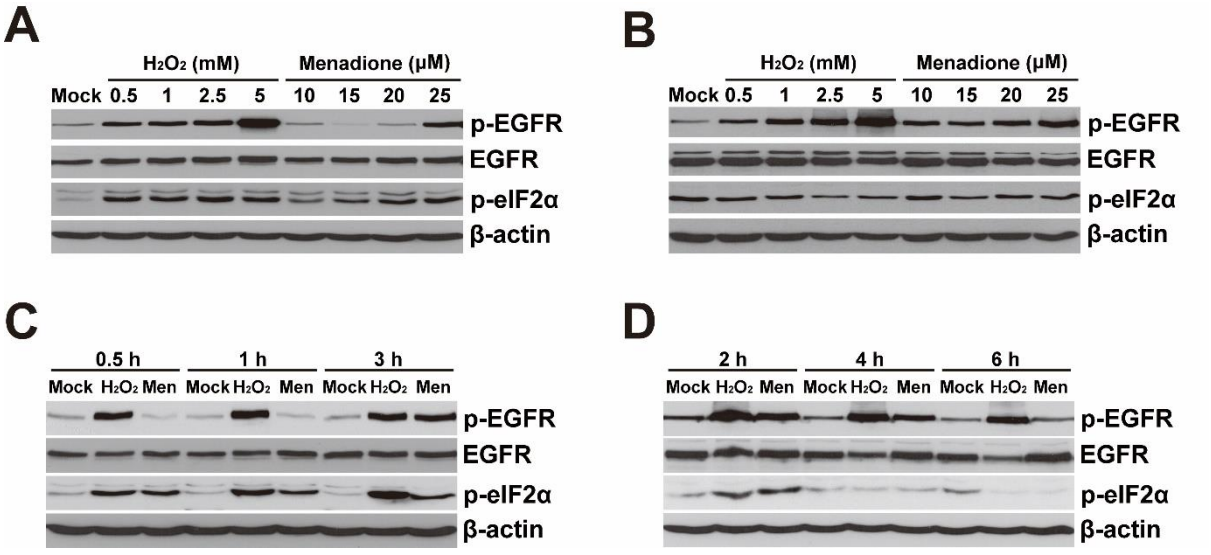
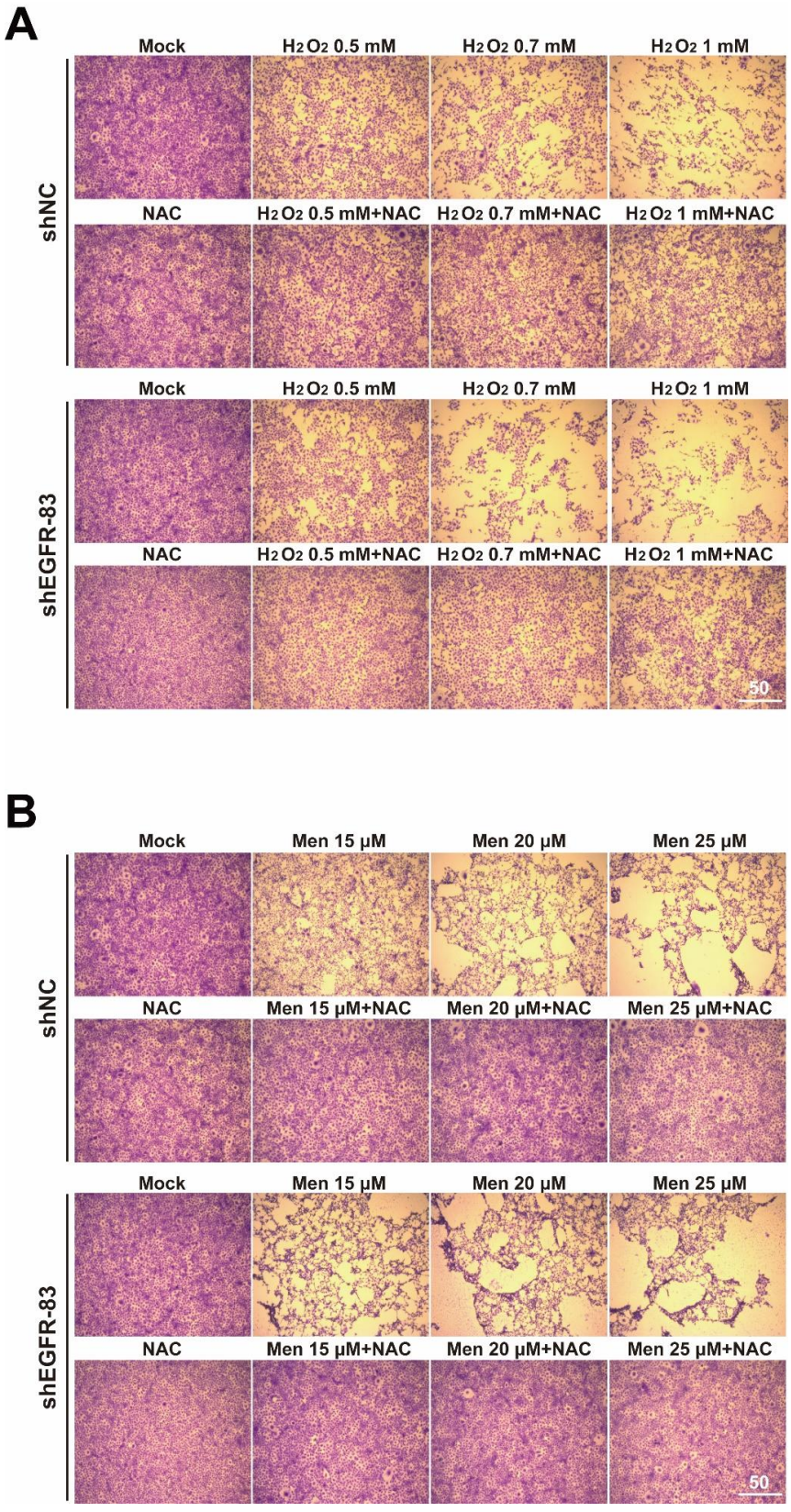
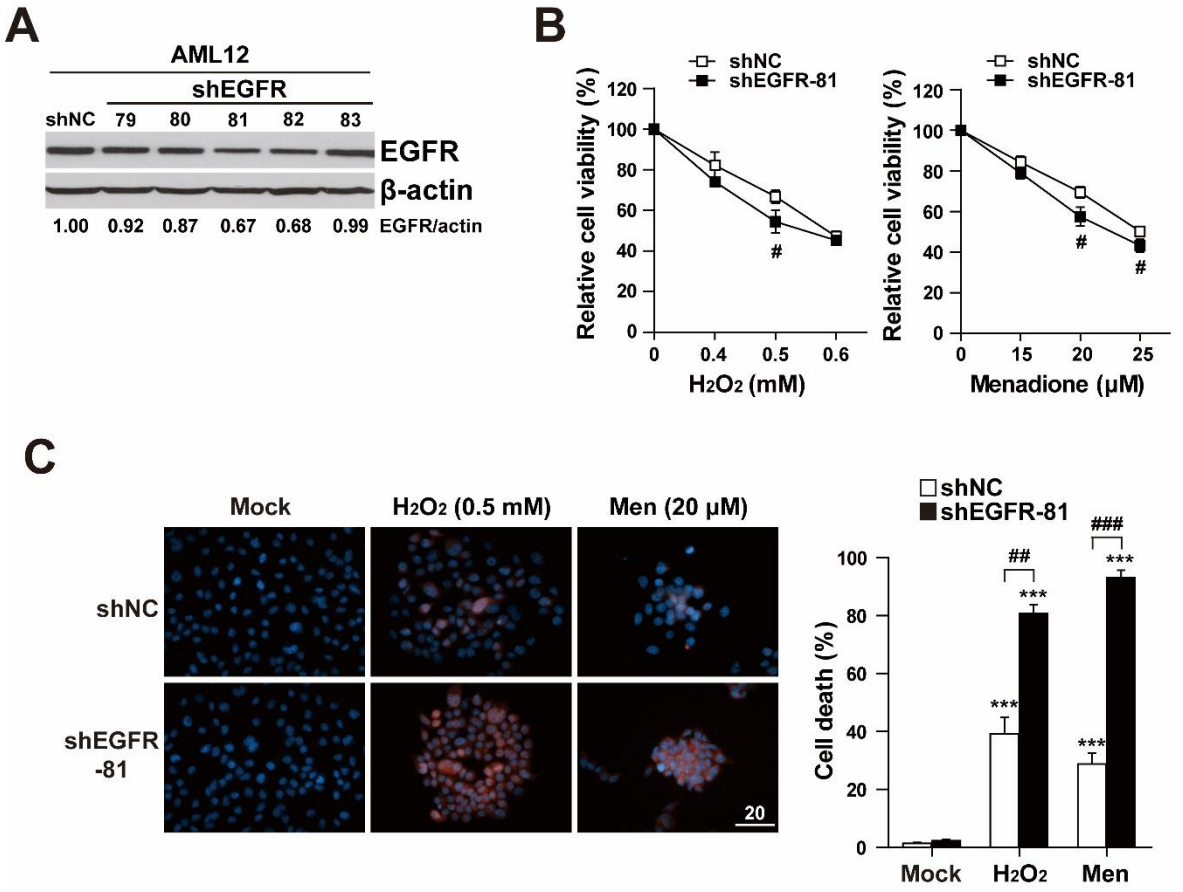


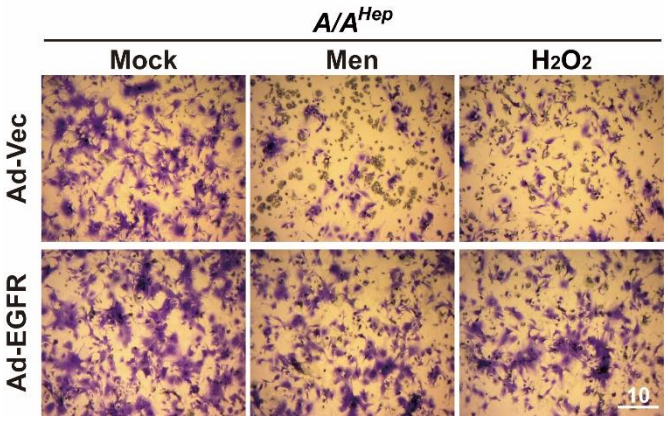
Supplementary Fig. S1. Concentration and time-dependent change of EGFR and eIF2α phosphorylation against reactive oxygen species. (A and B) Immortalized embryonic hepatocytes (A) and AML12 cells (B) were treated with hydrogen peroxide (H_2O_2) or menadione at indicated concentration for 6 h. (C and D) The immortalized embryonic hepatocytes (C) and AML12 cells (D) were treated with hydrogen peroxide (2.5 mM) or menadione (20 μM) for the indicated times. The cell lysates were subjected to SDS-PAGE, followed by immunoblot analyses using antibodies specific for p-EGFR, EGFR, p-eIF2α, eIF2α, and β-actin.



Supplementary Fig. S2. EGFR knockdown enhances susceptibility to reactive oxygen species in immortalized embryonic hepatocytes. (A and B) The shNC and shEGFR-83 cell lines were