Supplementary figures.

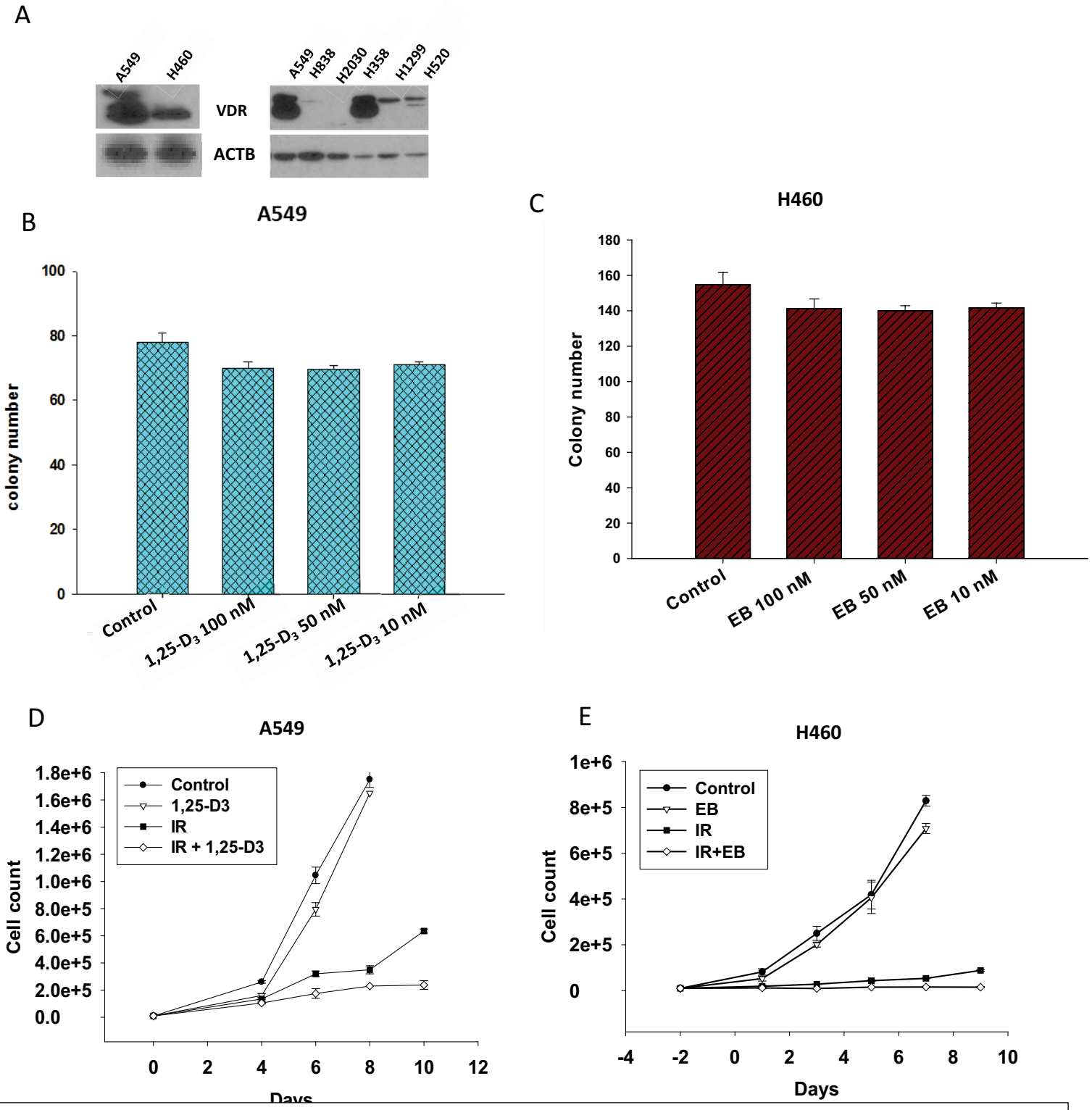


Figure S1. Vitamin D receptor Status in NSCLC cell lines and lack of effect of 1,25D_3 or EB 1089 alone. (**A**)**.** VDR status in select non-small cell lung cancer cell lines by Western blotting. (**B & C**) Clonogenic survival studies conducted with different doses of 1,25D_3 and EB 1089 in A549 and H460 cells indicates minimal inhibitory effects on survival. Studies were carried out for two weeks. (**D**) A549 cells were treated with either radiation alone, 100 nM 1,25D_3 alone or 100 nM 1,25D_3 in combination with radiation (IR, 6Gy). Viable cell number was determined at the indicated days following radiation exposure at day 0. (**E**) H460 cells were treated with radiation alone, 100 nM EB 1089 alone or the combination of 100 nM EB 1089 and radiation (IR, 6Gy). Viable cell number was determined at the indicated days following radiation exposure at day 0 (n=3 mean ± SE).

