

SUPPLEMENTARY FIGURE LEGENDS

Fig. S1. Cell death of TopBP1-deficient embryos

Merged images were obtained from representative wild-type and *TopBP1*^{Δ/Δ} embryos (E3.5 blastocyst) which were cultured for 24 h and subjected to DAPI and TUNEL staining. The magnification is ×40.

Fig. S2. Ablation of TopBP1 in the nucleus

TopBP1 in the nucleus of *TopBP1*^{+/+} and *TopBP1*^{fllox/fllox} MEF cells treated as described in Figure 4 was detected by immunostaining with anti-TopBP1 antibody.

Fig. S3. TopBP1-ablated cells containing 4N DNA content were arrested in the late G2 phase.

(A) At 120 h after Cre-retrovirus infection, *TopBP1*^{+/+} and *TopBP1*^{fllox/fllox} 3T3 cells were subjected to a double thymidine block (Thy/Thy). The cells were immunostained with anti-p-H3 antibody and counterstained with DAPI. (B) The cells in late G2 phase or mitosis were counted and described.

Fig. S4. Activation of DNA damage signaling in TopBP1-ablated cells.

The cells were treated as described in Figure 5A and B.

Fig.S5. TopBP1-ablated cells contain abnormal nuclei.

The cells were treated as described in Figure 5D.

Fig. S6. TopBP1 knockdown induced DNA damage signaling and reduction of DNA replication.

The cells were treated as described in Figure 7B.

Table S1. PCR primers used in genotyping

PCR reaction	Sequence	PCR product
①-a	5'-TTG AGA AGA TAG TTT GGG TCA CAG-3' 5'-CTC TAC CCA TAC CAC CCA CC-3'	255 bp
①-b	5'-CAC CTT GTG TTC TGA TGT GTC-3' 5'-GTC AGG TAG TGA AAC ATC ATG GGC-3'	154 bp
②	5'-TTG AGA AGA TAG TTT GGG TCA CAG-3' 5'-GTT GGC GCC TAC CGG TGG ATG TGG AAT GTG-3'	434 bp

③	5'-CAC CTT GTG TTC TGA TGT GTC-3' 5'-GTC AGG TAG TGA AAC ATC ATG GGC-3'	234 bp
④-a	5'-CCT GGG GAA AGT GGA ATA TG-3' 5'-GTC AGG TAG TGA AAC ATC ATG GGC-3'	383 bp
④-b	5'-CCT GGG GAA AGT GGA ATA TG-3' 5'-CAA TAA CAA GGA CAG TTC CTT AAT T-3'	290 bp

Table S2. Genotypes of progeny from TopBP1-heterozygous intercrosses

Age (dpc ^a)	No. (%) of mice with indicated genotype			Number (%)	
	+/+	+/ Δ	Δ/Δ	No. (%) of resorbed embryos	Total
E3.5	44 (21.4)	90 (43.7)	72 (34.9)		206
E8.5	16 (24.2)	40 (60.6)	0	10 (15.2)	66
E10.5	4 (15.4)	16 (61.5)	0	6 (23.1)	26
E13.5	4 (25.0)	12 (75.0)	0		16
Neonates	63 (37.5)	105 (62.5)	0		168
Blastocyst outgrowth ^b	12 (27.3)	24 (54.5)	8 (18.2)		44

