Supplementary Figure Legends

Supplementary Figure S1. Characterization of a Smurf2-deficient mouse model. (A) The integration site of the gene-trapping vector is determined by genomic PCR using primer En2-1 and one of the 12 primers (P1-P12) in the intron 1 of *Smurf2*. (B) PCR-based genotyping of the wild-type and trapped *Smurf2* alleles using primers shown in (A). (C) Western blot of Smurf2 expression in E12.5 embryos of wild-type (+/+), $Smurf2^{+/T}$ (+/T) and $Smurf2^{T/T}$ (T/T).

Supplementary Figure S2. Hematoxylin & Eosin staining of tissues from 2-month old wild-type (+/+) and $Smurf2^{T/T}$ (T/T) mice shows a normal development of Smurf2-deficient mice. Scale bars are 200 μm for 10X images and 100 μm for 50X images.

Supplementary Figure S3. Smurf2 induces senescence in Smurf2-deficient mouse embryonic fibroblasts (MEFs). Early passage (P4) and late passage (P28) already immortalized $Smurf2^{T/T}$ (T/T) MEFs were stained with crystal violet and for senescence-associated β-galactosidase (SA-β-gal) activity following ectopic expression of Smurf2, ligase mutant C716A or GFP control.

Supplementary Figure S4. Hematoxylin & Eosin and B220 staining of paraffin-embedded sections of lymphomas found in spleens of $Smurf2^{T/T}$ (T/T) and $Smurf2^{+/T}$ (+/T) mice. Scale bar: 100 μm.

Supplementary Figure S5. Hematoxylin & Eosin staining of paraffin-embedded

sections of kidney and liver with lymphomas in *Smurf2*$^{T/T}$ (T/T) and *Smurf2*$^{+/T}$ (+/T) mice. Scale bar: 100 μm.

Supplementary Figure S6. Analysis of loss of heterozygosity in lymphomas derived from *Smurf2*$^{+/T}$ mice. (A) Western blot of Smurf2 expression in lymphomas from *Smurf2*$^{+/T}$ and *Smurf2*$^{T/T}$ mice. Smurf2 expression in spleens of 2-month old wild-type (+/+), *Smurf2*$^{+/T}$ (+/T) and *Smurf2*$^{T/T}$ (T/T) mice is shown for comparison. Quantitation of abundance of (B) the wild-type *Smurf2* allele and (C) the trapped *Smurf2* allele after normalization with the *GAPDH* allele in tail and spleen DNA of 2-month old wild-type (+/+), *Smurf2*$^{+/T}$ (+/T) and *Smurf2*$^{T/T}$ (T/T) littermates. The relative level of the wild-type *Smurf2* allele in +/+ and the relative level of the trapped *Smurf2* allele in T/T mice were set to be 1. Quantitation of abundance of (D) the wild-type *Smurf2* allele and (E) the trapped *Smurf2* allele after normalization with *GAPDH* in DNA from lymphomas of *Smurf2*$^{+/T}$ (+/T) mice and their corresponding tail DNA. The relative level in tail DNA was set to be 1. Lymphoma samples analyzed in (D) and (E) correspond to those shown in (A). Error bars were calculated from standard deviations of three independent experiments.