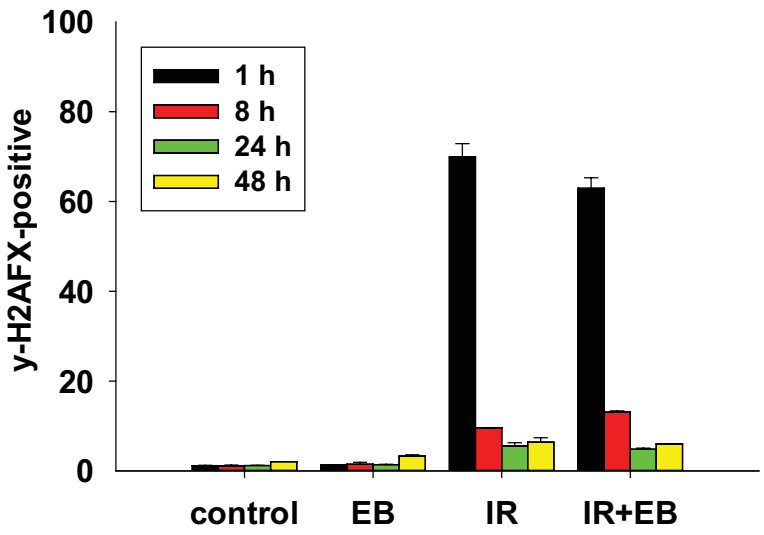
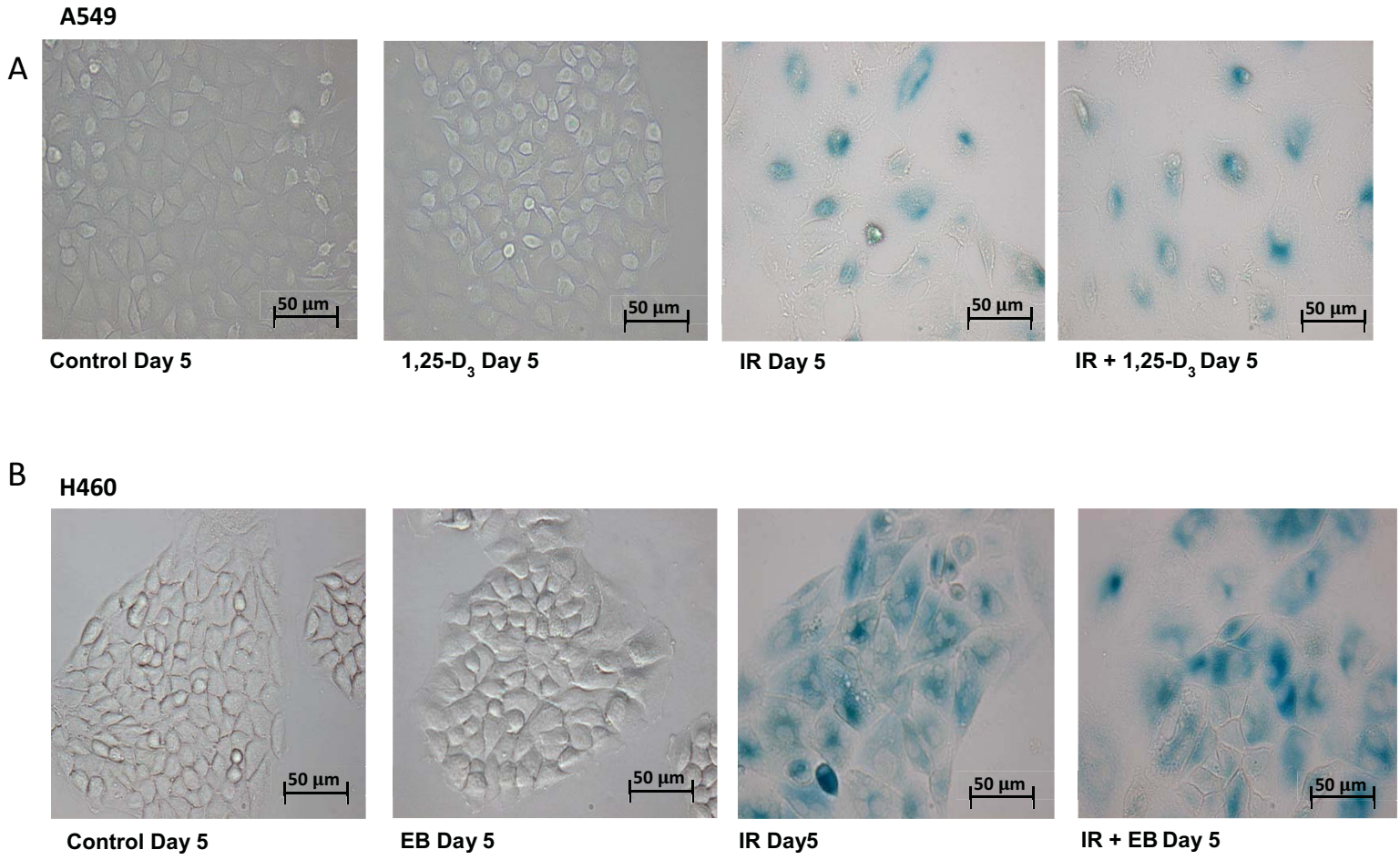


