Martínez et al., http://www.jcb.org/cgi/content/full/jcb.201110124/DC1

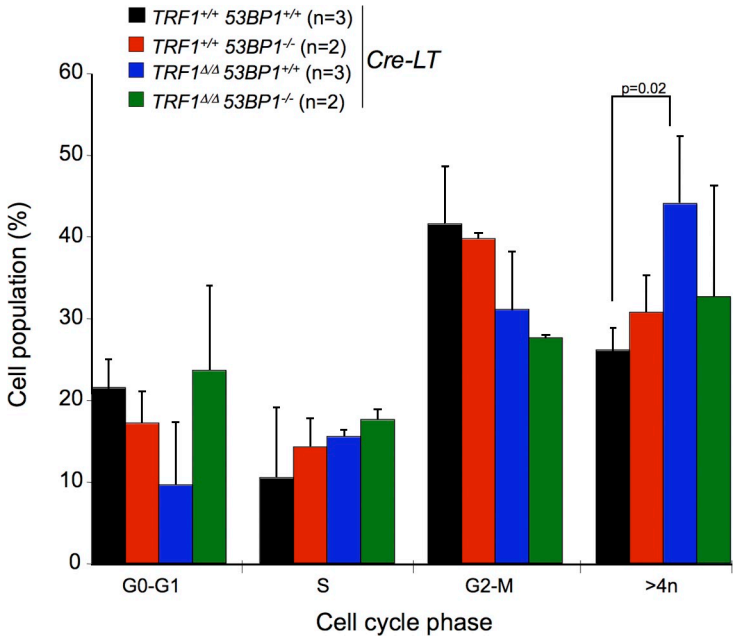


Figure S1. **Cell cycle profile of Cre-infected LT-immortalized MEFs.** Quantification of the percentage of cells at different phases of the cell cycle by FACS analysis of the indicated genotypes. Cells were stained with propidium iodide. *n*, number of independent MEFs used per genotype. Bars represent standard error. The Student's *t* test was used for statistical analysis, and p-values are indicated when significant.

