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Supporting Information

Molecular Responses of Human Lung Epithelial Cells to the Toxicity of Copper Oxide Nanoparticles Inferred from Whole Genome Expression Analysis

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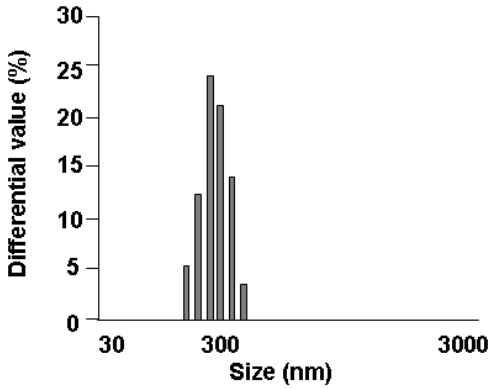


Figure S1. Particle size distribution of CuO-NPs (25 μg/mL) in culture medium assessed by using a laser diffraction particle size analyzer.

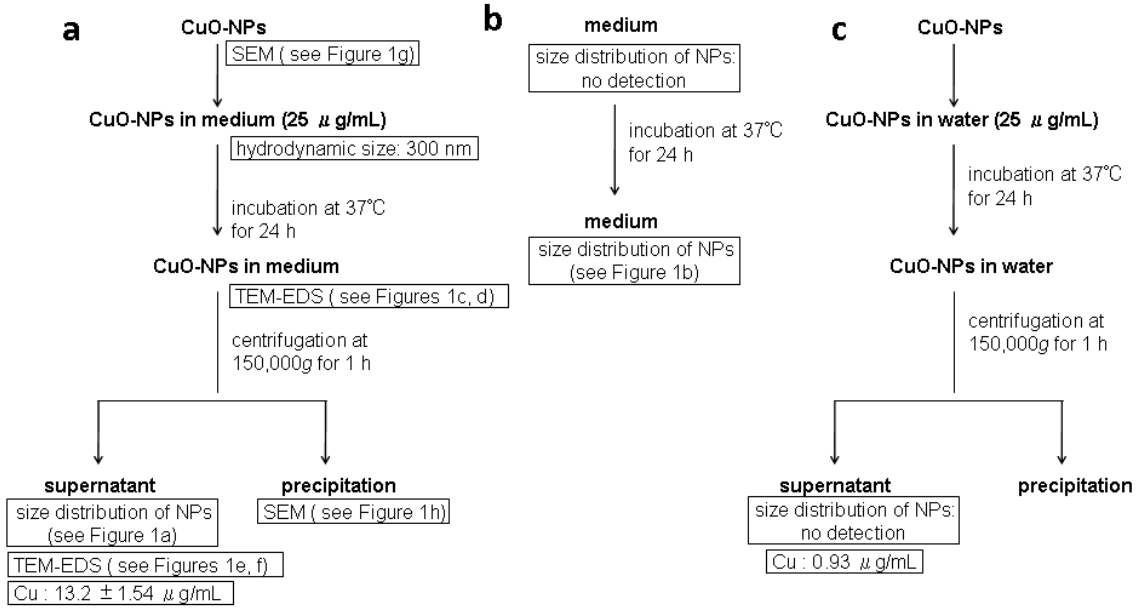


Figure S2. Preparation and characterization of medium containing Cu ions released from CuO-NPs. (**a)** The culture medium with CuO-NPs (25 μg/mL) was incubated at 37□ for 24 h, and then centrifuged. The supernatant was used to estimate contribution of Cu ions released from CuO-NPs into medium to CuO-NPs toxicity. (**b)** Culture medium without CuO-NPs was incubated at 37□ for 24 h, and then particle size distribution was measured with a laser diffraction size analyzer. (**c**) CuO-NPs in water were incubated at 37□ for 24 h, and then centrifuged. No particles were detected in the supernatant.

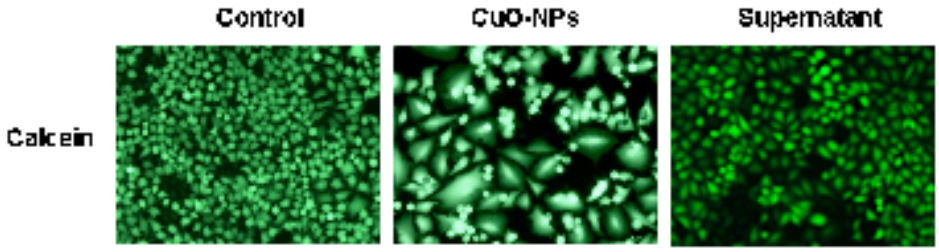


Figure S3. Cell viability as indicated by staining of cells that were exposed to CuO-NPs and the supernatant for 24 h with calcein acetoxymethyl ester (calcein-AM). A549 human lung epithelial cells were cultured in media containing 25 μg/mL CuO-NPs or the supernatant at 37□ for 24 h, and then the number of viable cells was compared to that of the control.

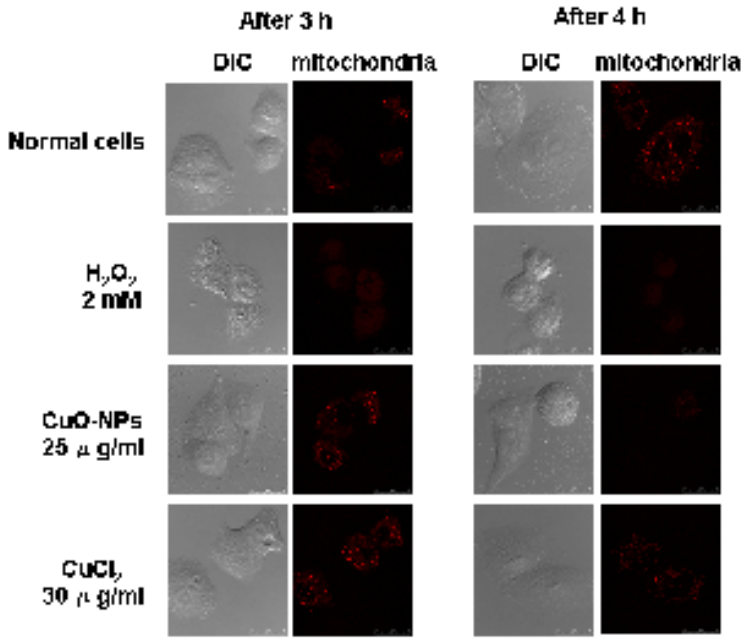


Figure S4. Damage to mitochondria by CuO-NPs. Mitochondrial damage in A549 human lung epithelial cells after exposure to H2O2 (2 mM), CuO-NPs (25 μg/mL), and CuCl2 (30 μg/mL) was measured by using 5,5′,6,6′-tetrachloro-1,1′,3,3′- tetraethylbenzimidazolylcarbocyanine iodide (JC-1; Invitrogen). The accumulation of JC-1 in mitochondria was measured by excitation at 543 nm and detection of fluorescence at 573–607 nm. Damaged mitochondria accumulated less JC-1, and therefore, exhibited less fluorescence. The mitochondria of cells that were exposed to CuO-NPs were damaged after 4 h. Cells that were exposed to CuCl2 also were damaged after 4 h; however, the damage was not as severe as that from CuO-NPs.

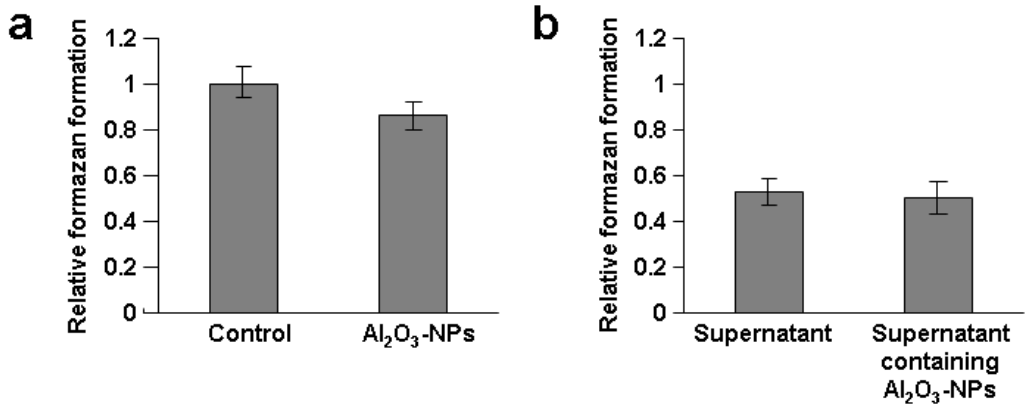


Figure S5. Effect of non-toxic dummy Al2O3-NPs on supernatant toxicity. (a) Cytotoxicity of Al2O3-NPs. The primary size of Al2O3-NPs was 50 nm and the hydrodynamic size was around 160 nm. A549 cells cultured for 48 h were exposed to Al2O3-NPs at a concentration of 25 μg/ml. After 24 h, a WST assay was performed. (b) Effect of Al2O3-NPs on the supernatant toxicity. A549 cells cultured for 48 h were exposed to supernatant and supernatant with Al2O3-NPs. The supernatant contained Cu ions released from CuO-NPs. After 24 h, a WST assay was performed. Zeta potential of Al2O3-NPs was -20.37 mV. Physicochemical character of Al2O3-NPs was previously reported (Xu et al., *Biomaterials* **2010**, 31, 8022-8031).

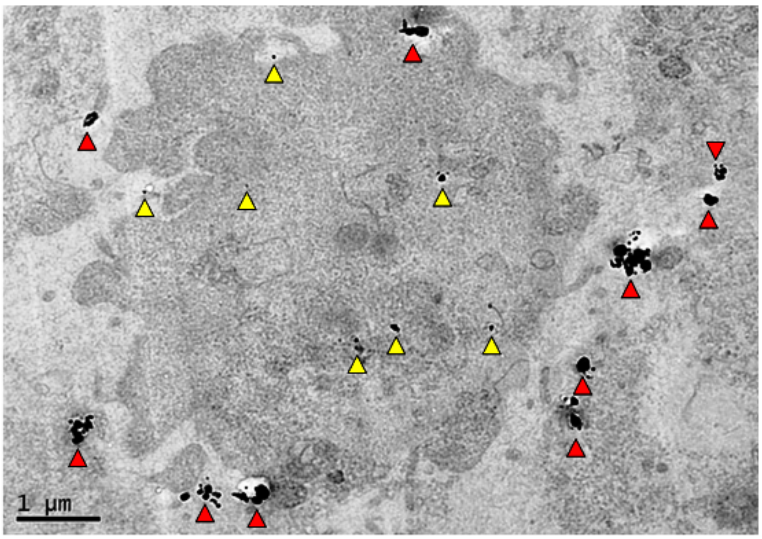


Figure S6. Internalized CuO-NPs observed by TEM. Yellow arrowheads indicate single or smaller (<100 nm) aggregated NPs. Red arrowheads indicate larger (> 100 nm) aggregated NPs. Cells were cultured in medium with 25 μ g/mL CuO-NPs for 24 h, and then living cells were harvested.

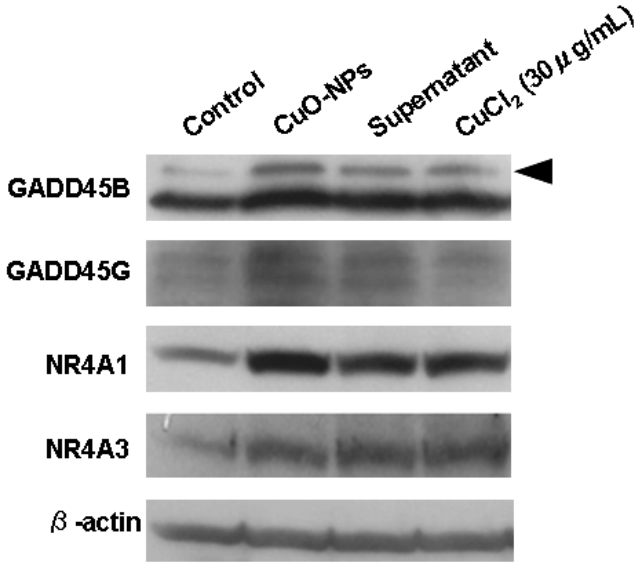


Figure S7. Western blotting analysis to confirm the change of gene expression. A549 cells were cultured for 48 h, and then exposed to 25 μg/mL CuO-NPs, supernatant and 30 μg/mL CuCl 2 for 24 h.

