

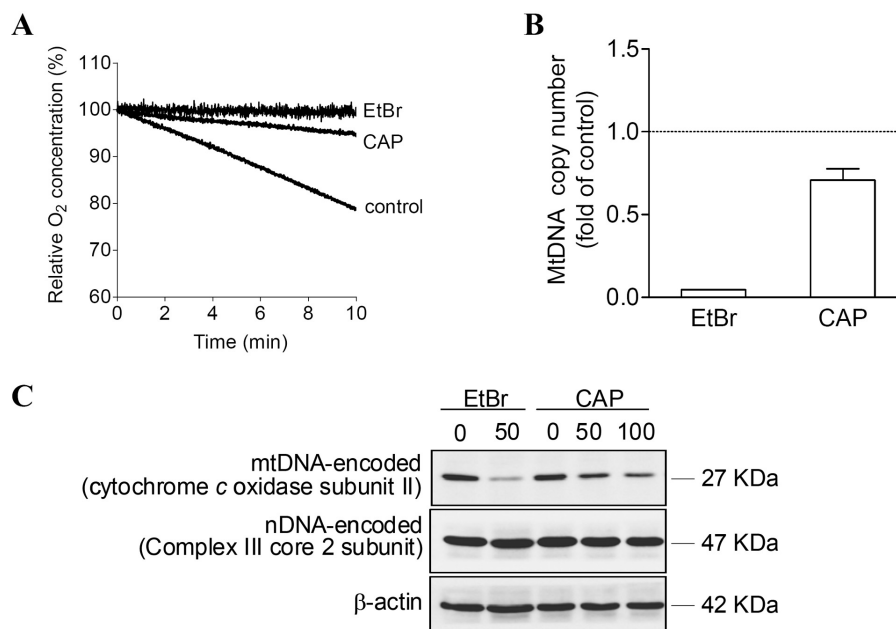
## Electronic supplementary material

### Supplemental Table

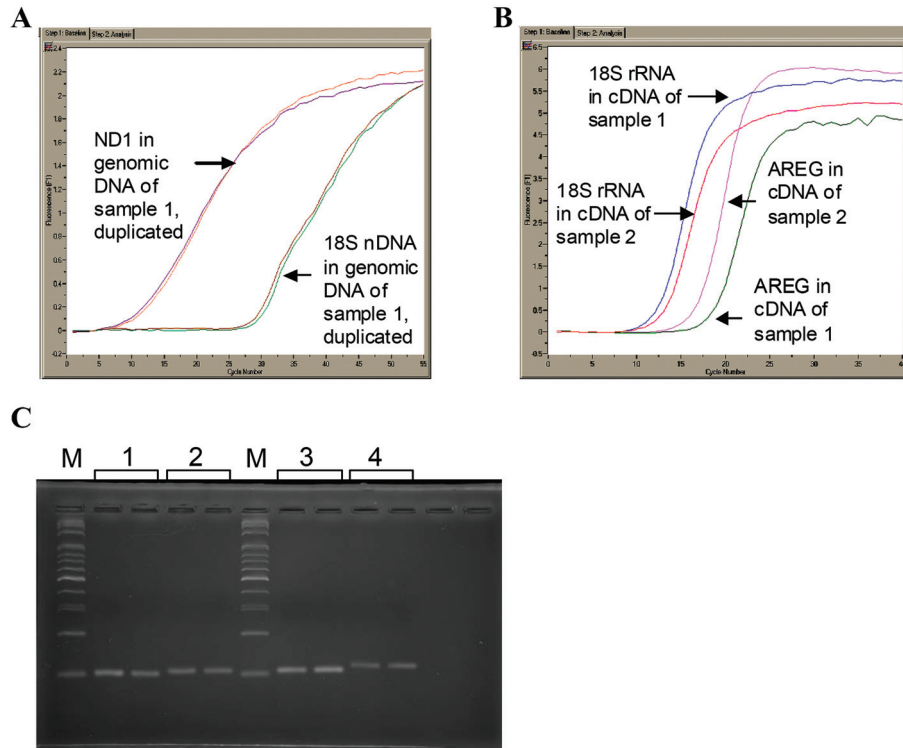
**Supplemental Table.** Candidate genes which were upregulated at least three-fold by EtBr- and CAP-induced mitochondrial dysfunction in HepG2 cells.