^a, days postcoitum

^b, genotyping after blastocyst outgrowth

Figure S1

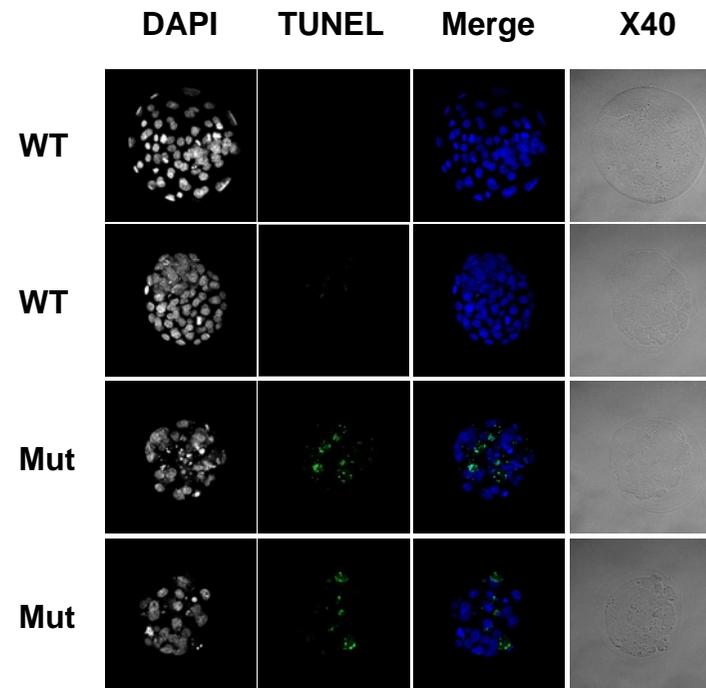


