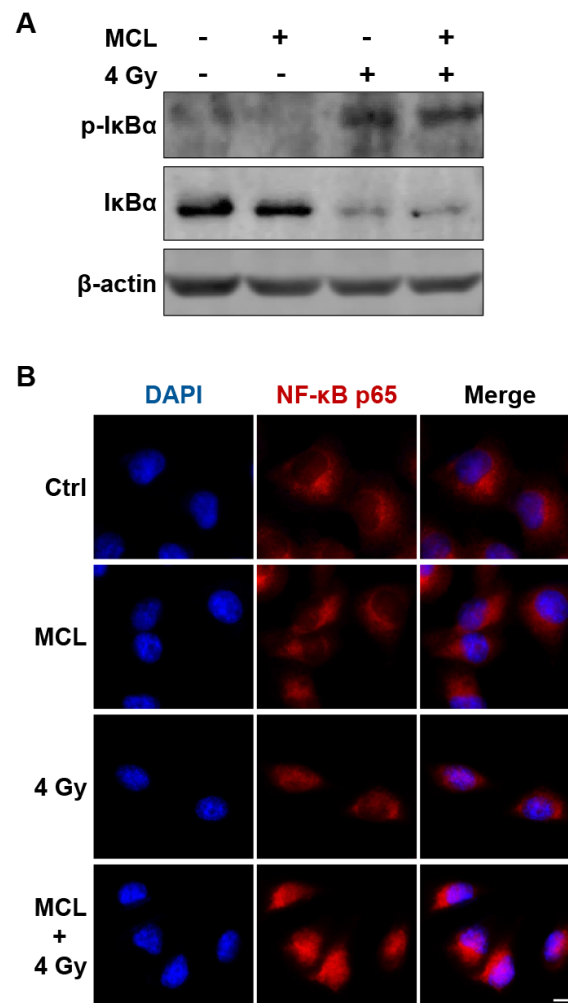
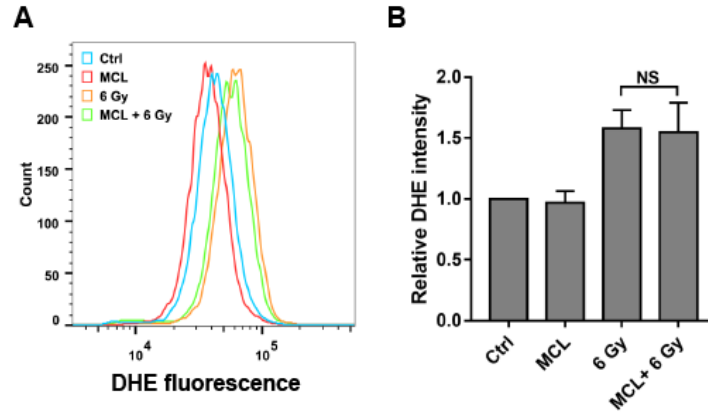


**Figure S1.** MCL sensitizes H1299 and Calu-1 cells to IR. (A) The relative cell viabilities of H1299 and Calu-1 cells were evaluated at 72 h after IR with or without MCL (5 or 10 μM) pretreatment under normoxia. \*,  $p < 0.05$ , \*\*,  $p < 0.01$ , compared with control (without radiation); #,  $p < 0.05$ , ##,  $p < 0.01$ , compared with counterpart (without MCL treatment). (B) The survival curves of H1299 and Calu-1 cells after IR with or without MCL (5 or 10 μM) pretreatment under normoxia. (C) The relative cell viabilities of H1299 and Calu-1 cells were evaluated at 72 h after IR with or without MCL (5 or 10 μM) pretreatment under hypoxia. \*\*,  $p < 0.01$ , compared with control (without radiation); ##,  $p < 0.01$ , compared with counterpart (without MCL treatment). (D) The survival curves of H1299 and Calu-1 cells after IR with or without MCL (5 or 10 μM) pretreatment under hypoxia.



**Figure S2.** MCL treatment does not affect the IR-activated NF- $\kappa$ B signaling pathway in H1299 cells. (A) Western blot analysis of phosphorylation and degradation of I $\kappa$ B $\alpha$  at 2 h after IR in H1299 cells pretreated with or without MCL (20  $\mu$ M). (B) Representative immunofluorescence images of intracellular localization of NF- $\kappa$ B p65 (red) in H1299 cells pretreated with or without MCL (20  $\mu$ M) at 2 h after IR. Nucleus (blue) was stained with DAPI. Scale bar, 10  $\mu$ m.





