**Supplementary materials and methods**

**DNA purification, library preparation, and sequencing**

DNA purification was done using the DNeasy Blood & Tissue Kit (Qiagen).  Fine hundred ng of genomic DNA was sheared randomly into 200 bp fragments with the CovarisTM S200 UltraSonicator (Covaris®). Sheared DNA was A-tailed and ligated with adaptor-embedded indexes using the NEBNext® UltraTM DNA Library Prep Kit for Illumina® (New England BioLabs, Inc.).  DNA quality, fragment size, and concentration of library preps were measured using Agilent’s DNA 1000 chips in conjunction with the 2100 Bioanalyzer (Agilent Technologies). Samples were equimolarly pooled prior to capture with a 2.2 Mbp SureSelectXT Custom Target Enrichment Kit (Agilent Technologies) targeting 108 genes previously implicated in melanomagenesis.  Paired-end sequencing was performed on the HiSeqTM 2000 sequencing system (Illumina) at the Perelman School of Medicine Next-Generation Sequencing Core Facility.

**Mutational analysis**

Short-sequenced reads were aligned to the hg19 human reference genome using the Burrows-Wheeler Alignment (BWA) tool. Duplicate reads were removed, as well as reads that map to more than one location, off-target reads, and variants annotated with the incorrect transcript. The Genome Analysis Toolkit (GATK) was used for data quality assurance as well as for Single Nucleotide Variant (SNV) and small insertion and deletion (indel) calling.  After downsampling by GATK, a mean target coverage of 197X was achieved.  Variants were annotated with wANNOVAR.

**SA-β-gal staining**

Cells were fixed with DPBS containing 2% formaldehyde (Sigma) and 0.2% glutaraldehyde (Sigma) for 30 minutes. Fixed cells were then incubated at 37°C (no CO2) with fresh SA-β-gal staining solution overnight. Images were acquired with Nikon TE2000 Inverted Microscope.

**Telomere dysfunction induced foci (TIF) assay**

The TIF assay is based on the co-localization detection of DNA damage by an antibody against gamma-H2AX, and telomeres using FITC-conjugated telomere sequence (TTAGGG)3-specific peptide nucleic acid (PNA) probe. Briefly, LOX-IMVI-BR cells were seeded to 6-well plate (50,000 cells/well). After cells adhered to the surface (next day), 6-thio-dG was added with fresh medium. Cells were treated with or without 6-thio-dG at 5 μM every two days for 4 days. Then cells were harvested and cell numbers were counted. 100,000 cells were re-plated in 4-well chamber slides. After cells adhered to the chamber slide (next day), cells were rinsed twice with 1xPBS and fixed in 4% paraformaldehyde in PBS for 10 minutes. Cells were washed twice with PBS and permeabilized in 0.5% Triton X-100 in PBS for 10 minutes. Following permeabilization, cells were washed three times with PBS. Cells were blocked with 0.2% Fish gelatin and 0.5% BSA in PBS for 30 minutes. Gamma-H2AX (mouse) (Millipore, Billerica, MA) was diluted 1:1000 in blocking solution and incubated with cells for 2 hrs. Following three washes with PBST (1x PBS in 0.1% Triton) and 3 washes with PBS, cells were incubated with Alexaflour 568 conjugated goat anti mouse (1:500) (Invitrogen, Grand Island, NY) for 40 minutes, then were washed five times with 0.1% PBST. Cells were fixed in 4% paraformaldehyde in PBS for 20 minutes at room temperature. The slides were sequentially dehydrated with 70%, 90%, 100% ethanol. Following dehydration, denaturation was conducted with hybridization buffer containing FITC-conjugated telomere sequence (TTAGGG)3-specific peptide nucleic acid (PNA) probe (PNA Bio, Thousand Oaks, CA), 70 % formamide, 30% 2xSSC, 10% (w/v) MgCl2.6H20 (Fisher Sci), 0.25% (w/v) blocking reagent for nucleic acid hybridization and detection (Roche) for 7 minutes at 80◦C on heat block, followed by overnight incubation at room temperature. Slides were washed sequentially with 70% formamide (Ambion, Life Technologies, Grand Island, NY) / 0.6 x SSC (Invitrogen) (2 x 1 hr), 2 x SSC (1 x 15 minutes), PBS (1 x 5 minutes) and sequentially dehydrated with 70%, 90%, 100% ethanol, then mounted with Vectashield mounting medium with DAPI (Vector Laboratories, Burlingame, CA). Images were captured with Deltavision wide-field microscope using the 60X objective, then deconvoluted using Autoquant X3. Gamma-H2AX and TIFs were quantified using Imaris software.

**Telomere length quantification**

Telomere length was measured by the ratio of the telomeric DNA and a single copy gene, 36B4. The forward and reverse primers used for amplifying telomeric DNA were tel1b and tel2b. The quantification of telomeric DNA and 36B4 was determined by quantitative real time PCR on Applied Biosystems 7500 Fast Real-Time PCR System. The reaction mixtures (20μL final volume) contained 10 μL Fast SYBR® Green Master Mix, 500nM each primer and 10ng genomic DNA. The reaction conditions were 95℃ for 20s, followed by 40 cycles of 95℃ for 3s and 60℃ for 30s. The telomere length was analyzed by 2-ΔΔCt method.

**Western blotting and antibodies**

Cells were washed with ice-cold PBS containing 100 µM Na3VO4 and scraped off culture dishes. After centrifugation, cell pellets were lysed in buffer containing 10 mM Tris-HCl, pH 7.8, 150 mM NaCl, 1 mM EDTA, 1% Nonidet P-40, 1 mM Na3VO4 and protease inhibitors (Roche complete protease inhibitor tablets). Lysates were cleared by micro-centrifugation and protein concentrations were determined with Protein Assay Dye Reagent Concentrate (Bio-Rad). For western blots, 20 µg of each lysate were run on 8% SDS-PAGE gels and transferred onto nitrocellulose membranes using a dye fast Trans-BlotR TurboTM transfer system (Bio-Rad). Blots were blocked in SEA BLOCK Blocking Buffer (Thermo Scientific) diluted with 1X TBS at 1:1 ratio at room temperature for 1 h, incubated overnight at 1:1000 dilutions with primary antibodies (anti-AXL: Bethyl Laboratories; anti-β-actin: Sigma; all other antibodies were purchased from Cell Signaling Technologies) at 4°C, stained with secondary antibodies conjugated to IRDye® Infrared Dyes (LI-COR Biosciences) and then visualized using an Odyssey flat bed scanner (LI-COR Biosciences).