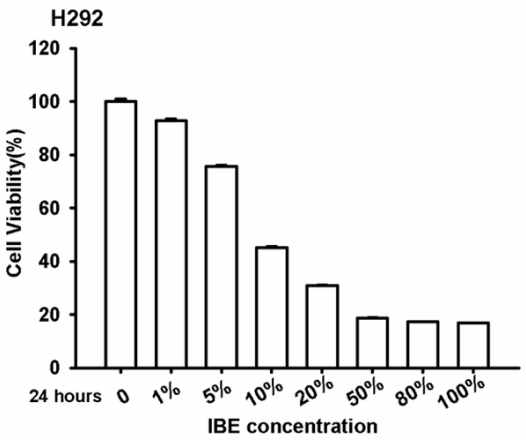
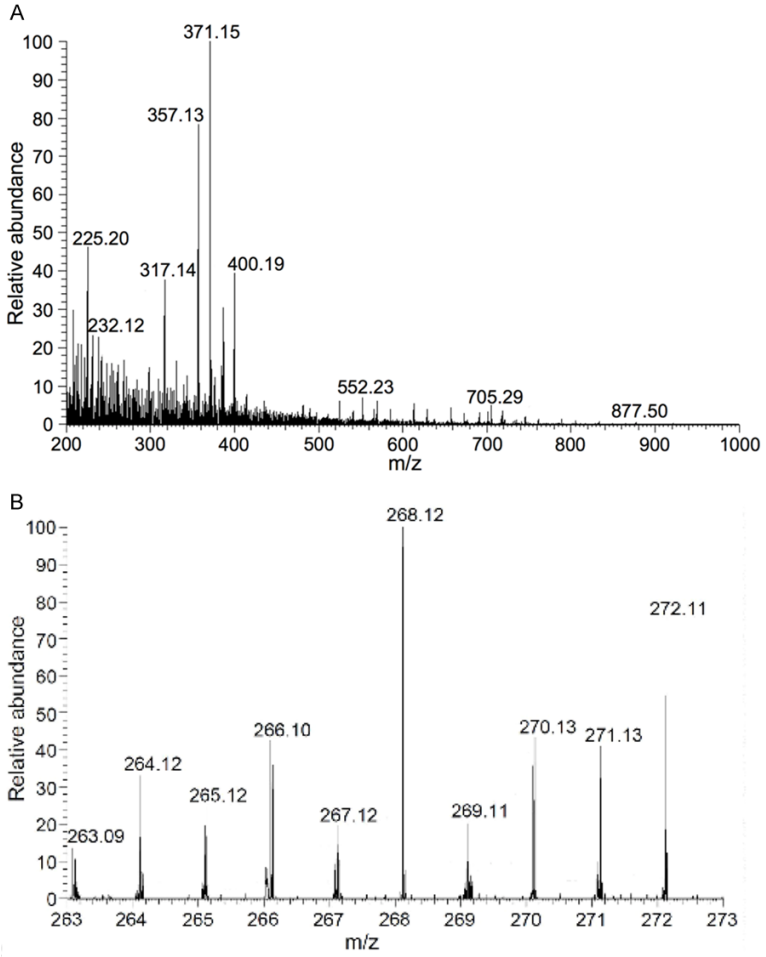
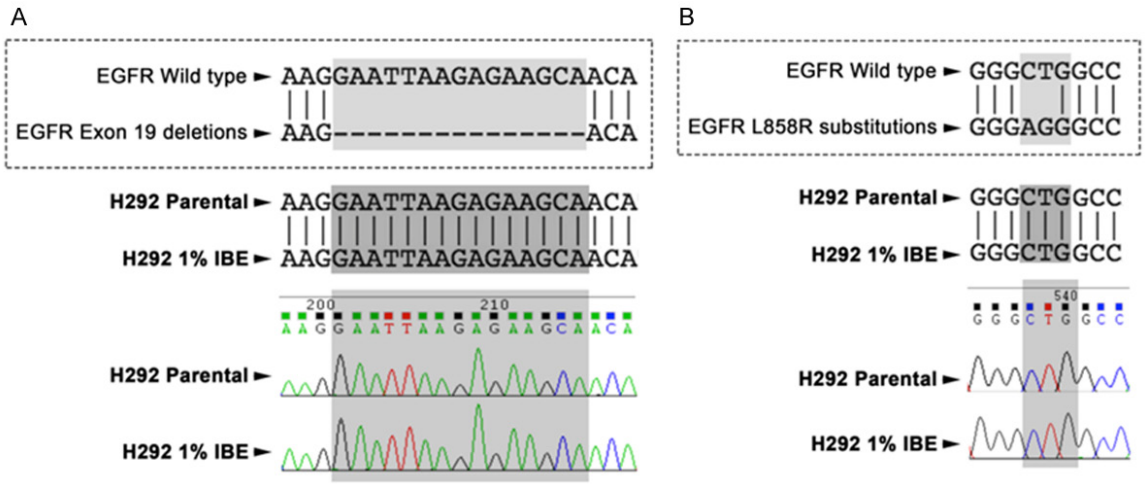


