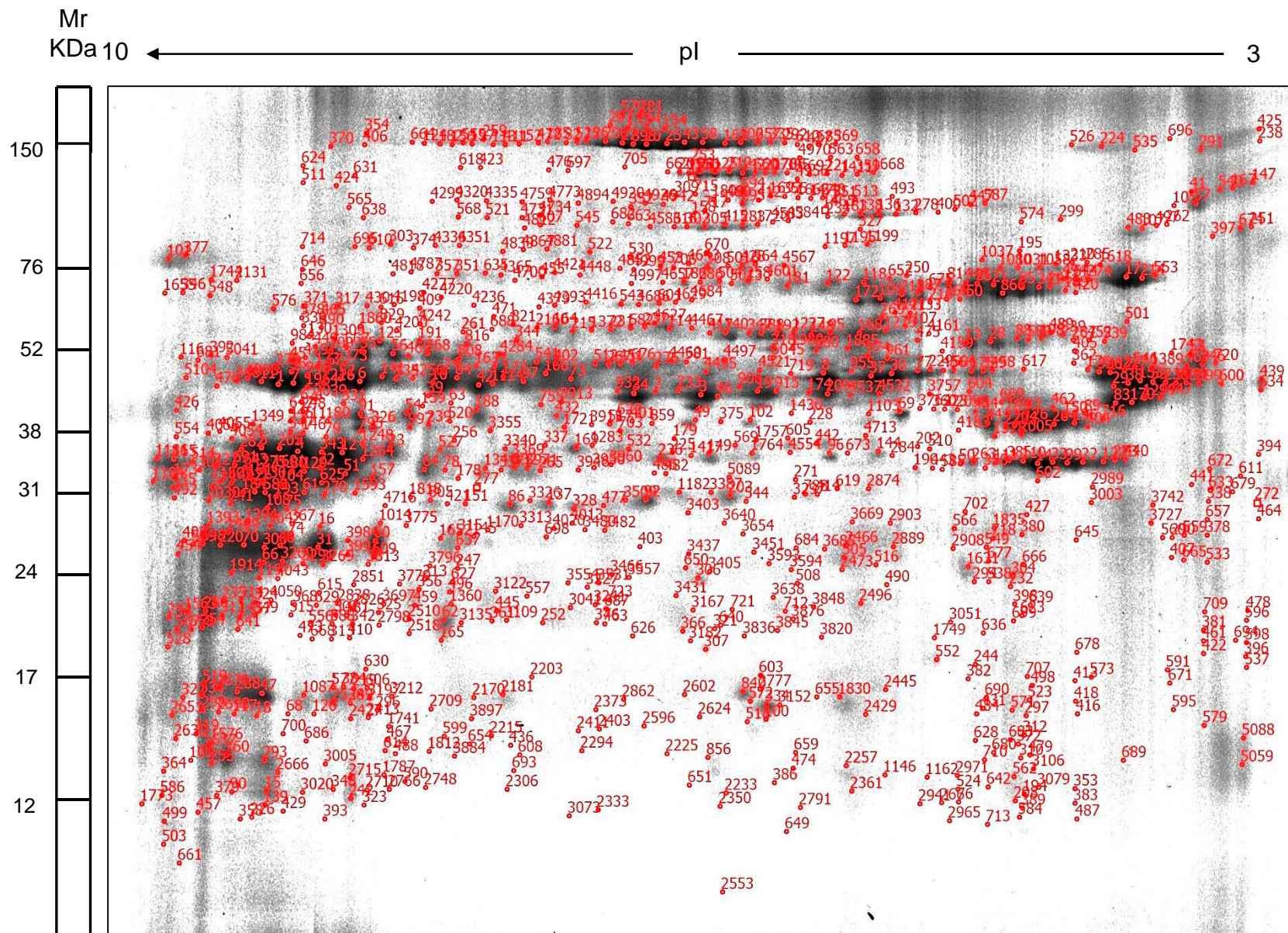
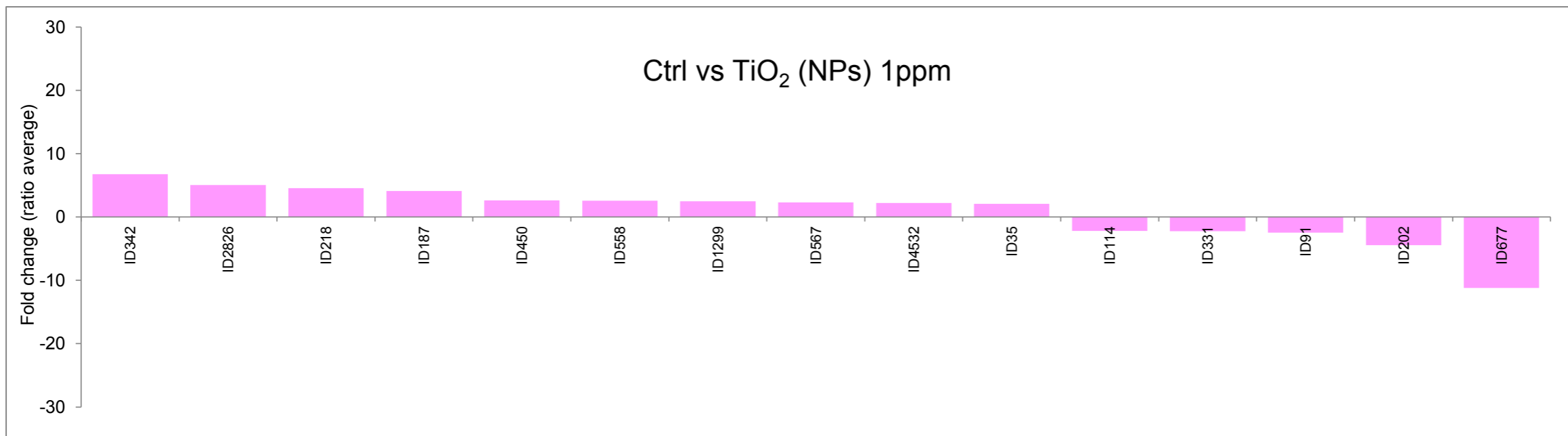
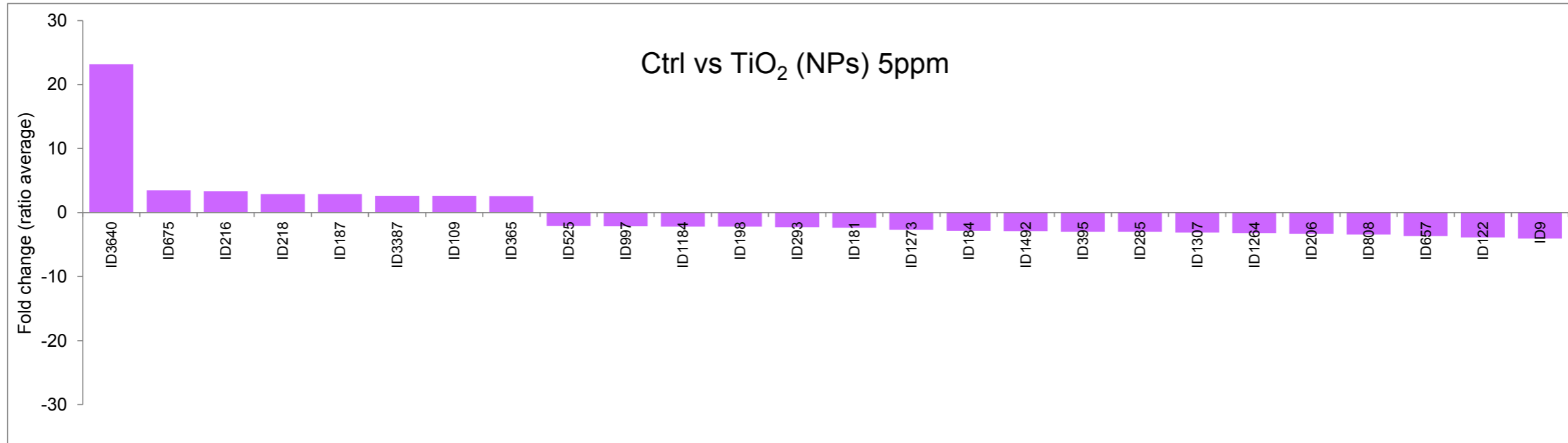


**Supplementary Figure S1.** Representative 2D-DIGE proteins from hepatocytes exposed to NPs. A total of 998 spots were detected by REDFIN software.

