

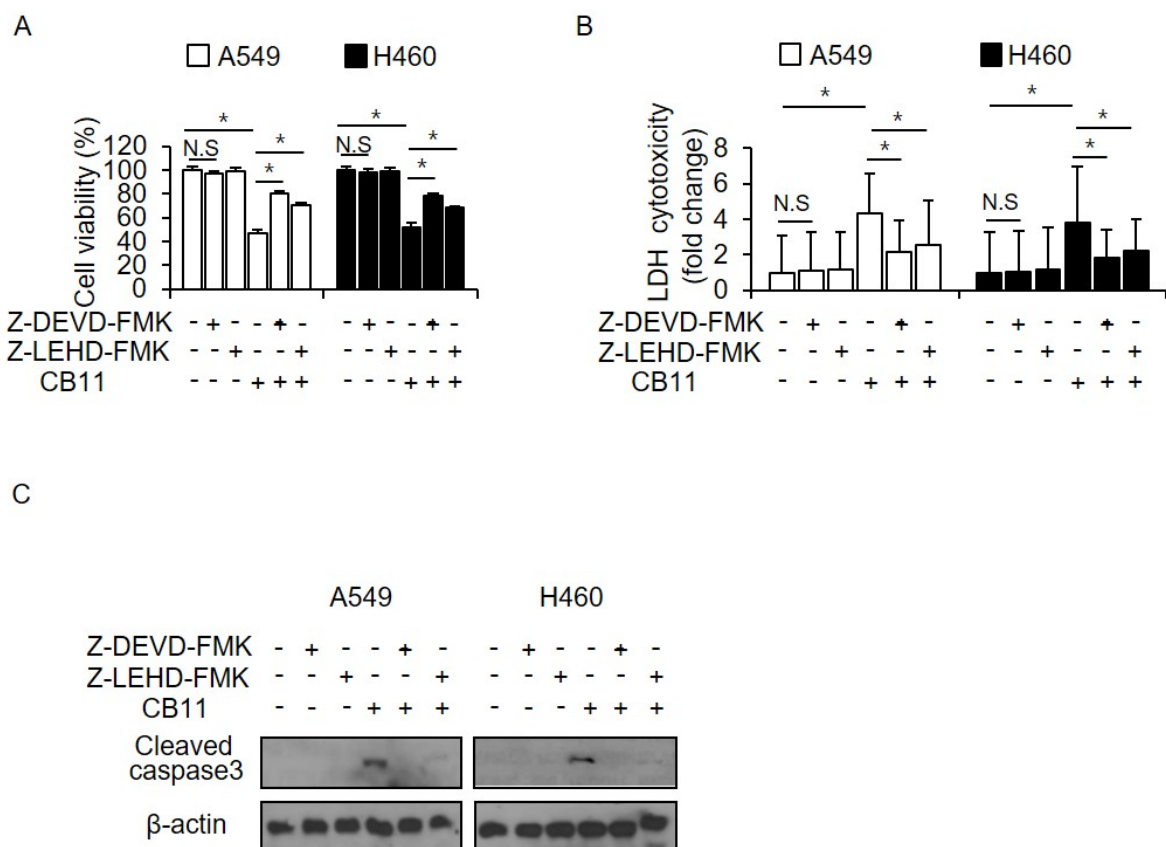
Supplemental Material

CB11, a novel purine-based PPAR γ ligand, overcomes radio-resistance by regulating ATM signaling and EMT in human non-small-cell lung cancer cells.