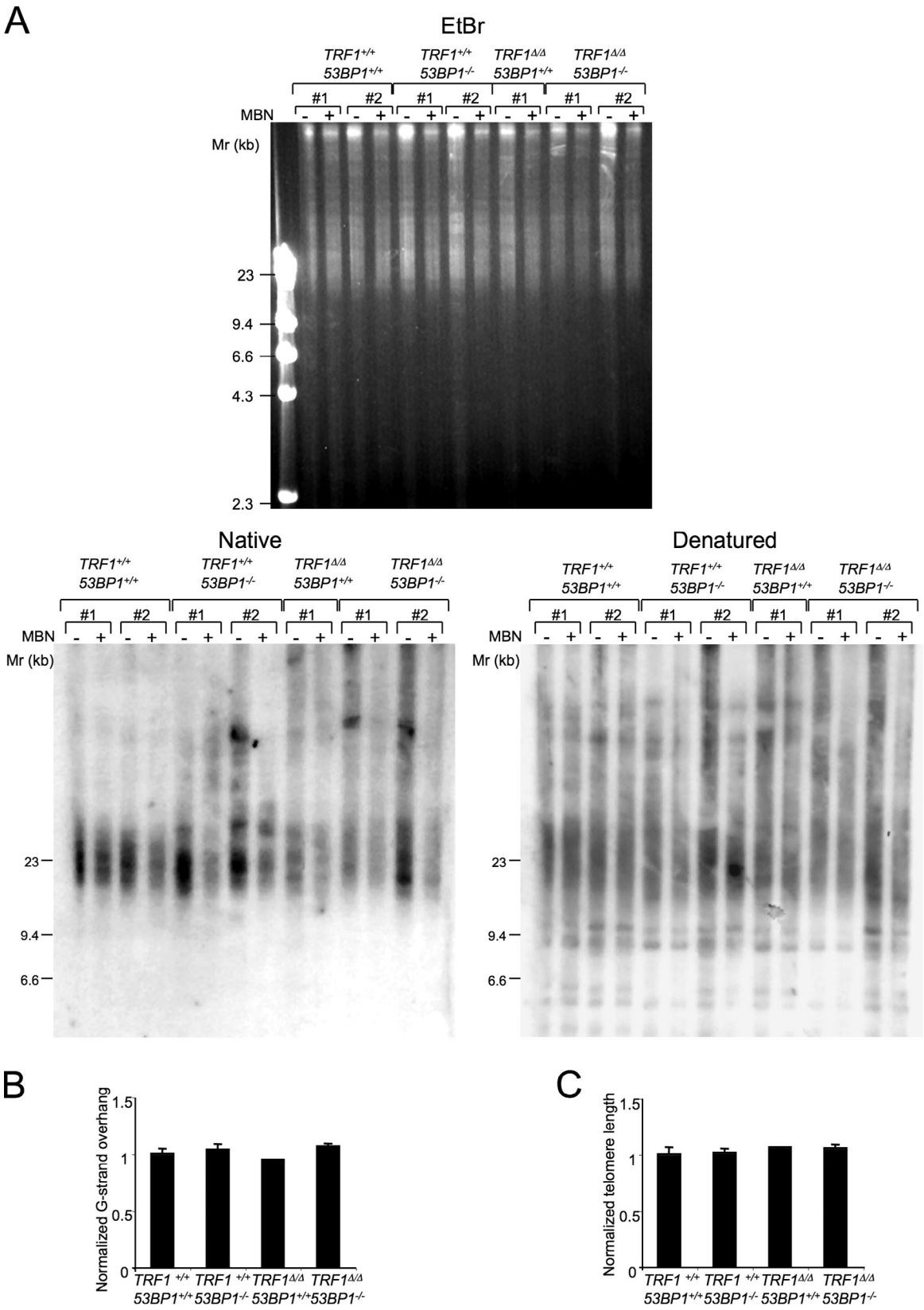


Figure S2. **Normal telomere length and G-strand overhangs in *TRF1*$^{\Delta/\Delta}$ *53BP1*$^{-/-}$ LT-immortalized MEFs.** (A) Ethidium bromide (EtBr)–stained gel (top), G-strand overhang signals in native gel conditions (bottom left), and total telomere signal in denaturing gel conditions (bottom right). (B) Quantification of G-strand length. The signals in native conditions were corrected by those in denaturing conditions and represented relative to the wild type. MBN, mung bean nuclease. (C) Quantification of telomere length. The signals in the denatured gel were corrected for loading by DNA intensity signals in ethidium bromide staining and represented relative to the wild type. Error bars correspond to standard deviation values. Mr, molecular marker.

