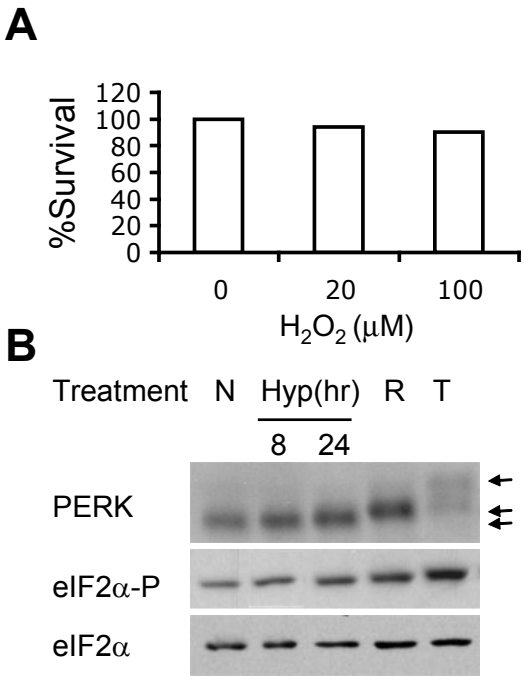
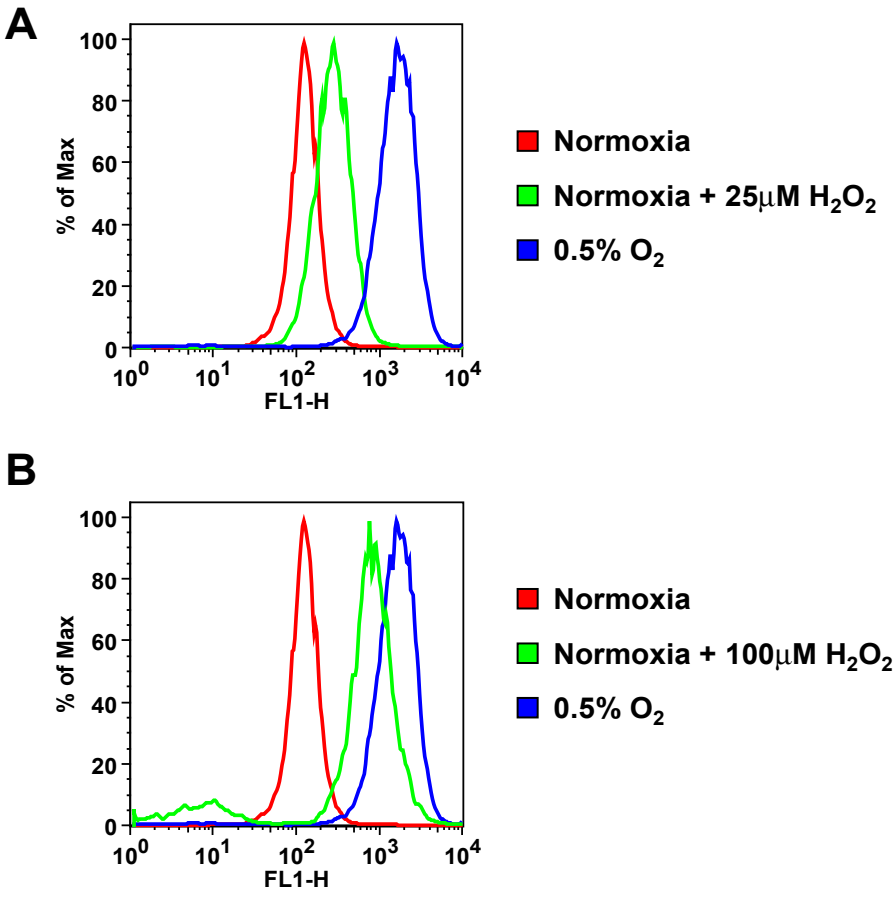
Supplementary Figure 1. **Effects of H_2O_2 on mRNA translation and cell survival.** A) MEF viability measured immediately after 1 hr H_2O_2 (0-100 ⌈M) exposure by trypan blue stain. B) Comparison of normoxia (N), hypoxia (Hyp) (0.5% O_2, 8 and 24 hr), H_2O_2 (R), (1 hr, 100 ⌈M), and thapsigargin (T), (0.8 ⌈M, 4 hr) effects on PERK protein mobility and eIF2⟨ phosphorylation.

Supplementary Figure 2. **Comparison of intracellular ROS levels in cells grown in moderate hypoxia versus H_2O_2.** Flow cytometry was used to evaluate 2', 7'-dichlorofluorescein-diacetate (DCFH-DA) fluorescence in cells exposed to 0.5% O_2 and 25 μM H_2O_2 (A) or 100 μM H_2O_2 (B). As shown here, 100 μM H_2O_2 treatment is closer to ROS levels achieved in cells grown at 0.5% O_2 than 25 μM H_2O_2..

Supplementary Figure 3. **Catalase expression suppresses ROS-activated ISR.** Effects of H_2O_2 (20 ⌈M,6 hr, replenished every 2 hrs) on the expression of ATF4 target genes GADD34, BiP, and CHOP (A) and PGK (B) in HEK293 cells transfected with catalase (CAT) or empty vector. **, $P<0.01$.


A
%Survival
120
100
80
60
40
20
0
0
20
100
H_2O_2 (μM)
B
Treatment N Hyp(hr) R T
8 24
PERK
eIF2α-P
eIF2α


A
100
80
60
40
20
0
% of Max
10^0
10^1
10^2
10^3
10^4
FL1-H
Normoxia
Normoxia + 25μM H_2O_2
0.5% O_2
B
100
80
60
40
20
0
% of Max
10^0
10^1
10^2
10^3
10^4
FL1-H
Normoxia
Normoxia + 100μM H_2O_2
0.5% O_2

Liu et al., Supplementary Figure 3