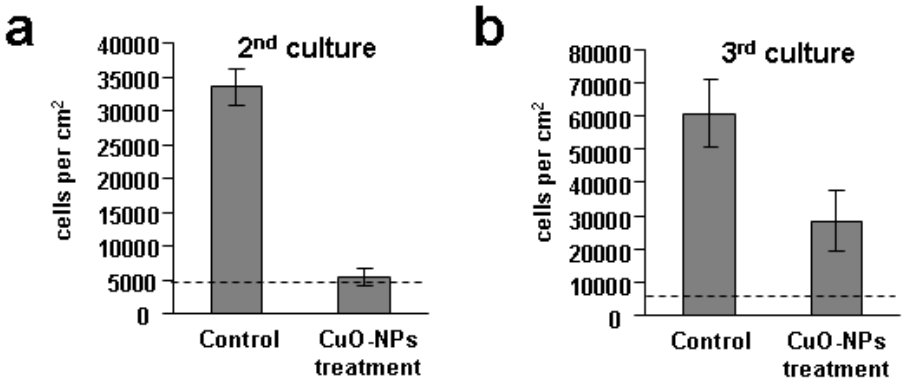


Figure S8. Cell cycle arrest due to CuO-NPs. Cells that were exposed to 25 μg/mL CuO-NPs were isolated, and then seeded in fresh culture medium that did not contain CuO-NPs at a density of 5000 cells/cm2. The left graph shows the number of cells after 72 h. The dotted line shows the number of cells at the time of the seeding. Cell proliferation was not observed. However, when the cells were harvested and seeded in fresh culture medium for an additional 72 h, cell proliferation resumed (right graph). Therefore, cell cycle arrest occurred after the cells were exposed to CuO-NPs.

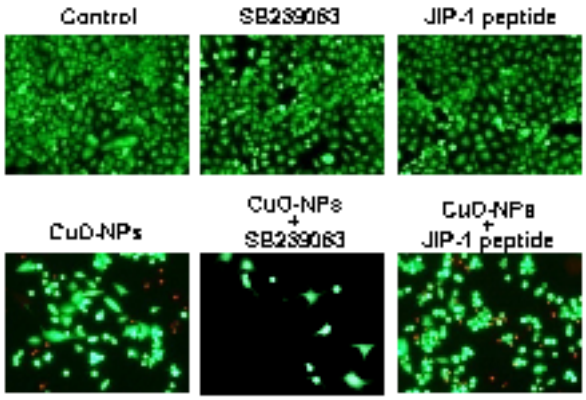


Figure S9. Effects of SB239063 and JNK interacting protein 1 (JIP-1), which are inhibitors of p38 and JNK, respectively. Double staining with calcein acetoxymethyl ester (calcein-AM) and propidium iodide (PI). SB239063 and CuO-NPs (CuO-NPs + SB239063) decreased the number of viable cells more than CuO-NPs alone. In the presence of SB239063, many cells that were exposed to CuO-NPs detached from the culture dish.

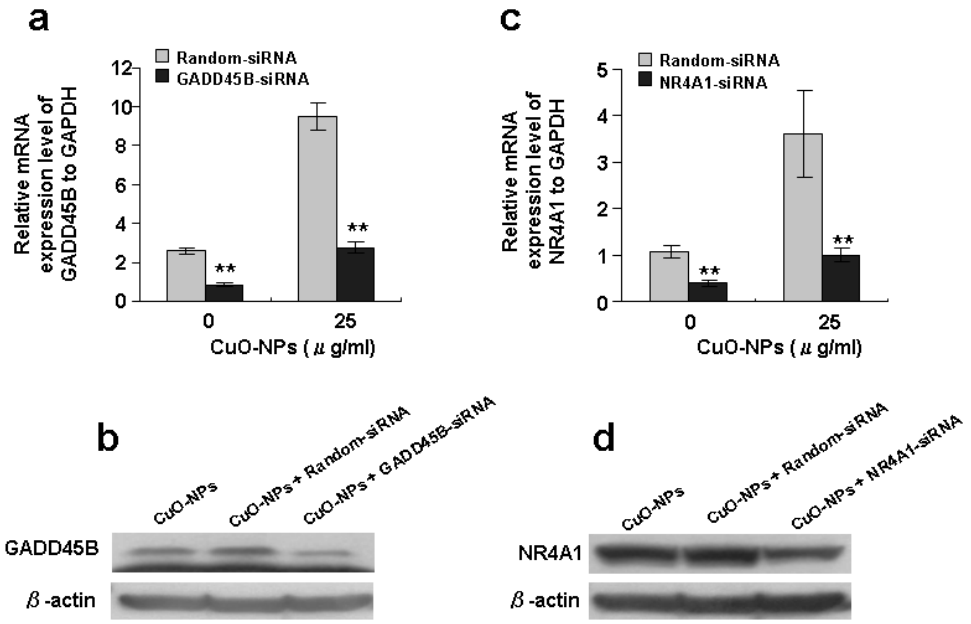


Figure S10. siRNA knockdown efficiency of *GADD45B* and *NR4A1*. (a) mRNA expression level of GADD45B. (b) Western blotting. The concentration of CuO-NPs was 25 μg/mL. GADD45B siRNA suppressed the expression at protein level. (c) mRNA expression level of NR4A1. (d) Western blotting. NR4A1 siRNA suppressed expression of NR4A1 at protein level.

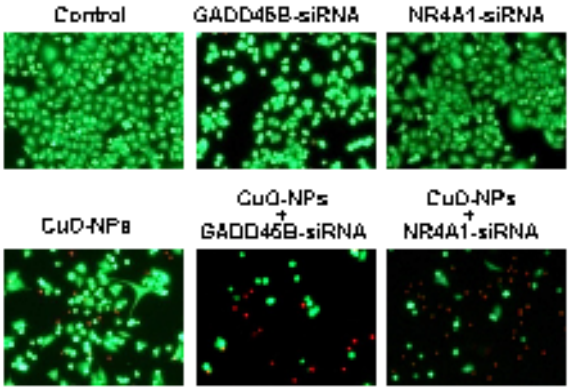


Figure S11. Effect of siRNA knockdown on the expression of *GADD45B* and *NR4A1* on the cytotoxicity of CuO-NPs. Double staining with calcein-AM and PI. Knockdown of *GADD45B* and *NR4A1* decreased the number of viable cells after cells were exposed to CuO-NPs. The number of dead cells as indicated by PI staining is not accurate because it included dead cells that detached from the surface of the culture dish.

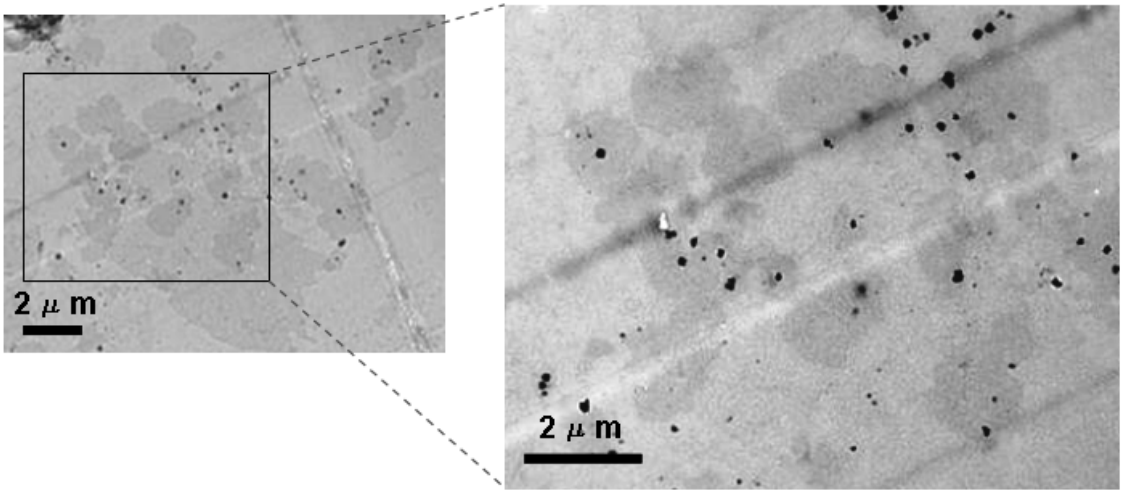


Figure S12. CuO-NPs in dead cell observed by TEM. Black dots indicate aggregates of CuO-NPs. Cells were cultured in medium with 25 μ g/mL CuO-NPs for 24 h, and then dead cells detached from culture dish were harvested. Right panel is a magnified image of leaflet in left panel.

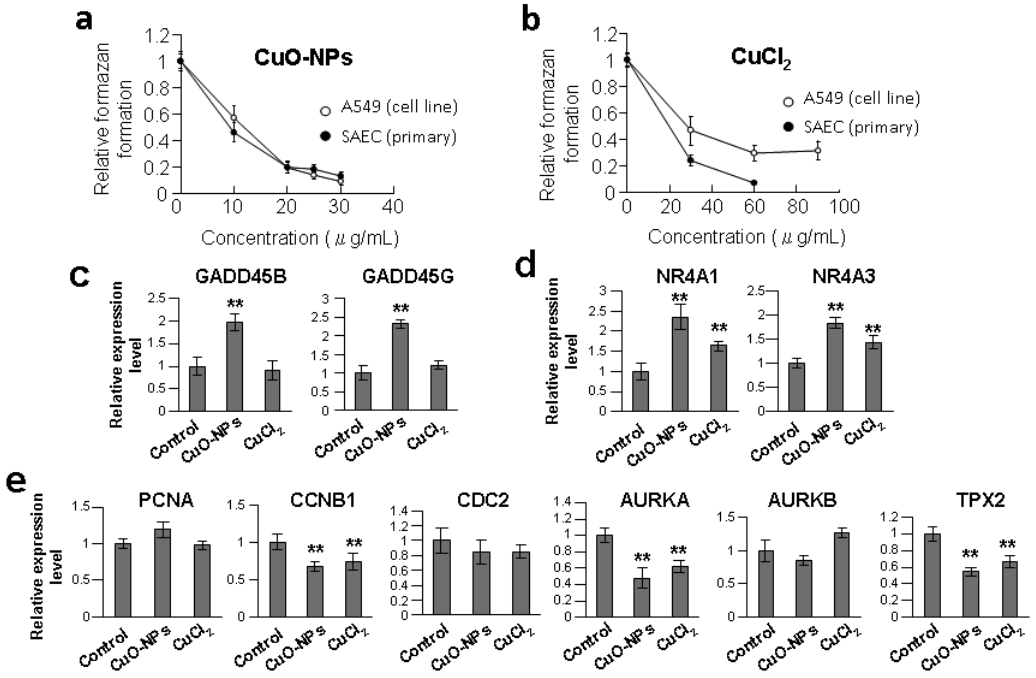


Figure S13. Cytotoxicity of CuO-NPs and Cu ions to primary human lung epithelial cells and change of gene expression. (a) Comparison of CuO-NPs toxicity between primary human epithelial cells (SAEC) and A549 cells. (b) Comparison of Cu ion toxicity between SAEC and A549 cells. (c-e) Expression level of genes in SAEC. Genes in (c) upregulated in CuO-NPs but not in 30 μ g/mL CuCl2 in A549 cells. SAEC cells showed similar pattern. Genes in (d) upregulated in both CuO-NPs and 30 μ g/mL CuCl2 in A549 cells. SAEC cells showed similar pattern. Genes in (e) downregulated in both CuO-NPs and 30 μ g/mL CuCl2 in A549 cells. SAEC cells showed similar pattern in CCNB1, AURKA and TPX2, but not PCNA, CDC2 and AURKB. For gene expression analysis, SAEC cells were exposed to media containing 25 μ g/mL CuO-NPs or 30 μ g/mL CuCl2 for 24 h.

Table S1. List of genes upregulated by CuO-NPs classified into the GO category of "Nucleobase, nucleoside, nucleotide and nucleic acid metabolic process". Fold-change is represented by logarithmic ratio (log_2 ratio) to expression level in control.

