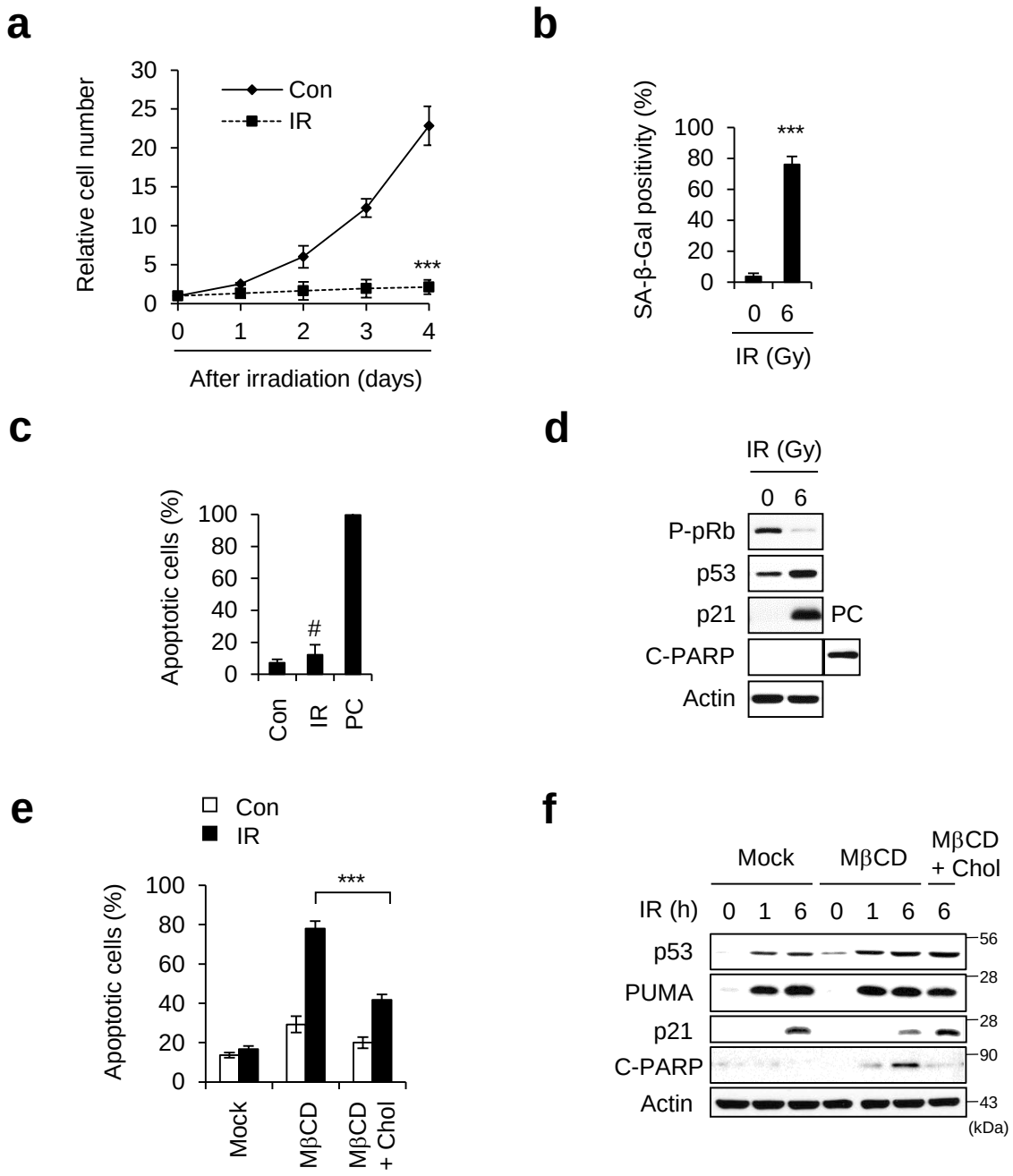
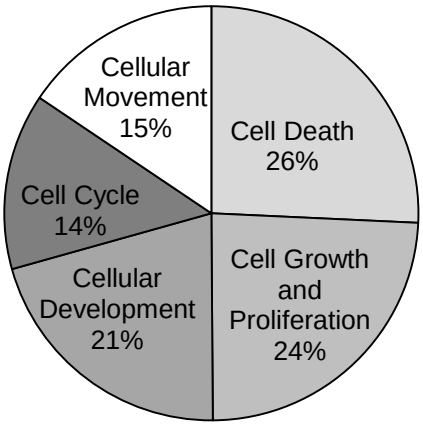


Supplementary Figure S1. MCF7 cells were irradiated with IR 6 Gy. **a**, Relative cell numbers were determined on the indicated days. Viable cell numbers on 0 day after irradiation was considered as 1. **b-d**, SA-β-Gal staining (**b**), Annexin V positivity (**c**), and immunoblotting (**d**) were performed at 4 days, 1 