Figure S2. Induction and repair of DNA damage by radiation and EB 1089 + radiation. Induction and decline of DNA damage in H460 NSCLC cells by FACS analysis of γH2AFX levels after treatment with 100 nM of EB 1089 and 6Gy radiation alone and in combination (n=3 mean ± SE).



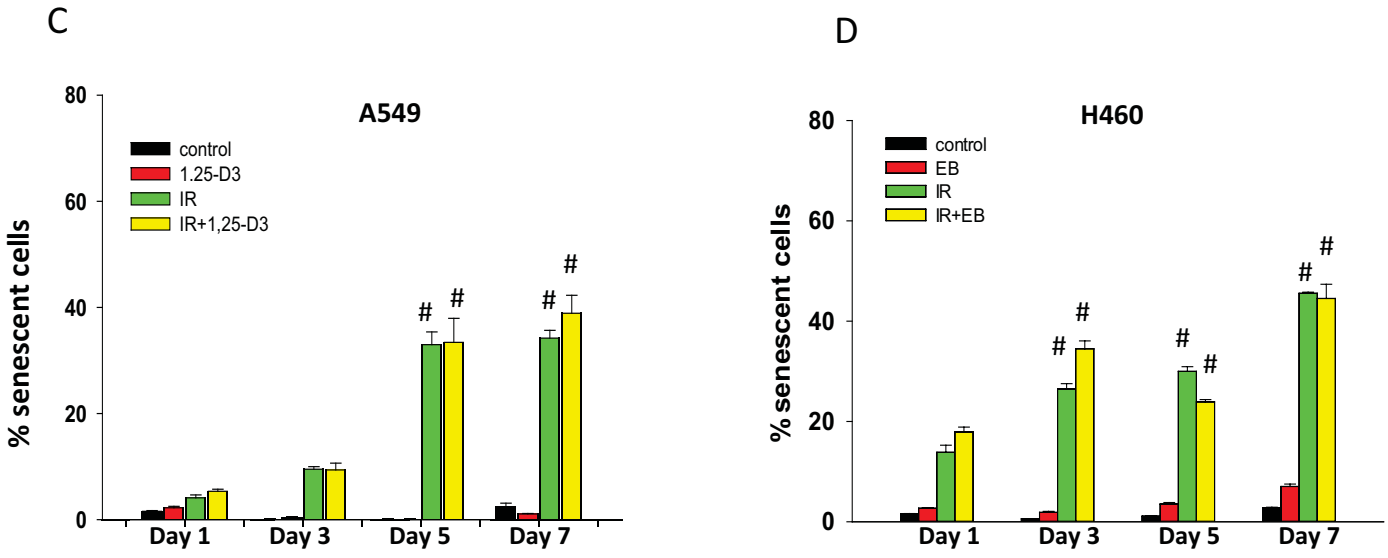


Figure S3. Senescence Induction by radiation and radiation + EB 1089 or 1,25-D_3. GLB/β-galactosidase staining indicative of senescence in A549 cells (**A**) and H460 cells (**B**) after 6 Gy radiation alone and the combination of IR (6Gy) + 1,25-D_3 or EB 1089. (**C/D**) Quantification of senescence by flow cytometry using C_{12}FDG in A549 cells (**C**) and H460 cells (**D**). (n=3, mean ± SE, #p<0.001 as compared to control)