Gene name	Description	Fold- change (log_2 ratio)
ACRC	Homo sapiens acidic repeat containing (ACRC), mRNA [NM_052957]	2.82
AFF1	Homo sapiens AF4/FMR2 family, member 1 (AFF1), mRNA [NM_005935]	2.18
ALS2	Homo sapiens amyotrophic lateral sclerosis 2 (juvenile) (ALS2), transcript variant 2, mRNA [NM_001135745]	2.00
ARC	Homo sapiens activity-regulated cytoskeleton-associated protein (ARC), mRNA [NM_015193]	3.06
ATF1	Homo sapiens activating transcription factor 1 (ATF1), mRNA [NM_005171]	1.11
ATF3	Homo sapiens activating transcription factor 3 (ATF3), transcript variant 4, mRNA [NM_001040619]	4.22
ATP6V1A	Homo sapiens ATPase, H+ transporting, lysosomal 70kDa, V1 subunit A (ATP6V1A), mRNA [NM_001690]	1.34
ATP6V1B2	Homo sapiens ATPase, H+ transporting, lysosomal 56/58kDa, V1 subunit B2 (ATP6V1B2), mRNA [NM_001693]	1.23
ATP6V1C1	Homo sapiens ATPase, H+ transporting, lysosomal 42kDa, V1 subunit C1 (ATP6V1C1), mRNA [NM_001695]	2.31
ATP6V1D	Homo sapiens ATPase, H+ transporting, lysosomal 34kDa, V1 subunit D (ATP6V1D), mRNA [NM_015994]	1.85
ATP6V1G1	Homo sapiens ATPase, H+ transporting, lysosomal 13kDa, V1 subunit G1 (ATP6V1G1), mRNA [NM_004888]	1.49
ATP6V1H	Homo sapiens ATPase, H+ transporting, lysosomal 50/57kDa, V1 subunit H (ATP6V1H), transcript variant 1, mRNA [NM_015941]	1.26
BLOC1S1	Homo sapiens biogenesis of lysosomal organelles complex-1, subunit 1 (BLOC1S1), mRNA [NM_001487]	1.06
BRF2	Homo sapiens BRF2, subunit of RNA polymerase III transcription initiation factor, BRF1-like (BRF2), mRNA [NM_018310]	1.86
CARD6	Homo sapiens caspase recruitment domain family, member 6 (CARD6), mRNA [NM_032587]	1.10
CCNK	Homo sapiens cyclin K (CCNK), transcript variant 2, mRNA [NM_003858]	4.88
CDC40	Homo sapiens cell division cycle 40 homolog (S. cerevisiae) (CDC40), mRNA [NM_015891]	1.32
CDKN2AIP	Homo sapiens CDKN2A interacting protein (CDKN2AIP), mRNA [NM_017632]	1.18
CEBPG	Homo sapiens CCAAT/enhancer binding protein (C/EBP), gamma (CEBPG), mRNA [NM_001806]	1.09
CIR	Homo sapiens CBF1 interacting corepressor (CIR), mRNA [NM_004882]	1.21
CLU	Homo sapiens clusterin (CLU), transcript variant 2, mRNA [NM_203339]	1.24
CPEB4	Homo sapiens cytoplasmic polyadenylation element binding protein 4 (CPEB4), mRNA [NM_030627]	1.57
CREM	Homo sapiens cAMP responsive element modulator (CREM), transcript variant 19, mRNA [NM_183013]	1.15
CRIPT	Homo sapiens cysteine-rich PDZ-binding protein (CRIPT), mRNA [NM_014171]	1.73
CUGBP1	Homo sapiens CUG triplet repeat, RNA binding protein 1 (CUGBP1), transcript variant 2, mRNA [NM_198700]	1.65
DHX58	Homo sapiens DEXH (Asp-Glu-X-His) box polypeptide 58 (DHX58), mRNA [NM_024119]	2.22
E2F6	Homo sapiens E2F transcription factor 6 (E2F6), mRNA [NM_198256]	1.06
EGR1	Homo sapiens early growth response 1 (EGR1), mRNA [NM_001964]	3.89
ELL	Homo sapiens elongation factor RNA polymerase II (ELL), mRNA [NM_006532]	1.46
FBXL19	Homo sapiens F-box and leucine-rich repeat protein 19 (FBXL19), mRNA [NM_001099784]	1.46
FOS	Homo sapiens v-fos FBJ murine osteosarcoma viral oncogene homolog (FOS), mRNA [NM_005252]	4.48
FOSB	Homo sapiens FBJ murine osteosarcoma viral oncogene homolog B (FOSB), transcript variant 1, mRNA [NM_006732]	5.70
FOXN3	Homo sapiens forkhead box N3 (FOXN3), transcript variant 2, mRNA [NM_005197]	1.47
FSD1L	Homo sapiens fibronectin type III and SPRY domain containing 1-like (FSD1L), transcript variant 2, mRNA [NM_031919]	1.61
GABPA	Homo sapiens GA binding protein transcription factor, alpha subunit 60kDa (GABPA), mRNA [NM_002040]	2.89
GEM	Homo sapiens GTP binding protein overexpressed in skeletal muscle (GEM), transcript	1.60

	variant 1, mRNA [NM_005261]	
GRN	Homo sapiens granulin (GRN), mRNA [NM_002087]	1.08
GTF2B	Homo sapiens general transcription factor IIB (GTF2B), mRNA [NM_001514]	1.32
HBP1	Homo sapiens HMG-box transcription factor 1 (HBP1), mRNA [NM_012257]	2.84
HES1	Homo sapiens hairy and enhancer of split 1, (Drosophila) (HES1), mRNA [NM_005524]	1.52
HEY1	Homo sapiens hairy/enhancer-of-split related with YRPW motif 1 (HEY1), transcript variant 2, mRNA [NM_001040708]	1.22
HINT3	Homo sapiens histidine triad nucleotide binding protein 3 (HINT3), mRNA [NM_138571]	1.60
HIST1H2AM	Homo sapiens histone cluster 1, H2am (HIST1H2AM), mRNA [NM_003514]	1.42
HIST2H2AA4	Homo sapiens histone cluster 2, H2aa4 (HIST2H2AA4), mRNA [NM_001040874]	1.66
HIST2H2AB	Homo sapiens histone cluster 2, H2ab (HIST2H2AB), mRNA [NM_175065]	1.20
HNRNPH2	Homo sapiens heterogeneous nuclear ribonucleoprotein H2 (H') (HNRNPH2), transcript variant 1, mRNA [NM_019597]	1.42
HSF2	Homo sapiens heat shock transcription factor 2 (HSF2), transcript variant 1, mRNA [NM_004506]	1.28
HUS1	Homo sapiens HUS1 checkpoint homolog (S. pombe) (HUS1), mRNA [NM_004507]	1.32
ING4	Homo sapiens inhibitor of growth family, member 4 (ING4), transcript variant 1, mRNA [NM_016162]	1.54
ISG20	Homo sapiens interferon stimulated exonuclease gene 20kDa (ISG20), mRNA [NM_002201]	1.08
ISY1	Homo sapiens ISY1 splicing factor homolog (S. cerevisiae) (ISY1), mRNA [NM_020701]	1.11
JDP2	Homo sapiens Jun dimerization protein 2 (JDP2), transcript variant 1, mRNA [NM_130469]	1.13
KBTBD4	Homo sapiens kelch repeat and BTB (POZ) domain containing 4 (KBTBD4), transcript variant 2, mRNA [NM_016506]	1.48
KBTBD8	Homo sapiens kelch repeat and BTB (POZ) domain containing 8 (KBTBD8), mRNA [NM_032505]	1.97
KIAA1627	Homo sapiens KIAA1627 protein (KIAA1627), mRNA [NM_020961]	1.32
KLF7	Homo sapiens Kruppel-like factor 7 (ubiquitous) (KLF7), mRNA [NM_003709]	1.21
KLHL18	Homo sapiens kelch-like 18 (Drosophila), mRNA (cDNA clone IMAGE:4081125), partial cds. [BC015962]	1.16
LARP4	Homo sapiens La ribonucleoprotein domain family, member 4 (LARP4), transcript variant 2, mRNA [NM_199188]	1.76
LAT	Homo sapiens linker for activation of T cells (LAT), transcript variant 1, mRNA [NM_014387]	2.03
LATS2	Homo sapiens LATS, large tumor suppressor, homolog 2 (Drosophila) (LATS2), mRNA [NM_014572]	1.20
MAFF	Homo sapiens v-maf musculoaponeurotic fibrosarcoma oncogene homolog F (avian) (MAFF), transcript variant 1, mRNA [NM_012323]	2.26
MAFG	Homo sapiens v-maf musculoaponeurotic fibrosarcoma oncogene homolog G (avian) (MAFG), transcript variant 1, mRNA [NM_002359]	1.34
MAFK	Homo sapiens v-maf musculoaponeurotic fibrosarcoma oncogene homolog K (avian) (MAFK), mRNA [NM_002360]	1.55
MAGOH	Homo sapiens mago-nashi homolog, proliferation-associated (Drosophila) (MAGOH), mRNA [NM_002370]	1.18
MED13	Homo sapiens mediator complex subunit 13 (MED13), mRNA [NM_005121]	1.89
MED21	Homo sapiens mediator complex subunit 21 (MED21), mRNA [NM_004264]	1.12
MLXIPL	Homo sapiens MLX interacting protein-like (MLXIPL), transcript variant 1, mRNA [NM_032951]	1.73
MSI2	Homo sapiens musashi homolog 2 (Drosophila) (MSI2), transcript variant 2, mRNA [NM_170721]	1.52
MT1A	Homo sapiens metallothionein 1A (MT1A), mRNA [NM_005946]	2.19
MTF1	Homo sapiens metal-regulatory transcription factor 1 (MTF1), mRNA [NM_005955]	1.65
MXI1	Homo sapiens MAX interactor 1 (MXI1), transcript variant 2, mRNA [NM_130439]	1.77
MYNN	Homo sapiens myoneurin (MYNN), mRNA [NM_018657]	1.08
NAP1L5	Homo sapiens nucleosome assembly protein 1-like 5 (NAP1L5), mRNA [NM_153757]	1.01
NFATC1	Homo sapiens nuclear factor of activated T-cells, cytoplasmic, calcineurin-dependent 1 (NFATC1), transcript variant 1, mRNA [NM_172390]	1.83
NFIL3	Homo sapiens nuclear factor, interleukin 3 regulated (NFIL3), mRNA [NM_005384]	1.08

