

## Proteomic and metabolomic profiling combined with in vitro studies reveal antiproliferative mechanism of silver nanoparticles in MDA-MB-231 breast carcinoma cells

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**Table S1:** Differentially expressed proteins in the T-AgNPs-treated cells

Uniprot ID	Protein Name	Peptide spectrum matches	Protein sequence coverage (%)	Protein Score	MW (kDa)	PI
P61604	10 kDa heat shock protein	7	45	131	10.9	8.92
P62820	Ras-related protein Rab-1A	19	45	257	22.7	6.21
E5RK69	Annexin	42	43	687	51.7	6.05
O14737	Programmed cell death protein 5	5	38	31	14.3	6.04
P35232	Prohibitin	13	36	270	29.8	5.76
Q15836	Vesicle-associated membrane protein 3	3	33	99	11.3	8.79
U3KQK0	Histone H2B	17	31	366	18.8	10.54
P51148	Ras-related protein Rab-5C	9	29	215	23.5	8.41
P42677	40S ribosomal protein S27	4	29	61	9.5	9.45
Q9Y281	Cofilin-2	9	28	222	18.7	7.88
P34897	Serine hydroxymethyltransferase	18	26	355	56	8.53
O95865	N(G),N(G)-dimethylarginine dimethylaminohydrolase 2	4	25	53	29.6	6.01
P25398	40S ribosomal protein S12	7	23	133	14.5	7.21

P26583	High mobility group protein B2	7	22	118	24	7.81
Q14320	Protein FAM50A	8	22	84	40.2	6.83
Q07021	Complement component 1 Q subcomponent-binding protein	9	22	167	31.3	4.84
P05141	ADP/ATP translocase 2	12	21	137	32.8	9.69
P39019	40S ribosomal protein S19	5	21	61	16.1	10.32
Q99714	3-hydroxyacyl-CoA dehydrogenase type-2	5	20	73	26.9	7.78
P51149	Ras-related protein Rab-7a	6	20	143	23.5	6.7
P62244	40S ribosomal protein S15a	7	19	120	14.8	10.13
P00367	Glutamate dehydrogenase 1	15	19	235	61.4	7.8
A8K878	Mesencephalic astrocyte-derived neurotrophic factor	6	19	105	21.1	8.92
Q03135	Caveolin-1	5	18	88	20.5	6.02
P49411	Elongation factor Tu	11	18	183	49.5	7.61
P14174	Macrophage migration inhibitory factor	2	17	36	12.5	7.88
P62851	40S ribosomal protein S25	4	16	63	13.7	10.11
A0A2R8YD14	40S ribosomal protein S24	3	16	40	19.2	10.98
P62266	40S ribosomal protein S23	3	15	56	15.8	10.49
P27824	Calnexin	12	15	152	67.5	4.6
P21796	Voltage-dependent anion-selective channel protein 1	5	15	76	30.8	8.54
Q99623	Prohibitin-2	5	15	116	33.3	9.83
H0YKD8	60S ribosomal protein L28	2	15	41	19.1	11.46
P53004	Biliverdin reductase A	7	15	81	33.4	6.44
O75367	Core histone macro-H2A.1	4	14	51	39.6	9.79
P45880	Voltage-dependent anion-selective channel protein 2	4	14	39	31.5	7.56
B0QYN7	SUMO-conjugating enzyme UBC9	3	14	36	20.4	8.46
F8W930	Insulin-like growth factor 2 mRNA-binding	11	14	194	66.7	8.46