Tae Woo Kim, Da-Won Hong, Joung Whan Park, and Sung Hee Hong*

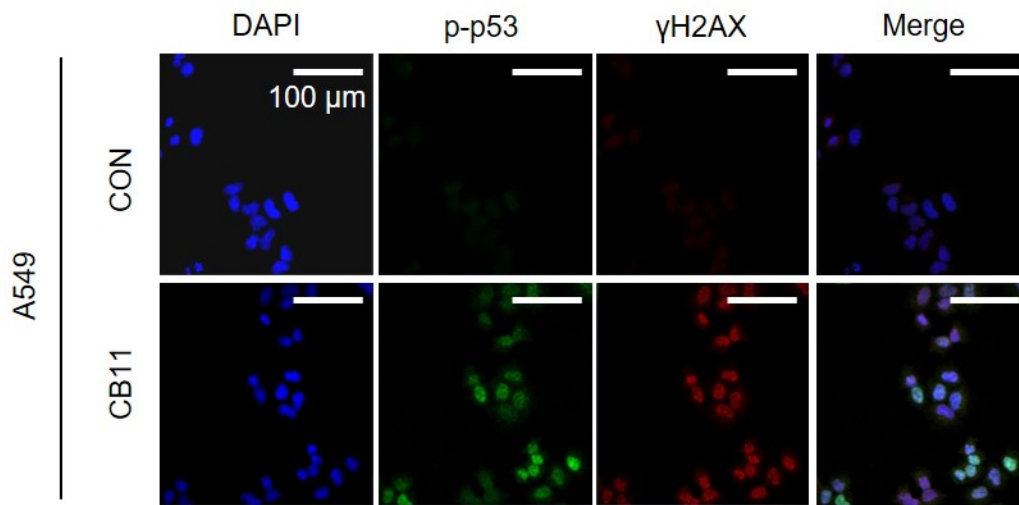
Supplementary Figure

Supplementary Figure 1.

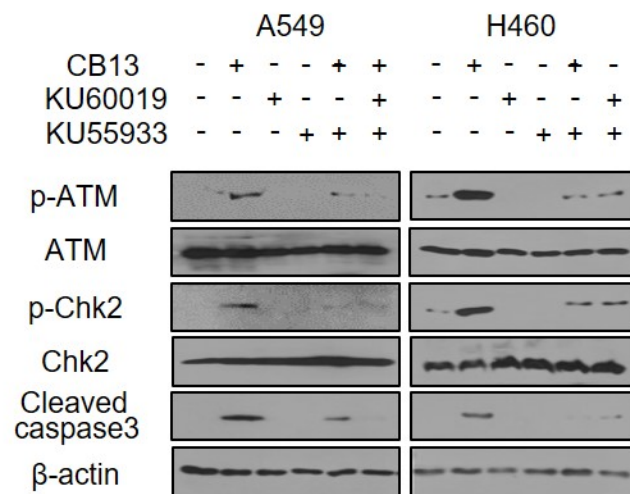


Supplementary Figure 2.