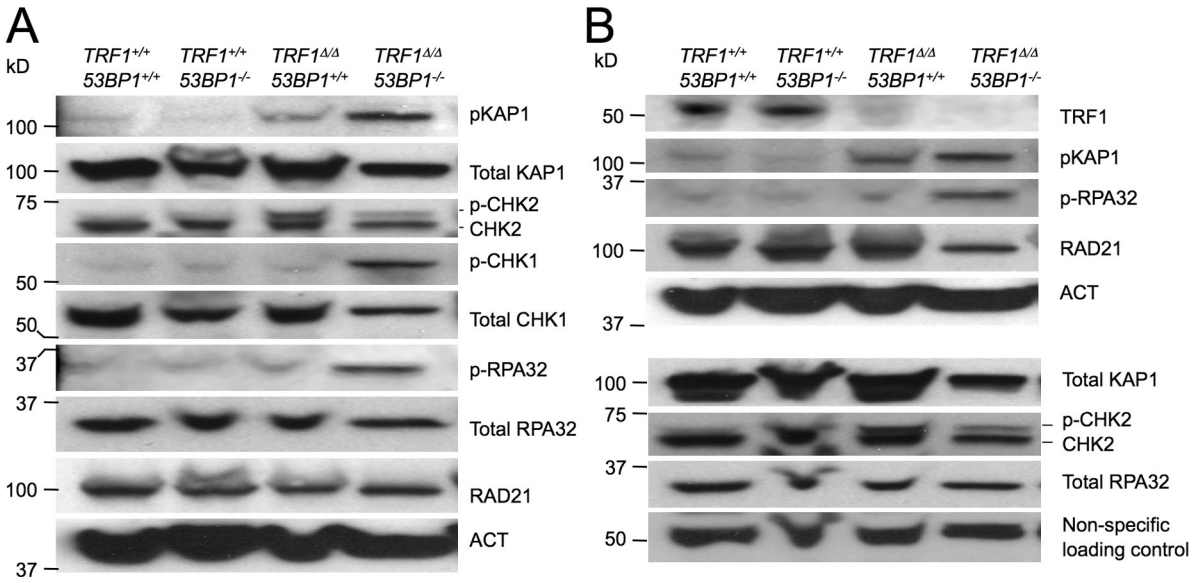
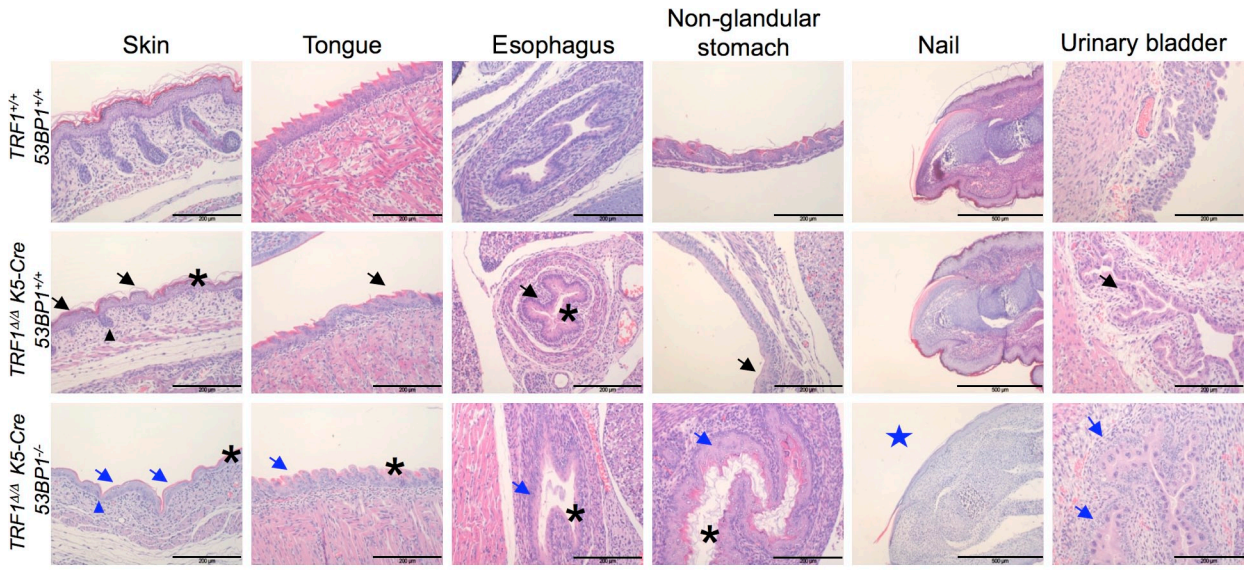


Figure S3. **53BP1 deficiency in *TRF1*$^{\Delta/\Delta}$-immortalized MEFs leads to increased levels of phosphorylated CHK1 and phosphorylated RPA.** (A and B) Western blot detection of DDR factors in Cre-infected LT-immortalized MEFs 4 d after selection of the indicated genotypes. The samples in A and B correspond to different extracts from the same infection of MEFs of the indicated genotypes. RAD21 and actin were used as loading controls. In B, the samples were run in duplicate on the same gel. The membrane was cut into two parts, each one containing one of the duplicates. One half was used to test TRF1, pKAP1, p-RPA32, RAD21, and actin, and the other half was used to test total KAP1, CHK2, total RPA32, and a nonspecific band detected by the anti-CHK2 antibody that was used as a loading control. The data shown here correspond to four independent MEFs different from those shown in Fig. 2 D.