NR4A1	Homo sapiens nuclear receptor subfamily 4, group A, member 1 (NR4A1), transcript variant 1, mRNA [NM_002135]	5.28
NR4A3	Homo sapiens nuclear receptor subfamily 4, group A, member 3 (NR4A3), transcript variant 4, mRNA [NM_173199]	3.06
OGT	Homo sapiens O-linked N-acetylglucosamine (GlcNAc) transferase (UDP-N-acetylglucosamine:polypeptide-N-acetylglucosaminyl transferase) (OGT), transcript variant 1, mRNA [NM_181672]	1.38
PAIP2	Homo sapiens poly(A) binding protein interacting protein 2 (PAIP2), transcript variant 1, mRNA [NM_001033112]	1.12
PAPOLA	Homo sapiens poly(A) polymerase alpha (PAPOLA), mRNA [NM_032632]	1.60
PCF11	Homo sapiens PCF11, cleavage and polyadenylation factor subunit, homolog (S. cerevisiae) (PCF11), mRNA [NM_015885]	3.27
PHC3	Homo sapiens polyhomeotic homolog 3 (Drosophila) (PHC3), mRNA [NM_024947]	1.68
PHF1	Homo sapiens PHD finger protein 1 (PHF1), transcript variant 2, mRNA [NM_024165]	1.04
PHTF1	Homo sapiens putative homeodomain transcription factor 1 (PHTF1), mRNA [NM_006608]	1.39
PLRG1	Homo sapiens pleiotropic regulator 1 (PRL1 homolog, Arabidopsis) (PLRG1), mRNA [NM_002669]	1.38
PMS2L2	Homo sapiens postmeiotic segregation increased 2-like 2 pseudogene (PMS2L2), non-coding RNA [NR_003614]	1.02
PROP1	Homo sapiens PROP paired-like homeobox 1 (PROP1), mRNA [NM_006261]	1.95
PRPF18	Homo sapiens PRP18 pre-mRNA processing factor 18 homolog (S. cerevisiae) (PRPF18), mRNA [NM_003675]	1.43
RBBP6	Homo sapiens retinoblastoma binding protein 6 (RBBP6), transcript variant 1, mRNA [NM_006910]	1.10
RIOK3	Homo sapiens RIO kinase 3 (yeast) (RIOK3), mRNA [NM_003831]	2.38
RIT1	Homo sapiens Ras-like without CAAX 1 (RIT1), mRNA [NM_006912]	1.89
RLF	Homo sapiens rearranged L-myc fusion (RLF), mRNA [NM_012421]	1.44
RNF11	Homo sapiens ring finger protein 11 (RNF11), mRNA [NM_014372]	1.15
RNF12	Homo sapiens ring finger protein 12 (RNF12), transcript variant 1, mRNA [NM_016120]	1.68
RNF185	Homo sapiens ring finger protein 185 (RNF185), transcript variant 1, mRNA [NM_152267]	1.07
RNMT	Homo sapiens RNA (guanine-7-) methyltransferase (RNMT), mRNA [NM_003799]	1.27
RP2	Homo sapiens retinitis pigmentosa 2 (X-linked recessive) (RP2), mRNA [NM_006915]	1.35
RPUSD4	Homo sapiens RNA pseudouridylate synthase domain containing 4 (RPUSD4), mRNA [NM_032795]	1.06
RYBP	Homo sapiens RING1 and YY1 binding protein (RYBP), mRNA [NM_012234]	1.02
SBNO1	Homo sapiens cDNA FLJ23676 fis, clone HEP08548, highly similar to Homo sapiens mRNA for MOP-3. [AK074256]	1.19
SCML1	Homo sapiens sex comb on midleg-like 1 (Drosophila) (SCML1), transcript variant 1, mRNA [NM_001037540]	2.00
SIN3B	Homo sapiens SIN3 homolog B, transcription regulator (yeast), mRNA (cDNA clone IMAGE:3923074), partial cds. [BC025026]	1.28
SIRT6	Homo sapiens sirtuin (silent mating type information regulation 2 homolog) 6 (S. cerevisiae) (SIRT6), mRNA [NM_016539]	1.68
SLC25A44	Homo sapiens solute carrier family 25, member 44 (SLC25A44), transcript variant 1, mRNA [NM_014655]	1.12
SLU7	Homo sapiens SLU7 splicing factor homolog (S. cerevisiae) (SLU7), mRNA [NM_006425]	1.93
SNAI1	Homo sapiens snail homolog 1 (Drosophila) (SNAI1), mRNA [NM_005985]	3.18
SNIP1	Homo sapiens Smad nuclear interacting protein 1 (SNIP1), mRNA [NM_024700]	3.07
SOX8	Homo sapiens SRY (sex determining region Y)-box 8 (SOX8), mRNA [NM_014587]	1.93
SP1	Homo sapiens Sp1 transcription factor (SP1), transcript variant 1, mRNA [NM_138473]	2.03
SREBF2	Homo sapiens sterol regulatory element binding transcription factor 2 (SREBF2), mRNA [NM_004599]	1.32
SUPT4H1	Homo sapiens suppressor of Ty 4 homolog 1 (S. cerevisiae) (SUPT4H1), mRNA [NM_003168]	1.23
TAF13	Homo sapiens TAF13 RNA polymerase II, TATA box binding protein (TBP)-associated factor, 18kDa (TAF13), mRNA [NM_005645]	1.98
TAF7	Homo sapiens TAF7 RNA polymerase II, TATA box binding protein (TBP)-associated factor, 55kDa (TAF7), mRNA [NM_005642]	1.41

TAF8	Homo sapiens TAF8 RNA polymerase II, TATA box binding protein (TBP)-associated factor, 43kDa, mRNA (cDNA clone IMAGE:5166848), with apparent retained intron. [BC033728]	1.29
TDG	Homo sapiens thymine-DNA glycosylase (TDG), mRNA [NM_003211]	1.14
TEAD1	Homo sapiens TEA domain family member 1 (SV40 transcriptional enhancer factor) (TEAD1), mRNA [NM_021961]	1.30
TFIP11	Homo sapiens tuftelin interacting protein 11 (TFIP11), transcript variant 1, mRNA [NM_001008697]	1.28
THAP1	Homo sapiens THAP domain containing, apoptosis associated protein 1 (THAP1), transcript variant 1, mRNA [NM_018105]	1.16
TTF1	Homo sapiens transcription termination factor, RNA polymerase I (TTF1), mRNA [NM_007344]	1.00
UHMK1	Homo sapiens U2AF homology motif (UHM) kinase 1 (UHMK1), mRNA [NM_175866]	2.05
USP15	Homo sapiens ubiquitin specific peptidase 15 (USP15), mRNA [NM_006313]	1.33
USP32	Homo sapiens ubiquitin specific peptidase 32 (USP32), mRNA [NM_032582]	1.52
UTP11L	Homo sapiens UTP11-like, U3 small nucleolar ribonucleoprotein, (yeast) (UTP11L), mRNA [NM_016037]	1.28
ZBTB43	Homo sapiens zinc finger and BTB domain containing 43 (ZBTB43), transcript variant 1, mRNA [NM_014007]	1.89
ZBTB5	Homo sapiens zinc finger and BTB domain containing 5 (ZBTB5), mRNA [NM_014872]	1.43
ZNF10	Homo sapiens zinc finger protein 10 (ZNF10), mRNA [NM_015394]	2.81
ZNF12	Homo sapiens zinc finger protein 12 (ZNF12), transcript variant 1, mRNA [NM_016265]	1.00
ZNF121	Homo sapiens zinc finger protein 121 (ZNF121), mRNA [NM_001008727]	1.03
ZNF143	Homo sapiens zinc finger protein 143 (ZNF143), mRNA [NM_003442]	1.90
ZNF175	Homo sapiens zinc finger protein 175, mRNA (cDNA clone IMAGE:4301632), partial cds. [BC007778]	2.43
ZNF211	Homo sapiens zinc finger protein 211 (ZNF211), transcript variant 2, mRNA [NM_198855]	1.50
ZNF222	Homo sapiens zinc finger protein 222 (ZNF222), transcript variant 2, mRNA [NM_013360]	2.06
ZNF224	Homo sapiens cDNA FLJ78762 complete cds, highly similar to Homo sapiens zinc finger protein 224, mRNA. [AK292500]	1.61
ZNF236	Homo sapiens zinc finger protein 236 (ZNF236), mRNA [NM_007345]	1.02
ZNF256	Homo sapiens zinc finger protein 256 (ZNF256), mRNA [NM_005773]	1.65
ZNF257	Homo sapiens zinc finger protein 257 (ZNF257), mRNA [NM_033468]	1.47
ZNF266	Homo sapiens zinc finger protein 266 (ZNF266), mRNA [NM_006631]	1.12
ZNF274	Homo sapiens zinc finger protein 274 (ZNF274), transcript variant ZNF274c, mRNA [NM_133502]	1.19
ZNF277	Homo sapiens zinc finger protein 277 (ZNF277), mRNA [NM_021994]	1.17
ZNF286A	Homo sapiens zinc finger protein 286A (ZNF286A), transcript variant 1, mRNA [NM_020652]	2.20
ZNF324	Homo sapiens zinc finger protein 324 (ZNF324), mRNA [NM_014347]	1.09
ZNF331	Homo sapiens zinc finger protein 331 (ZNF331), transcript variant 1, mRNA [NM_018555]	1.48
ZNF34	Homo sapiens zinc finger protein 34 (ZNF34), mRNA [NM_030580]	1.40
ZNF37A	Homo sapiens zinc finger protein 37A (ZNF37A), transcript variant 1, mRNA [NM_001007094]	1.09
ZNF383	Homo sapiens zinc finger protein 383 (ZNF383), mRNA [NM_152604]	1.08
ZNF394	Homo sapiens zinc finger protein 394 (ZNF394), mRNA [NM_032164]	1.35
ZNF436	Homo sapiens zinc finger protein 436 (ZNF436), transcript variant 1, mRNA [NM_001077195]	1.76
ZNF461	Homo sapiens zinc finger protein 461 (ZNF461), mRNA [NM_153257]	1.68
ZNF473	Homo sapiens zinc finger protein 473 (ZNF473), transcript variant 1, mRNA [NM_015428]	1.92
ZNF484	Homo sapiens zinc finger protein 484 (ZNF484), transcript variant 2, mRNA [NM_001007101]	1.16
ZNF507	Homo sapiens zinc finger protein 507 (ZNF507), transcript variant 2, mRNA [NM_014910]	1.19
ZNF512	Homo sapiens zinc finger protein 512 (ZNF512), mRNA [NM_032434]	1.19
ZNF550	Homo sapiens zinc finger protein 550, mRNA (cDNA clone IMAGE:6044705). [BC053858]	1.04
ZNF557	Homo sapiens zinc finger protein 557 (ZNF557), transcript variant 1, mRNA [NM_024341]	1.78

ZNF558	Homo sapiens zinc finger protein 558 (ZNF558), mRNA [NM_144693]	1.05
ZNF565	Homo sapiens zinc finger protein 565 (ZNF565), transcript variant 1, mRNA [NM_001042474]	1.23
ZNF625	Homo sapiens zinc finger protein 625 (ZNF625), mRNA [NM_145233]	1.20
ZNF626	Homo sapiens zinc finger protein 626 (ZNF626), transcript variant 2, mRNA [NM_145297]	1.31
ZNF669	Homo sapiens zinc finger protein 669 (ZNF669), transcript variant 1, mRNA [NM_024804]	3.33
ZNF707	Homo sapiens zinc finger protein 707 (ZNF707), transcript variant 1, mRNA [NM_173831]	1.63
ZNF721	Homo sapiens zinc finger protein 721 (ZNF721), mRNA [NM_133474]	1.17
ZNF780B	Homo sapiens zinc finger protein 780B (ZNF780B), mRNA [NM_001005851]	1.14
ZNF79	Homo sapiens zinc finger protein 79 (ZNF79), mRNA [NM_007135]	1.08
ZNF8	Homo sapiens zinc finger protein 8 (ZNF8), mRNA [NM_021089]	2.14
ZRANB2	Homo sapiens zinc finger, RAN-binding domain containing 2 (ZRANB2), transcript variant 1, mRNA [NM_203350]	2.14
ZRSR2	Homo sapiens zinc finger (CCCH type), RNA-binding motif and serine/arginine rich 2 (ZRSR2), mRNA [NM_005089]	1.42
ZSCAN2	Homo sapiens zinc finger and SCAN domain containing 2 (ZSCAN2), transcript variant 2, mRNA [NM_017894]	1.12
ZSCAN20	Homo sapiens zinc finger and SCAN domain containing 20 (ZSCAN20), mRNA [NM_145238]	1.05

Table S2. List of genes upregulated by CuO-NPs classified into the GO category of "response to stress". Fold-change is represented by logarithmic ratio (log_2 ratio) to expression level in control.

Gene name	Description	Fold-change (log_2 ratio)
ATF1	Homo sapiens activating transcription factor 1 (ATF1), mRNA [NM_005171]	1.11
CDKL3	Homo sapiens cyclin-dependent kinase-like 3 (CDKL3), transcript variant 2, mRNA [NM_016508]	2.37
CLK1	Homo sapiens CDC-like kinase 1 (CLK1), mRNA [NM_004071]	2.18
CREM	Homo sapiens cAMP responsive element modulator (CREM), transcript variant 19, mRNA [NM_183013]	1.15
CRYAB	Homo sapiens crystallin, alpha B (CRYAB), mRNA [NM_001885]	4.36
DNAJA1	Homo sapiens DnaJ (Hsp40) homolog, subfamily A, member 1 (DNAJA1), mRNA [NM_001539]	1.33
DNAJA4	Homo sapiens PRO1472 mRNA, complete cds. [AF116663]	5.65
DNAJB1	Homo sapiens DnaJ (Hsp40) homolog, subfamily B, member 1 (DNAJB1), mRNA [NM_006145]	2.94
DNAJB6	Homo sapiens DnaJ (Hsp40) homolog, subfamily B, member 6 (DNAJB6), transcript variant 1, mRNA [NM_058246]	2.17
DNAJB9	Homo sapiens DnaJ (Hsp40) homolog, subfamily B, member 9 (DNAJB9), mRNA [NM_012328]	1.55
DNAJC3	Homo sapiens DnaJ (Hsp40) homolog, subfamily C, member 3, mRNA (cDNA clone IMAGE:5218144), with apparent retained intron. [BC033823]	1.60
FOS	Homo sapiens v-fos FBJ murine osteosarcoma viral oncogene homolog (FOS), mRNA [NM_005252]	4.48
FOSB	Homo sapiens FBJ murine osteosarcoma viral oncogene homolog B (FOSB), transcript variant 1, mRNA [NM_006732]	5.70
FSD1L	Homo sapiens fibronectin type III and SPRY domain containing 1-like (FSD1L), transcript variant 2, mRNA [NM_031919]	1.61
GADD45B	Homo sapiens growth arrest and DNA-damage-inducible, beta (GADD45B), mRNA [NM_015675]	2.96
GADD45G	Homo sapiens growth arrest and DNA-damage-inducible, gamma (GADD45G), mRNA [NM_006705]	3.59
HRH1	Homo sapiens histamine receptor H1 (HRH1), transcript variant 4, mRNA [NM_000861]	1.00
HSF2	Homo sapiens heat shock transcription factor 2 (HSF2), transcript variant 1, mRNA [NM_004506]	1.28
HSP90AA1	Homo sapiens heat shock protein 90kDa alpha (cytosolic), class A member 1 (HSP90AA1), transcript variant 2, mRNA [NM_005348]	1.20
HSPA13	Homo sapiens heat shock protein 70kDa family, member 13 (HSPA13), mRNA [NM_006948]	1.10
HSPA6	Homo sapiens heat shock 70kDa protein 6 (HSP70B') (HSPA6), mRNA [NM_002155]	4.67
HSPB8	Homo sapiens heat shock 22kDa protein 8 (HSPB8), mRNA [NM_014365]	1.99
HSPH1	Homo sapiens heat shock 105kDa/110kDa protein 1 (HSPH1), mRNA [NM_006644]	2.06
JDP2	Homo sapiens Jun dimerization protein 2 (JDP2), transcript variant 1, mRNA [NM_130469]	1.13
NLK	Homo sapiens nemo-like kinase (NLK), mRNA [NM_016231]	1.32
NR4A1	Homo sapiens nuclear receptor subfamily 4, group A, member 1 (NR4A1), transcript variant 1, mRNA [NM_002135]	5.28
NR4A3	Homo sapiens nuclear receptor subfamily 4, group A, member 3 (NR4A3), transcript variant 4, mRNA [NM_173199]	3.06
ST13	Homo sapiens suppression of tumorigenicity 13 (colon carcinoma) (Hsp70 interacting protein) (ST13), mRNA [NM_003932]	1.07
TTC1	Homo sapiens tetratricopeptide repeat domain 1 (TTC1), mRNA [NM_003314]	1.32
VEGFA	Homo sapiens vascular endothelial growth factor A (VEGFA), transcript variant 1, mRNA [NM_001025366]	1.24