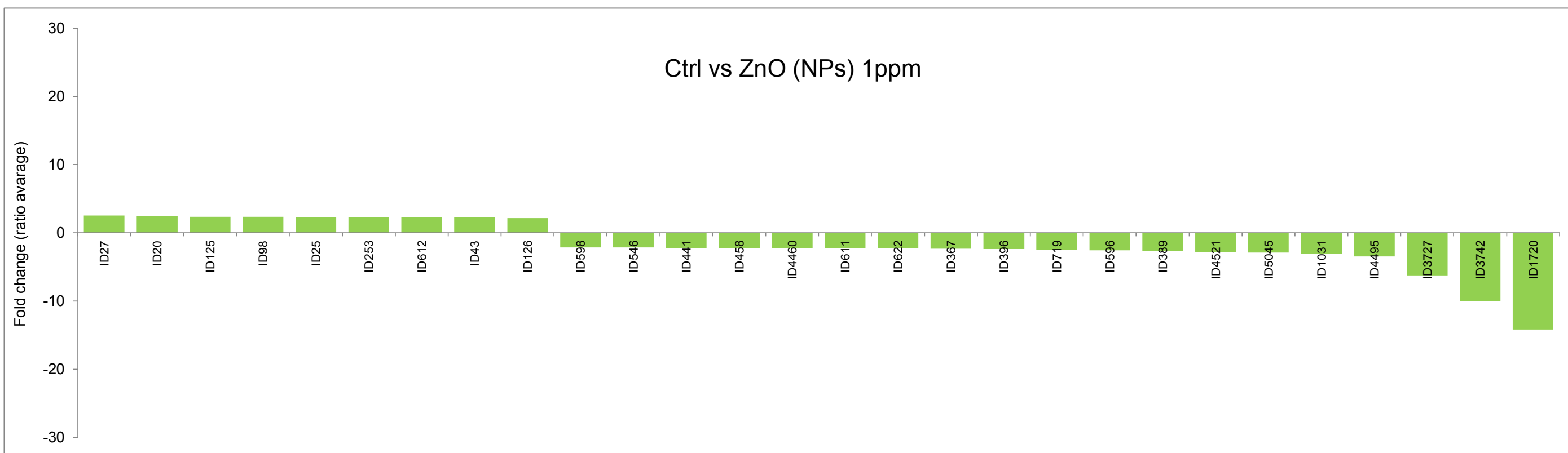
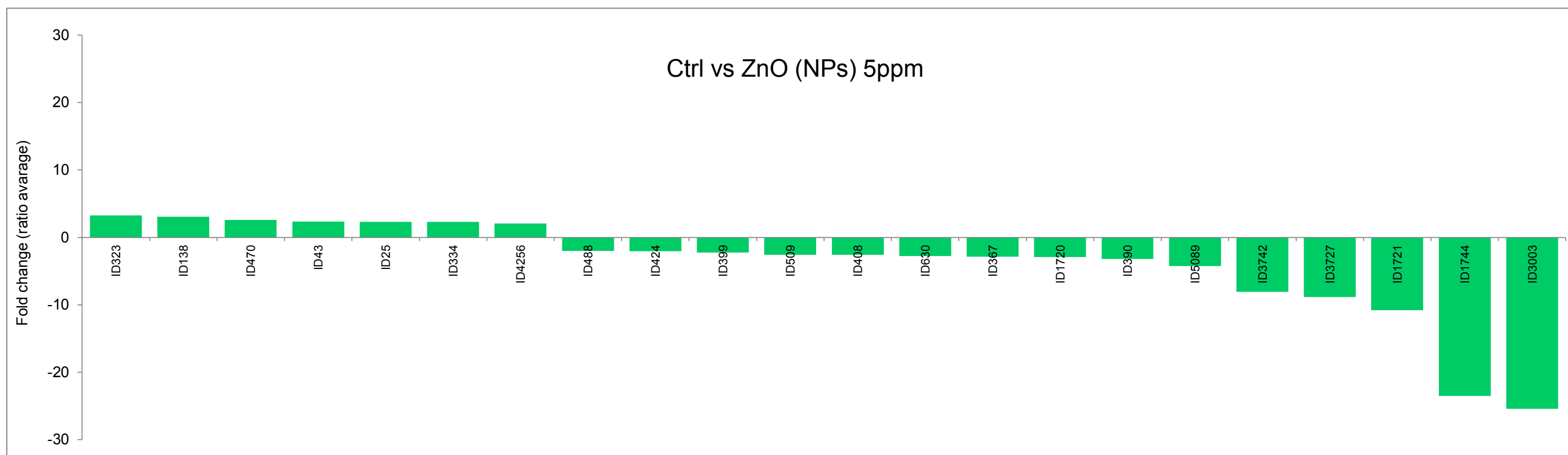


**Supplementary Figure S2:** Proteins up- and down-regulated by NPs along with fold change (F.C.). All data from comparisons control (ctrl) versus each NPs were selected by F.C.  $\geq 2$  and  $p < 0.05$ . **A)** Ctrl vs TiO<sub>2</sub> NPs at 5 ppm showed ID2203 with F.C. = -10498.64, ID2233 with F.C. = -259.78, ID3051 with F.C. = 259.78, ID474 with F.C. = 67.76; Ctrl vs TiO<sub>2</sub> NPs at 1 ppm showed ID439 with F.C. = - Inf. (- Infinite, not detected at the specific NPs exposure). **B)** Ctrl vs ZnO NPs at 5ppm showed ID589 with F.C. = -83.50, ID1430 with F.C. = -203.84 and ID502, ID629, ID2473, ID2798, ID3403, ID3451, ID3654 with F.C. = - Inf.; Ctrl vs ZnO NPs at 1 ppm showed ID299 with F.C. = -35.60, ID2473 with F.C. = -55.15 and ID5089, ID439, ID634 with F.C. = - Inf. **C)** Ctrl vs CuO NPs at 5 ppm and 1ppm concentrations. **D)** Ctrl vs Ag NPs at 5 ppm showed ID2466 with F.C. = -58.78, ID252, ID342, ID439, ID470, ID481, ID617, ID634, ID1195, ID1721, ID1744, Id2160, ID2715, ID2826, ID2838, ID2851, ID3405, ID3685, ID4421, ID4448, ID4773, ID4881 with F.C. = - Inf.; Ctrl vs AgNPs at 1 ppm showed ID489 with F.C. = -37.73.

