

Figure S1. A, Growth of *p53* knockout cell lines in the presence or absence of reversine in colony formation assays. Representative images and averaged growth from three independent experiments are shown. **B**, Reversine concentrations that were used during adaptation of the respective cell lines. **C**, DNA sequencing chromatograms of the *TP53* target sites of wildtype and the CRISPR/Cas9 mutated cell lines. **D**, Copy number deviations from euploidy in *p53* knockout cell lines before adaptation as measured by next generation sequencing. Copy number changes are depicted as number of genes. **E**, Copy number profiles of wildtype cell lines and corresponding *p53* knockouts. Shown are copy numbers with each dot representing a 500 kb bin in the genome of cell populations. Segments above 0.5 threshold for gain are colored in red, segments below threshold for loss are colored in blue. Thresholding occurs relative to the parental wildtype. Dotted green lines mark the centromeres in each chromosome. **F**, Bar graphs showing flow cytometric analysis of wildtype (full bar) and corresponding *p53* knockout (empty bar) cell lines before and 24 hours after radiation with 6.22-Gy. Cells were stained with PI and anti-MPM2. Flow cytometry was done as described in the methods. 10,000 cells were analyzed in each experiment. S-Phase percentages are not shown.