Table S3. List of genes downregulated by CuO-NPs classified into the GO category of "cell cycle". Fold-change is represented by logarithmic ratio (log_2 ratio) to expression level in control. *, also classified into the category of "mitosis".

Gene name	Description	Fold-change (log_2 ratio)
ACTR3B*	Homo sapiens ARP3 actin-related protein 3 homolog B (yeast) (ACTR3B), transcript variant 2, mRNA [NM_001040135]	-1.07
ATR	Homo sapiens ataxia telangiectasia and Rad3 related (ATR), mRNA [NM_001184]	-1.11
AURKA*	Homo sapiens aurora kinase A (AURKA), transcript variant 1, mRNA [NM_198433]	-1.21
AURKB*	Homo sapiens aurora kinase B (AURKB), mRNA [NM_004217]	-1.13
AXL	Homo sapiens AXL receptor tyrosine kinase (AXL), transcript variant 1, mRNA [NM_021913]	-1.81
BCL2A1	Homo sapiens BCL2-related protein A1 (BCL2A1), transcript variant 1, mRNA [NM_004049]	-1.11
CCNA2*	Homo sapiens cyclin A2 (CCNA2), mRNA [NM_001237]	-1.39
CCNB1*	Homo sapiens cyclin B1 (CCNB1), mRNA [NM_031966]	-1.74
CCNB2*	Homo sapiens cyclin B2 (CCNB2), mRNA [NM_004701]	-1.44
CDC2*	Homo sapiens cell division cycle 2, G1 to S and G2 to M (CDC2), transcript variant 1, mRNA [NM_001786]	-1.41
CDC20	Homo sapiens cell division cycle 20 homolog (S. cerevisiae) (CDC20), mRNA [NM_001255]	-1.23
CDK6*	Homo sapiens cyclin-dependent kinase 6 (CDK6), mRNA [NM_001259]	-1.28
CDKN1B	Homo sapiens cyclin-dependent kinase inhibitor 1B (p27, Kip1) (CDKN1B), mRNA [NM_004064]	-1.30
CDKN2C	Homo sapiens cyclin-dependent kinase inhibitor 2C (p18, inhibits CDK4) (CDKN2C), transcript variant 2, mRNA [NM_078626]	-1.57
CIT*	Homo sapiens citron (rho-interacting, serine/threonine kinase 21) (CIT), mRNA [NM_007174]	-1.82
CKAP5	Homo sapiens cytoskeleton associated protein 5 (CKAP5), transcript variant 1, mRNA [NM_001008938]	-1.07
DBF4	Homo sapiens DBF4 homolog (S. cerevisiae) (DBF4), mRNA [NM_006716]	-1.37
DIS3L*	Homo sapiens DIS3 mitotic control homolog (S. cerevisiae)-like (DIS3L), transcript variant 2, mRNA [NM_133375]	-1.71
DLC1	Homo sapiens deleted in liver cancer 1 (DLC1), transcript variant 1, mRNA [NM_182643]	-1.09
DNAJC5	full-length cDNA clone CS0DN003YL17 of Adult brain of Homo sapiens (human). [CR607484]	-1.38
DST	Homo sapiens cDNA: FLJ21489 fis, clone COL05450. [AK025142]	-1.03
E2F7	Homo sapiens E2F transcription factor 7 (E2F7), mRNA [NM_203394]	-1.28
E2F8	Homo sapiens E2F transcription factor 8 (E2F8), mRNA [NM_024680]	-1.61
EFHB	Homo sapiens EF-hand domain family, member B (EFHB), mRNA [NM_144715]	-1.56
EIF2AK4	Homo sapiens eukaryotic translation initiation factor 2 alpha kinase 4 (EIF2AK4), mRNA [NM_001013703]	-1.17
EPHB2	Homo sapiens EPH receptor B2 (EPHB2), transcript variant 2, mRNA [NM_004442]	-1.28
ERBB2	Homo sapiens v-erb-b2 erythroblastic leukemia viral oncogene homolog 2, neuro/glioblastoma derived oncogene homolog (avian) (ERBB2), transcript variant 2, mRNA [NM_001005862]	-1.33
FBXL4	Homo sapiens F-box and leucine-rich repeat protein 4 (FBXL4), mRNA [NM_012160]	-1.09
FKBP7	Homo sapiens FK506 binding protein 7 (FKBP7), transcript variant 1, mRNA [NM_181342]	-1.06
FOXF2	Homo sapiens forkhead box F2 (FOXF2), mRNA [NM_001452]	-1.14
GPSM2*	Homo sapiens G-protein signaling modulator 2 (AGS3-like, C. elegans) (GPSM2), mRNA [NM_013296]	-1.19
GTSE1	Homo sapiens G-2 and S-phase expressed 1 (GTSE1), mRNA [NM_016426]	-1.42
JUB*	Homo sapiens jub, ajuba homolog (Xenopus laevis) (JUB), transcript variant 1, mRNA [NM_032876]	-1.41
KIAA1274	Homo sapiens KIAA1274 (KIAA1274), mRNA [NM_014431]	-1.14
KIAA1804	Homo sapiens mixed lineage kinase 4 (KIAA1804), mRNA [NM_032435]	-1.37
KIF18A*	Homo sapiens kinesin family member 18A (KIF18A), mRNA [NM_031217]	-1.17
KIF18B*	Homo sapiens hypothetical protein LOC146909, mRNA (cDNA clone IMAGE:4418755), partial cds. [BC048263]	-2.07
KIF20A*	Homo sapiens kinesin family member 20A (KIF20A), mRNA [NM_005733]	-2.05

KIF23*	Homo sapiens kinesin family member 23 (KIF23), transcript variant 1, mRNA [NM_138555]	-1.56
KIFC1*	Homo sapiens kinesin family member C1 (KIFC1), mRNA [NM_002263]	-1.26
MCM4	Homo sapiens minichromosome maintenance complex component 4 (MCM4), transcript variant 1, mRNA [NM_005914]	-1.09
MCM6	Homo sapiens minichromosome maintenance complex component 6 (MCM6), mRNA [NM_005915]	-1.10
MELK	Homo sapiens maternal embryonic leucine zipper kinase (MELK), mRNA [NM_014791]	-1.11
MOBKL2B*	Homo sapiens MOB1, Mps One Binder kinase activator-like 2B (yeast) (MOBKL2B), mRNA [NM_024761]	-1.11
MYBBP1A	Homo sapiens MYB binding protein (P160) 1a (MYBBP1A), transcript variant 2, mRNA [NM_014520]	-1.02
MYBL1	Homo sapiens v-myb myeloblastosis viral oncogene homolog (avian)-like 1 (MYBL1), mRNA [NM_001080416]	-1.84
MYC	Homo sapiens v-myc myelocytomatosis viral oncogene homolog (avian) (MYC), mRNA [NM_002467]	-1.48
MYH9*	Homo sapiens myosin, heavy chain 9, non-muscle (MYH9), mRNA [NM_002473]	-1.21
MYO5C*	Homo sapiens myosin VC (MYO5C), mRNA [NM_018728]	-1.39
NCAPD2*	Homo sapiens non-SMC condensin I complex, subunit D2 (NCAPD2), mRNA [NM_014865]	-1.12
NDC80	Homo sapiens NDC80 homolog, kinetochore complex component (S. cerevisiae) (NDC80), mRNA [NM_006101]	-1.01
NR2F2	Homo sapiens nuclear receptor subfamily 2, group F, member 2 (NR2F2), mRNA [NM_021005]	-1.11
NUF2*	Homo sapiens NUF2, NDC80 kinetochore complex component, homolog (S. cerevisiae) (NUF2), transcript variant 1, mRNA [NM_145697]	-1.17
OTUD4*	Homo sapiens OTU domain containing 4 (OTUD4), transcript variant 1, mRNA [NM_199324]	-1.47
PARP4	Homo sapiens poly (ADP-ribose) polymerase family, member 4 (PARP4), mRNA [NM_006437]	-1.18
PCNA	Homo sapiens proliferating cell nuclear antigen (PCNA), transcript variant 1, mRNA [NM_002592]	-1.37
PDGFA	Homo sapiens platelet-derived growth factor alpha polypeptide (PDGFA), transcript variant 1, mRNA [NM_002607]	-1.04
PLK2	Homo sapiens polo-like kinase 2 (Drosophila) (PLK2), mRNA [NM_006622]	-1.29
PMS1	Homo sapiens PMS1 postmeiotic segregation increased 1 (S. cerevisiae) (PMS1), transcript variant 1, mRNA [NM_000534]	-1.66
POLI*	Homo sapiens polymerase (DNA directed) iota (POLI), mRNA [NM_007195]	-1.58
PSKH1*	Homo sapiens protein serine kinase H1 (PSKH1), mRNA [NM_006742]	-1.28
PSRC1	Homo sapiens proline/serine-rich coiled-coil 1 (PSRC1), transcript variant 1, mRNA [NM_032636]	-1.61
PTPN13	Homo sapiens protein tyrosine phosphatase, non-receptor type 13 (APO-1/CD95 (Fas)-associated phosphatase) (PTPN13), transcript variant 4, mRNA [NM_080685]	-1.77
PTTG1*	Homo sapiens pituitary tumor-transforming 1 (PTTG1), mRNA [NM_004219]	-1.04
RAPGEF6*	Homo sapiens Rap guanine nucleotide exchange factor (GEF) 6 (RAPGEF6), mRNA [NM_016340]	-1.08
RBBP8	Homo sapiens retinoblastoma binding protein 8 (RBBP8), transcript variant 1, mRNA [NM_002894]	-1.31
ROR1	Tyrosine-protein kinase transmembrane receptor ROR1 Precursor (EC 2.7.10.1)(Neurotrophic tyrosine kinase, receptor-related 1) [Source:UniProtKB/Swiss-Prot;Acc:Q01973] [ENST00000371079]	-1.43
SASS6*	Homo sapiens spindle assembly 6 homolog (C. elegans) (SASS6), mRNA [NM_194292]	-1.07
SPTBN1	Homo sapiens spectrin, beta, non-erythrocytic 1 (SPTBN1), transcript variant 1, mRNA [NM_003128]	-1.21
SRGAP2	Homo sapiens SLIT-ROBO Rho GTPase activating protein 2 (SRGAP2), transcript variant 1, mRNA [NM_015326]	-1.17
TNS3	Homo sapiens tensin 3 (TNS3), mRNA [NM_022748]	-1.98
TOP2A*	Homo sapiens topoisomerase (DNA) II alpha 170kDa (TOP2A), mRNA [NM_001067]	-2.00
TPX2*	Homo sapiens TPX2, microtubule-associated, homolog (Xenopus laevis) (TPX2), mRNA [NM_012112]	-1.25
TRAF7	Homo sapiens TNF receptor-associated factor 7 (TRAF7), mRNA [NM_032271]	-1.01
TRIM14	Homo sapiens tripartite motif-containing 14 (TRIM14), transcript variant 1, mRNA	-1.87