Figure S2

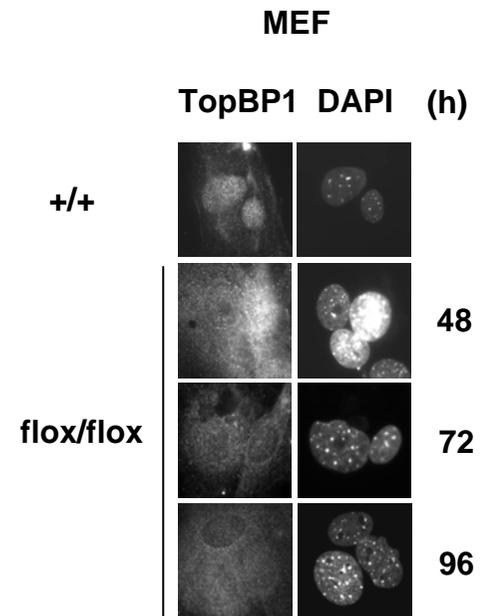


Figure S3

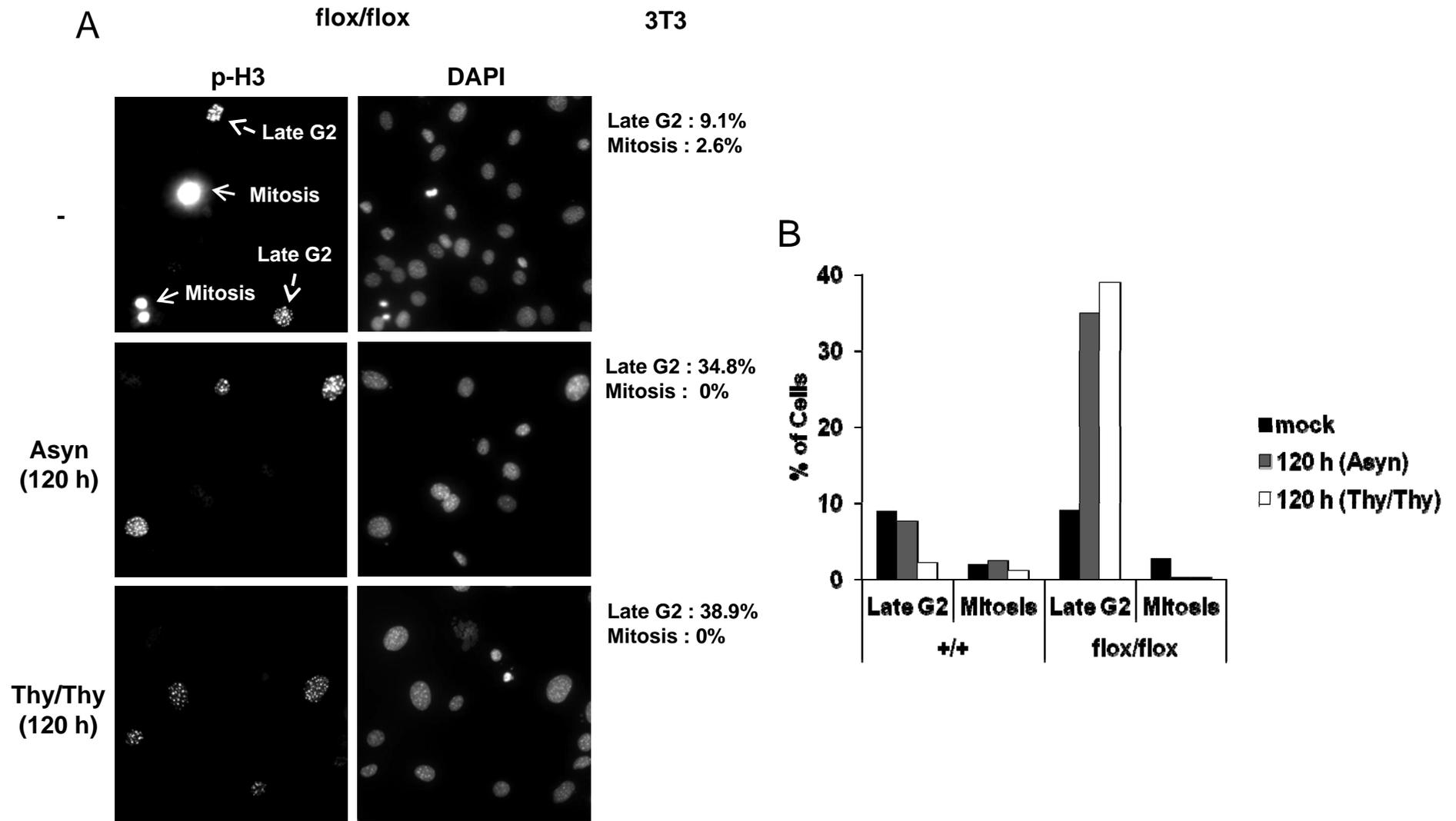