treated with hydrogen peroxide (H_2O_2) or menadione at indicated concentrations with/without NAC (1 mM) for 7 h. The remaining cells were stained with crystal violet staining solution (scale bar = 50 μm).



Supplementary Fig. S3. EGFR knockdown enhances susceptibility to reactive oxygen species in AML12 cells. (A) From AML12 cells stably expressing five EGFR shRNAs (79-83) or shNC, the cell lysates were subjected to SDS-PAGE, followed by immunoblot analyses using antibodies specific for EGFR and β-actin. For the EGFR/β-actin ratio, densitometry scanning was performed and quantified using NIH Image software. (B) AML12 shNC and AML12 shEGFR-81 cell lines were treated with menadione or hydrogen peroxide (H_2O_2) at indicated concentration for 7 h. Cell viability was determined using the crystal violet assay. The data are expressed as mean ± SEM of three independent experiments. $^{\#}P < 0.05$; shNC vs shEGFR. (C) AML12 shNC and AML12 shEGFR-81 cell lines were treated with hydrogen peroxide (H_2O_2, 0.5 mM) or menadione (20 μM) for 7 h. Cell death (apoptotic and necrotic cells) was determined using double staining with Hoechst 33258 and propidium iodide (PI). Representative images are shown (scale bar = 20 μm). At least 500 cells were counted, and cell death is expressed as a percentage of total cells. The data are expressed as mean ± SEM of three independent experiments. $^{***}P < 0.001$; Mock vs Chemicals in the same group, $^{\#\#}P < 0.01$ and $^{\#\#\#}P < 0.001$; shNC vs shEGFR.



Supplementary Fig. S4. EGFR overexpression reduces the susceptibility of eIF2α phosphorylation-deficient primary hepatocytes to reactive oxygen species. The Ad-EGFR-Flag or Ad-Vec infected *A/A*^{Hep} primary hepatocytes were treated with menadione (6 μM) or hydrogen peroxide (H_2O_2, 0.7 mM) for 30 h. The remaining cells were stained with crystal violet staining solution (scale bar = 10 μm).