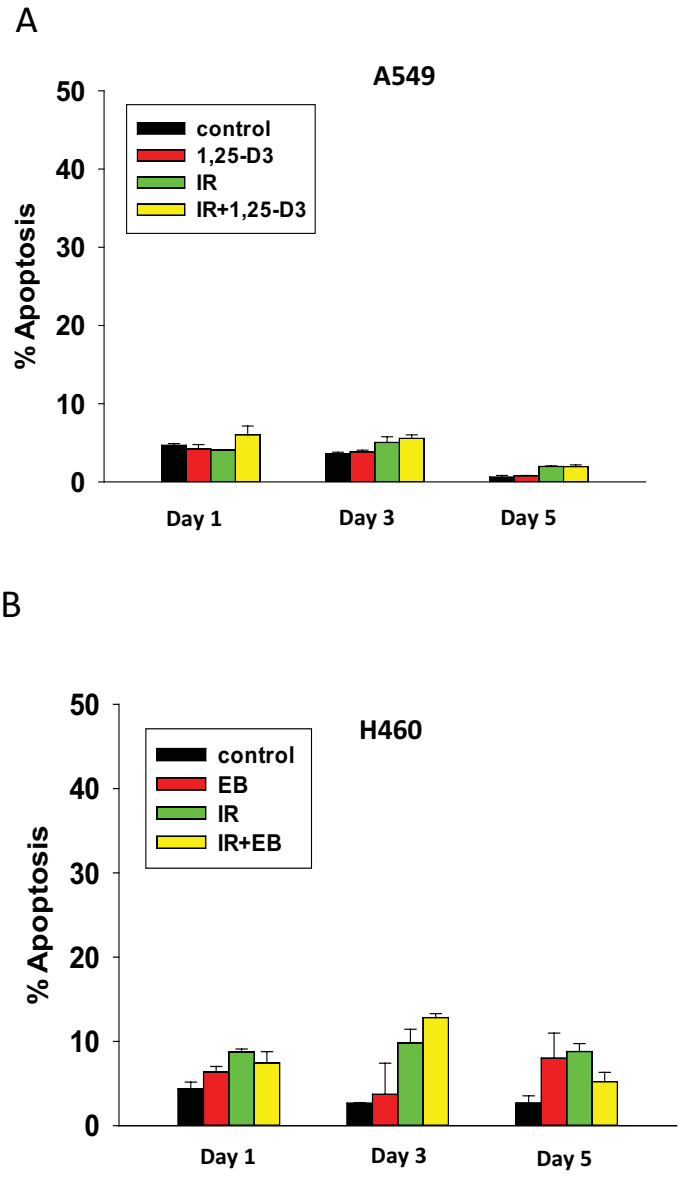


Figure S4. Absence of increased apoptosis associated with radiation sensitization. Apoptosis induction was quantified in A549 cells (**A**) and H460 cells (**B**) using annexin V and propidium iodide staining and flow cytometry. Quadrants indicating both early and late apoptosis were taken into account. (n=3, mean ± SE)

