Supplemental Figure Legends and Supplemental Tables

Supplemental Figure S1: Parasigittal sections of E9.5 Cop1 wild-type (+/+) and null (-/-) embryos. Immunohistochemistry for the mitosis marker phosphorylated histone H3 (P-H3) did not reveal any obvious cell proliferation defects in Cop1-deficient embryos. The heart (indicated by the arrow) of Cop1-null embryos do not form properly. The scale bar is 1mm.

Supplemental Figure S2: *Cop1*$^{h/h}$ mice have reduced body weight and exhibit a ventral white spotting phenotype. (A) Pictures of P4, P20 and P40 mice with the indicated genotypes. (B) Graph of the body weight of *Cop1*$^{h/h}$ and *Cop1*$^{h/h}$ control littermates at P4, P10, P20 and P40. The values are the mean (+ SD) of 20 different mice.

Supplemental Figure S3: (A) to (E) *Cop1*-deficiency does not affect p53 levels or transcriptional activity. (A) Total lysates were prepared from E9.5 embryos with the indicated *Cop1* genotypes. p53 and Vinculin (Vinc.) were detected by Western blotting. Extracts from *Trp53*$^{-/-}$ MEFs and Adeno-Cre-infected *p53*$^{LSL/-}$;*Mdm2*$^{-/-}$ (Francoz et al., 2006) were used as negative and positive controls, respectively. (B) Lysates were prepared from MEFs with the indicated *Cop1* genotypes. Cop1, p53, p19ARF and p21 were detected by Western blotting. Vinculin (Vinc.) serves as loading control. (C) Determination of p53 half-life in early passage MEFs. MEFs were treated with cycloheximide for the times indicated, then analyzed by Western blotting. (D) Early passage MEFs were exposed to 30J/m^2 and extracted in the appropriate lysis buffers at the times indicated. Samples were analyzed by Western blotting for protein expression as indicated. Vinculin (Vinc.) serves as loading control. (E) Transcriptional analysis of p53 target genes by Q-RT-PCR analyses. The data were normalized to the level of expression in non-treated control, which is set to 1. The data represent the mean (+ SD) of three independent experiments. (F) loss of p53 does not rescue phenotypes associated with Cop1-deficiency. No rescue or delay of the

embryonic lethality associated with ablation of Cop1 expression was observed (top panel). Hydrops fetalis observed in E14.5-15.5 *Cop1*$^{hypo/-}$ embryos is not rescued on a *p53*-null background (lower panel).

Supplemental Figure S4: (A) to (C) *Cop1*-deficiency does not impact on cell proliferation of p53 wild-type cells. (A) Growth curve of early passage *Cop1*$^{+/+}$ and *Cop1*$^{h/-}$ MEFs; cells were seeded in triplicate at 10^5 cells/100 mm dish. The numbers refer to the mean values (+/- SD) of three independent MEF cultures. (B) Percentage of BrdU incorporation (1hr pulse) of P3 *Cop1*$^{+/+}$ and *Cop1*$^{h/-}$ MEFs. No significant differences were observed. (C) Proliferation of *Cop1*$^{+/+}$ and *Cop1*$^{h/-}$ MEF cultures on a 3T3 schedule. The relative cumulative cell numbers is shown on a linear scale on the y axis.

Supplemental Table S1: Genotyping Analysis of Progeny from *Cop1* Heterozygous Intercrosses

Stage	No. of Litters	Total No.	+/+	+/-	-/-	-/- (%)	Abnormal	Abnormal (%)
E 9.5	7	50	12	26	12	24	8 smaller	67
E 10.5	10	67	17	37	13	19	13 smaller	100
E11.5	6	48	14	29	5	10	5 dead	100
E 12.5	4	24	7	17	0	0	0	0
F2	36	215	70	145	0	0	0	0

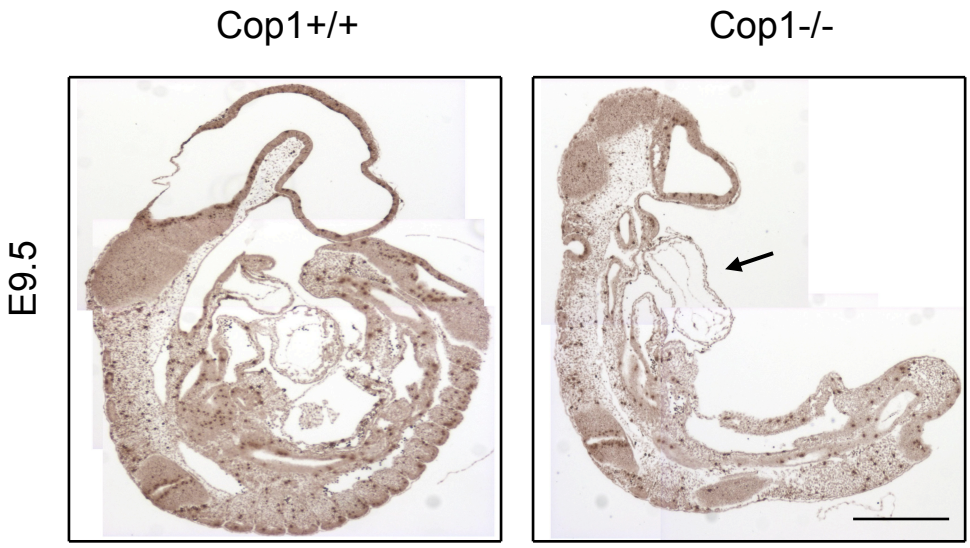
Supplemental Table S2: Genotyping Analysis of Progeny from *Cop1*$^{hypo/+}$ mice crossed with *Cop1*$^{+/-}$