	protein 2					
O00762	Ubiquitin-conjugating enzyme E2 C	3	13	33	19.6	7.37
P22087	rRNA 2'-O-methyltransferase fibrillar	4	13	42	33.8	10.18
P62269	40S ribosomal protein S18	3	13	38	17.7	10.99
B7Z4C8	60S ribosomal protein L31	3	13	48	15.1	10.37
H0YFD6	Trifunctional enzyme subunit alpha	11	13	128	86.3	9.1
P36551	Oxygen-dependent coproporphyrinogen-III oxidase	7	13	152	50.1	8.25
P04181	Ornithine aminotransferase	7	13	167	48.5	7.03
P13726	Tissue factor	3	13	47	33	7.03
P31350	Ribonucleoside-diphosphate reductase subunit M2	4	13	94	44.8	5.38
P11766	Alcohol dehydrogenase class-3	5	13	66	39.7	7.49
Q9UJZ1	Stomatin-like protein 2	4	12	107	38.5	7.39
P00374	Dihydrofolate reductase	2	12	44	21.4	7.42
Q96I99	Succinate--CoA ligase [GDP-forming] subunit beta	6	12	89	46.5	6.39
P09110	3-ketoacyl-CoA thiolase	5	12	61	44.3	8.44
C9J5N1	PTGES3L-AARSD1 readthrough	6	12	85	55	6.55
Q9P287	BRCA2 and CDKN1A-interacting protein	6	11	67	36	4.61
Q8N1G4	Leucine-rich repeat-containing protein 47	8	11	189	63.4	8.28
P49755	Transmembrane emp24 domain-containing protein 10	5	11	79	25	7.44
P30084	Enoyl-CoA hydratase	5	10	94	31.4	8.07
P21589	5'-nucleotidase	6	10	104	63.3	7.03
D6RBW1	Eukaryotic translation initiation factor 4E	6	10	90	28.5	8.12
F8WAR4	MICOS complex subunit	3	10	63	27.7	6.64
P61019	Ras-related protein Rab-2A	3	10	54	23.5	6.54
P49748	Very long-chain specific acyl-CoA	9	9	182	70.3	8.75