EtBr (fold of control)	CAP (fold of control)	Gene name	Gene symbol	PANTHER molecular function [50]	PANTHER biological process
11.0	20.8	Very low density lipoprotein receptor	VLDLR	Other receptor	Oogenesis
9.6	3.0	Amphiregulin	AREG	Growth factor	Ligand-mediated signaling; Cell proliferation and differentiation
8.6	4.5	Serpin peptidase inhibitor, member 2	SERPINE2	Serine protease inhibitor	Proteolysis
7.7	4.2	Leukocyte-associated Ig-like receptor 2	LAIR2	Immunoglobulin receptor family member; Defense/immunity protein	Ligand-mediated signaling; Natural killer cell mediated immunity
7.4	6.5	Early growth response 1	EGR1	KRAB box transcription factor; Nucleic acid binding	mRNA transcription regulation
5.7	3.8	Vanin 1	VNN1	Other hydrolase	Vitamin metabolism
5.5	3.4	Aquaporin 7	AQP7	Other transporter	Other transport; Other homeostasis activities
5.1	4.7	Insulin-like growth factor binding protein 1	IGFBP1	Other miscellaneous function protein	Extracellular matrix protein-mediated signaling; Growth factor homeostasis
4.5	5.4	Hexokinase domain containing 1	HKDC1	Carbohydrate kinase	Glycolysis
4.2	5.6	AXL receptor tyrosine kinase	AXL	Tyrosine protein kinase receptor; Protein kinase	Immunity and defense; Cell proliferation and differentiation; Oncogenesis
3.6	4.9	Synaptogyrin 3	SYNGR3	Membrane traffic regulatory protein	Neuronal activities

## Supplemental Figures

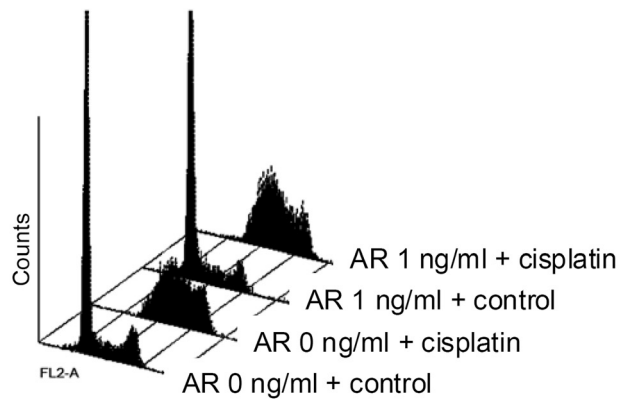


**Supplemental Figure 1.** Treatment of HepG2 cells with ethidium bromide (EtBr), and chloramphenicol (CAP) resulted in mitochondrial dysfunction. These treatments caused (A) decline in oxygen consumption, (B) depletion of mitochondrial DNA (mtDNA), (C) downregulation of mtDNA encoded cytochrome *c* oxidase subunit II, but not nuclear DNA encoded core 2 subunit of Complex III in HepG2 cells. The copy number of mtDNA was measured by  $\Delta$ Ct value of mitochondrial ND1/18S nDNA in genomic DNA. Data are the mean  $\pm$  SEM of the results from three independent experiments.

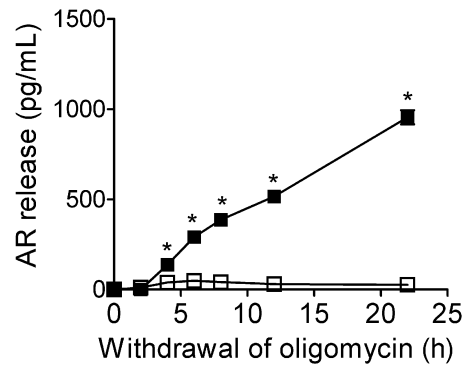


1. 18S nDNA in genomic DNA of sample 1
2. ND1 in genomic DNA of sample 1
3. 18S rRNA in cDNA of sample 1
4. AREG in cDNA of sample 1

**Supplemental Figure 2.** Validation of the real-time quantitative PCR in the measurement of the relative mtDNA copy number (A) and AR transcript in cDNA (B). The specificities of the ND1 and AR primers were demonstrated by RT-PCR (C).



**Supplemental Figure 3.** The addition of recombinant AR had no effect on cisplatin-sensitivity of HepG2 cells. Human recombinant AR (0 and 1 ng/ml) was added to the culture medium 1 hr before treatment of cisplatin, and the HepG2 cells were then maintained in the medium containing cisplatin (0 or 10  $\mu$ M). After 36 h of incubation, the DNA content was measured by flow cytometry as described in Materials and methods.



**Supplemental Figure 4.** Oligomycin induced AR release in a time-dependent manner. Cells had been cultured with the medium containing 0.5  $\mu\text{g}/\text{mL}$  oligomycin for 1 h, and were then washed thoroughly with a fresh medium. After incubation for indicated periods of time, AR concentration in the condition medium was measured by ELISA.