Supplementary Figure 1. Cell viability of H292 cells in response to short-term IBE treatment. H292 cells were treated with different concentration of IBE as indicated for 24 hours, and then the cell viabilities were determined by MTT assay.



Supplementary Figure 2. Mass spectrometry analysis of incense burning smoke solution. Incense-burning smoke was dissolved into de-ionized water by suction with pump. The relative abundance of IBE compositions was performed in the Orbitrap LC-MS with a mass resolution of 60,000 at *m/z* 200 (A). The survey scan of IBE compositions at 268.12 was similar with commercial standard Auramine O [38] (B).



Supplementary Figure 3. Activating mutations of EGFR were not detected in IBE stable clone of H292 cells. EGFR sequence at Exon 19 deletion (A) and L858R point mutation (B) in 1% IBE-treated clone of H292 cells was aligned and compared with that in the parental cells.

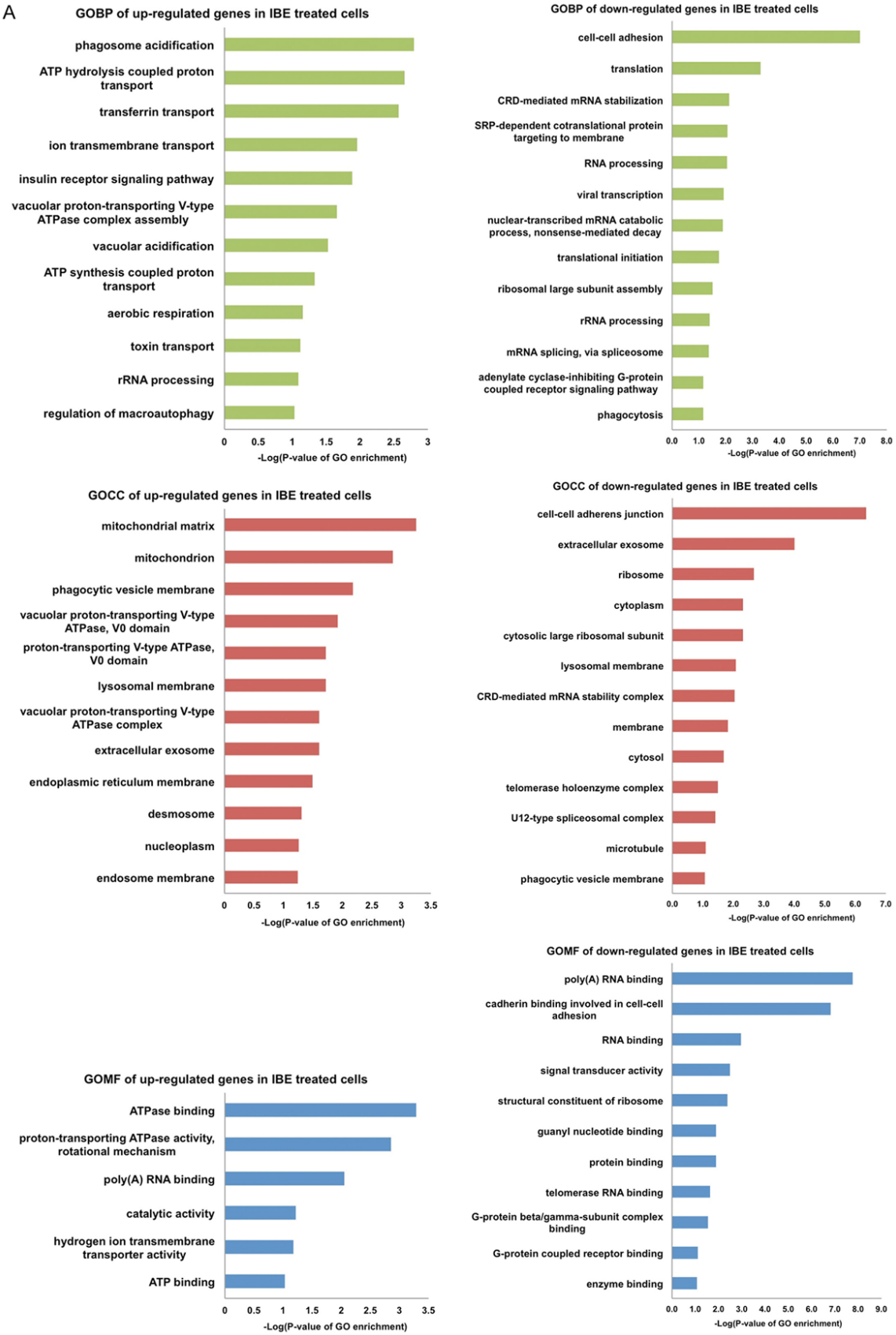
Supplementary Materials and Methods

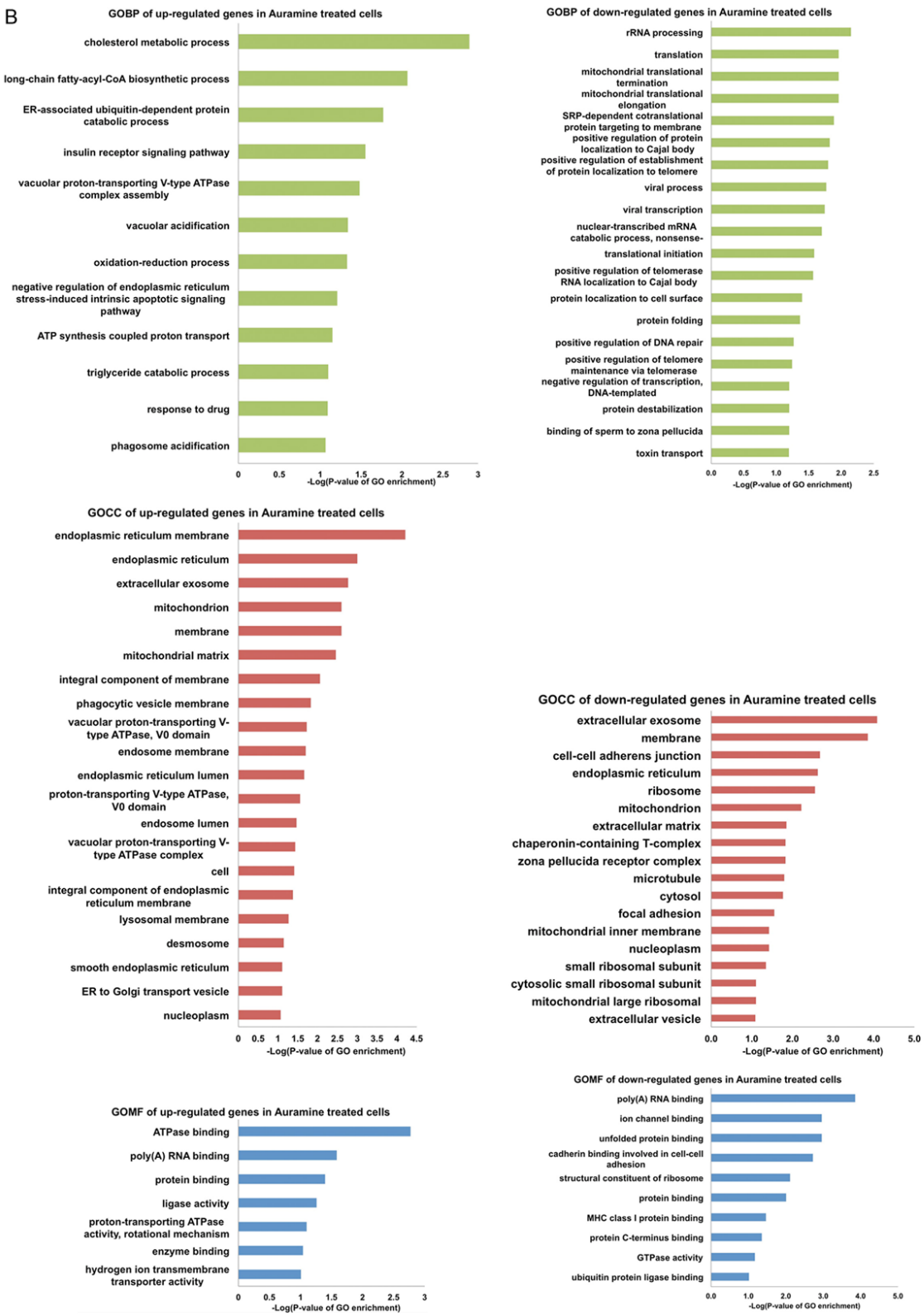
Mass spectrometry analysis

Incense-burning smoke was continuously dissolved into water by suction with pump. The survey scan of IBE compositions was performed in the Orbitrap LC-MS (ThermoFisher scientific) with a mass resolution of 60,000 at *m/z* 200. The flow rate of HPLC was 50 μL/min, and solution gradient was from 0% to 100% B (B = 80% acetonitrile, 0.1% formic acid) over 30 min minutes.