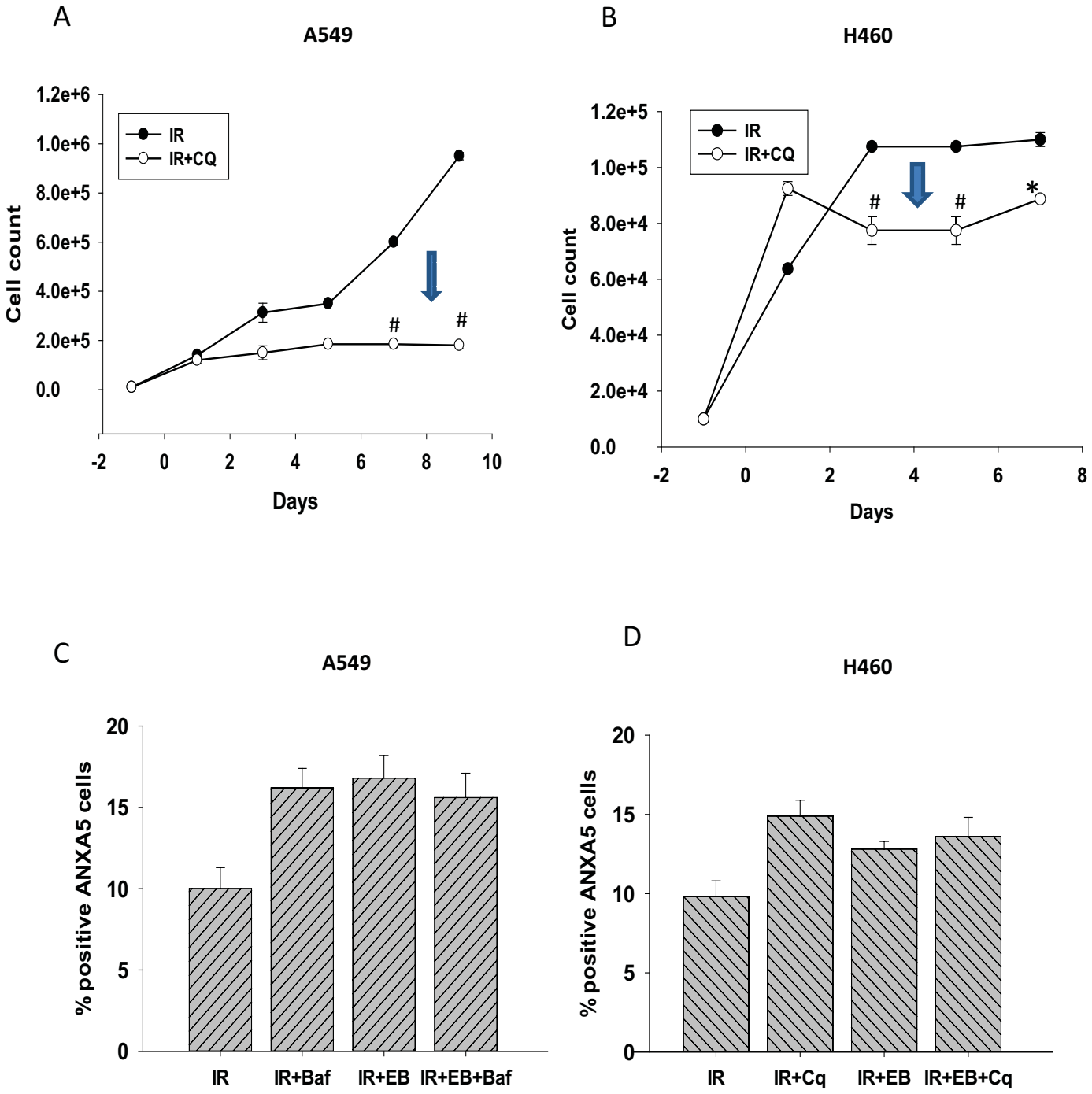


Figure S5. Cytoprotective Autophagy induced by Radiation**.** Evidence that autophagy induced by radiation (IR, 6 Gy) alone is cytoprotective in (**A**) A549 cells and (**B**) H460 cells based on increase in radiation sensitivity when autophagy is blocked by chloroquine (n=3, mean ± SE, #p<0.001; *p<0.05). (**C/D**) Blockade of autophagy induced by radiation alone by either bafilomycin or chloroquine results in an increase in apoptosis. Apoptosis was not increased when autophagy was blocked for the combination treatment of EB 1089 + IR in H460 NSCLC cells (n=3, mean ± SE).