	[NM_014788]	
TRIM59	Homo sapiens tripartite motif-containing 59 (TRIM59), mRNA [NM_173084]	-1.86
TRIM6	Homo sapiens tripartite motif-containing 6 (TRIM6), transcript variant 1, mRNA [NM_001003818]	-1.64
TUBA3D*	Homo sapiens tubulin, alpha 3d (TUBA3D), mRNA [NM_080386]	-1.20
TUBB2B*	Homo sapiens tubulin, beta 2B (TUBB2B), mRNA [NM_178012]	-1.07
TUBB6*	Homo sapiens tubulin, beta 6 (TUBB6), mRNA [NM_032525]	-1.21
UBE2T*	Homo sapiens ubiquitin-conjugating enzyme E2T (putative) (UBE2T), mRNA [NM_014176]	-1.14
UHRF1	Homo sapiens ubiquitin-like with PHD and ring finger domains 1 (UHRF1), transcript variant 2, mRNA [NM_013282]	-1.37
UTRN	Homo sapiens utrophin (UTRN), mRNA [NM_007124]	-1.01
YWHAH	Homo sapiens tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, eta polypeptide (YWHAH), mRNA [NM_003405]	-1.34
ZFP36L1*	Homo sapiens zinc finger protein 36, C3H type-like 1 (ZFP36L1), mRNA [NM_004926]	-1.45
ZFP36L2*	Homo sapiens zinc finger protein 36, C3H type-like 2 (ZFP36L2), mRNA [NM_006887]	-1.22

Table S4. List of genes downregulated by CuO-NPs classified into the GO category of "cytokinesis". Fold-change is represented by logarithmic ratio (log_2 ratio) to expression level in control.

Gene name	Description	Fold-change (log_2 ratio)
ACTR3B	Homo sapiens ARP3 actin-related protein 3 homolog B (yeast) (ACTR3B), transcript variant 2, mRNA [NM_001040135]	-1.069
AURKA	Homo sapiens aurora kinase A (AURKA), transcript variant 1, mRNA [NM_198433]	-1.206
AURKB	Homo sapiens aurora kinase B (AURKB), mRNA [NM_004217]	-1.129
CIT	Homo sapiens citron (rho-interacting, serine/threonine kinase 21) (CIT), mRNA [NM_007174]	-1.821
GPSM2	Homo sapiens G-protein signaling modulator 2 (AGS3-like, C. elegans) (GPSM2), mRNA [NM_013296]	-1.185
KIF18A	Homo sapiens kinesin family member 18A (KIF18A), mRNA [NM_031217]	-1.165
KIF18B	Homo sapiens hypothetical protein LOC146909, mRNA (cDNA clone IMAGE:4418755), partial cds. [BC048263]	-2.068
KIF20A	Homo sapiens kinesin family member 20A (KIF20A), mRNA [NM_005733]	-2.049
KIF20B	Homo sapiens kinesin family member 20B (KIF20B), mRNA [NM_016195]	-1.253
KIF23	Homo sapiens kinesin family member 23 (KIF23), transcript variant 1, mRNA [NM_138555]	-1.562
KIFC1	Homo sapiens kinesin family member C1 (KIFC1), mRNA [NM_002263]	-1.264
MOBKL2B	Homo sapiens MOB1, Mps One Binder kinase activator-like 2B (yeast) (MOBKL2B), mRNA [NM_024761]	-1.112
MYH9	Homo sapiens myosin, heavy chain 9, non-muscle (MYH9), mRNA [NM_002473]	-1.213
MYO5C	Homo sapiens myosin VC (MYO5C), mRNA [NM_018728]	-1.393
PSKH1	Homo sapiens protein serine kinase H1 (PSKH1), mRNA [NM_006742]	-1.281
PTPN13	Homo sapiens protein tyrosine phosphatase, non-receptor type 13 (APO-1/CD95 (Fas)-associated phosphatase) (PTPN13), transcript variant 4, mRNA [NM_080685]	-1.774

Table S5. List of genes downregulated by CuO-NPs classified into the GO category of "chromosome segregation". Fold-change is represented by logarithmic ratio (log_2 ratio) to expression level in control.

Gene name	Description	Fold-change (log_2 ratio)
KIF18A	Homo sapiens kinesin family member 18A (KIF18A), mRNA [NM_031217]	-1.17
KIF18B	Homo sapiens hypothetical protein LOC146909, mRNA (cDNA clone IMAGE:4418755), partial cds. [BC048263]	-2.07
KIF20A	Homo sapiens kinesin family member 20A (KIF20A), mRNA [NM_005733]	-2.05
KIF20B	Homo sapiens kinesin family member 20B (KIF20B), mRNA [NM_016195]	-1.25
KIF23	Homo sapiens kinesin family member 23 (KIF23), transcript variant 1, mRNA [NM_138555]	-1.56
KIFC1	Homo sapiens kinesin family member C1 (KIFC1), mRNA [NM_002263]	-1.26
NUF2	Homo sapiens NUF2, NDC80 kinetochore complex component, homolog (S. cerevisiae) (NUF2), transcript variant 1, mRNA [NM_145697]	-1.17
OTUD4	Homo sapiens OTU domain containing 4 (OTUD4), transcript variant 1, mRNA [NM_199324]	-1.47
POLI	Homo sapiens polymerase (DNA directed) iota (POLI), mRNA [NM_007195]	-1.58
PTTG1	Homo sapiens pituitary tumor-transforming 1 (PTTG1), mRNA [NM_004219]	-1.04
SASS6	Homo sapiens spindle assembly 6 homolog (C. elegans) (SASS6), mRNA [NM_194292]	-1.07
TOP2A	Homo sapiens topoisomerase (DNA) II alpha 170kDa (TOP2A), mRNA [NM_001067]	-2.00
TPX2	Homo sapiens TPX2, microtubule-associated, homolog (Xenopus laevis) (TPX2), mRNA [NM_012112]	-1.25
TUBA3D	Homo sapiens tubulin, alpha 3d (TUBA3D), mRNA [NM_080386]	-1.20
TUBB2B	Homo sapiens tubulin, beta 2B (TUBB2B), mRNA [NM_178012]	-1.07
TUBB6	Homo sapiens tubulin, beta 6 (TUBB6), mRNA [NM_032525]	-1.21
UBE2T	Homo sapiens ubiquitin-conjugating enzyme E2T (putative) (UBE2T), mRNA [NM_014176]	-1.14

Table S6. List of genes upregulated by CuO-NPs classified into the GO category of "cellular component organization". Fold-change is represented by logarithmic ratio (log_2 ratio) to expression level in control. *, Also classified into the category of "cellular component morphogenesis"

Gene name	Description	Fold-change (log_2 ratio)
ACTR3B*	Homo sapiens ARP3 actin-related protein 3 homolog B (yeast) (ACTR3B), transcript variant 2, mRNA [NM_001040135]	-1.07
ANGPTL4*	Homo sapiens angiopoietin-like 4 (ANGPTL4), transcript variant 1, mRNA [NM_139314]	-1.09
ATR	Homo sapiens ataxia telangiectasia and Rad3 related (ATR), mRNA [NM_001184]	-1.11
ATRX	Homo sapiens alpha thalassemia/mental retardation syndrome X-linked (RAD54 homolog, S. cerevisiae) (ATRX), transcript variant 1, mRNA [NM_000489]	-1.04
CENPA	Homo sapiens centromere protein A (CENPA), transcript variant 1, mRNA [NM_001809]	-1.80
CIT*	Homo sapiens citron (rho-interacting, serine/threonine kinase 21) (CIT), mRNA [NM_007174]	-1.82
CKAP5*	Homo sapiens cytoskeleton associated protein 5 (CKAP5), transcript variant 1, mRNA [NM_001008938]	-1.07
CLDN23*	Homo sapiens claudin 23 (CLDN23), mRNA [NM_194284]	-1.11
COCH*	Homo sapiens coagulation factor C homolog, cochlin (Limulus polyphemus) (COCH), transcript variant 2, mRNA [NM_004086]	-1.05
COL4A1*	Homo sapiens collagen, type IV, alpha 1 (COL4A1), mRNA [NM_001845]	-1.01
COL5A1*	Homo sapiens collagen, type V, alpha 1 (COL5A1), mRNA [NM_000093]	-1.30
COL5A2*	Homo sapiens collagen, type V, alpha 2 (COL5A2), mRNA [NM_000393]	-1.03
DAPK1*	Homo sapiens death-associated protein kinase 1 (DAPK1), mRNA [NM_004938]	-1.44
DLC1*	Homo sapiens deleted in liver cancer 1 (DLC1), transcript variant 1, mRNA [NM_182643]	-1.09
DLG5*	Homo sapiens discs, large homolog 5 (Drosophila) (DLG5), mRNA [NM_004747]	-1.36
DST*	Homo sapiens cDNA: FLJ21489 fis, clone COL05450. [AK025142]	-1.03
EHMT1	Homo sapiens euchromatic histone-lysine N-methyltransferase 1 (EHMT1), mRNA [NM_024757]	-1.18
EVI5*	Homo sapiens ecotropic viral integration site 5 (EVI5), mRNA [NM_005665]	-1.08
FOXF2*	Homo sapiens forkhead box F2 (FOXF2), mRNA [NM_001452]	-1.14
GEMIN5	Homo sapiens gem (nuclear organelle) associated protein 5 (GEMIN5), mRNA [NM_015465]	-1.59
GTSE1*	Homo sapiens G-2 and S-phase expressed 1 (GTSE1), mRNA [NM_016426]	-1.42
H1FX	Homo sapiens H1 histone family, member X (H1FX), mRNA [NM_006026]	-1.52
H2AFX	Homo sapiens H2A histone family, member X (H2AFX), mRNA [NM_002105]	-1.16
HMGB2	Homo sapiens high-mobility group box 2 (HMGB2), transcript variant 1, mRNA [NM_002129]	-2.06
IPP*	Homo sapiens intracisternal A particle-promoted polypeptide (IPP), mRNA [NM_005897]	-1.05
JUB*	Homo sapiens jub, ajuba homolog (Xenopus laevis) (JUB), transcript variant 1, mRNA [NM_032876]	-1.41
KIAA1804*	Homo sapiens mixed lineage kinase 4 (KIAA1804), mRNA [NM_032435]	-1.37
KIF18A*	Homo sapiens kinesin family member 18A (KIF18A), mRNA [NM_031217]	-1.17
KIF18B*	Homo sapiens hypothetical protein LOC146909, mRNA (cDNA clone IMAGE:4418755), partial cds. [BC048263]	-2.07
KIF20A*	Homo sapiens kinesin family member 20A (KIF20A), mRNA [NM_005733]	-2.05
KIF20B	Homo sapiens kinesin family member 20B (KIF20B), mRNA [NM_016195]	-1.25
KIF23*	Homo sapiens kinesin family member 23 (KIF23), transcript variant 1, mRNA [NM_138555]	-1.56
KIFC1*	Homo sapiens kinesin family member C1 (KIFC1), mRNA [NM_002263]	-1.26
KLHDC5*	Homo sapiens kelch domain containing 5 (KLHDC5), mRNA [NM_020782]	-1.43
LIMK2*	Homo sapiens LIM domain kinase 2 (LIMK2), transcript variant 2b, mRNA [NM_016733]	-1.18
LMNB1*	Homo sapiens lamin B1 (LMNB1), mRNA [NM_005573]	-2.04
LMNB2*	Homo sapiens lamin B2 (LMNB2), mRNA [NM_032737]	-1.71
MELK*	Homo sapiens maternal embryonic leucine zipper kinase (MELK), mRNA [NM_014791]	-1.11
MESDC1*	Homo sapiens mesoderm development candidate 1 (MESDC1), mRNA [NM_022566]	-1.01
MYO1B*	Homo sapiens myosin IB (MYO1B), transcript variant 2, mRNA [NM_012223]	-1.30
MYO5C*	Homo sapiens myosin VC (MYO5C), mRNA [NM_018728]	-1.39