Figure S4

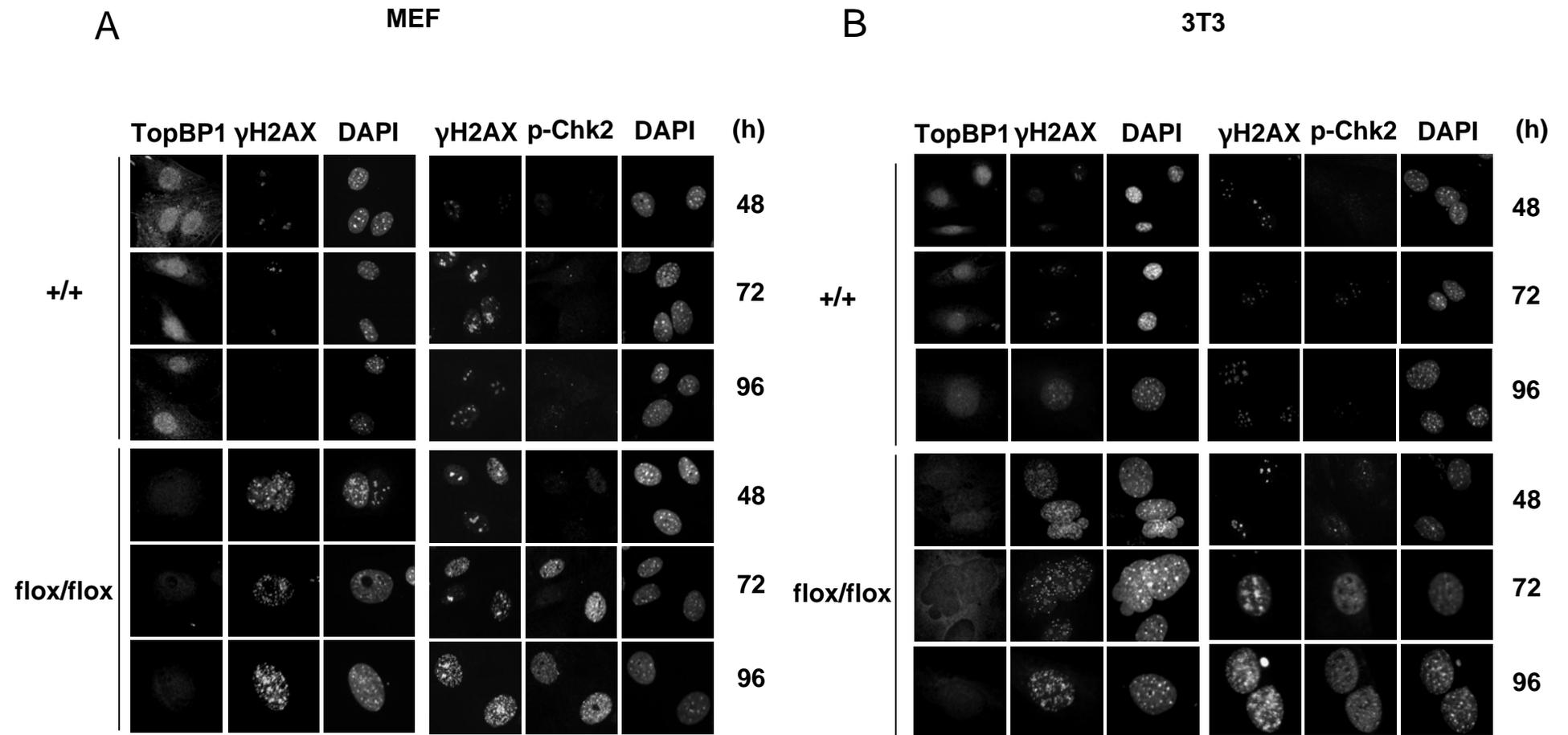


Figure S5

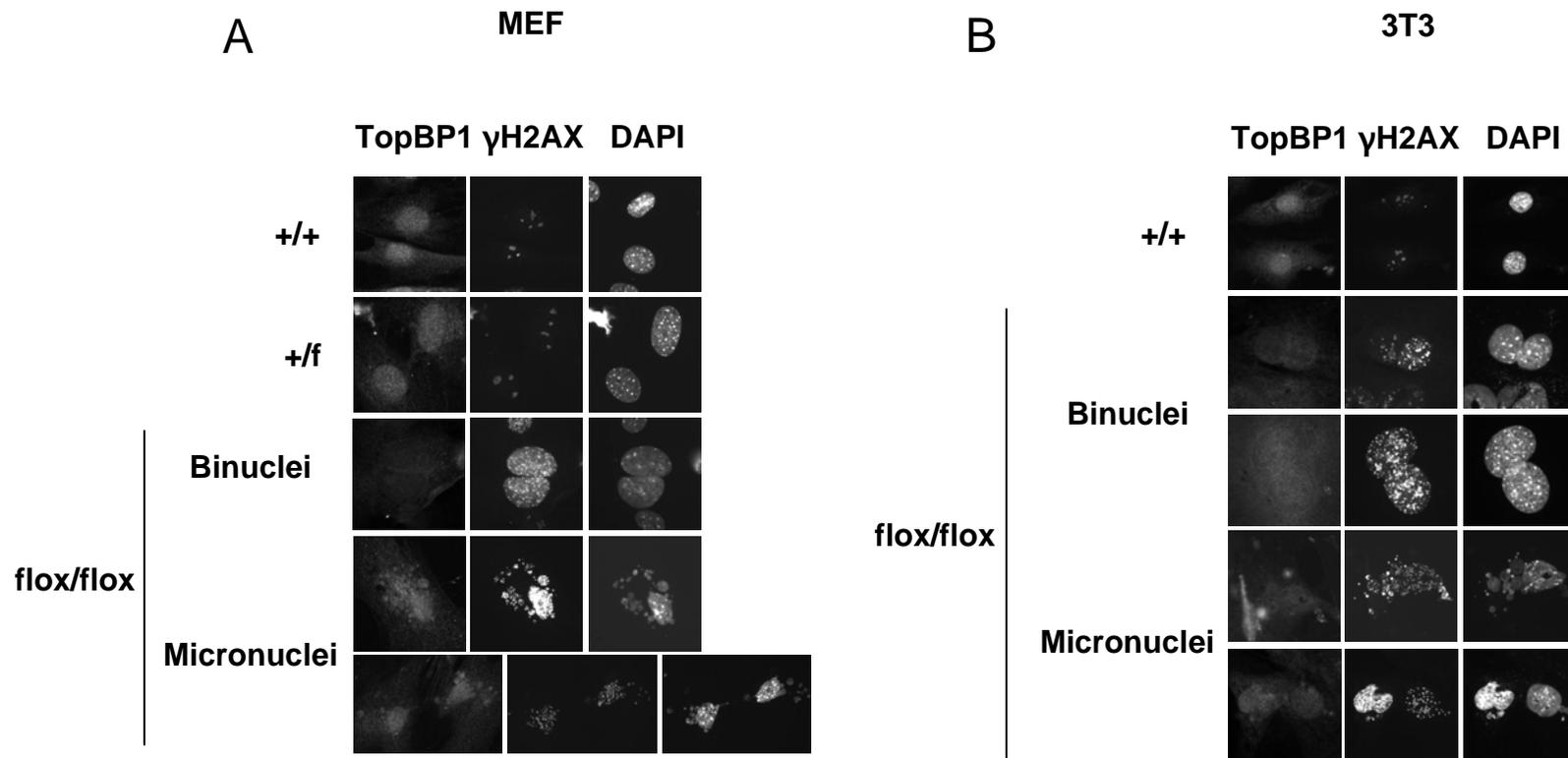


Figure S6