A

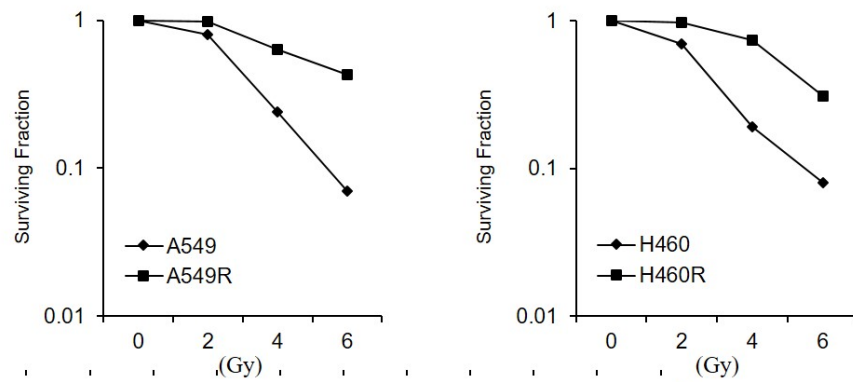


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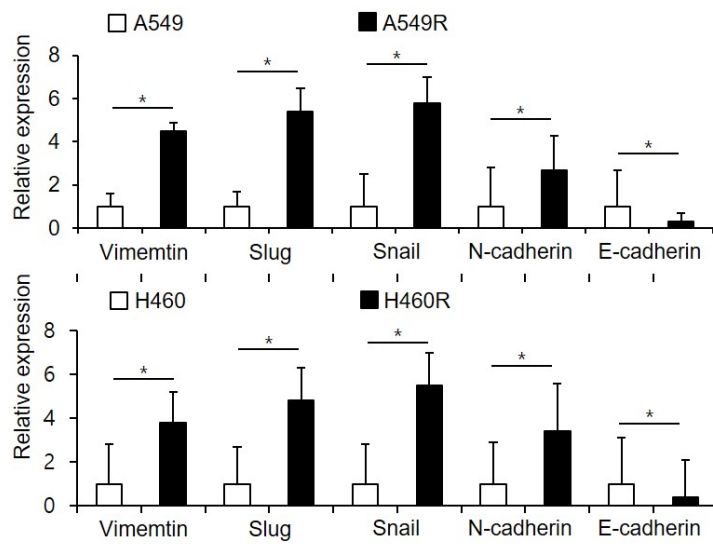


Supplementary Figure 3.

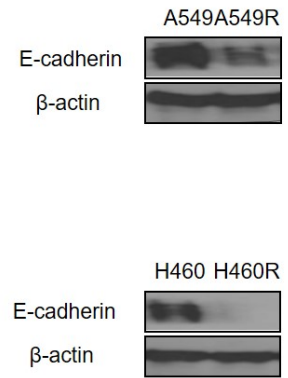
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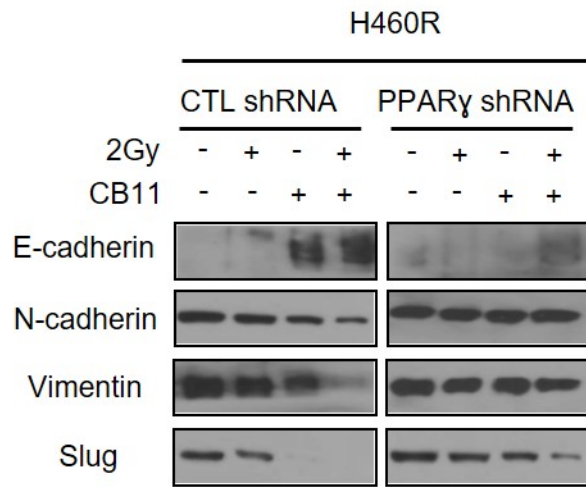
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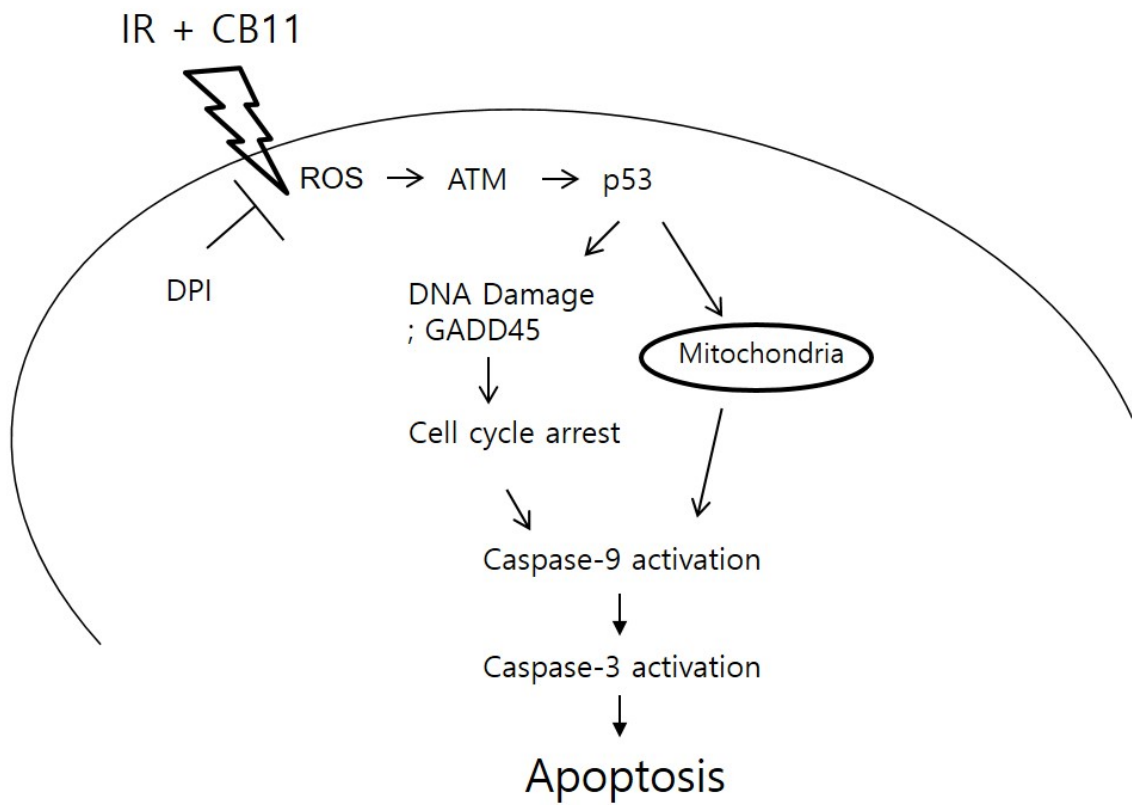
C