**Figure S5.** MCL does not affect the ROS production after IR in H1299 cells. (A) Determination of ROS with its specific fluorescent probe dihydroethidium (DHE) at 12 h after IR in H1299 cells pretreated with or without MCL (20  $\mu$ M). (B) Quantification of (A).

**Table S1.** The survival curve parameters of H1299 and Calu-1 cells after IR with pretreatment of MCL (5 or 10  $\mu$ M ) under normoxia.

|                | H1299           |      |       | Calu-1          |      |       |
|----------------|-----------------|------|-------|-----------------|------|-------|
|                | SF2             | Dq   | SERDq | SF2             | Dq   | SERDq |
| Ctrl           | 0.67 $\pm$ 0.06 | 1.75 | -     | 0.58 $\pm$ 0.05 | 1.13 | -     |
| 5 $\mu$ M MCL  | 0.63 $\pm$ 0.07 | 1.47 | 1.18  | 0.55 $\pm$ 0.04 | 1.03 | 1.10  |
| 10 $\mu$ M MCL | 0.58 $\pm$ 0.04 | 1.26 | 1.39  | 0.49 $\pm$ 0.02 | 0.76 | 1.48  |

<sup>1</sup> SF2, survival fraction at 2 Gy. <sup>2</sup> Dq, quasithreshold dose. <sup>3</sup> SERDq, sensitization enhancement ratio for Dq.

**Table S2.** The survival curve parameters of H1299 and Calu-1 cells after IR with pretreatment of MCL (5 or 10  $\mu$ M ) under hypoxia.

|                | H1299           |      |       | Calu-1          |      |       |
|----------------|-----------------|------|-------|-----------------|------|-------|
|                | SF2             | Dq   | SERDq | SF2             | Dq   | SERDq |
| Ctrl           | 0.76 $\pm$ 0.03 | 2.37 | -     | 0.63 $\pm$ 0.03 | 1.42 | -     |
| 5 $\mu$ M MCL  | 0.68 $\pm$ 0.04 | 1.75 | 1.36  | 0.59 $\pm$ 0.05 | 1.17 | 1.21  |
| 10 $\mu$ M MCL | 0.59 $\pm$ 0.06 | 1.39 | 1.71  | 0.51 $\pm$ 0.04 | 0.90 | 1.59  |

<sup>1</sup> SF2, survival fraction at 2 Gy. <sup>2</sup> Dq, quasithreshold dose. <sup>3</sup> SERDq, sensitization enhancement ratio for Dq.

## Materials and Methods

### 1. Immunofluorescence

Cells were fixed with 4% paraformaldehyde and permeabilised with TNBS solution (PBS supplemented with 0.5% Triton X-100 and 1% FBS) for 1 h. The cells were then incubated with specific primary antibodies for different proteins as follows: anti- $\gamma$ -H2AX (phospho S139) antibody (1:200, Abcam) or anti-NF- $\kappa$ B p65 antibody (1:200, Cell Signaling Technology) at 37  $^{\circ}$ C for 2 h. After rinsing with TNBS, the cells were incubated with Goat Anti-Rabbit IgG H&L (TRITC) (1:1000, Abcam) at 37  $^{\circ}$ C for 1 h. DAPI (5 mg/mL; Sigma-Aldrich) was used to stain the nuclei. The cells were visualized with a fluorescence microscope (Leica DMI 4000B).

### 2. ROS measurement

ROS measurement was performed by flow cytometry in cells incubated with Dihydroethidium (DHE) (Molecular Probes) at a final concentration of 10  $\mu$ M for 30 min at 37  $^{\circ}$ C.

### *3. Cell cycle analysis*

Cells were harvested, fixed with 70% ethanol and stored at -20 °C for 24 h. Samples were then harvested by centrifugation at 1000 rpm for 5 min, washed twice with PBS and incubated with RNase A (0.25 mg/ml) and propidium iodide (20 µg/ml, BD Biosciences) for 30 min at 37 °C. Propidium iodide staining analysis was performed using a BD Accuri C6 analyzer (BD Biosciences). Cell cycle analysis was performed using Modfit LT 3.1 software.