

Figure S1. Compound C induces EGR-1 expression in skin cancer cells. (A) Compound C was involved in p53-EGR-1 pathway in BCC cells. Arrows were indicated as TP53 and EGR-1. (B) For the time-dependent assay, C32 and A375 cells were treated with 40 μM compound C for 0, 1, 2, 4, 6, 8, 12 or 24 h. For the dose-dependent assay, C32 cells were treated with 0, 1, 5, 10, 20, or 40 μM compound C for 8 h. A375 cells were treated with 0, 1, 5, 10, 20 or 40 μM compound C for 6 h. Protein expression level of EGR-1 was detected by immunoblotting. (C) HaCaT and C32 cells were treated with 0 or 40 μM compound C for 6 or 8 h. Immunofluorescence staining images were captured by confocal microscopy. Scale bar, 20 μm . EGR-1, early growth response 1; BCC, basal cell carcinoma; cDNA, complimentary DNA.

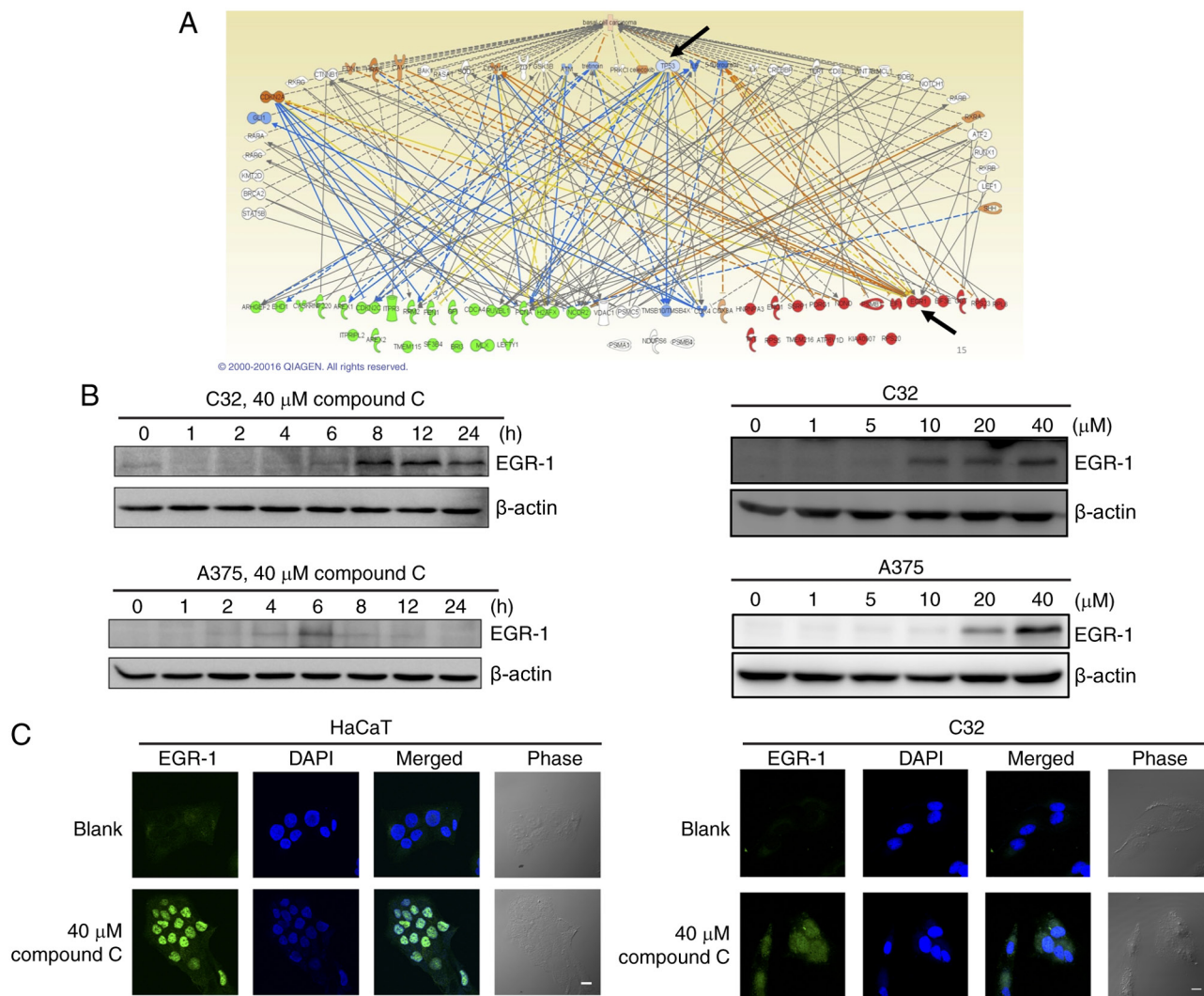