day, and 2 days after IR exposure, respectively. **e** and **f**, MCF7 cells were treated without (Mock) or with 0.1 mM MβCD. MβCD+chol indicates cholesterol repletion with the MβCD/cholesterol mixture. Quantification of Annexin V positivity (**e**) and immunoblotting (**f**) were performed at 1 day and 2 days, respectively. The values represent the mean ± SD of three independent experiments. ***, ** and # indicates the statistical significance of $p< 0.001$, $p< 0.01$, and $p>0.05$ by t-test, respectively.

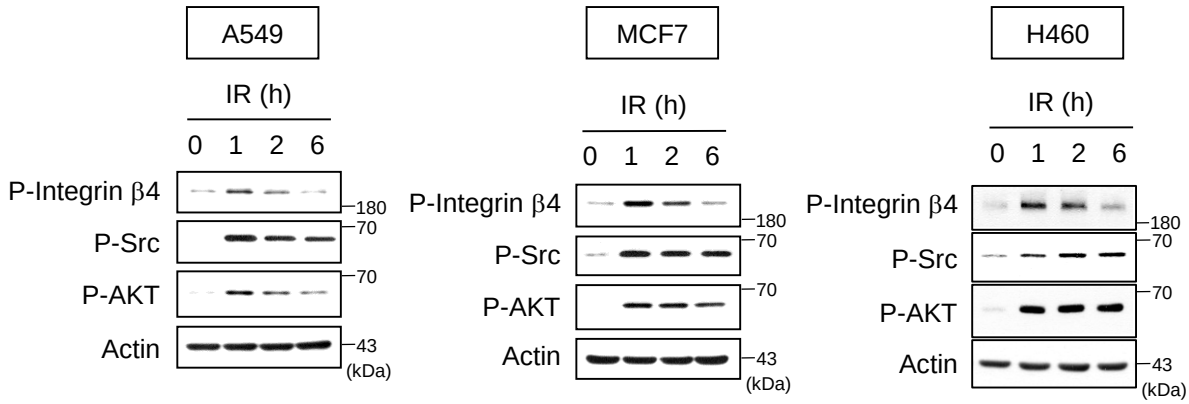
a



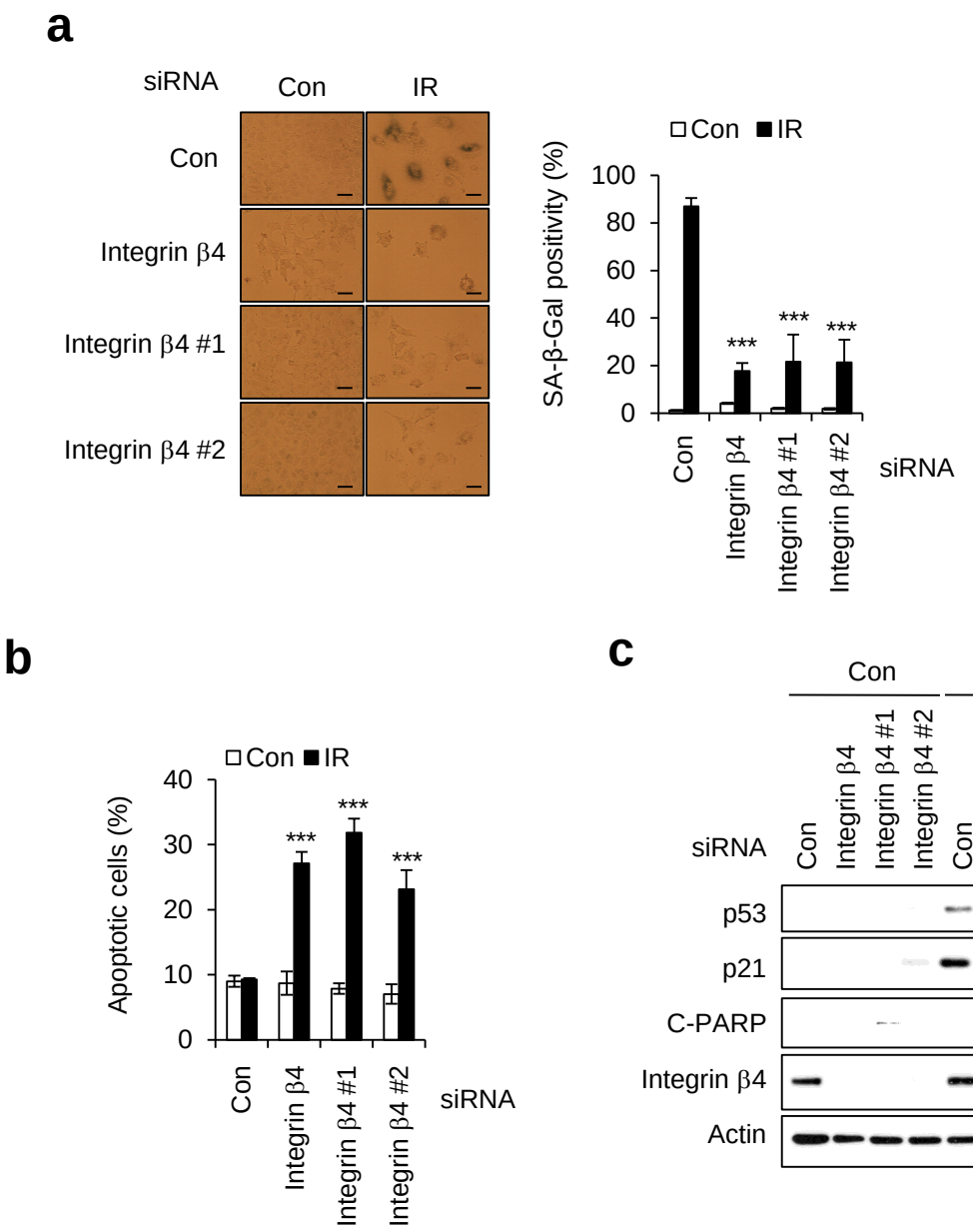
b

Identified Proteins in the integrin-related signaling pathway
Integrin β4 (Tyr1510)
Src (Ser75)
AKT1 (Ser246)
PAK1/2/3 (Ser141)
FAK (Tyr407)
AKT2 (Ser473)

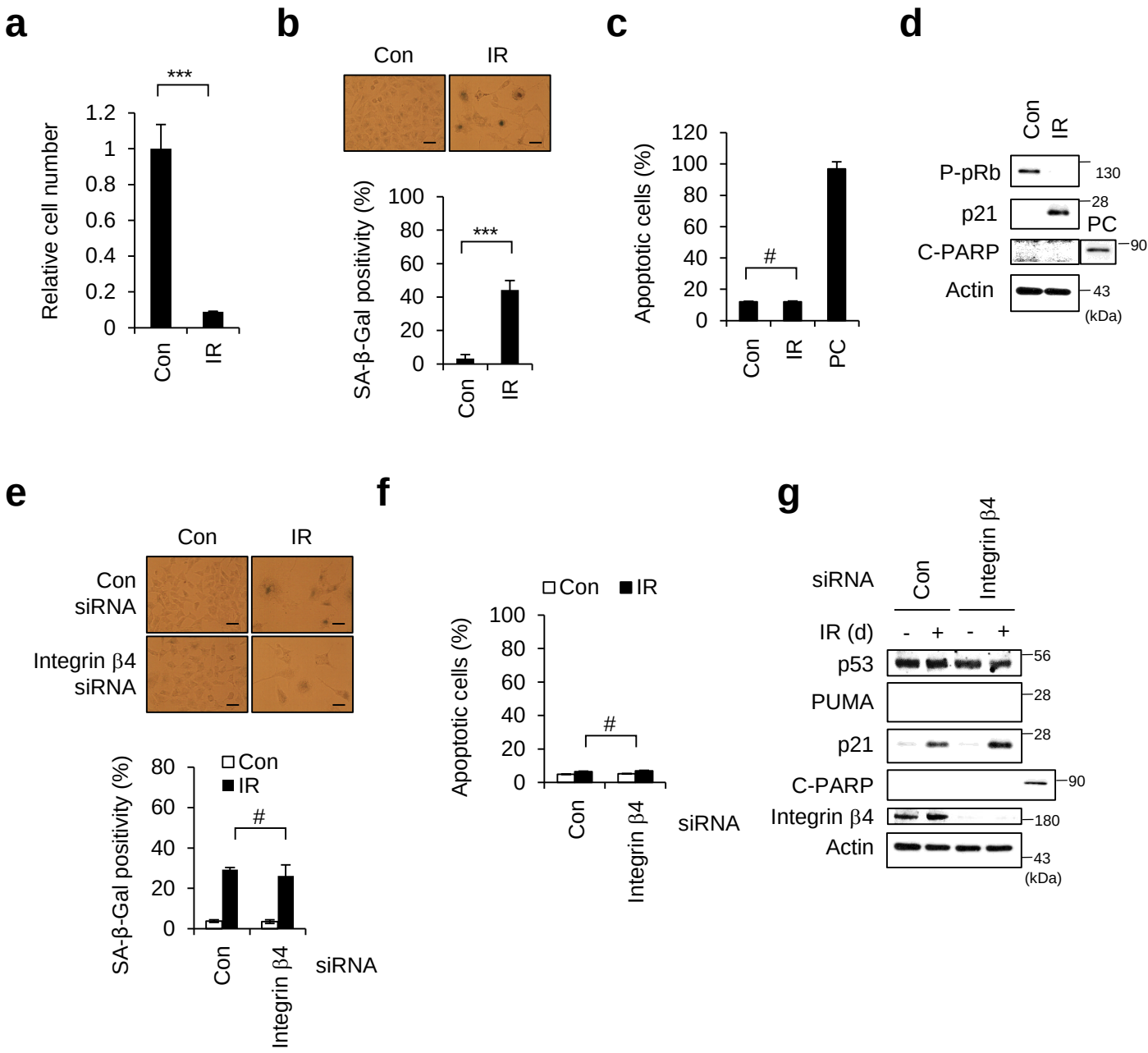
c



