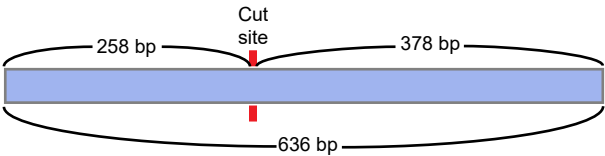


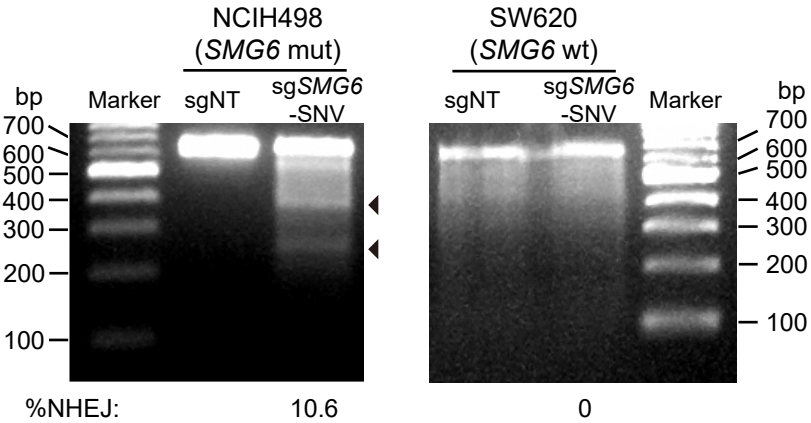
a.

Wild-type *SMG6* GGCCTCCCGCGGGCTGGGTCTGTCGTGGGT
Mutant *SMG6* GGCCTCCCGCGGGCTGGGTCAATCGTGGGT
sg*SMG6*-SNV + PAM TCCCGCGGGCTGGGTCAATCGTGG

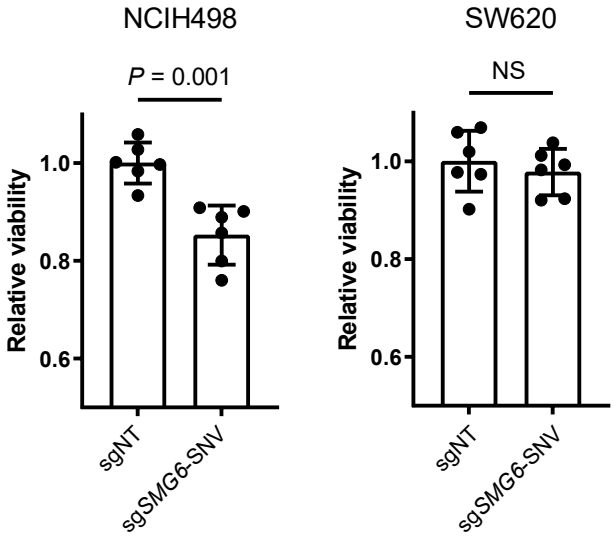
b.



c.



d.



Supplementary Figure 2. Experimental validation of the therapeutic strategy with haploinsufficient gene *SMG6* in human colorectal cancer cell lines. **(a)** Genomic DNA sequences of wild-type *SMG6* and *SMG6* of the NCIH498 cell line, and single-guide RNA (sgRNA) with the protospacer adjacent motif (PAM) sequence targeting passenger single-nucleotide variant (SNV) of NCIH498 *SMG6*. The SNV is represented in red and the PAM sequence in blue. **(b)** Schematic of PCR amplicon design for T7E1 assay. **(c)** Non-homologous end joining (NHEJ) frequency with the T7E1 assay. Gel images of T7E1-treated PCR products amplified from the target site of sg*SMG6*-SNV in control sgRNA or sg*SMG6*-SNV transduced NCIH498 cells and SW620 cells. **(d)** Effect of sgRNA targeting the *SMG6* SNV on cell growth of NCIH498 and SW620. Statistical significance of the difference in cell growth was determined using two-tailed Student t test. Data are presented as mean $\pm$ standard deviation (s.d.). NS, not significant.