |
| P13639 | x | x | 54 | 53 | 2719.6 | Elongation factor 2 OS=Homo sapiens GN=EEF2 PE=1 SV=4 - [EF2_HUMAN] | 9.93E-07 | 4.20E-01 | 3.98E-07 | 2.64E-06 | -0.16 | -1.66 | -1.50 |
| Q06830 | x | | 17 | 15 | 836.61 | Peroxiredoxin-1 OS=Homo sapiens GN=PRDX1 PE=1 SV=1 - [PRDX1_HUMAN] | 5.28E-07 | 2.24E-04 | 6.39E-08 | 2.60E-04 | -0.81 | -1.66 | -0.86 |
| P06493 | x | x | 4 | 3 | 197.08 | Cyclin-dependent kinase 1 OS=Homo sapiens GN=CDK1 PE=1 SV=3 - [CDK1_HUMAN] | 4.89E-04 | 1.00E+00 | 7.69E-04 | 7.78E-04 | 0.37 | -1.67 | -2.03 |
| Q92769 | x | | 2 | 2 | 89.77 | Histone deacetylase 2 OS=Homo sapiens GN=HDAC2 PE=1 SV=2 - [HDAC2_HUMAN] | 1.09E-03 | 1.90E-02 | 5.34E-04 | 2.03E-01 | -0.91 | -1.68 | -0.77 |
| P11413 | x | x | 24 | 23 | 857.62 | Glucose-6-phosphate 1-dehydrogenase OS=Homo sapiens GN=G6PD PE=1 SV=4 - [G6PD_HUMAN] | 6.88E-10 | 3.09E-05 | 1.41E-11 | 4.16E-09 | -0.55 | -1.69 | -1.13 |
| P15121 | x | | 8 | 6 | 356.92 | Aldose reductase OS=Homo sapiens GN=AKR1B1 PE=1 SV=3 - [ALDR_HUMAN] | 2.10E-07 | 2.26E-05 | 2.12E-08 | 5.22E-04 | -1.03 | -1.83 | -0.81 |
| P36776 | x | x | 10 | 9 | 546.85 | Lon protease homolog, mitochondrial OS=Homo sapiens GN=LONP1 PE=1 SV=2 - [LONM_HUMAN] | 2.49E-10 | 1.68E-03 | 5.79E-12 | 1.49E-10 | -0.41 | -1.93 | -1.52 |
| P32322 | x | | 17 | 15 | 854.98 | Pyrroline-5-carboxylate reductase 1, mitochondrial OS=Homo sapiens GN=PYCR1 PE=1 SV=2 - [P5CR1_HUMAN] | 2.71E-07 | 2.74E-06 | 4.33E-08 | 2.23E-02 | -1.42 | -1.99 | -0.57 |
| O75874 | x | x | 21 | 19 | 1205.32 | Isocitrate dehydrogenase [NADP] cytoplasmic OS=Homo sapiens GN=IDH1 PE=1 SV=2 - [IDHC_HUMAN] | 1.73E-09 | 7.27E-04 | 6.15E-11 | 5.57E-09 | -0.54 | -2.04 | -1.49 |
| P48637 | x | | 10 | 10 | 644.74 | Glutathione synthetase OS=Homo sapiens GN=GSS PE=1 SV=1 - [GSHB_HUMAN] | 1.37E-08 | 2.48E-06 | 6.00E-10 | 1.39E-05 | -1.11 | -2.10 | -0.99 |
| O00244 | x | x | 2 | 2 | 60.94 | Copper transport protein ATOX1 OS=Homo sapiens GN=ATOX1 PE=1 SV=1 - [ATOX1_HUMAN] | 8.71E-06 | 6.55E-01 | 5.68E-06 | 2.49E-05 | -0.12 | -2.11 | -1.99 |
| P42330 | x | x | 20 | 10 | 1032.71 | Aldo-keto reductase family 1 member C3 OS=Homo sapiens GN=AKR1C3 PE=1 SV=4 - [AK1C3_HUMAN] | 2.60E-07 | 5.23E-03 | 3.36E-08 | 6.20E-06 | -0.70 | -2.27 | -1.56 |
| O00629 | x | | 3 | 3 | 79.78 | Importin subunit alpha-4 OS=Homo sapiens GN=KPNA4 PE=1 SV=1 - [IMA4_HUMAN] | 3.25E-06 | 1.57E-05 | 1.30E-06 | 2.87E-01 | -1.99 | -2.46 | -0.47 |
| Q96C36 | x | | 6 | 4 | 373.52 | Pyrroline-5-carboxylate reductase 2 OS=Homo sapiens GN=PYCR2 PE=1 SV=1 - [P5CR2_HUMAN] | 1.66E-09 | 3.09E-09 | 6.88E-11 | 2.87E-03 | -2.47 | -3.23 | -0.77 |
| O43396 | x | x | 7 | 6 | 292.95 | Thioredoxin-like protein 1 OS=Homo sapiens GN=TXNL1 PE=1 SV=3 - [TXNL1_HUMAN] | 8.91E-07 | 5.22E-03 | 1.41E-07 | 4.25E-05 | -1.22 | -3.89 | -2.66 |

**Table S3.** Overview of LC-MS/MS runs analyzed in the proteomics study. Using the respective sample identifiers, deposited mass spectrometric data can be assigned to the investigated experimental groups.

| LC-MS/MS run | Experimental group |
|---|---|
| OEII15601 | Cu complex |
| OEII15603 | Mn complex |
| OEII15605 | DMSO |
| OEII15607 | Cu complex |
| OEII15609 | DMSO |
| OEII15611 | DMSO |
| OEII15615 | Mn complex |
| OEII15617 | Cu complex |
| OEII15619 | DMSO |
| OEII15621 | Mn complex |
| OEII15623 | DMSO |
| OEII15625 | Mn complex |
| OEII15629 | Cu complex |
| OEII15631 | DMSO |
| OEII15633 | Mn complex |
| OEII15635 | Cu complex |
| OEII15637 | Cu complex |
| OEII15639 | Mn complex |