**SUPPLEMENTAL MATERIALS AND METHODS**

**Plasmids**

SA2 is full length SA2 with an amino terminal triple Flag tag cloned into pLPCX (Clontech). SA2.D793K (1) was generated by substituting aspartate (D) to lysine (K) at amino acid position 793 using site-directed mutagenesis with the sense oligonucleotide 5’ ggctgaagatcatcaaaattttacacagaatagtgaaggc 3’. The following shRNA plasmids against SA2 were obtained from the MISSION shRNA library by Sigma-Aldrich: TRCN0000153201 (shSA2-3) and TRCN0000154078 (shSA2-4).

**Lentiviral infection**

Lentiviruses were produced by transfection of 293FT (Invitrogen) packaging cells with a three-plasmid system as described previously (2,3). 293FT cells were seeded in a 6-cm dish at 1.2 × 106 cells and 24 hr later were transfected with 1 µg lentiviral vector, 1 µg pCMVΔR.89 packaging plasmid, and 100 ng pMD.G envelope plasmid using Lipofectamine 2000 (Invitrogen) according to the manufacturer’s instructions. Lentiviral supernatants were collected at 48 hr after transfection, filtered with a 0.45-µm filter (Millipore), and frozen at −80°C. Twenty-four hr before infection, target cells were seeded at a density of 2.2 × 105. Target cells were infected for 48-72 hr with lentiviral supernatants supplemented with 8 µg/ml polybrene (Sigma-Aldrich). Infected cells were selected using 2 µg/ml puromycin and propagated in media containing 2 µg/ml puromycin.

**Retroviral Infection**

For isolation of LOX-IMVI single cell clones, cells were retrovirally infected with pBABE-hygro as described previously (4), seeded at low density, and single cell colonies isolated 10 to 14 days post seeding using cloning cylinders.

**siRNA and plasmid transfection**

siRNA transfections were performed with Oligofectamine (Invitrogen) according to the manufacturer’s protocol for 72 hr. The final concentration of siRNA was 100 nM. The following siRNAs (synthesized by Dharmacon Research Inc.) were used: siSCC1 5′-GGUGAAAAUGGCAUUACGGUU-3′) described previously (Watrin et al., 2006) and siGFP Duplex I. For plasmids, cells were transfected with Lipofectamine 2000 (Invitrogen) according to the manufacturers protocol for 18 hr.

**Chromosome specific FISH f**or measurement of aneuploidy

Asynchronous BJ cells were trypsinized, washed with media, fixed twice in methanol:acetic acid (3:1) for 15 min, and processed as described above. FITC-conjugated 6 cen and TRITC-conjugated 10 cen probes (Cytocell) were used. Monosomy and trisomy was scored to determine aneuploidy for each chromosome at early and late PD.

**Sister chromatid exchange (SCE) assay**

SCE was measured by Giemsa staining (5). Cells were seeded at low confluency in media containing 20μM BrdU and were grown for 36 hr, followed by colcemide (0.1 μg/mL) for 4 hr. Cells were harvested by trypsinization, hypotonically swollen in 10 mM Tris, pH 7.4, 10 mM NaCl, and 5 mM MgCl2 for 10 min at 37°C, and fixed twice for 15 min in methanol/acetic acid (3:1). Metaphase spreads were prepared by dropping fixed cells on coverslips followed by centrifugation at 1000 rpm for 10 sec in an Eppendorf 5810R centrifuge. Spreads were stained with Hoechest (10 μg/mL) in ddH2O for 20 min, washed once with Gurr Buffer pH 6.8 (Thermofisher Scientific), and exposed to 365-nm UV light (Stratalinker 1800 UV irradiator) for 60 min. Coverslips were washed with 2xSCC at 60°C for 30 min and were stained with 4x Geimsa stain for 10 min at room temperature. 4x Geimsa stain was made by diluting 100x Geimsa stain (1g Geimsa dissolved in 66 mL glycerol at 60°C for 2h then 66 mL methanol added) with Gurr Buffer. Cells were washed with ddH2O twice, air dried and sealed with Cytoseal 60 (Thermofisher Scientific).

**SUPPLEMENTAL REFERENCES**

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