

## **Supplementary Information**

**to**

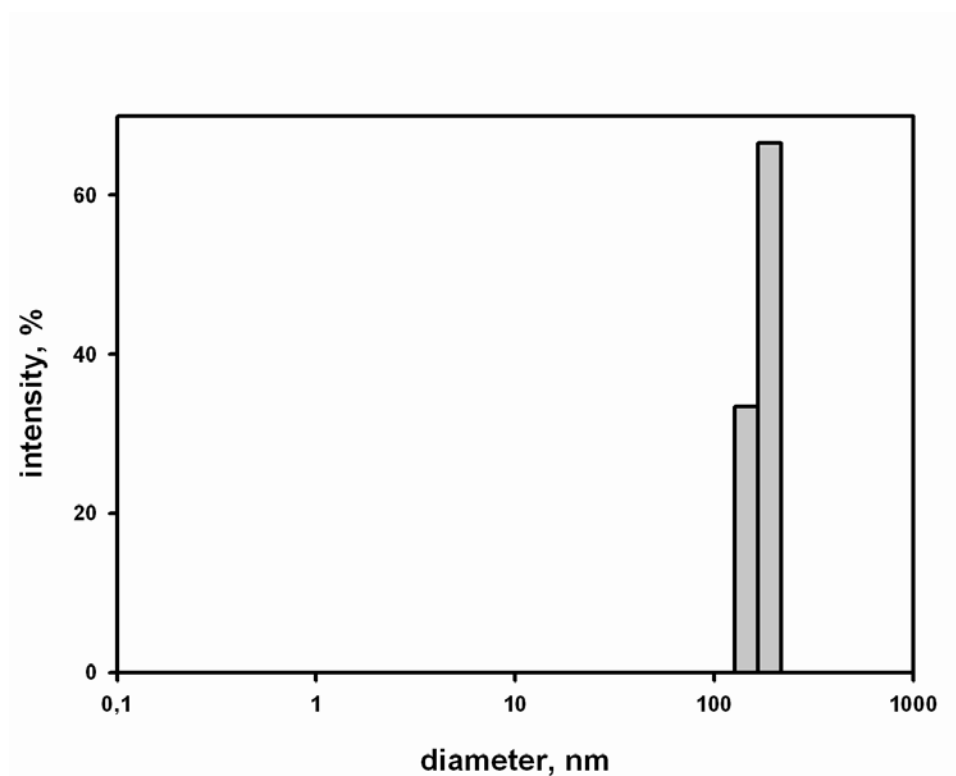
### **Interference of CuO nanoparticles with metal homeostasis in hepatocytes under sub-toxic conditions**

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**Table S1. Quantitative real time polymerase chain reaction primer sequences**

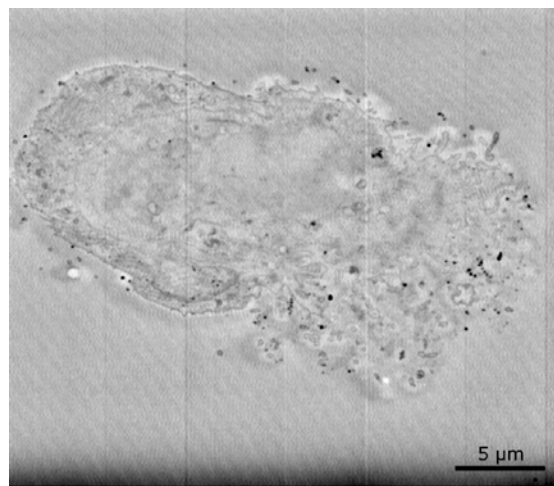
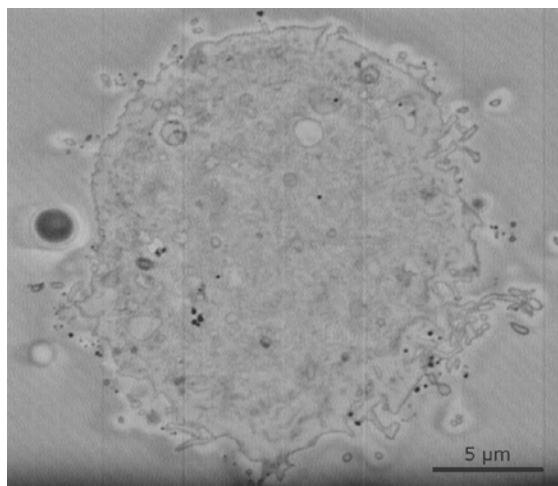
Gene	Forward primer sequence	Reverse primer sequence
HMOX1	ATG ACA CCA AGG ACC AGA GC	GTG TAA GGA CCC ATC GGA GA
HSPA6	AGG AGG TGG AGA GGA TGG TT	TGT CCT CTT CGG GAA TCT TG
SOD1	TGG CCG ATG TGT CTA TTG AA	ACC TTT GCC CAA GTC ATC TG
ZNT1	CGC AGC CAT GGG GTG TTG GG	CAT CGC CAG CGA GGT CA
GCLM	CCT CCT GCT GTG TGA TGC CAC	CGT GCG CTT GAA TGT CAG GAA TGC
ATP7B	TGG CAA AGT CCC CAC AAT CAA C	TCA AGG CAA CCA ACA CGG AGA G
MTF1	CGA AGG AGA AGC CAT TTG AG	ATT TGC TGC AGC CTT CAG AT
MET1X	GCT TCT CCT TGC CTC GAA A	TGA CGT CCC TTT GCA GAT G
36B4	GAA ATC CTG GGT GTC CGC AAT GTT	AGA CAA GGC CAG GAC TCG TTT GTA
HPRT	ATG GAC AGG ACT GAA CGT CTT GCT	TTG AGC ACA CAG AGG GCT ACA ATG

**Figure S1. Size distribution of CuO-NP** after sonication in water and coating with PVP-40. The population of CuO-NP is mono dispersed ( $PI\ 18.2 \pm 4.9$ ) and its mean diameter is  $175 \pm 9\text{ nm}$ . See reference (40) in the main text for SEM images of the powder.



**Figure S2. SEM images of HepG2 cells after 24 h incubation with 250  $\mu$ M CuO-NP.**

On the left, low magnification of the cell shown in Figure 2. On the right, another cell with a lot of CuO-NP in contact with protrusions at one extremity, suggesting macropinocytosis.



**Figure S3. qPCR and microarray measurements of ZNT1, GCLM, HSPA6, HMOX1 and MET1X mRNA from HepG2 cells.** The cells were exposed to copper salt or CuO-NP for various times at indicated concentrations :

□ 100  $\mu$ M Cu (1), ◇ 100  $\mu$ M Cu (2), ▽ 200  $\mu$ M Cu (2), △ 400  $\mu$ M Cu (2)

○ 60 $\mu$ M and 250  $\mu$ M Cu (this study, Fig. 5), ● 60 $\mu$ M & 250  $\mu$ M CuO-NP (this study, Fig. 5)

(1) P. Muller, H. van Bakel, B. van de Sluis, F. Holstege, C. Wijmenga and L. W. Klomp, *J Biol Inorg Chem*, 2007, **12**, 495.

(2) M. O. Song, J. Li and J. H. Freedman, *Physiological genomics*, 2009, **38**, 386.