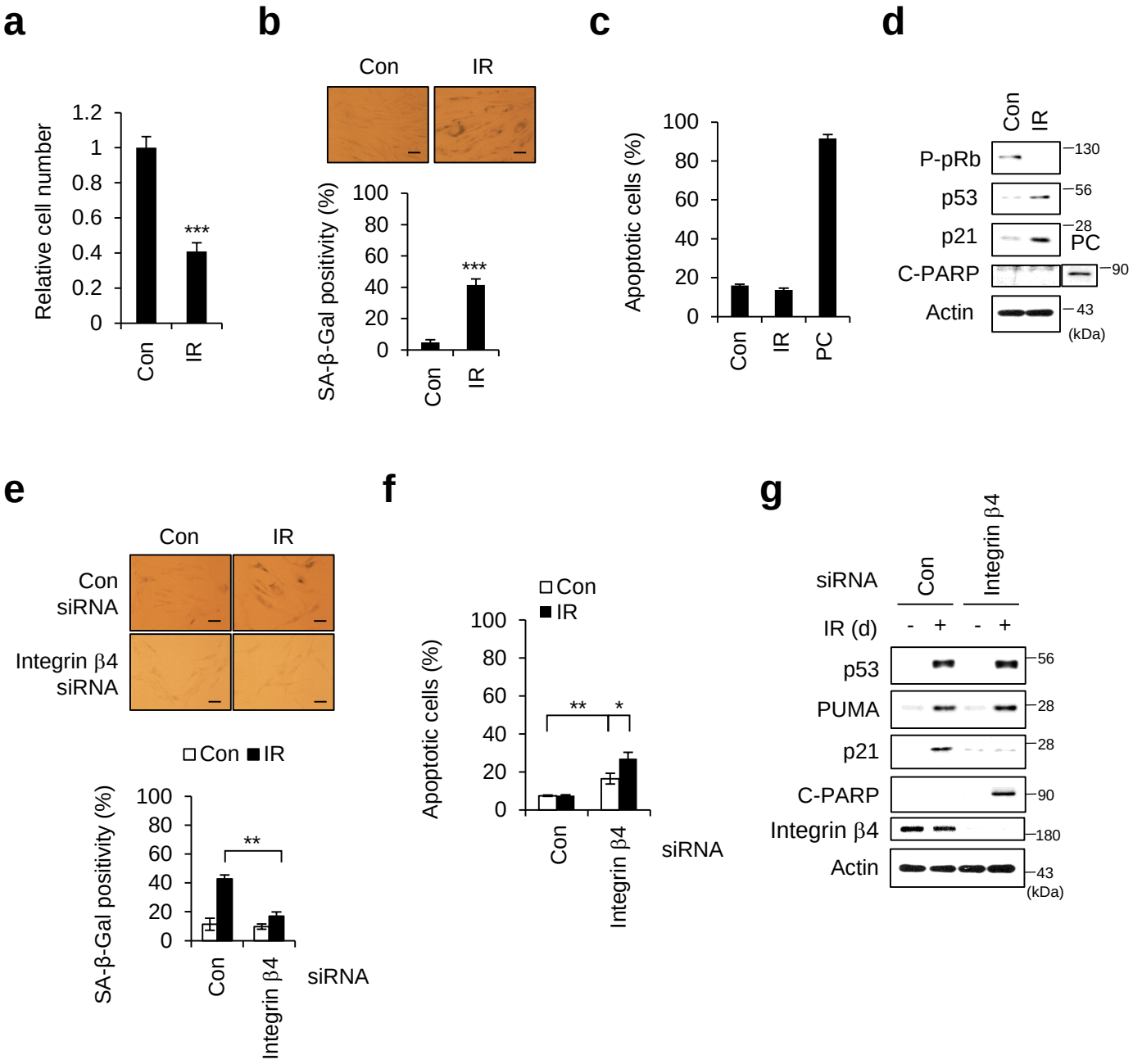
Supplementary Figure S2. Functional annotations and putative signaling pathways of IR-induced cellular senescence. **a**, Molecular functions of identified phosphoproteins by the Ingenuity Pathway Analysis (IPA) tool. **b**, The phospho-antibody microarray identified a list of integrin-related signaling molecules whose phosphorylation states increased in 6 Gy of IR exposed MCF7 cells. **c**, A549 (left pannel), MCF7 (middle pannel), H460 (right pannel) cells were irradiated with 6 Gy of IR, and then incubated for the indicated hours. Immunoblot were performed with indicated antibodies. **d**, A549 cells were exposed to 6 Gy of IR and lipid rafts were fractionated 2 hrs. Equal volume for each fraction were resolved by SDS-PAGE and immunoblotting was performed with the indicated antibodies.