Figure S2. AMPK activation was not involved in compound C-induced EGR-1 expression in C32 and A375 cells. C32 and A375 cells were co-treated with or without 4 mM metformin and 40 μ M compound C for 8 or 6 h. Expression levels of EGR-1, AMPK, p-AMPK and β -actin were detected by immunoblotting.

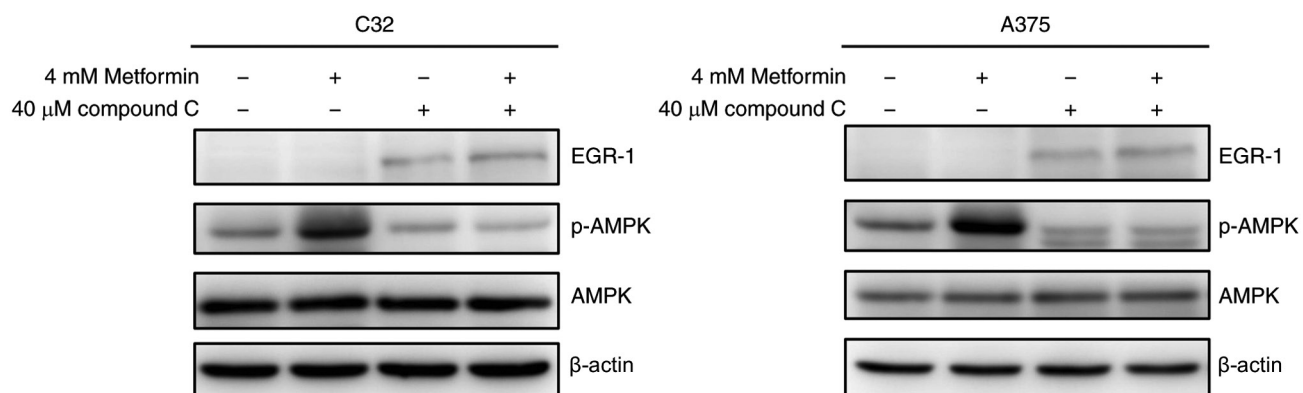


Figure S3. Compound C upregulates the EGR-1 expression mediated by the ERK signaling pathway. (A) C32 and A375 cells were treated with 40 μ M compound C for 8 or 6 h. (B) C32 cells were pretreated with 10 μ M U0126 for 1 h and then treated with 40 μ M compound C for 8 h. (C and D) C32 cells were pretreated with 2 mM NAC for 1 h and then treated with 40 μ M compound C for 4 or 8 h to evaluate the ROS or protein expression levels. Expression levels of EGR-1. This statistical result was analyzed using one-way ANOVA. ***P<0.001 vs. control. p-ERK, ERK and β -actin were detected by immunoblotting. EGR-1, early growth response 1; NAC, N-acetyl-cysteine; p-, phosphorylated.