Total proteins (40 μg) lysate of parental, IBE-treated, or auramine-treated H292 cells were separated by 10% SDS-PAGE and divided into eight gel fractions. After in-gel trypsin digestion, the tryptic peptides of each fraction were injected into the linear ion trap-Fourier transform ion cyclotron resonance mass spectrometer (LTQ-FTICR MS) (Thermo Electron) for mass identification. The survey scan (*m/z* range: 320-2,000) was performed in FTICR MS with a mass resolution of 100,000 at *m/z* 400. The top ten most abundant multiply charged ions were sequentially isolated for MS/MS assay by LTQ. Protein identification and label-free quantitative analysis were performed by MaxQuant and MaxLFQ softwares, respectively. The significance threshold for the identification was set as $P < 0.01$.

A


GOBP of up-regulated genes in IBE treated cells
phagosome acidification
ATP hydrolysis coupled proton transport
transferrin transport
ion transmembrane transport
insulin receptor signaling pathway
vacuolar proton-transporting V-type ATPase complex assembly
vacuolar acidification
ATP synthesis coupled proton transport
aerobic respiration
toxin transport
rRNA processing
regulation of macroautophagy
0 0.5 1 1.5 2 2.5 3
-Log(P-value of GO enrichment)
GOBP of down-regulated genes in IBE treated cells
cell-cell adhesion
translation
CRD-mediated mRNA stabilization
SRP-dependent cotranslational protein targeting to membrane
RNA processing
viral transcription
nuclear-transcribed mRNA catabolic process, nonsense-mediated decay
translational initiation
ribosomal large subunit assembly
rRNA processing
mRNA splicing, via spliceosome
adenylate cyclase-inhibiting G-protein coupled receptor signaling pathway
phagocytosis
0.0 1.0 2.0 3.0 4.0 5.0 6.0 7.0 8.0
-Log(P-value of GO enrichment)
GOCC of up-regulated genes in IBE treated cells
mitochondrial matrix
mitochondrion
phagocytic vesicle membrane
vacuolar proton-transporting V-type ATPase, V0 domain
proton-transporting V-type ATPase, V0 domain
lysosomal membrane
vacuolar proton-transporting V-type ATPase complex
extracellular exosome
endoplasmic reticulum membrane
desmosome
nucleoplasm
endosome membrane
0 0.5 1 1.5 2 2.5 3 3.5
-Log(P-value of GO enrichment)
GOCC of down-regulated genes in IBE treated cells
cell-cell adherens junction
extracellular exosome
ribosome
cytoplasm
cytosolic large ribosomal subunit
lysosomal membrane
CRD-mediated mRNA stability complex
membrane
cytosol
telomerase holoenzyme complex
U12-type spliceosomal complex
microtubule
phagocytic vesicle membrane
0.0 1.0 2.0 3.0 4.0 5.0 6.0 7.0
-Log(P-value of GO enrichment)
GOMF of down-regulated genes in IBE treated cells
poly(A) RNA binding
cadherin binding involved in cell-cell adhesion
RNA binding
signal transducer activity
structural constituent of ribosome
guanyl nucleotide binding
protein binding
telomerase RNA binding
G-protein beta/gamma-subunit complex binding
G-protein coupled receptor binding
enzyme binding
0.0 1.0 2.0 3.0 4.0 5.0 6.0 7.0 8.0 9.0
-Log(P-value of GO enrichment)
GOMF of up-regulated genes in IBE treated cells
ATPase binding
proton-transporting ATPase activity, rotational mechanism
poly(A) RNA binding
catalytic activity
hydrogen ion transmembrane transporter activity
ATP binding
0 0.5 1 1.5 2 2.5 3 3.5
-Log(P-value of GO enrichment)



Supplementary Figure 4. Enrichment of Gene Ontology (GO) terms in up- or down-regulated genes in H292 IBE/Auramine cells vs. parental cells. GO terms belong to cellular components (GOCC), biological processes (GOBP) and molecular functions (GOMF) of H292 IBE- (A) or auramine- (B) treated cells were shown in red, green, and blue, respectively. GO terms were analyzed by David functional annotation tools (https://david.ncifcrf.gov/tools.jsp).