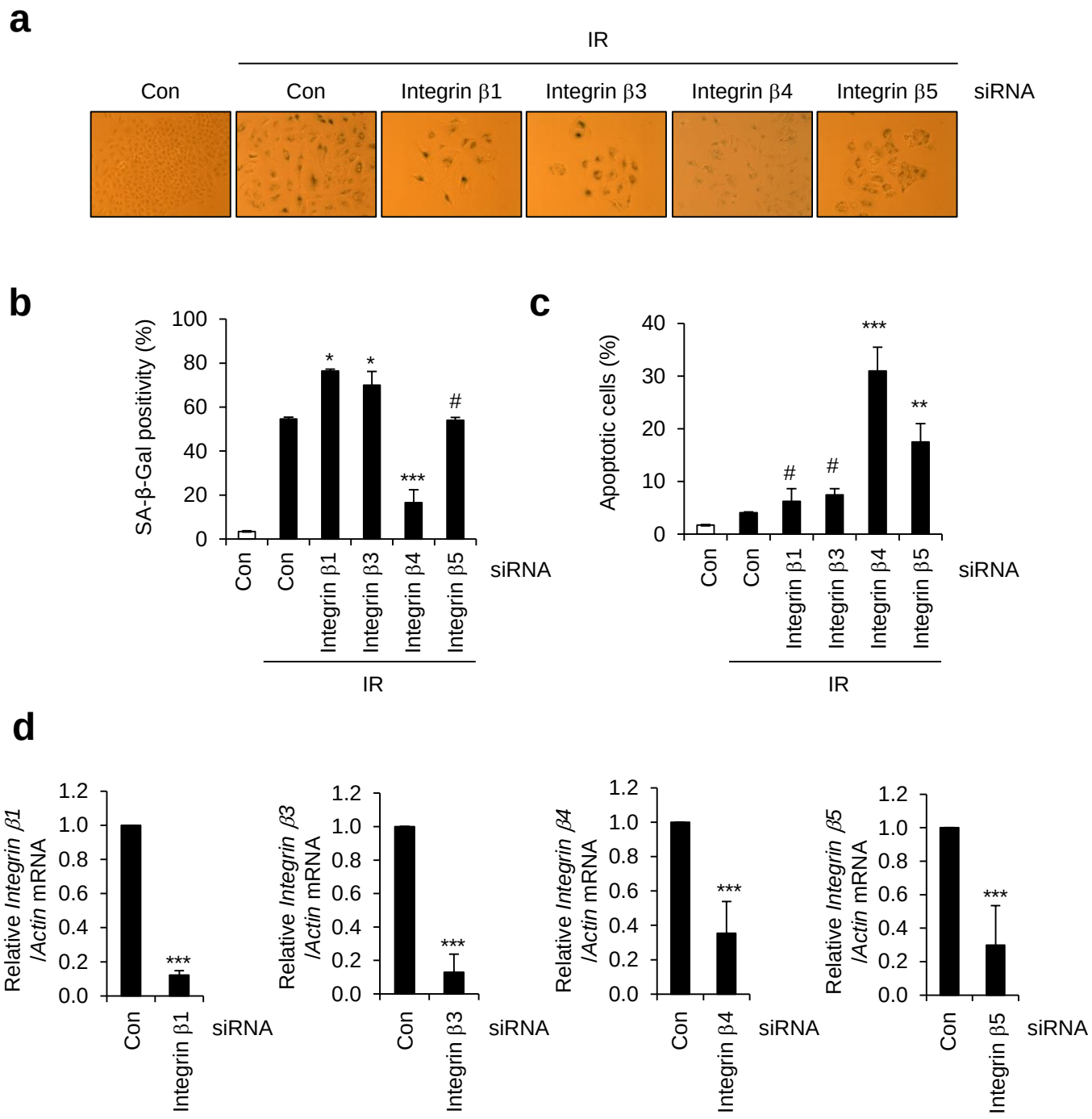
Supplementary Figure S3. A549 cells were transfected with two more additional integrin β4 siRNAs and then irradiated with 6 Gy of IR. **a–b**, Assays of SA-β-Gal (a) and Annexin V (**b**) were assessed in each group on days 4 and 1 after irradiation, respectively. **c**, Immunoblotting was performed with the indicated antibodies after irradiation. Actin served as the loading control. The values represent the means ± SD; *** indicates $p < 0.001$ as assessed by t-test.