NCAPD2	Homo sapiens non-SMC condensin I complex, subunit D2 (NCAPD2), mRNA [NM_014865]	-1.12
OBSL1*	Homo sapiens obscurin-like 1 (OBSL1), mRNA [NM_015311]	-1.11
OLFML2A*	Homo sapiens olfactomedin-like 2A (OLFML2A), mRNA [NM_182487]	-1.15
PCDH9*	Homo sapiens protocadherin 9 (PCDH9), transcript variant 1, mRNA [NM_203487]	-1.43
PDGFA*	Homo sapiens platelet-derived growth factor alpha polypeptide (PDGFA), transcript variant 1, mRNA [NM_002607]	-1.04
PODXL*	Homo sapiens podocalyxin-like (PODXL), transcript variant 1, mRNA [NM_001018111]	-1.69
PSKH1*	Homo sapiens protein serine kinase H1 (PSKH1), mRNA [NM_006742]	-1.28
PSRC1*	Homo sapiens proline/serine-rich coiled-coil 1 (PSRC1), transcript variant 1, mRNA [NM_032636]	-1.61
SASS6	Homo sapiens spindle assembly 6 homolog (C. elegans) (SASS6), mRNA [NM_194292]	-1.07
SETBP1	Homo sapiens SET binding protein 1 (SETBP1), transcript variant 1, mRNA [NM_015559]	-1.04
SIM2	Homo sapiens single-minded homolog 2 (Drosophila) (SIM2), transcript variant SIM2, mRNA [NM_005069]	-1.41
SPTBN1*	Homo sapiens spectrin, beta, non-erythrocytic 1 (SPTBN1), transcript variant 1, mRNA [NM_003128]	-1.21
TBC1D9B*	Homo sapiens TBC1 domain family, member 9B (with GRAM domain) (TBC1D9B), transcript variant 1, mRNA [NM_198868]	-1.08
THSD7A*	Homo sapiens cDNA FLJ11022 fis, clone PLACE1003771. [AK001884]	-1.39
TPM1*	Homo sapiens tropomyosin 1 (alpha) (TPM1), transcript variant 5, mRNA [NM_000366]	-1.09
TRIOBP*	Homo sapiens TRIO and F-actin binding protein (TRIOBP), transcript variant 6, mRNA [NM_001039141]	-1.20
TUBA3D*	Homo sapiens tubulin, alpha 3d (TUBA3D), mRNA [NM_080386]	-1.20
TUBB2B*	Homo sapiens tubulin, beta 2B (TUBB2B), mRNA [NM_178012]	-1.07
TUBB6*	Homo sapiens tubulin, beta 6 (TUBB6), mRNA [NM_032525]	-1.21
UTRN*	Homo sapiens utrophin (UTRN), mRNA [NM_007124]	-1.01

Table S7. List of shared genes whose expressions were upregulated in cells exposed to both CuO-NPs and released Cu ions. Fold-change is represented by logarithmic ratio (log_2 ratio) to expression level in control.

Gene name	Description	Fold-change (log_2 ratio)	
		CuO-NPs	Cu ions
MT1F	Homo sapiens metallothionein 1F (MT1F), mRNA [NM_005949]	4.80	4.59
NR4A1	Homo sapiens nuclear receptor subfamily 4, group A, member 1 (NR4A1), transcript variant 1, mRNA [NM_002135]	5.28	2.71
LOC100129113	Homo sapiens cDNA FLJ37158 fis, clone BRACE2026293. [AK094477]	2.71	2.31
DHRS2	Homo sapiens dehydrogenase/reductase (SDR family) member 2 (DHRS2), transcript variant 1, mRNA [NM_182908]	2.45	2.24
CSTA	Homo sapiens cystatin A (stefin A) (CSTA), mRNA [NM_005213]	2.15	2.12
VCX3A	Homo sapiens variable charge, X-linked 3A (VCX3A), mRNA [NM_016379]	5.29	2.11
MT1G	Homo sapiens metallothionein 1G (MT1G), mRNA [NM_005950]	2.31	2.10
NUPR1	Homo sapiens nuclear protein 1 (NUPR1), transcript variant 1, mRNA [NM_001042483]	2.40	2.10
MT2A	Homo sapiens metallothionein 2A (MT2A), mRNA [NM_005953]	2.24	1.98
CDK5R2	Homo sapiens cyclin-dependent kinase 5, regulatory subunit 2 (p39) (CDK5R2), mRNA [NM_003936]	2.06	1.96
MT1E	Homo sapiens unknown mRNA. [AF495759]	2.16	1.95
HTRA3	Homo sapiens HtrA serine peptidase 3 (HTRA3), mRNA [NM_053044]	2.51	1.93
LOC133874	Homo sapiens hypothetical gene LOC133874 (LOC133874), mRNA [NM_001102609]	1.92	1.84
S100P	Homo sapiens S100 calcium binding protein P (S100P), mRNA [NM_005980]	2.15	1.84
MT1A	Homo sapiens metallothionein 1A (MT1A), mRNA [NM_005946]	2.19	1.75
MT1X	Homo sapiens metallothionein 1X (MT1X), mRNA [NM_005952]	1.98	1.71
SPANXD	Homo sapiens SPANX family, member D (SPANXD), mRNA [NM_032417]	2.54	1.68
GABARAPL1	Homo sapiens GABA(A) receptor-associated protein like 1 (GABARAPL1), mRNA [NM_031412]	4.44	1.62
MT1B	Homo sapiens metallothionein 1B (MT1B), mRNA [NM_005947]	2.24	1.60
INSIG1	Homo sapiens insulin induced gene 1 (INSIG1), transcript variant 2, mRNA [NM_198336]	2.42	1.58
MT1H	Homo sapiens metallothionein 1H (MT1H), mRNA [NM_005951]	1.98	1.57
SPANXA1	Homo sapiens sperm protein associated with the nucleus, X-linked, family member A1 (SPANXA1), mRNA [NM_013453]	2.18	1.55
MT1L	Homo sapiens metallothionein 1L (gene/pseudogene) (MT1L), non-coding RNA [NR_001447]	1.79	1.52
BEX2	Homo sapiens brain expressed X-linked 2 (BEX2), mRNA [NM_032621]	3.29	1.49
SPANXB2	Homo sapiens SPANX family, member B2 (SPANXB2), mRNA [NM_145664]	2.20	1.48
SNX8	Homo sapiens sorting nexin 8 (SNX8), mRNA [NM_013321]	1.80	1.45
KIAA0430	Homo sapiens KIAA0430 (KIAA0430), mRNA [NM_014647]	1.47	1.44
IGF2	Homo sapiens insulin-like growth factor 2 (somatomedin A) (IGF2), transcript variant 1, mRNA [NM_000612]	1.36	1.47
CLCN6	Homo sapiens chloride channel 6 (CLCN6), transcript variant ClC-6a, mRNA [NM_001286]	1.73	1.32
ASNS	Homo sapiens asparagine synthetase, mRNA (cDNA clone IMAGE:5266877), **** WARNING: chimeric clone ****. [BC030024]	1.58	1.32
PNPLA8	Homo sapiens patatin-like phospholipase domain containing 8 (PNPLA8), mRNA [NM_015723]	2.06	1.27
TAF8	Homo sapiens TAF8 RNA polymerase II, TATA box binding protein (TBP)-associated factor, 43kDa, mRNA (cDNA clone IMAGE:5166848), with apparent retained intron. [BC033728]	1.29	1.24
TRIB3	Homo sapiens tribbles homolog 3 (Drosophila) (TRIB3), mRNA [NM_021158]	1.57	1.20
SEC61A2	Homo sapiens Sec61 alpha 2 subunit (S. cerevisiae) (SEC61A2), transcript variant 1, mRNA [NM_018144]	1.72	1.15
OR5L2	Homo sapiens olfactory receptor, family 5, subfamily L, member 2 (OR5L2), mRNA [NM_001004739]	1.36	1.14

FXC1	Homo sapiens fracture callus 1 homolog (rat) (FXC1), nuclear gene encoding mitochondrial protein, mRNA [NM_012192]	1.13	1.14
BNIP3L	Homo sapiens BCL2/adenovirus E1B 19kDa interacting protein 3-like (BNIP3L), mRNA [NM_004331]	2.17	1.11
PPP1R3B	Homo sapiens protein phosphatase 1, regulatory (inhibitor) subunit 3B (PPP1R3B), mRNA [NM_024607]	1.14	1.10
SIRT6	Homo sapiens sirtuin (silent mating type information regulation 2 homolog) 6 (S. cerevisiae) (SIRT6), mRNA [NM_016539]	1.68	1.10
CYB5R2	Homo sapiens cytochrome b5 reductase 2 (CYB5R2), mRNA [NM_016229]	1.08	1.11
GDF15	Homo sapiens growth differentiation factor 15 (GDF15), mRNA [NM_004864]	1.08	1.95
CTSL2	Homo sapiens cathepsin L2 (CTSL2), mRNA [NM_001333]	1.44	1.07
SOD2	Homo sapiens superoxide dismutase 2, mitochondrial (SOD2), nuclear gene encoding mitochondrial protein, transcript variant 2, mRNA [NM_001024465]	1.28	1.07
C1S	Homo sapiens complement component 1, s subcomponent (C1S), transcript variant 1, mRNA [NM_001734]	1.06	1.21
MSI2	Homo sapiens musashi homolog 2 (Drosophila) (MSI2), transcript variant 2, mRNA [NM_170721]	1.52	1.06
SREBF2	Homo sapiens sterol regulatory element binding transcription factor 2 (SREBF2), mRNA [NM_004599]	1.32	1.06
LARP4	Homo sapiens La ribonucleoprotein domain family, member 4 (LARP4), transcript variant 2, mRNA [NM_199188]	1.76	1.05
MVD	Homo sapiens mevalonate (diphospho) decarboxylase (MVD), mRNA [NM_002461]	1.04	1.61
SEC14L1	Homo sapiens SEC14-like 1 (S. cerevisiae) (SEC14L1), transcript variant 1, mRNA [NM_003003]	1.72	1.03
NFATC1	Homo sapiens nuclear factor of activated T-cells, cytoplasmic, calcineurin-dependent 1 (NFATC1), transcript variant 1, mRNA [NM_172390]	1.83	1.03
TBC1D15	Homo sapiens TBC1 domain family, member 15 (TBC1D15), mRNA [NM_022771]	1.98	1.02
SAT1	Homo sapiens spermidine/spermine N1-acetyltransferase 1 (SAT1), mRNA [NM_002970]	1.53	1.02
C10orf35	Homo sapiens chromosome 10 open reading frame 35 (C10orf35), mRNA [NM_145306]	1.37	1.02
RNF12	Homo sapiens ring finger protein 12 (RNF12), transcript variant 1, mRNA [NM_016120]	1.68	1.01

Table S8. List of shared genes whose expressions were downregulated in cells exposed to both CuO-NPs and released Cu ions. Fold-change is represented by logarithmic ratio (log_2 ratio) to expression level in control.