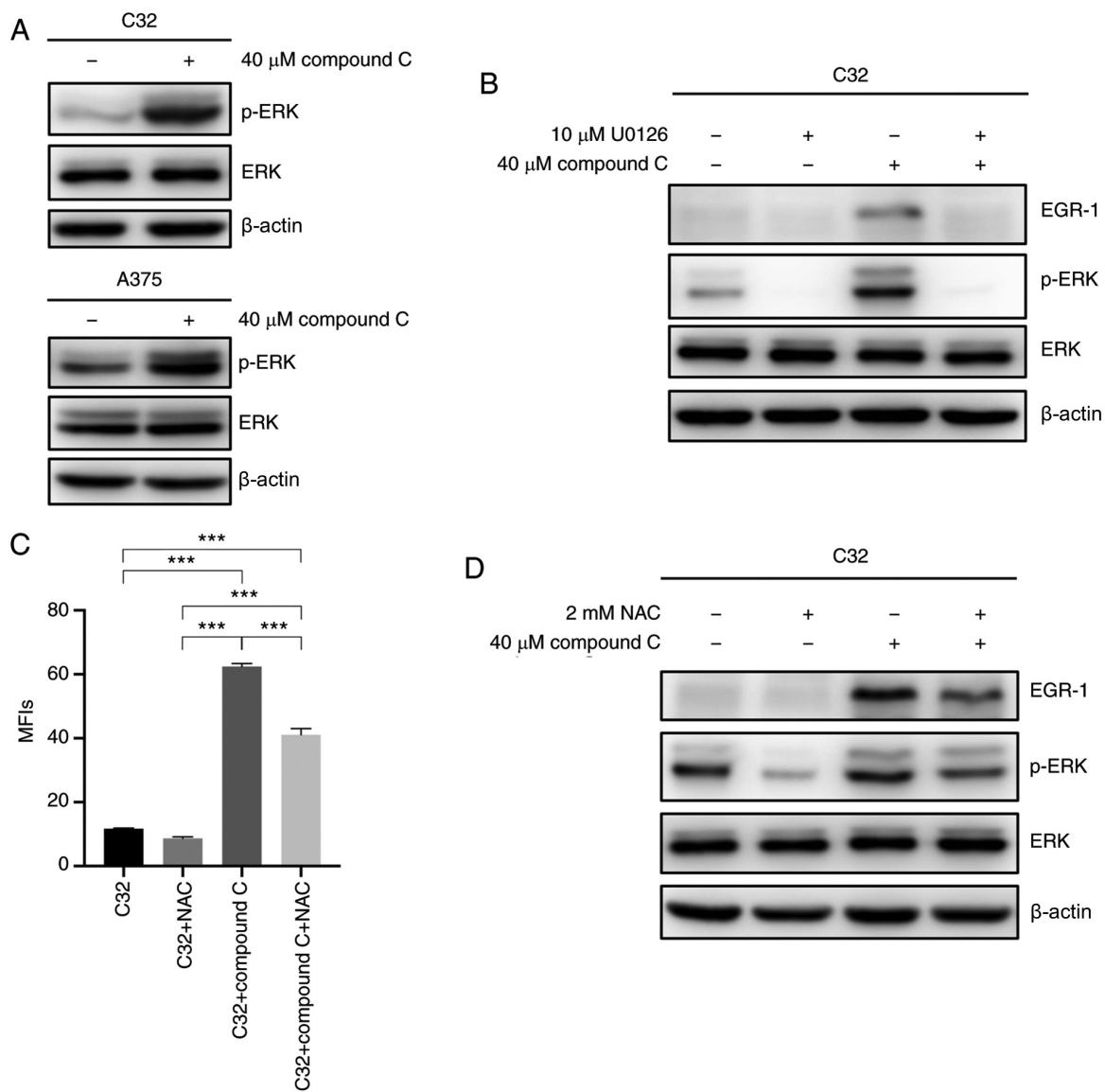


Figure S4. Compound C-induced p53 expression is EGR-1-independent. Control and EGR-1-knockdown BCC cells were treated with 40 μ M compound C for 6 h. Expression levels of EGR-1, p53 and β -actin were detected by immunoblotting. EGR-1, early growth response 1; BCC, basal cell carcinoma.

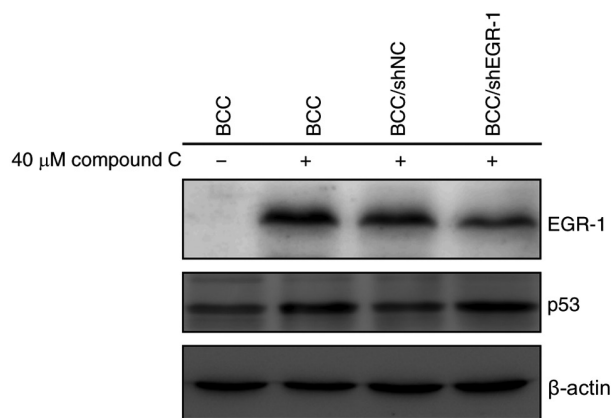


Table SI. The top-five genes were significantly upregulated by CC.

Gene	CC/Con [\log_2 (Ratio)]	P-value
FOS	4.11	3.04×10^{-11}
EGR-1	3.93	1.02×10^{-15}
BAAT	3.89	1.26×10^{-23}
GDF15, PGPEP1	3.73	6.03×10^{-17}
INSIG1	3.34	2.99×10^{-13}

CC, compound C; Con, control.