Stage	No. of Litters	Total No.	hypo/+	+/+	+/-	hypo/-	hypo/- (%)	Abnormal	Abnormal (%)
E 10.5	2	13	3	4	3	3	23	0	0
E 12.5	5	42	10	12	11	9	21	4 smaller	44
E 14.5	6	39	9	11	11	8	20	7 paler	87
E 15.5	2	14	4	4	4	2	14	2 paler	100
E18.5	3	20	7	6	6	1	5	1 dead	100
P4	11	66	20	25	21	0	0	0	0

Supplemental Table S3: Genotyping Analysis of Progeny from *Cop1*$^{hypo/+}$ Intercrosses

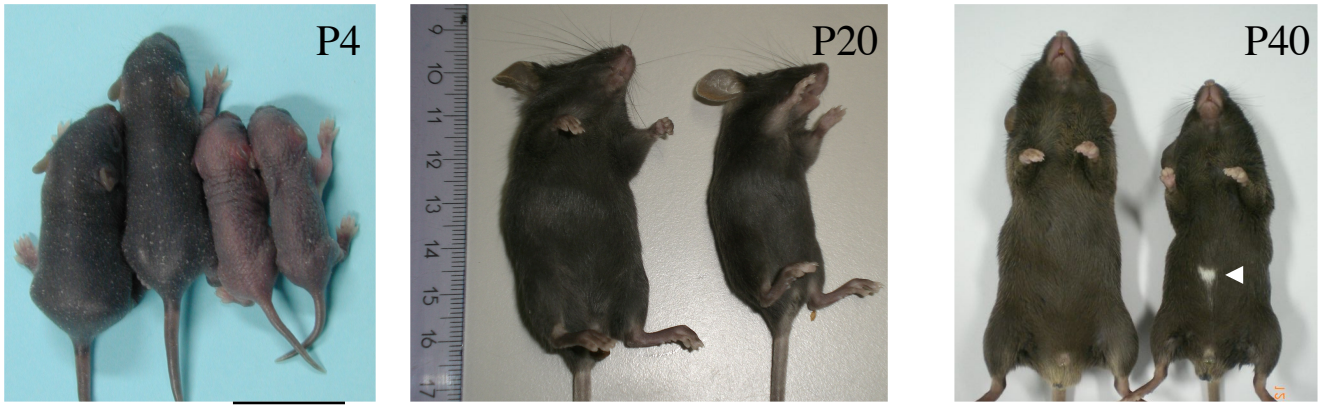
Stage	No. of Litters	Total No.	+/+	hypo/+	hypo/hypo	hypo/hypo (%)	Abnormal	Abnormal (%)
E12.5	2	17	4	8	5	29	0	0
E 15.5	3	26	7	13	6	23	0	0
P4	6	42	10	24	8	19	18 smaller	95