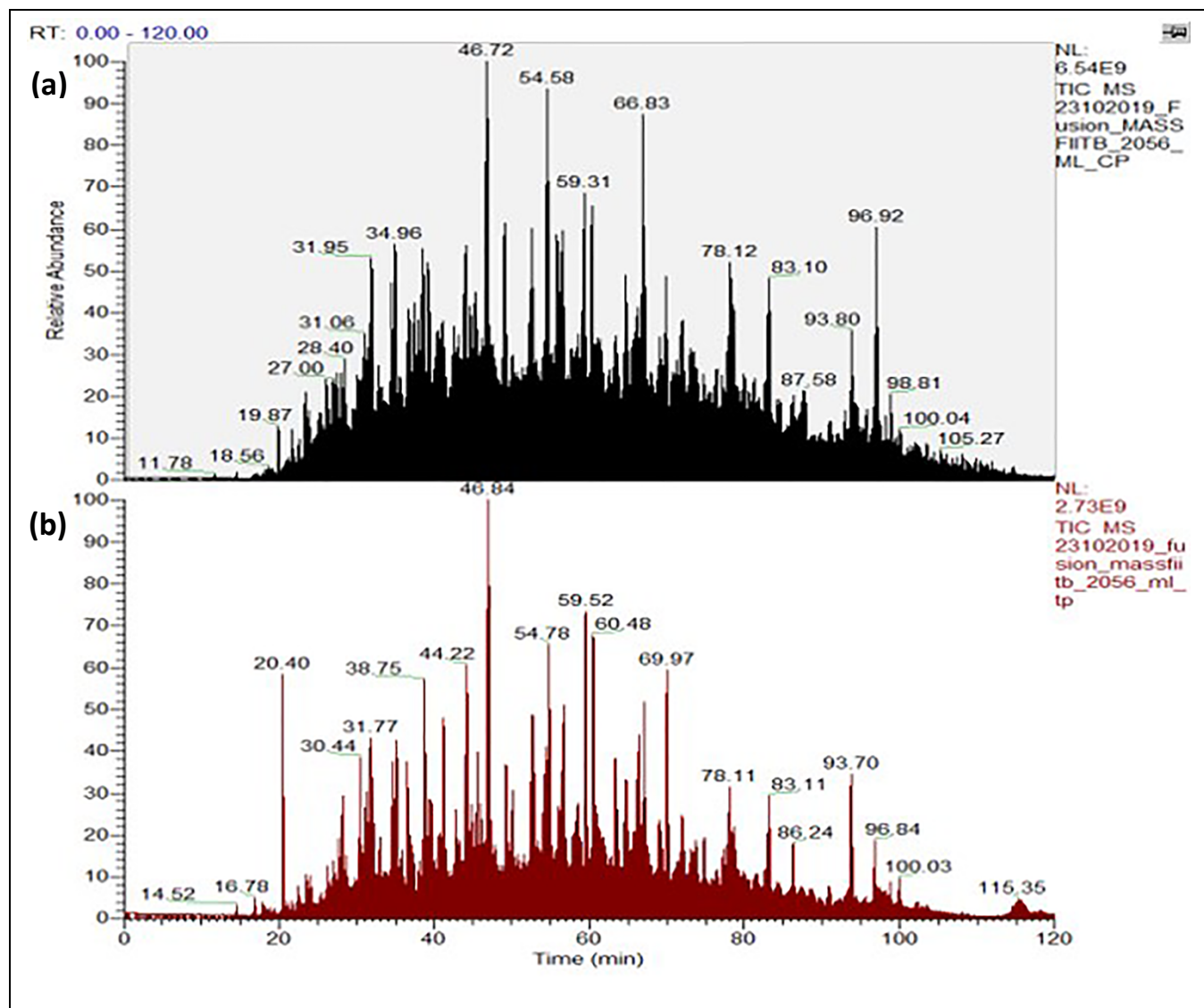
	dehydrogenase					
P05412	Transcription factor AP-1	3	9	42	35.7	8.76
Q96C36	Pyrroline-5-carboxylate reductase 2	2	8	31	33.6	7.77
Q8IVD9	NudC domain-containing protein 3	3	8	111	40.8	5.25
E9PF18	Hydroxyacyl-coenzyme A dehydrogenase	4	8	52	42.1	9.26
Q14558	Phosphoribosyl pyrophosphate synthase-associated protein 1	2	8	55	39.4	7.2
Q92615	La-related protein 4B	7	8	162	80.5	6.92
Q9H9A6	Leucine-rich repeat-containing protein 40	6	8	102	68.2	6.43
P02786	Transferrin receptor protein 1	7	8	127	84.8	6.61
P48147	Prolyl endopeptidase	4	7	108	80.6	5.86
O75792	Ribonuclease H2 subunit A	3	7	60	33.4	5.25
P05556	Integrin beta-1	7	7	80	88.4	5.39
Q13642	Four and a half LIM domains protein 1	3	7	67	36.2	8.97
Q16643	Drebrin	4	7	29	71.4	4.45
Q7L5N1	COP9 signalosome complex subunit 6	2	7	35	36.1	5.73
Q9UBS4	DnaJ homolog subfamily B member 11	3	7	65	40.5	6.18
P07686	Beta-hexosaminidase subunit beta	5	7	70	63.1	6.76
P52306	Rap1 GTPase-GDP dissociation stimulator 1	6	6	91	66.3	5.31
Q86U42	Polyadenylate-binding protein 2	4	6	67	32.7	5.06
Q01970	1-phosphatidylinositol 4,5-bisphosphate phosphodiesterase beta-3	6	6	113	138.7	5.9
P11498	Pyruvate carboxylase	6	6	70	129.6	6.84
P13674	Prolyl 4-hydroxylase subunit alpha-1	4	6	76	61	6.01
O43493	Trans-Golgi network integral membrane protein 2	4	6	60	51	5.73
A0A0G2JLB3	Glucosylceramidase	6	6	83	59.6	7.42
Q9Y5U2	Protein TSSC4	3	6	47	34.3	5.19
Q8N335	Glycerol-3-phosphate dehydrogenase 1-like protein	2	6	24	38.4	7.02

O43815	Striatin	5	6	109	86.1	5.27
Q70UQ0	Inhibitor of nuclear factor kappa-B kinase-interacting protein	4	5	70	39.3	9.17
Q8TDN6	Ribosome biogenesis protein BRX1 homolog	2	5	41	41.4	9.92
Q14683	Structural maintenance of chromosomes protein 1A	9	5	102	143.1	7.64
P53990	IST1 homolog	2	5	32	39.7	5.35
O75410	Transforming acidic coiled-coil-containing protein 1	4	5	108	87.7	4.88
Q96T60	Bifunctional polynucleotide phosphatase/kinase	6	5	110	57	8.46
A0A499FI31	Squamous cell carcinoma antigen recognized by T-cells 3	6	5	95	111.9	5.5
P55084	Trifunctional enzyme subunit beta	3	5	27	51.3	9.41
P48960	CD97 antigen	8	5	200	91.8	6.87
A0A2R8Y5Y7	60S ribosomal protein L9	3	5	53	25	9.74
Q9NVX2	Notchless protein homolog 1	2	5	32	53.3	7.34
P51003	Poly(A) polymerase alpha	3	5	27	82.8	7.37
A2A274	Aconitate hydratase	4	4	62	87.8	7.37
V9GYM8	Rho guanine nucleotide exchange factor 2	6	4	105	116	7.37
Q9NY93	Probable ATP-dependent RNA helicase DDX56	3	4	75	61.6	9.26
Q96JB5	CDK5 regulatory subunit-associated protein 3	3	4	58	56.9	4.75
O94925	Glutaminase kidney isoform	3	4	37	73.4	7.77
Q9BYT8	Neurolysin	4	4	76	80.6	6.64
Q96GA3	Protein LTV1 homolog	3	4	52	54.8	4.91
P10515	Dihydrolipoyllysine-residue acetyltransferase component of pyruvate dehydrogenase complex	3	4	112	69	7.84
Q9UFC0	Leucine-rich repeat and WD repeat-containing	2	4	55	70.8	7.21