Gene name	Description	Fold-change (log_2 ratio)	
		CuO-NPs	Cu ions
FAM83D	Homo sapiens family with sequence similarity 83, member D (FAM83D), mRNA [NM_030919]	-2.40	-2.25
HMGB2	Homo sapiens high-mobility group box 2 (HMGB2), transcript variant 1, mRNA [NM_002129]	-2.06	-1.83
IGFBP3	Homo sapiens insulin-like growth factor binding protein 3 (IGFBP3), transcript variant 1, mRNA [NM_001013398]	-2.40	-1.81
CENPA	Homo sapiens centromere protein A (CENPA), transcript variant 1, mRNA [NM_001809]	-1.80	-2.04
TRIM59	Homo sapiens tripartite motif-containing 59 (TRIM59), mRNA [NM_173084]	-1.86	-1.59
KIF20A	Homo sapiens kinesin family member 20A (KIF20A), mRNA [NM_005733]	-2.05	-1.53
MYBL1	Homo sapiens v-myb myeloblastosis viral oncogene homolog (avian)-like 1 (MYBL1), mRNA [NM_001080416]	-1.84	-1.48
CKAP2	Homo sapiens cytoskeleton associated protein 2 (CKAP2), transcript variant 1, mRNA [NM_018204]	-1.76	-1.44
LOC338620	Homo sapiens hypothetical protein LOC338620, mRNA (cDNA clone IMAGE:6023208), partial cds. [BC043009]	-2.01	-1.42
TOP2A	Homo sapiens topoisomerase (DNA) II alpha 170kDa (TOP2A), mRNA [NM_001067]	-2.00	-1.41
CCDC80	Homo sapiens coiled-coil domain containing 80 (CCDC80), transcript variant 1, mRNA [NM_199511]	-1.40	-1.41
BARD1	Homo sapiens BRCA1 associated RING domain 1 (BARD1), mRNA [NM_000465]	-1.35	-1.55
CCNB1	Homo sapiens cyclin B1 (CCNB1), mRNA [NM_031966]	-1.74	-1.33
G0S2	Homo sapiens G0/G1switch 2 (G0S2), mRNA [NM_015714]	-1.33	-1.56
NFE2L3	Homo sapiens nuclear factor (erythroid-derived 2)-like 3 (NFE2L3), mRNA [NM_004289]	-1.99	-1.32
ZNF185	Homo sapiens zinc finger protein 185 (LIM domain) (ZNF185), mRNA [NM_007150]	-1.28	-1.77
ALPK2	Homo sapiens alpha-kinase 2 (ALPK2), mRNA [NM_052947]	-1.58	-1.28
PABPC3	Homo sapiens poly(A) binding protein, cytoplasmic 3 (PABPC3), mRNA [NM_030979]	-1.71	-1.26
SLC27A2	Homo sapiens solute carrier family 27 (fatty acid transporter), member 2 (SLC27A2), mRNA [NM_003645]	-1.26	-1.57
HN1	Homo sapiens hematological and neurological expressed 1 (HN1), transcript variant 3, mRNA [NM_001002033]	-1.25	-1.32
C15orf23	Homo sapiens chromosome 15 open reading frame 23 (C15orf23), transcript variant 2, mRNA [NM_001142761]	-1.63	-1.24
CDC20	Homo sapiens cell division cycle 20 homolog (S. cerevisiae) (CDC20), mRNA [NM_001255]	-1.23	-1.42
EFEMP1	Homo sapiens EGF-containing fibulin-like extracellular matrix protein 1 (EFEMP1), transcript variant 1, mRNA [NM_004105]	-1.78	-1.22
RACGAP1	Homo sapiens Rac GTPase activating protein 1 (RACGAP1), transcript variant 1, mRNA [NM_013277]	-1.56	-1.22
KIF23	Homo sapiens kinesin family member 23 (KIF23), transcript variant 1, mRNA [NM_138555]	-1.56	-1.21
TUBA3D	Homo sapiens tubulin, alpha 3d (TUBA3D), mRNA [NM_080386]	-1.20	-1.32
LOC100128974	PREDICTED: Homo sapiens misc_RNA (LOC100128974), miscRNA [XR_037045]	-1.31	-1.19
LMNB2	Homo sapiens lamin B2 (LMNB2), mRNA [NM_032737]	-1.71	-1.19
PLAGL1	Homo sapiens pleiomorphic adenoma gene-like 1 (PLAGL1), transcript variant 2, mRNA [NM_006718]	-1.18	-1.50
CCNA2	Homo sapiens cyclin A2 (CCNA2), mRNA [NM_001237]	-1.39	-1.18
PRSS23	Homo sapiens protease, serine, 23 (PRSS23), mRNA [NM_007173]	-1.80	-1.17
TPX2	Homo sapiens TPX2, microtubule-associated, homolog (Xenopus laevis) (TPX2), mRNA [NM_012112]	-1.25	-1.17
PIF1	Homo sapiens PIF1 5'-to-3' DNA helicase homolog (S. cerevisiae) (PIF1), mRNA [NM_025049]	-1.65	-1.16

CDC2	Homo sapiens cell division cycle 2, G1 to S and G2 to M (CDC2), transcript variant 1, mRNA [NM_001786]	-1.41	-1.16
RRM2	Homo sapiens ribonucleotide reductase M2 polypeptide (RRM2), mRNA [NM_001034]	-1.38	-1.15
SFRP1	Homo sapiens secreted frizzled-related protein 1 (SFRP1), mRNA [NM_003012]	-1.14	-1.16
TMEM171	Homo sapiens transmembrane protein 171 (TMEM171), mRNA [NM_173490]	-1.15	-1.14
GPSM2	Homo sapiens G-protein signaling modulator 2 (AGS3-like, C. elegans) (GPSM2), mRNA [NM_013296]	-1.19	-1.14
TRIM14	Homo sapiens tripartite motif-containing 14 (TRIM14), transcript variant 1, mRNA [NM_014788]	-1.87	-1.13
TRAM1	Homo sapiens translocation associated membrane protein 1 (TRAM1), mRNA [NM_014294]	-1.11	-1.40
LOC389842	PREDICTED: Homo sapiens similar to RanBP1 (LOC389842), mRNA [XM_372200]	-1.44	-1.11
TPM1	Homo sapiens tropomyosin 1 (alpha) (TPM1), transcript variant 5, mRNA [NM_000366]	-1.09	-1.55
HYLS1	Homo sapiens hydrolethalus syndrome 1 (HYLS1), transcript variant 1, mRNA [NM_145014]	-1.25	-1.09
TMSB4X	Homo sapiens thymosin beta 4, X-linked (TMSB4X), mRNA [NM_021109]	-1.13	-1.09
IRS1	Homo sapiens insulin receptor substrate 1 (IRS1), mRNA [NM_005544]	-2.21	-1.08
ABCB10	Homo sapiens ATP-binding cassette, sub-family B (MDR/TAP), member 10 (ABCB10), nuclear gene encoding mitochondrial protein, mRNA [NM_012089]	-1.70	-1.07
KIF18B	Homo sapiens hypothetical protein LOC146909, mRNA (cDNA clone IMAGE:4418755), partial cds. [BC048263]	-2.07	-1.07
LOC100132658	PREDICTED: Homo sapiens misc_RNA (LOC100132658), miscRNA [XR_038952]	-1.15	-1.07
FBXO5	Homo sapiens F-box protein 5 (FBXO5), transcript variant 1, mRNA [NM_012177]	-1.17	-1.06
TGFB2	Homo sapiens transforming growth factor, beta 2 (TGFB2), transcript variant 1, mRNA [NM_001135599]	-2.11	-1.05
CDCA3	Homo sapiens cell division cycle associated 3 (CDCA3), mRNA [NM_031299]	-1.34	-1.04
AREG	Homo sapiens amphiregulin (AREG), mRNA [NM_001657]	-1.50	-1.02
ZFP36L1	Homo sapiens zinc finger protein 36, C3H type-like 1 (ZFP36L1), mRNA [NM_004926]	-1.45	-1.02
DLGAP5	Homo sapiens discs, large (Drosophila) homolog-associated protein 5 (DLGAP5), mRNA [NM_014750]	-1.34	-1.01
BCAR3	Homo sapiens breast cancer anti-estrogen resistance 3 (BCAR3), mRNA [NM_003567]	-1.10	-1.00

Table S9. Shared downregulated genes by CuO-NPs and released Cu ions, which fall into the categories of "mitosis", chromosome segregation", and "cell cycle".

GO category	Gene name	Description
mitosis	CCNA2	Homo sapiens cyclin A2 (CCNA2), mRNA [NM_001237]
	CCNB1	Homo sapiens cyclin B1 (CCNB1), mRNA [NM_031966]
	CDC2	Homo sapiens cell division cycle 2, G1 to S and G2 to M (CDC2), transcript variant 1, mRNA [NM_001786]
	GPSM2	Homo sapiens G-protein signaling modulator 2 (AGS3-like, C. elegans) (GPSM2), mRNA [NM_013296]
	KIF18B	Homo sapiens hypothetical protein LOC146909, mRNA (cDNA clone IMAGE:4418755), partial cds. [BC048263]
	KIF20A	Homo sapiens kinesin family member 20A (KIF20A), mRNA [NM_005733]
	KIF23	Homo sapiens kinesin family member 20A (KIF20A), mRNA [NM_005733]
	TOP2A	Homo sapiens topoisomerase (DNA) II alpha 170kDa (TOP2A), mRNA [NM_001067]
	TPX2	Homo sapiens TPX2, microtubule-associated, homolog (Xenopus laevis) (TPX2), mRNA [NM_012112]
	TUBA3D	Homo sapiens tubulin, alpha 3d (TUBA3D), mRNA [NM_080386]
	ZFP36L1	Homo sapiens zinc finger protein 36, C3H type-like 1 (ZFP36L1), mRNA [NM_004926]
chromosome segregation	KIF18B	Homo sapiens hypothetical protein LOC146909, mRNA (cDNA clone IMAGE:4418755), partial cds. [BC048263]
	KIF20A	Homo sapiens kinesin family member 20A (KIF20A), mRNA [NM_005733]
	KIF23	Homo sapiens kinesin family member 20A (KIF20A), mRNA [NM_005733]
	TOP2A	Homo sapiens topoisomerase (DNA) II alpha 170kDa (TOP2A), mRNA [NM_001067]
	TPX2	Homo sapiens TPX2, microtubule-associated, homolog (Xenopus laevis) (TPX2), mRNA [NM_012112]
	TUBA3D	Homo sapiens tubulin, alpha 3d (TUBA3D), mRNA [NM_080386]
cell cycle	CCNA2	Homo sapiens cyclin A2 (CCNA2), mRNA [NM_001237]
	CCNB1	Homo sapiens cyclin B1 (CCNB1), mRNA [NM_031966]
	CDC2	Homo sapiens cell division cycle 2, G1 to S and G2 to M (CDC2), transcript variant 1, mRNA [NM_001786]
	CDC20	Homo sapiens cell division cycle 20 homolog (S. cerevisiae) (CDC20), mRNA [NM_001255]
	GPSM2	Homo sapiens G-protein signaling modulator 2 (AGS3-like, C. elegans) (GPSM2), mRNA [NM_013296]
	KIF18B	Homo sapiens hypothetical protein LOC146909, mRNA (cDNA clone IMAGE:4418755), partial cds.

		[BC048263]
	KIF20A	Homo sapiens kinesin family member 20A (KIF20A), mRNA [NM_005733]
	KIF23	Homo sapiens kinesin family member 20A (KIF20A), mRNA [NM_005733]
	MYBL1	Homo sapiens v-myb myeloblastosis viral oncogene homolog (avian)-like 1 (MYBL1), mRNA [NM_001080416]
	TOP2A	Homo sapiens topoisomerase (DNA) II alpha 170kDa (TOP2A), mRNA [NM_001067]
cell cycle	TPX2	Homo sapiens TPX2, microtubule-associated, homolog (Xenopus laevis) (TPX2), mRNA [NM_012112]
	TRIM14	Homo sapiens tripartite motif-containing 14 (TRIM14), transcript variant 1, mRNA [NM_014788]
	TRIM59	Homo sapiens tripartite motif-containing 59 (TRIM59), mRNA [NM_173084]
	TUBA3D	Homo sapiens tubulin, alpha 3d (TUBA3D), mRNA [NM_080386]
	ZFP36L1	Homo sapiens zinc finger protein 36, C3H type-like 1 (ZFP36L1), mRNA [NM_004926]

Table S10. Primer sequences for qPCR

Gene Name	**Forward sequence (5'→3')**	**Reverse sequence (5'→3')**
GADD45A	ctgaacggtgatggcatctg	ccccttggcatcagtttctg
GADD45B	taccgttggtttccgcaact	gccagagagcccaaaacctt
GADD45G	gtgctgagctctggctgtca	gctgtgctttccggaactgt
PCNA	ggtgttggaggcactcaagg	ccaaagagacgtgggacgag
CDC2	ttcagagctttgggcactcc	gggatgctaggcttcctggt
CCNB1	actgcaggccaaaatgccta	aggttctggctctggcactg
CDKN1A	tcctctagctgtgggggtga	aaggtcgctggacgatttga
FOS	cctcgtactccaaccgcatc	tgggtaggagcacggtcact
FOSB	caagaggtacagcggcatcc	caacgtcccgttccaacaat
ATF3	tgggtccagaagacctgcat	aaaccctggtgatgccacag
JDP2	tgaaggaggcaggacagagg	tcatggcttttcctggctgt
ATR	gctctggtccaagggtgatg	accctcaggtggggtttcat
TP53	cgtcccaagcaatggatgat	tggcattctgggagcttcat
NR4A1	gcaccttcatggacggctac	ctgaggagcatggctggact
NR4A2	tgtaccaaatgcccctgtcc	gagtgcggcatcatctcctc
NR4A3	agccttcctgcgtgtaccaa	aatggatggctgctgatgct
AURKA	tcagcgggtcttgtgtcctt	aaccggcttgtgactggaga
AURKB	ccccatctgcacttgtcctc	tgtgaagtgccgcgttaaga
TPX2	ccccctcggatttcatcaat	ttggccttctcctcaaacca