Supplemental Figure S1



Supplemental Figure S2

A



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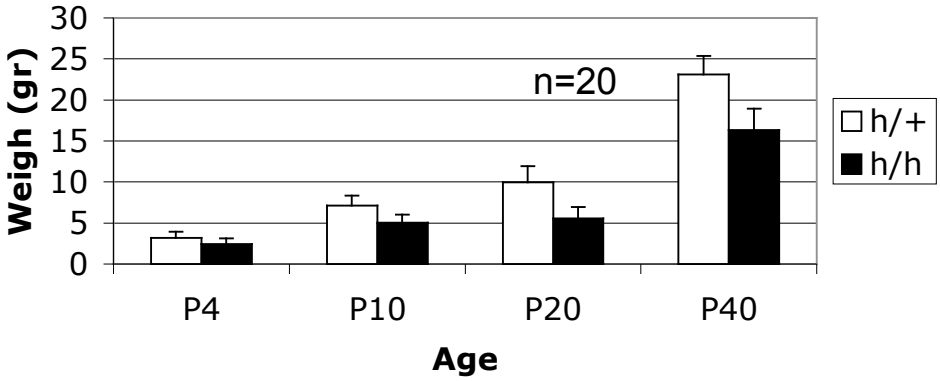
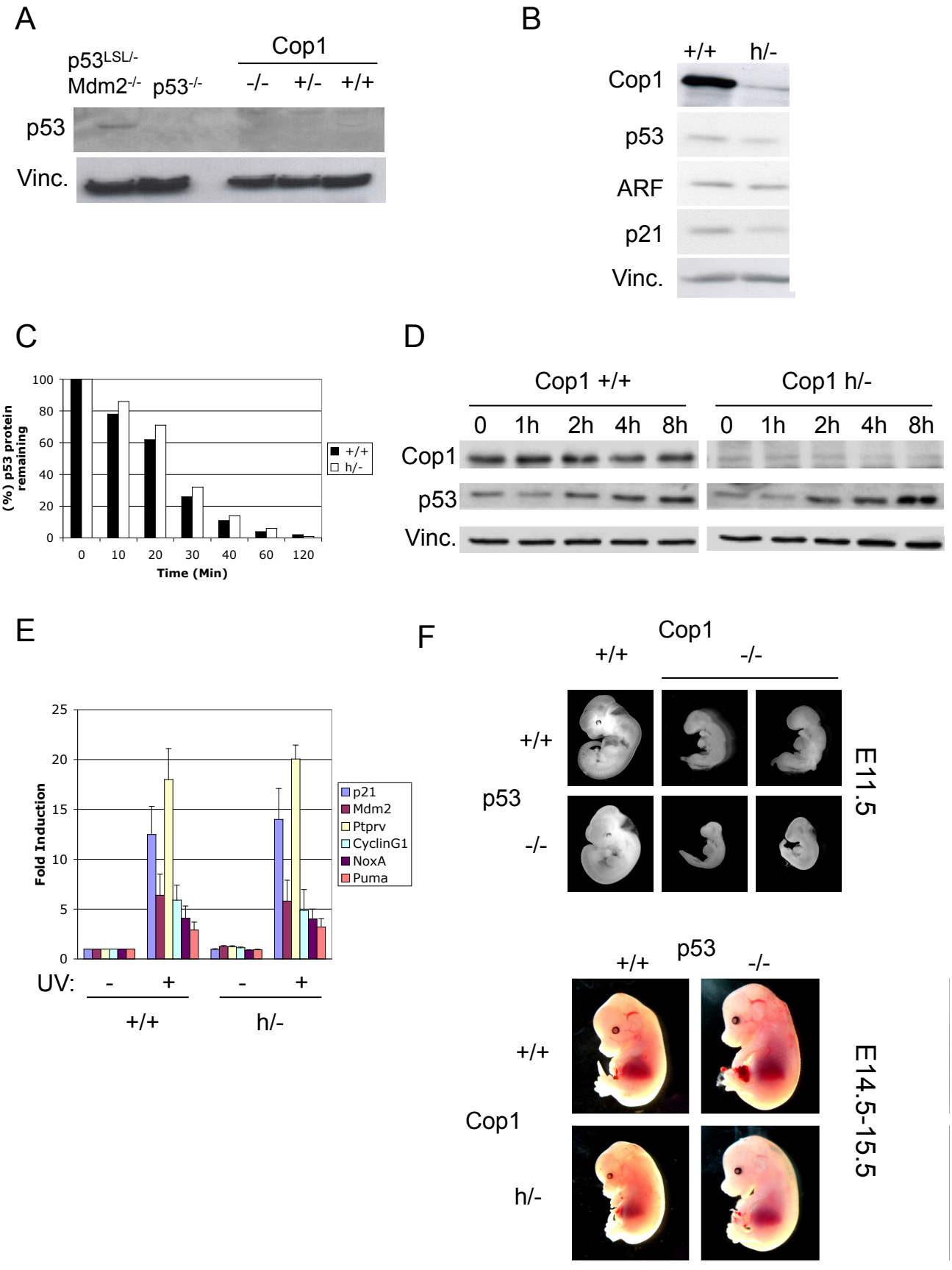
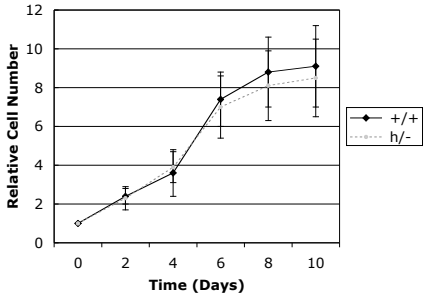


Supplemental Figure S3



Supplemental Figure S4

A



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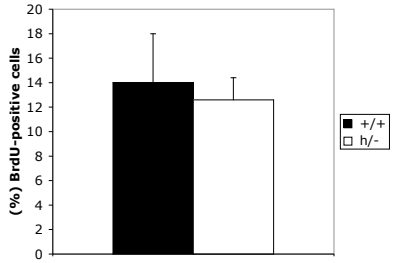

C