	protein 1					
Q9H4L5	Oxysterol-binding protein-related protein 3	3	3	73	101.2	6.87
P54886	Delta-1-pyrroline-5-carboxylate synthase	3	3	52	87.2	7.12
O95202	Mitochondrial proton/calcium exchanger protein	4	3	71	83.3	6.7
Q92542	Nicastrin	3	3	33	78.4	5.99
A0A1B0GTL5	Rab11 family-interacting protein 5	4	3	45	138.3	5.21
O60568	Multifunctional procollagen lysine hydroxylase and glycosyltransferase LH3	3	3	63	84.7	6.05
O00469	Procollagen-lysine,2-oxoglutarate 5-dioxygenase 2	3	3	73	84.6	6.71
Q16891	MICOS complex subunit MIC60	2	3		83.6	6.48
Q96ST2	Protein IWS1 homolog	3	2	53	91.9	4.69
O43747	AP-1 complex subunit gamma-1	2	2	72	91.3	6.8
Q9NYF8	Bcl-2-associated transcription factor 1	3	2	44	106.1	9.98
Q9Y6A5	Transforming acidic coiled-coil-containing protein 3	2	2	59	90.3	5.05
P23229	Integrin alpha-6	2	2	65	126.5	6.61
A0A087X117	Nodal modulator 1	5	2	92	139.4	5.85
Q13751	Laminin subunit beta-3	5	2	111	129.5	7.21
P42704	Leucine-rich PPR motif-containing protein	3	2	74	157.8	6.13
Q14980	Nuclear mitotic apparatus protein 1	5	1	60	238.1	5.78
P27708	CAD protein	2	1	48	242.8	6.46

