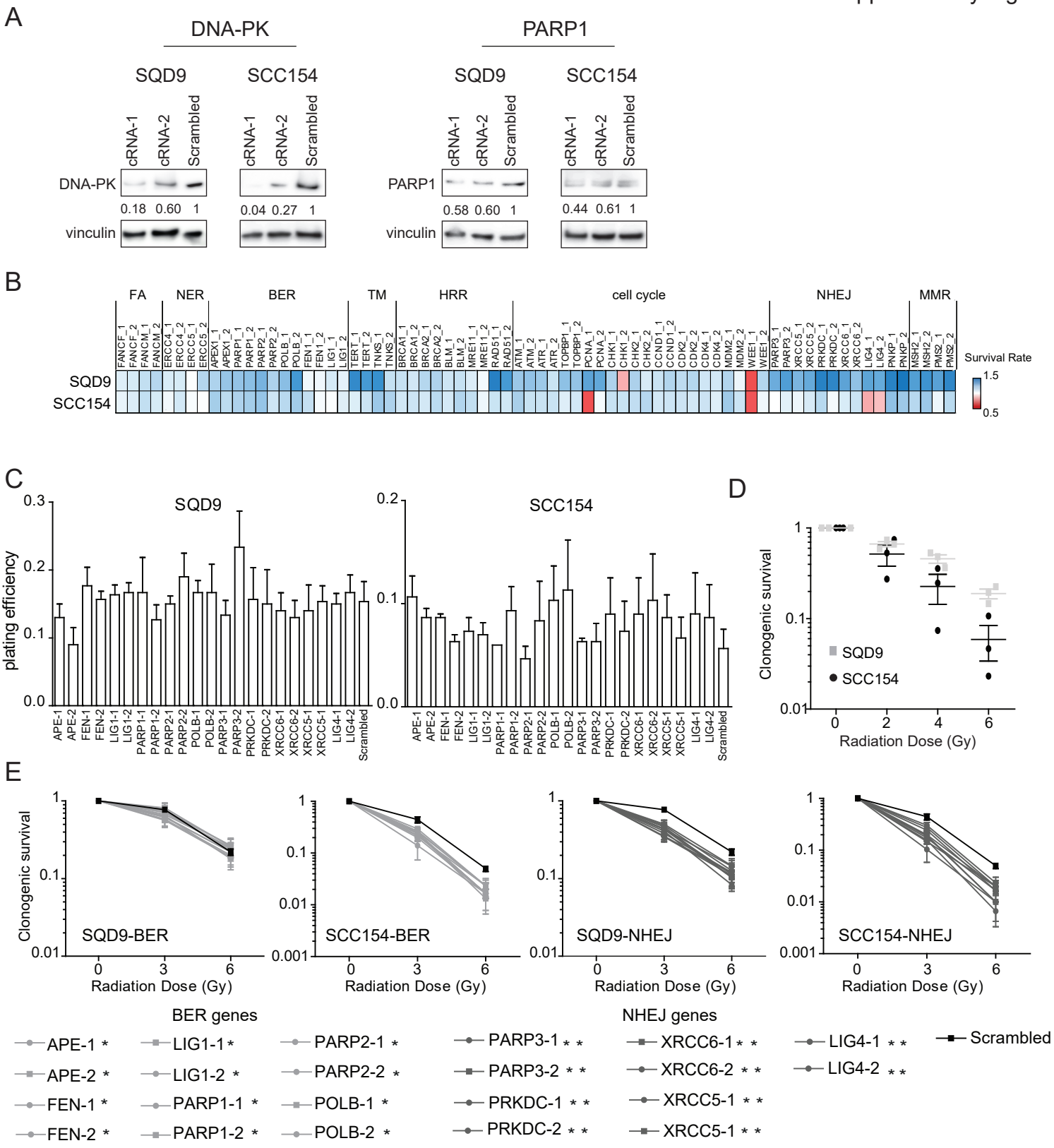

Supplementary Figure 1. (A) Immunoblot analysis of HPV-negative SQD9 and HPV-positive SCC154 cells 48 hours after co-transfection with Cas9 and scrambled crRNA or cRNAs specific for DNA-PK or PARP-1 using the indicated antibodies. Band intensities were measured by densitometry and normalized to vinculin expression (below). (B) Relative survival of non-RT HNSCC cells transfected with the indicated crRNA-Cas9 compared to scambled cRNA-Cas9 assessed by the SRB assay. (C) Plating efficiency of HPV-positive and HPV-negative SQD9 cells treated with cRNA-Cas9 targeting the BER genes, the NHEJ genes or scrambled cRNA. Data are presented as mean clonogenic survival at 0Gy ± s.e.m relative to the number of plated cells, n=3. (D) Clonogenic assay of SQD9 and SCC154 cells to determine the optimal RT dose for the CRISPR screen. Clonogenic cell survival is shown as mean± s.e.m. relative to non-irradiated cells, n=3. (E) Clonogenic assay of HPV-negative SQD9 and HPV-positive SCC154 cells treated with cRNA-Cas9 targeting the BER genes, the NHEJ genes, or scrambled cRNA. Data are presented as mean ± s.e.m. relative to non-irradiated cells, n=3. (C, E)* P-values<0.05 were assessed by comparing the cRNAs to the scrambled cRNAs by 2-way ANOVA. * signficant for SCC154, ** signficant for both SCC154 and SQD9 cells at 3Gy.