**SUPPLEMENTAL FIGURE LEGENDS**

**Fig. S1. Analysis of STAG2 tumorcell lines.**

(A) List of STAG2 cell lines used in this study. (B) Immunoblot analysis of STAG2 tumor cell lines with the indicated antibodies.

**Fig. S2. Analysis of T-SCE and SCE in HCT116 SA2 KO cells.**

(A) CO-FISH analysis of metaphase spreads from HCT116 WT or SA2 KO metaphase spreads probed with TTAGGG (red). (B) Quantification of the frequency of T-SCE. (n=1626-2432 chromosome ends from 31-40 metaphase spreads) ±SEM. (C) CO-FISH analysis metaphase spreads from HCT116 SA2 KO cells transfected with GFP or SCC1 siRNA probed with TTAGGG (red). (D) Quantification of the frequency of T-SCE. Average of two independent experiments (n=1142-1218 chromosome ends from 15-18 metaphase spreads) ±SEM. (A and C) DNA was stained with DAPI. Scale bar, 5 μm. Inset scale bar, 2 μm. (B and D) \*\*\*\*p≤0.0001, students unpaired t-test. (E) Giemsa stained HCT116 WT or SA2 KO metaphase spreads. Scale bar, 10 μm. (F) Quantification of the frequency of sister chromatid exchanges (SCE). (n=338-461 chromosomes from 15-20 metaphase spreads) ±SEM. ns (not significant), students unpaired t-test. (G) List of modal chromosome #, the source, and the approximate average telomere length (based on the analysis shown in Fig. 3E) for STAG2 tumor cell lines.

**Fig. S3. Analysis of BJ-1 and BJ-2 SA2-depleted stable cell lines.**

(A) Immunoblot analysis of vector and SA2 depleted early BJ-2 cell lines (PD34; day 21). (B) FISH analysis of mitotic cells from the indicated early BJ-2 cell lines using a 16p telo (green) probe. DNA was stained with DAPI. Scale bar, 5 μm. (C) Quantification of the percentage of BJ-2 mitotic cells with cohered telomeres using a 16p telo probe. Average of two independent experiments (n=49-57 cells each) ± SEM. (D) Quantification of CO-FISH analysis of metaphase spreads from the indicated early BJ-2 cell lines probed with TTAGGG (red). Average of two independent experiments (n=1132-1986 chromosome ends from 17-32 metaphase spreads) ±SEM. (E) Growth curve analysis of vector or SA2 depleted BJ-1 stable cell lines, generated by lentiviral infection of BJ cells at PD 40. (F) Quantification of the percentage of the indicated late BJ-1 cells (PD 47, 50, 50; day 30) with more than 10 γH2AX/53BP1 colocalizing foci. Average of three independent experiments (n=62-65 cells each) ± SEM. (G) Quantification of senescent β-galactosidase positive late BJ-1 cells (PD 47, 50, 50; day 30). Average of two independent experiments (n=874-1186 cells each) ± SEM. (H) Analysis of telomere restriction fragments isolated from late BJ-2 cells (PD 46, 48, 48; day 66), fractionated on 0.8% agarose gel and hybridized under native conditions with a 32P-[CCCATT]3 probe to detect the G-stand overhang, and then, denatured and reprobed to detect the total G-strand telomeric DNA. (I-J) Measurement of aneuploidy. (I) FISH analysis of BJ-2 interphase cells at early (32) and late (54) PD using 10 cen (red) and 6 cen (green) probes. DNA was stained with DAPI. Scale bar, 10 μm. (J) Quantification of chromosome-specific aneuploidy based on the frequency of monosomy and trisomy. Average of three independent experiments (n=61-277 cells each) ± SEM. No events were detected in shvec early cells. (D, F, G, J) \*p≤0.05, \*\*p≤0.01, \*\*\*p≤0.001, students unpaired t-test.