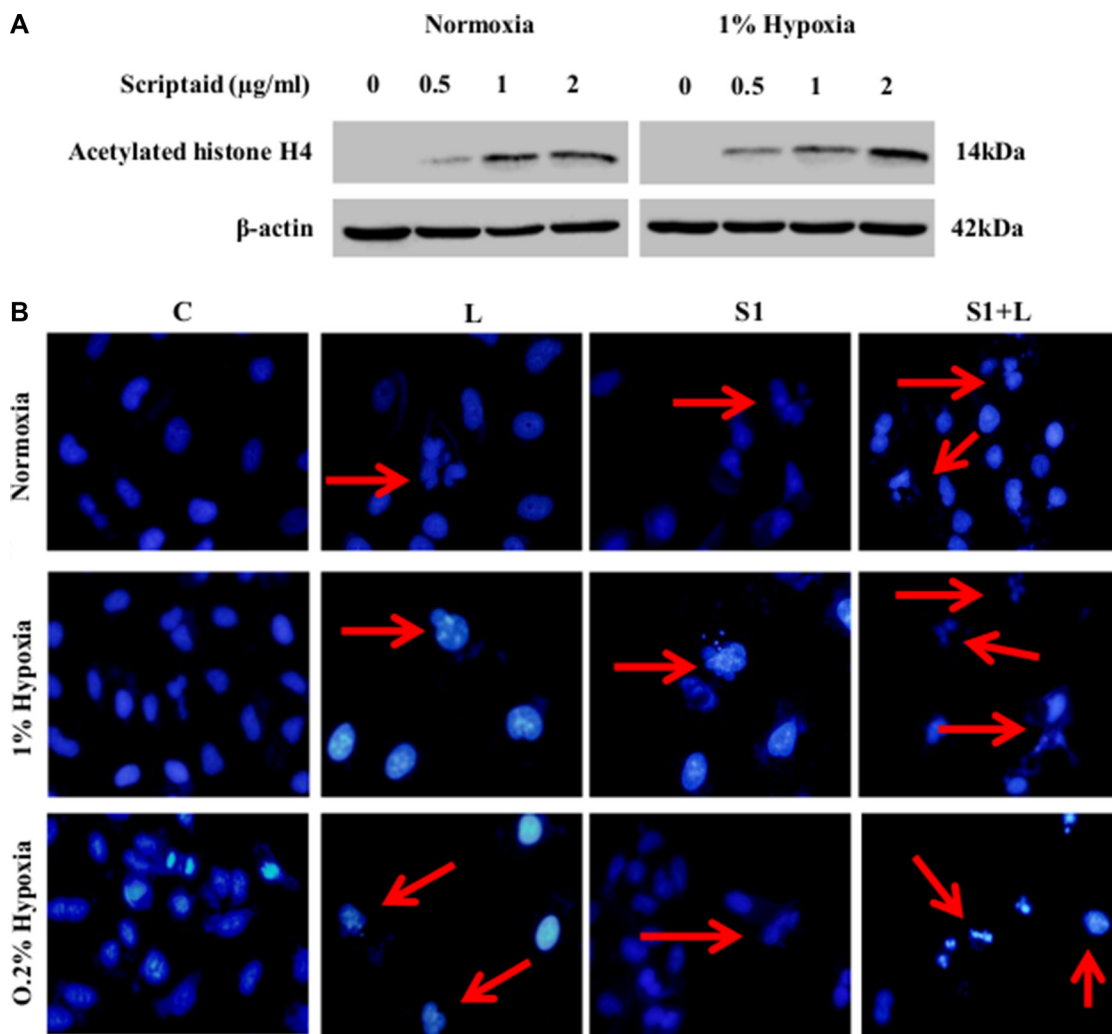
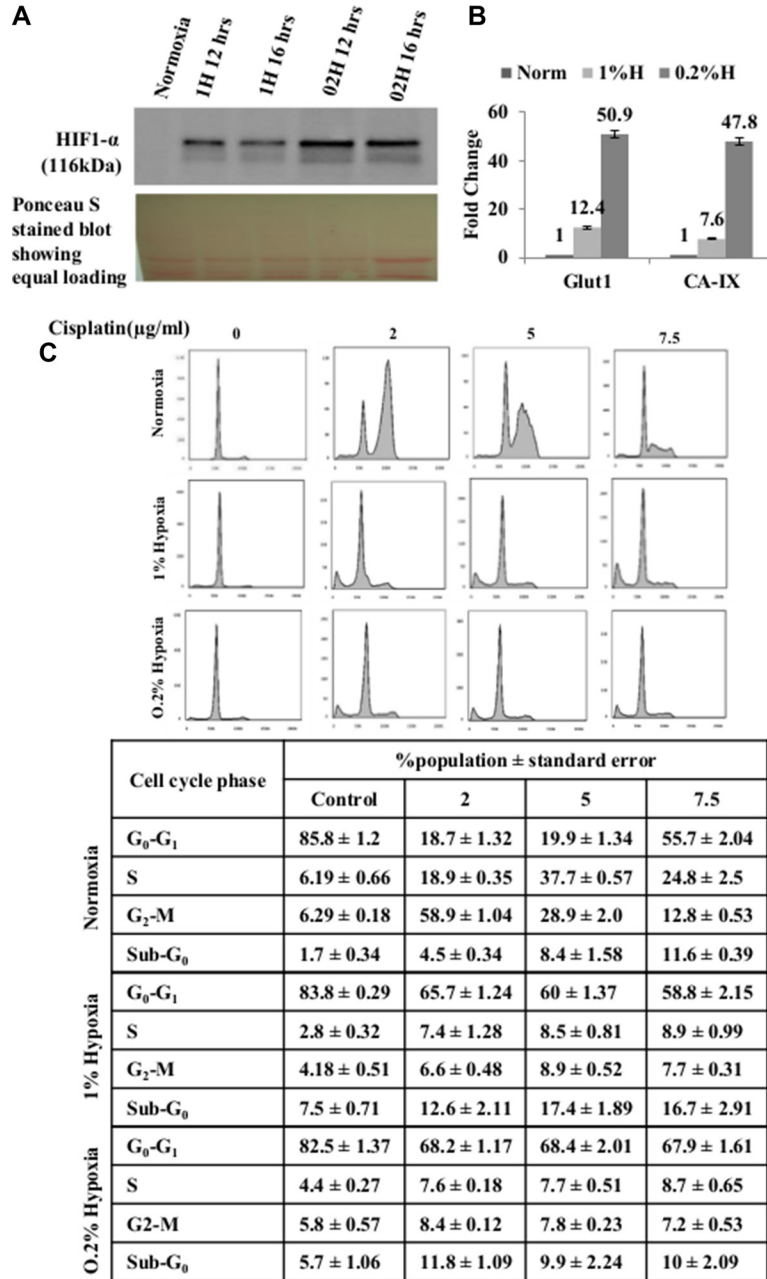


Scriptaid overcomes hypoxia-induced cisplatin resistance in both wild-type and mutant p53 lung cancer cells

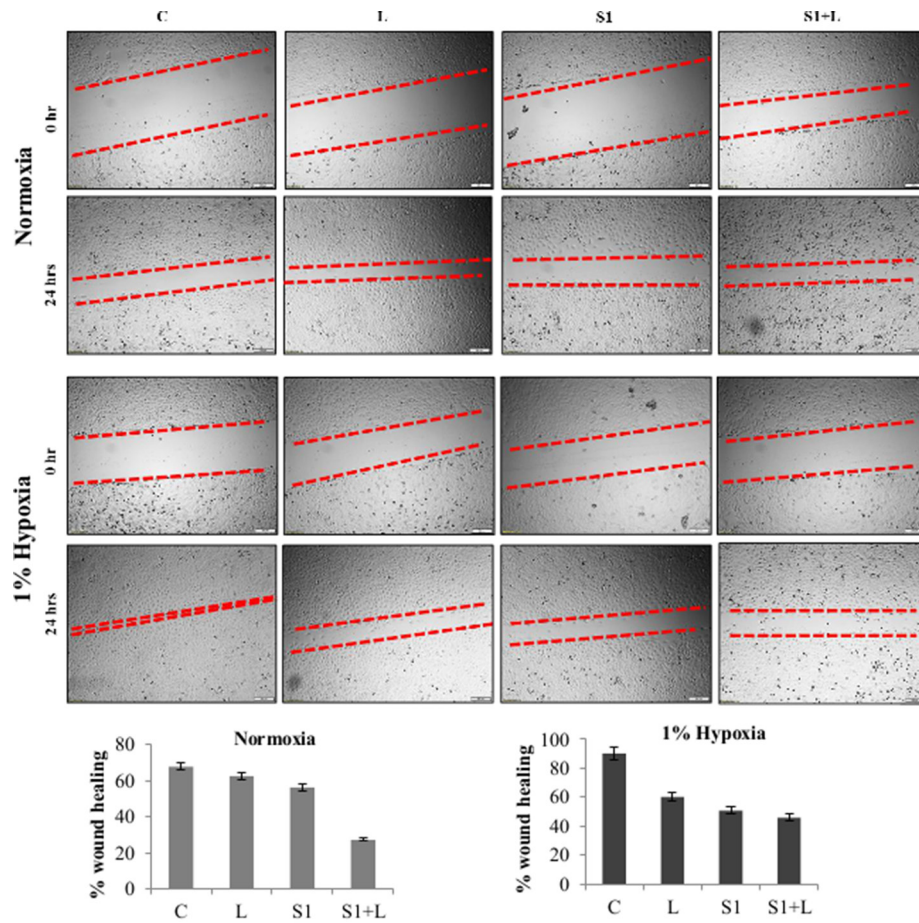
Supplementary Materials



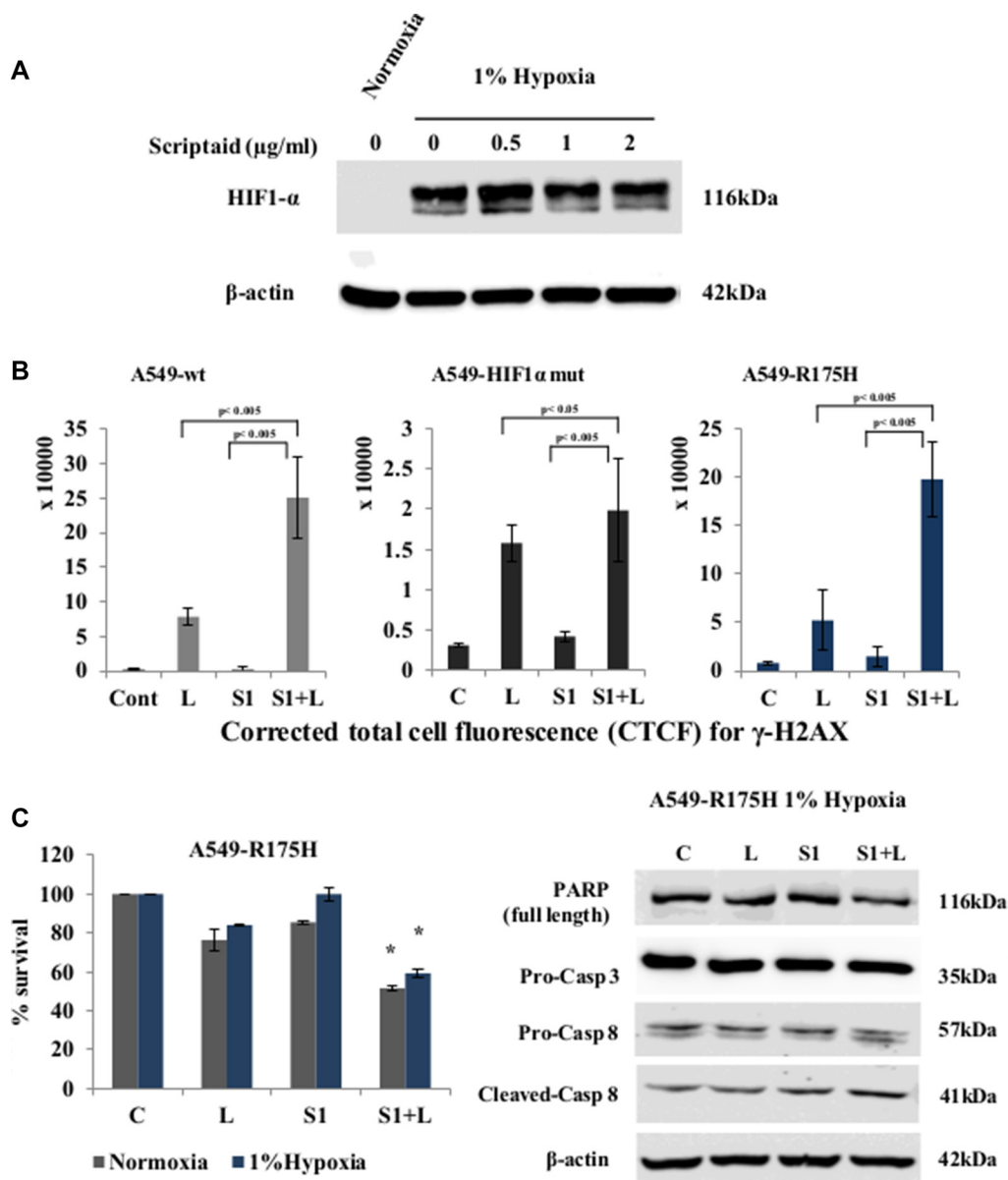
Supplementary Figure S1: (A) Western blot analysis showing up overexpression of acetylated histone H4 in response to scriptaid treatment in A549 cell line in a dose-dependent manner in normoxia and hypoxia. (B) DAPI stained nuclei showing morphological features of apoptotic cells in response