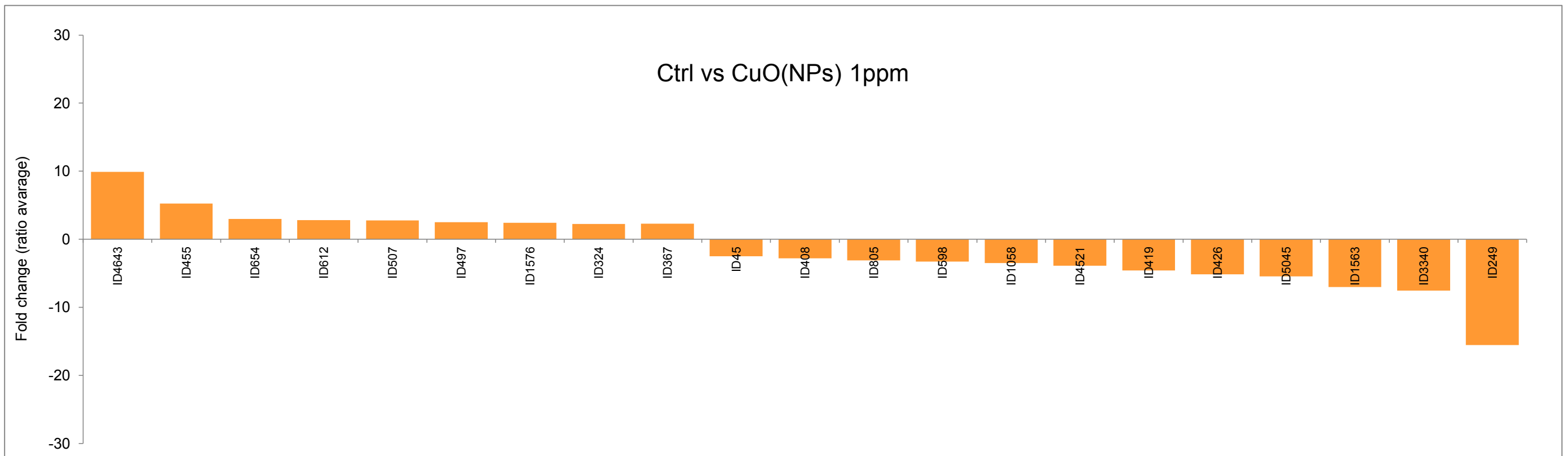
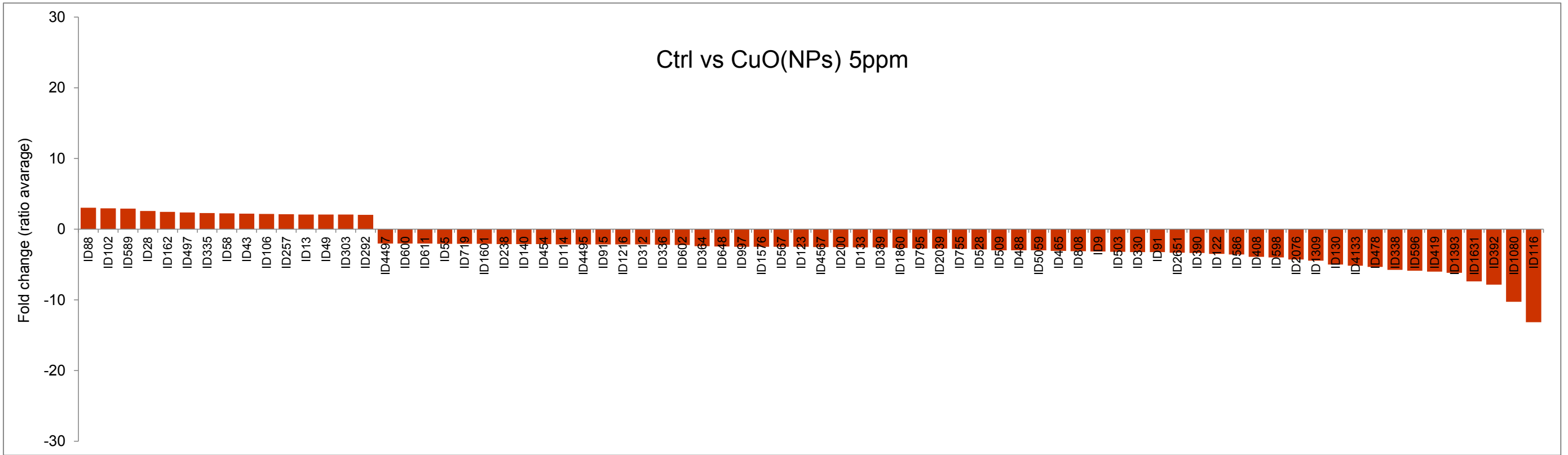
**A**



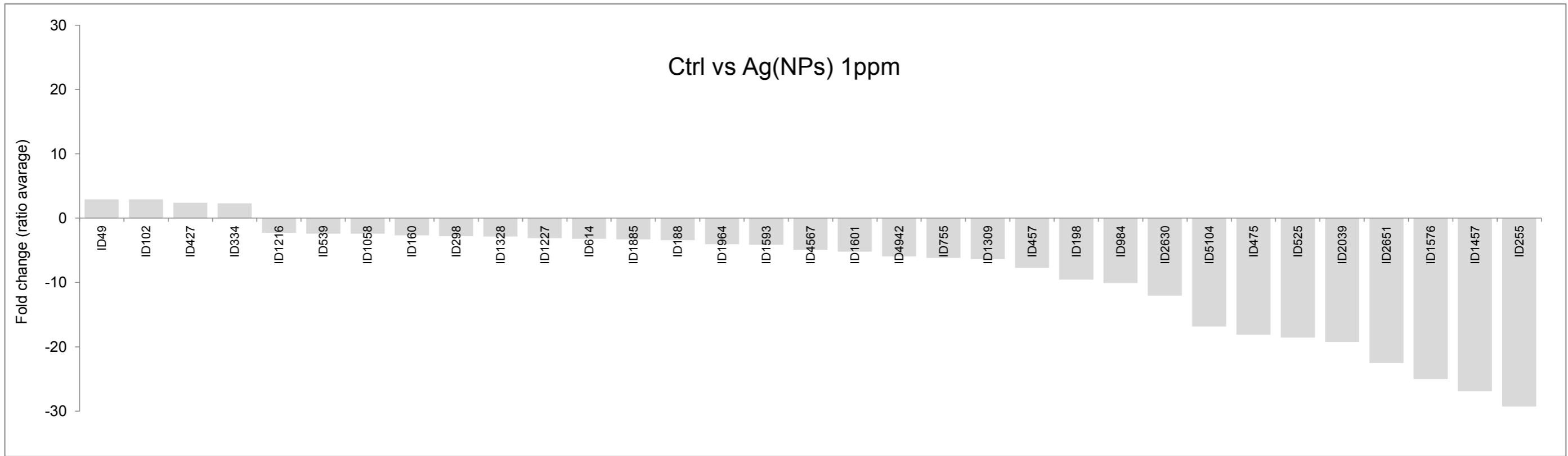
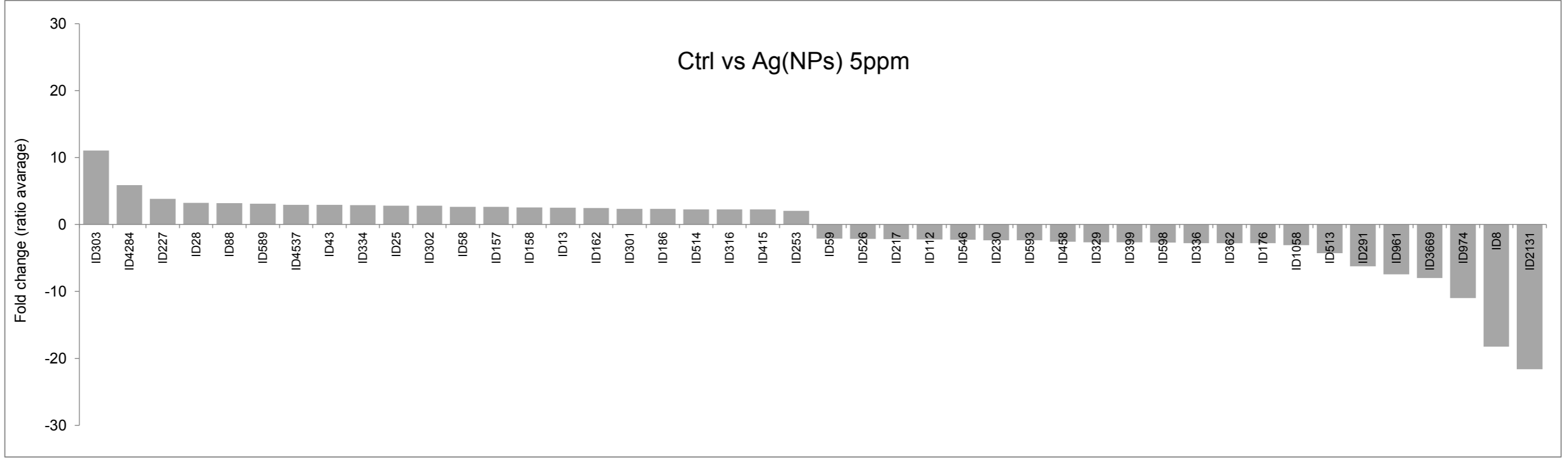
**B**



C



D



**Supplementary Table S1. Lipid composition**

	Control	TiO <sub>2</sub> NPs	ZnO NPs	CuO NPs	Ag NPs
Total lipid (nmol/protein mg)	443.4 ±145.0	490.5 ±133.0	468.0 ±145.3	496.4 ±89.7	630.8 ±103.1*
TG (nmol/protein mg)	307.8 ±128.1	345.1 ±137.8	357.6 ±92.6	372.7 ±69.3	465.4 ±108.1*
Total phospholipid (nmol/protein mg)	84.41 ±22.72	90.70 ±31.87	99.23 ±26.7	72.58 ±20.19	110.06 ±38.19
Total cholesterol (nmol/protein mg)	51.14 ±10.84	54.64 ±9.45	70.87 ±24.00	51.06 ±6.57	55.40 ±11.93