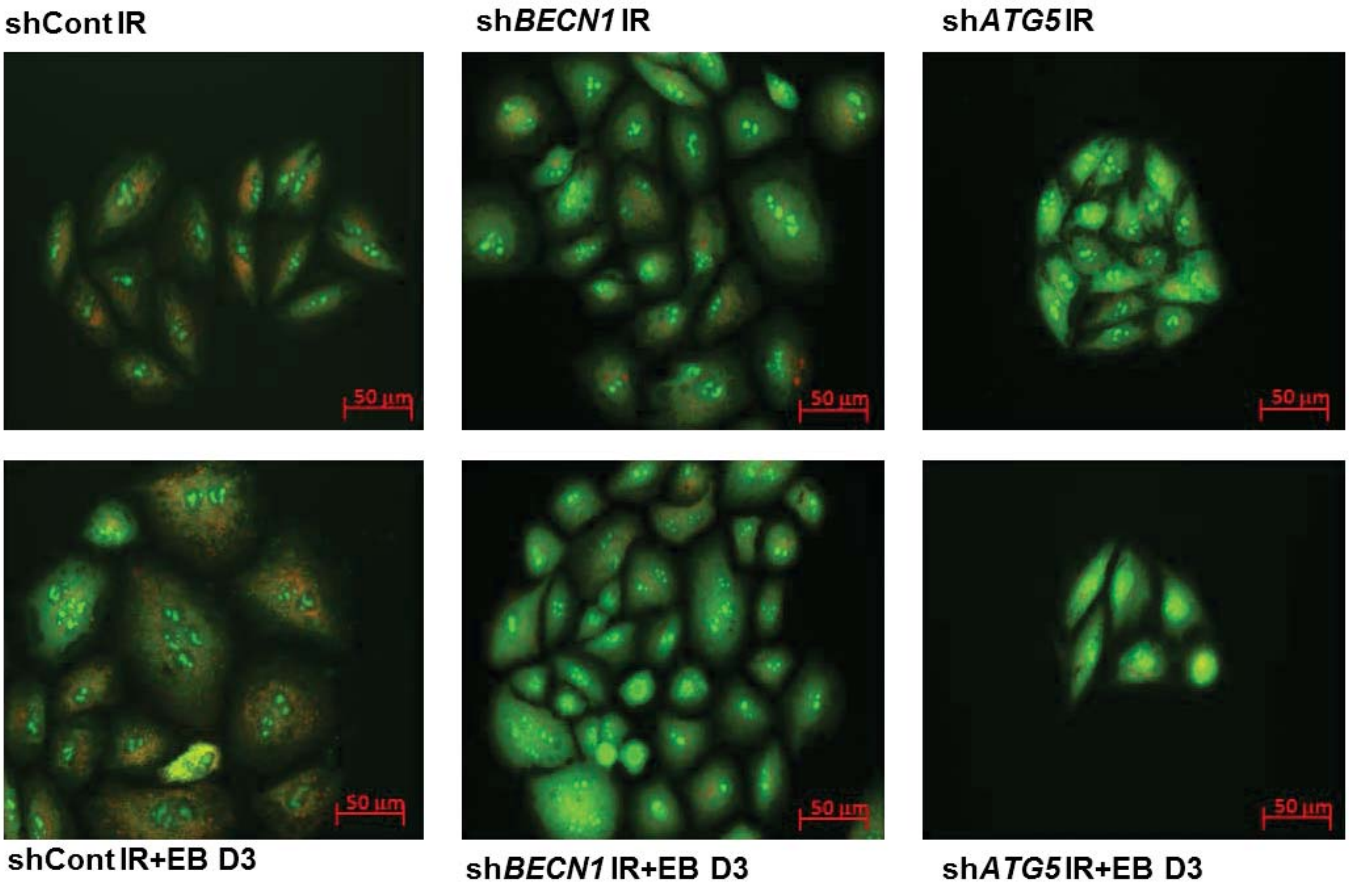
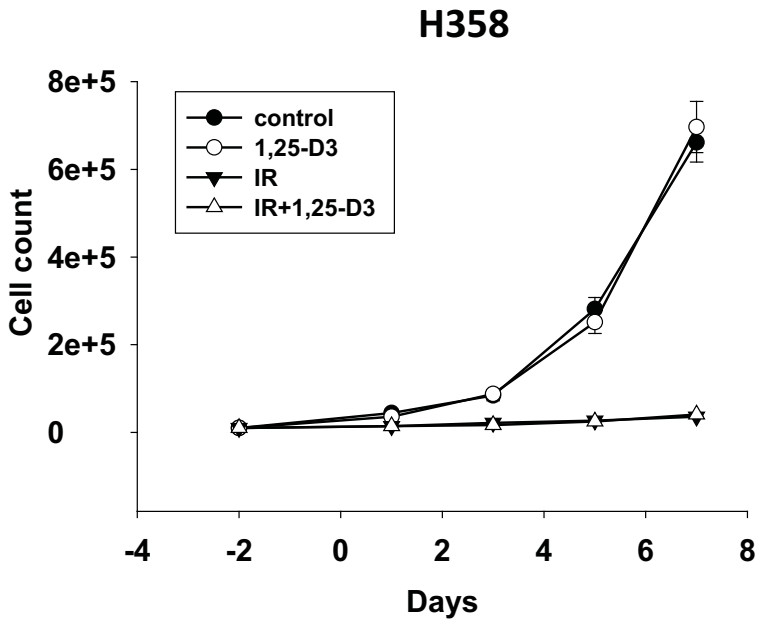


Figure S6. Inhibition of autophagy by genetic silencing**.** H460 cells with and without silencing of *ATG5* or *BECN1* were exposed to radiation alone or EB 1089 + radiation and autophagic vesicle formation was assessed based on acridine orange staining.