to treatment. Arrows indicate blebs in the nucleus, a hallmark of cells undergoing apoptosis. Combination treated cells showed higher number of apoptosing cells.



Supplementary Figure S2: Confirmation of *in vitro* hypoxia by (A) western blot showing stabilization of hypoxia inducible factor (HIF) 1 α and up-regulation of HIF1 α -regulated genes (B) in A549. (C) Cell cycle analysis by flow cytometry showing G₂-M and S phase arrest of A549 cells in response to cisplatin treatment in normoxia. Arrest was overcome in hypoxia accompanied by increase in G₀-G₁ population.



Supplementary Figure S3: Wound healing assay showing inhibition of migration in response to treatment. Compared to normoxia, A549 cells showed aggressive migratory potency under hypoxic condition in untreated controls. The combination treatment was inhibitory to cell migration in both conditions. C = control, L = 2 µg/ml cisplatin, S1 = 1 µg/ml scriptaid. C = control, L = 2 µg/ml cisplatin, S1 = 1 µg/ml scriptaid. * indicates $p < 0.05$.



Supplementary Figure S4: (A) Western blot for HIF1 α shows no significant change in expression after 24 hrs treatment with various concentration of scriptaid in A549 cells. β -actin is used as the loading control. (B) CTCF for γ -H2AX was calculated using Image J software; in all 3 cell lines, the combination treatment resulted in significantly more DNA damage than single agent treatment. (C) MTT for single and combination in normoxia and hypoxia in A549-R175H cells showing effectiveness of the combination in both conditions; western blot for apoptosis markers in hypoxia for A549-R175H shows increased cell death in combination than that in single agent treatment. C = control, L = 2 μ g/ml cisplatin, S1 = 1 μ g/ml scriptaid. * indicates $p < 0.05$.