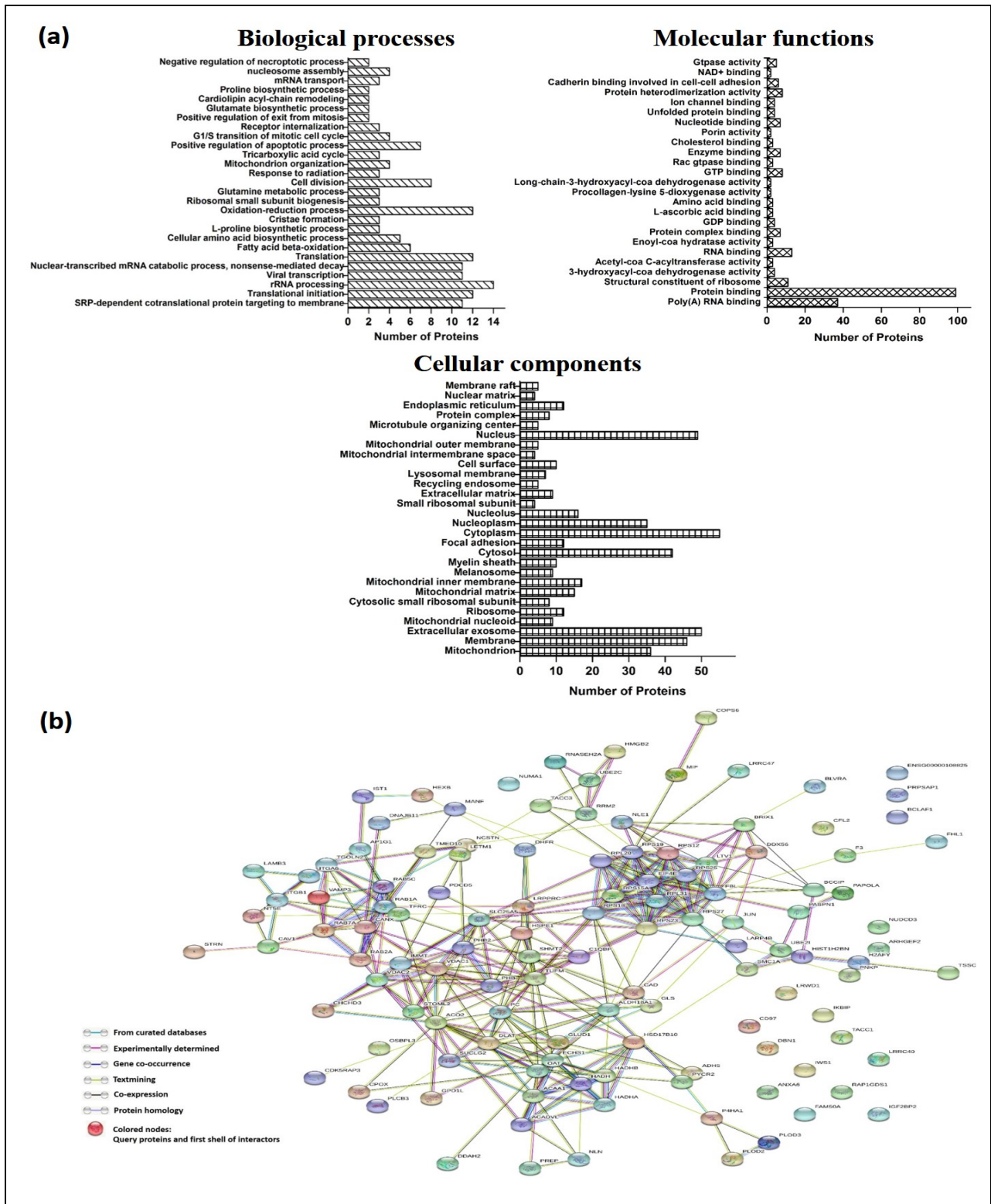
**Table S2.** Down-regulated proteins involved in metabolic pathways

<b>S.No</b>	<b>Uniprot ID</b>	<b>Protein Name</b>
1.	Q99714	3-hydroxyacyl-CoA dehydrogenase type-2
2.	P54886	Delta-1-pyrroline-5-carboxylate synthase
3.	P00367	Glutamate dehydrogenase 1
4.	P07686	Beta-hexosaminidase subunit beta
5.	P11766	Alcohol dehydrogenase class-3
6.	P30084	Enoyl-CoA hydratase
7.	P27708	CAD protein
8.	H0YFD6	Trifunctional enzyme subunit alpha
9.	P55084	Trifunctional enzyme subunit beta
10.	Q01970	1-phosphatidylinositol 4,5-bisphosphate phosphodiesterase beta-3
11.	P13674	Prolyl 4-hydroxylase subunit alpha-1
12.	P36551	Oxygen-dependent coproporphyrinogen-III oxidase
13.	E9PF18	Hydroxyacyl-coenzyme A dehydrogenase
14.	P21589	5'-nucleotidase
15.	A0A0G2JLB3	Glucosylceramidase
16.	P34897	Serine hydroxymethyltransferase
17.	A2A274	Aconitate hydratase
18.	Q96I99	Succinate--CoA ligase [GDP-forming] subunit beta
19.	P10515	Dihydrolipoyllysine-residue acetyltransferase component of pyruvate dehydrogenase complex
20.	P49748	Very long-chain specific acyl-CoA dehydrogenase
21.	Q96C36	Pyrroline-5-carboxylate reductase 2
22.	P00374	Dihydrofolate reductase
23.	P31350	Ribonucleoside-diphosphate reductase subunit M2
24.	O94925	Glutaminase kidney isoform
25.	P04181	Ornithine aminotransferase
26.	P09110	3-ketoacyl-CoA thiolase
27.	P11498	Pyruvate carboxylase