Supplementary Figure 4.



Supplementary Figure 5.



Supplementary Figure Legends

Supplementary Fig 1. The effects of Z-DEVD-FMK and Z-LEHD-FMK on CB11-treated A549 and H460 cells. **A-C** A549 and H460 cells were pretreated with Z-DEVD-FMK (20 μ M) or Z-LEHD-FMK (20 μ M) for 4 h and subsequently treated with CB11 (30 μ M, 24 h). Cell viability and cytotoxicity were determined using WST-1 and LDH assays, respectively; *, $p < 0.05$. A Western blot analysis was conducted on protein samples to determine cleaved caspase-3 levels. β -actin was used as a protein loading control.

Supplementary Fig 2. A Analyses of p-p53 and γ H2AX responses to CB11. p-p53 and γ H2AX confocal immunofluorescence staining in A549 cells treated with CB11 (30 μ M, 24 h). p-p53 was labeled in green, γ -H2AX was labeled in red, and nuclei were stained in blue with DAPI (4',6-diamidino-2-phenylindole). **B** ATM inhibitors suppress CB13-mediated ATM signaling. A549 and H460 cells were treated with or without CB13 (30 μ M, 24 h), KU60019 (10 μ M, 24 h) and KU55933 (10 μ M, 24 h) for 24 h. Western blot analysis was conducted on protein samples to determine p-ATM, ATM, p-chk2, chk2 and cleaved caspase-3 levels. β -actin was used as a protein loading control.

Supplementary Fig 3. Generated radio-resistant A549R and H460R cells acquire an EMT phenotype. **A** A clonogenic cell survival assay was performed with various doses (0, 2, 4, or 6 Gy) of radiation, and the survival fraction was calculated using the surviving fraction formula in A549, A549R, H460, and H460R cells; *, $p < 0.05$. **B-C** Real-time RT-PCR was used to detect the expression of E-cadherin, N-cadherin, vimentin, slug, and snail in A549, A549R, H460, and H460R cells, and Western blot analysis was used to detect the protein expression of E-cadherin in A549, A549R, H460, and H460R cells; *, $p < 0.05$. β -actin was used as an RNA and protein loading control.

Supplementary Fig 4. PPAR γ shRNA-stable cell lines were established after H460R cells were transfected with PPAR γ shRNA. These cells were treated with CB11 (30 μ M) and Western blot analyses were performed to examine the levels of E-cadherin, N-cadherin, vimentin, and slug proteins; *, $p < 0.05$. β -actin was used as a protein loading control.

Supplementary Fig 5. Schematic representation of the apoptotic cell death signaling pathway induced by 2Gy + CB01 in radio-resistant NSCLC cells.