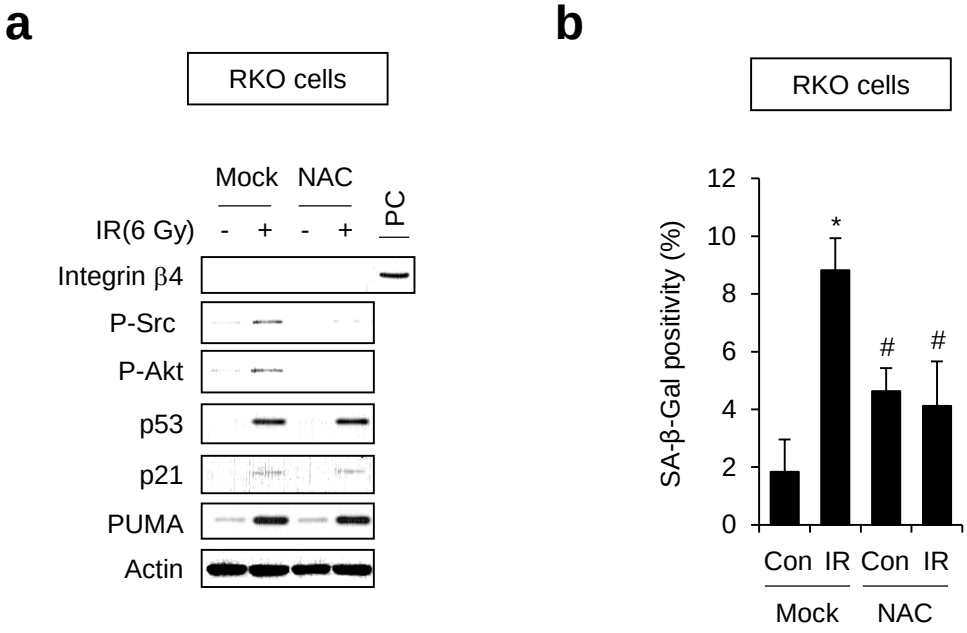
Supplementary Figure S4. Human breast adenocarcinoma MDA-MB231 cells having mutant *p53* R280K were irradiated with 6 Gy of IR. **a,** Relative cell numbers were determined 4 days after irradiation. **b–d,** Cells were subjected to SA-β-Gal staining (**b**), Annexin V staining (**c**), and immunoblotting (**d**) on days 4, 1, and 2, respectively. **e**–**g,** MDA-MB231 cells were transfected with integrin β4 Si and then exposed to 6 Gy IR. SA-β-Gal positivity (**e**), Annexin V positivity (**f**), and immunoblotting (**g**) were conducted on days 4, 1, and 2 after irradiation, respectively. Immunoblotting was performed with the indicated antibodies, and actin served as the loading control. The values represent the means ± SD; *** and # indicate $p < 0.001$ and $p > 0.05$, respectively, as assessed by t-test.



Supplementary Figure S5. Non-transformed human diploid fibroblast (HDF) cells were irradiated with 6 Gy of IR. Relative cell numbers were determined 4 days after irradiation. **b–d,** Cells were subjected to SA-β-Gal staining (**b**), Annexin V staining (**c**), and immunoblotting (**d**) on days 4, 1, and 2, respectively. **e**–**g,** HDF cells were transfected with integrin β4 Si and then exposed to 6 Gy IR. SA-β-Gal positivity (**e**), Annexin V positivity (**f**), and immunoblotting (**g**) were conducted on days 4, 1, and 2 after irradiation, respectively. Immunoblotting was performed with the indicated antibodies and actin served as the loading control. The values represent the means ± SD; ***, **, and * indicate $p< 0.001$, $p<0.01$, and $p< 0.05$, respectively, as assessed by t-test.



Supplementary Figure S6. A549 cells were transfected with the indicated siRNA prior to 6 Gy of IR exposure. **a** and **b**, SA-β-Gal staining and its quantification were performed 4 days after irradiation. **c**, Annexin V positive cells were determined 1 day after irradiation. **d**, A549 cells were transfected with the indicated siRNA prior to exposed IR at 6 Gy. qRT-PCR analyses were performed to detect mRNA levels of integrin β1 Si, integrin β3 Si, integrin β4 Si, and integrin β5 Si after each siRNA transfection. The values represent the mean ± SD of three independent experiments. ***, **, * and # indicate the statistical significance of $p< 0.001$, $p< 0.01$, $p<0.05$, and $p>0.05$ by t-test, comparing to cells irradiated Con Si transfected cells..



Supplementary Figure S7. RKO cells were pretreated with NAC, a ROS scavenger, and then irradiated with 6 Gy of IR. **a–b**, Immunoblot assay (**a**) and quantification of SA-β-Gal staining (**b**) were performed 6 h and 4 days after irradiation, respectively. PC indicates positive control. The values represent the means ± SD; * and # indicate $p<0.05$ and $p>0.05$, respectively, as assessed by t-test.