↘ Low-grade dysplasia: Atypical hyperplasia, irregular stratification, enlarged cells and nuclei and in some cases loss of nuclear polarity

↘ High-grade dysplasia with marked cytological atypia: irregular stratification, loss of cellular polarity, nuclear polymorphism, giant nuclei, loss of nuclear polarity and prominent nucleoli

▲ Primordial hair follicles

▲ Absence of hair follicle

* Hyperkeratosis

★ Nail dysplasia

Figure S4. **Histopathological findings in different stratified epithelia of *TRF1*$^{\Delta/\Delta}$ *K5-Cre 53BP1*$^{-/-}$ mice at birth.** Representative images of skin, tongue, esophagus, nonglandular stomach, nail, and urinary bladder of wild-type, *TRF1*$^{\Delta/\Delta}$ *K5-Cre*, and *TRF1*$^{\Delta/\Delta}$ *K5-Cre* 53BP1$^{-/-}$ mice. The *TRF1*$^{\Delta/\Delta}$ *K5-Cre* mice show a low-grade dysplasia pattern characterized by atypical hyperplasia, irregular stratification, enlarged cells and nuclei, and in some cases, loss of nuclear polarity. The back skin show primordial hair follicles. The *TRF1*$^{\Delta/\Delta}$ *K5-Cre* 53BP1$^{-/-}$ mice show a high-grade dysplasia pattern with marked cytological atypia, irregular stratification, loss of cellular polarity, nuclear polymorphism, giant nuclei, loss of nuclear polarity, and prominent nucleoli. The back skin presents complete absence of hair follicles. There is nail atrophy. The level of hyperkeratosis is higher in *TRF1*$^{\Delta/\Delta}$ *K5-Cre 53BP1*$^{-/-}$ than in the *TRF1*$^{\Delta/\Delta}$*K5-Cre* mice.

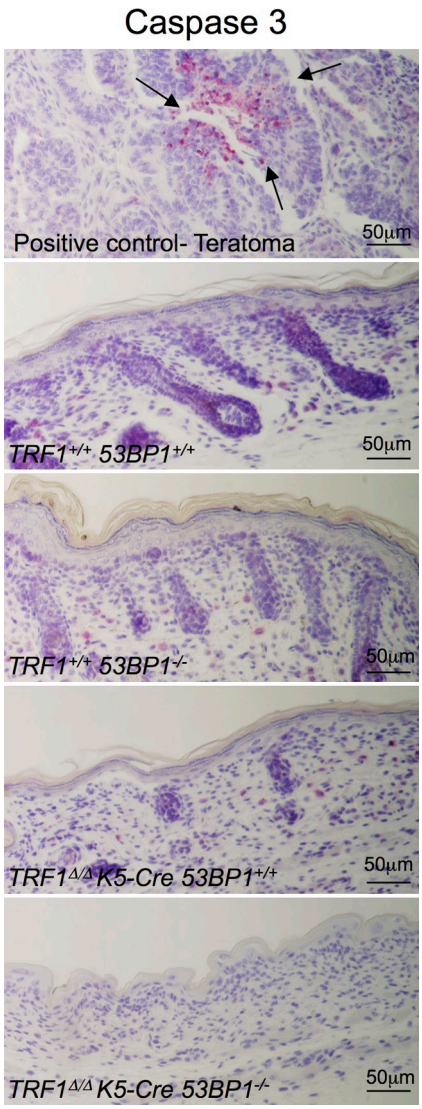


Figure S5. **No apoptotic cells are detected in *TRF1*$^{\Delta/\Delta}$ *K5-Cre 53BP1*$^{-/-}$ neonate skin.** Representative images of caspase 3 active immunohistochemistry detection on neonate skin of the indicated genotypes. A section of a teratoma was used as a positive control. Apoptotic cells are marked with arrows.