A



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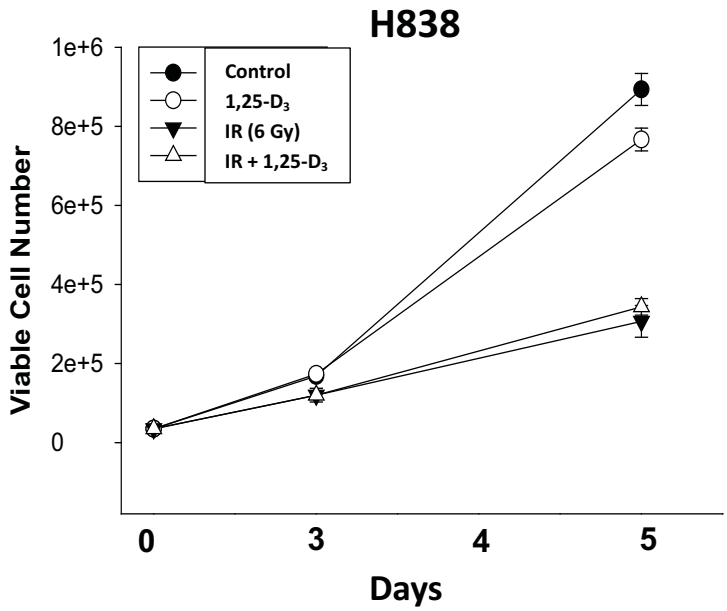


Figure S7. Lack of sensitization in NSCLC cells that are mutant in TP53 or lacking the VDR. (**A**) H358 cells that express the VDR but are mutant in TP53 were exposed to the vehicle control, 100 nM 1,25-D_3, radiation (IR, 6 Gy), or 100 nM 1,25-D_3 in combination with radiation. (**B**) H838 cells, which lacks the VDR but are wt in TP53 were exposed to radiation (IR, 6 Gy) and the combination treatment of IR+1,25-D_3. (n=3, mean ± SE)

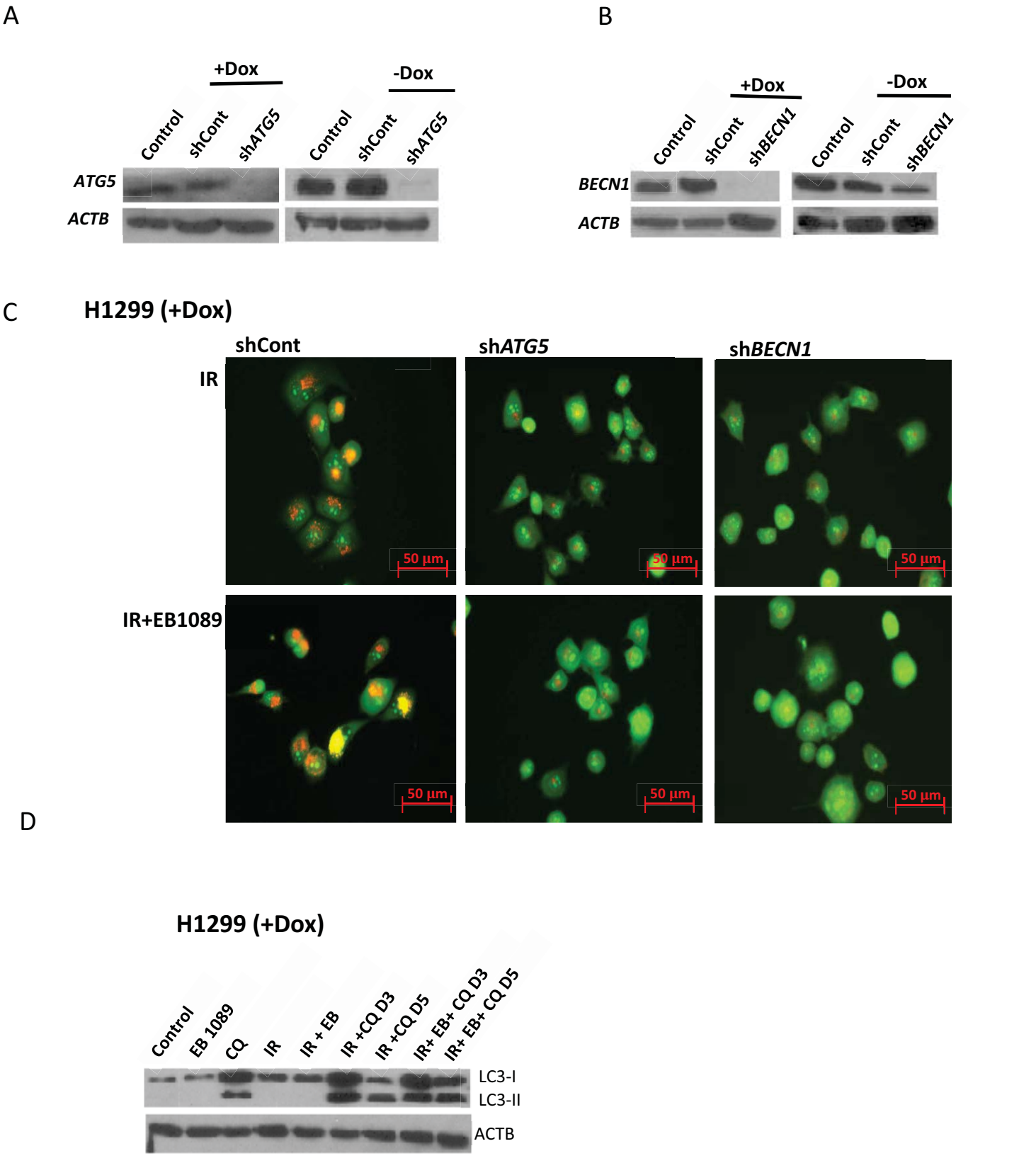
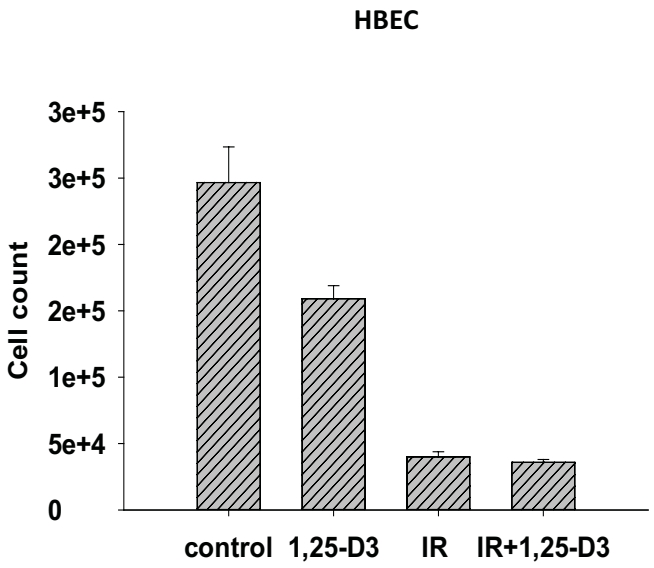