TG%	67.76 ±7.62	68.87 ±10.22	56.39 ±28.87	75.04 ±3.03	73.18 ±6.53
CE%	3.60 ± 1.59	3.66 ±2.05	4.29 ±2.25	3.04 ±1.00	2.17 ±0.41
FC%	8.60 ±2.39	8.11 ±2.20	15.67 ±17.88	7.36 ±1.85	6.75 ±2.19
PC%	11.81 ±3.07	11.11 ±4.81	12.14 ±4.01	9.90 ±4.01	13.34 ±7.67
PE%	2.43 ±0.94	3.45 ±2.02	4.58 ±3.93	1.07 ±0.69*	1.66 ±0.71
PS%	0.92 ±0.33	0.64 ±0.12	0.747 ±0.12	1.247 ±0.16	0.48 ±0.28
PI%	3.17 ±1.20	2.79 ±1.39	4.16 ±3.63	1.55 ±0.77*	1.92 ±0.86
SM%	2.24 ±0.49	1.59 ±0.28*	2.27 ±1.06	1.63 ±1.01	0.80 ±0.43***
PC/PE	5.29 ±10.84	3.81 ±1.51	4.83 ±3.73	13.44 ±9.00*	9.14 ±5.98
CL/PL	0.435 ±0.083	0.450 ±0.135	0.585 ±0.367	0.534 ±0.217	0.481 ±0.364
Ratio Hydrophobic-Amphipathic	2.68 ±0.96	2.97 ±1.32	2.26 ±1.40	3.64 ±0.66	3.32 ±1.31

TG, triacylglycerol; CE, cholesteryl ester; FC, free cholesterol; PC, phosphatidylcholine; PE, phosphatidylethanolamine; PS, phosphatidylserine; PI, phosphatidylinositol; SM, sphingomyelin. Total lipid quantities correspond to the summation of all measured lipid species, which are expressed as the percentage of the summation. Total phospholipid quantities correspond to the summation of PC, PE, SM, PS and PI and total cholesterol to the summation of FC and CE. Data are expressed as the mean ± SEM and correspond to the results obtained using 5 ppm concentration of nanoparticles in the culture medium. Control vs. treated: \*P ≤ 0.05, \*\*\*P ≤ 0.001.