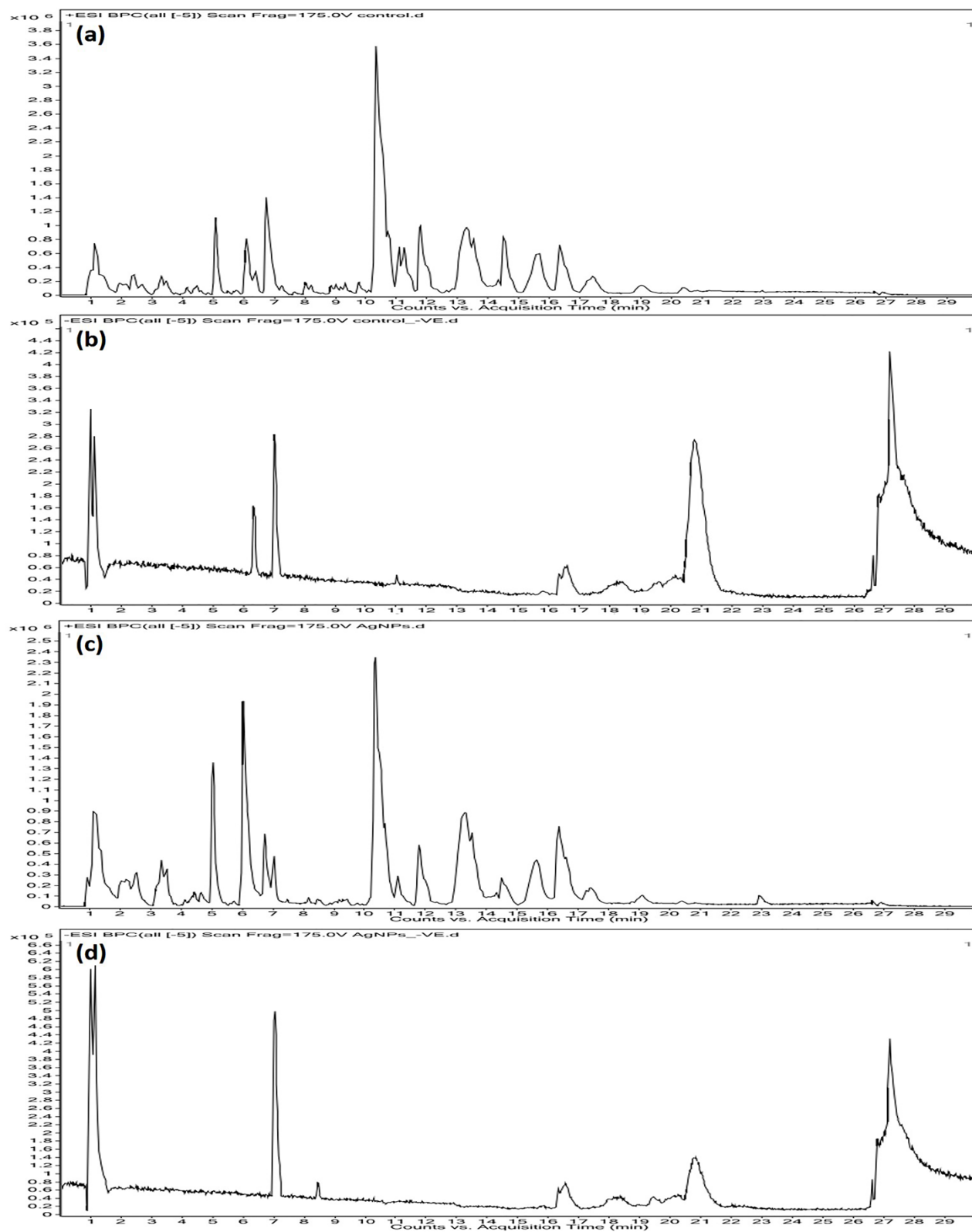


**Supplementary Figure 1.** Mass spectrometry-assisted proteomic analysis. (a) Total ion chromatogram plots for the (a) control and (b) T-AgNPs treated cells.





**Supplementary Figure 2.** (a) Differentially expressed proteins in treated cells grouped into GO terms. (b) The protein-protein interaction network of the 127 identified differentially expressed-proteins using STRING 11.5 database



**Supplementary Figure 3.** Mass spectrometry-assisted metabolomic analysis. Base peak chromatograms (BPC) in ESI  $^{+/-}$  mode. BPC of control cells in (a) positive and (b) negative mode; BPC of treated cells in (c) positive and (d) negative mode.