Figure S8. Inhibition of Autophagy by genetic silencing or exposure to chloroquine. (**A & B**) Autophagy genes *ATG5* and *BECN1* were silenced. (**C**) Inhibition of autophagy by silencing *ATG5* and *BECN1* is shown by reduced acidic vesicle formation using acridine orange staining. (**D**) Interference with autophagic flux as indicated by accumulation of LC3-II by western blotting.

A



B

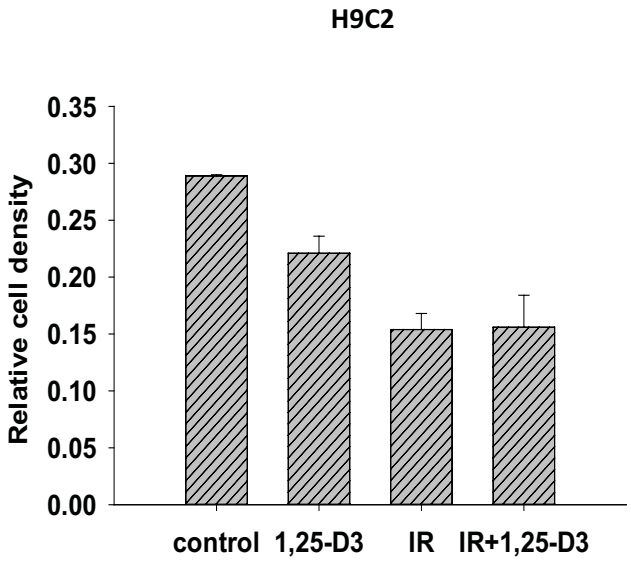


Figure S9. Lack of sensitization in human bronchial epithelial cells and cardiomyocytes**.** (**A**) Human bronchial epithelial cells were exposed to the vehicle control, 100 nM 1,25-D_3, radiation (IR, 6 Gy), or 100 nM 1,25-D_3 prior to irradiation (6 Gy). (**B**) H9C2 cardiomyocyes in culture were exposed to 100 nM 1,25-D_3 for 72 hours followed by radiation (5 Gy). (n=3, mean ± SE).