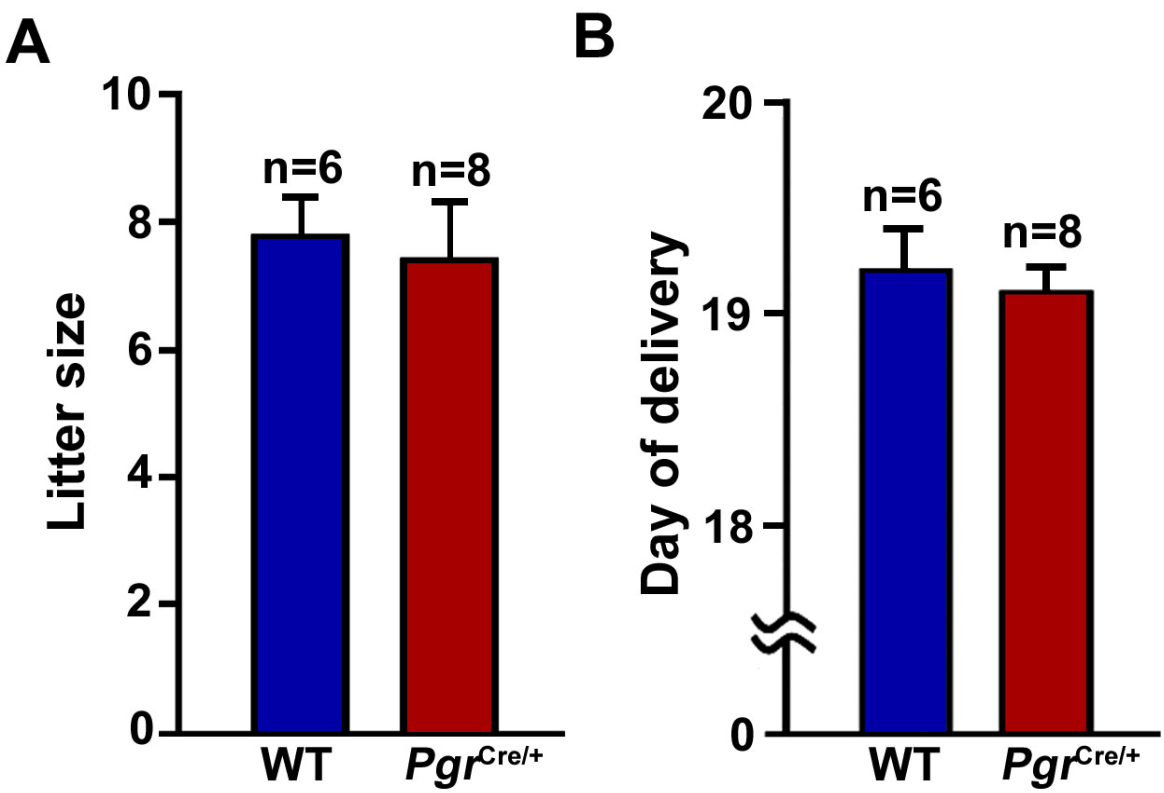
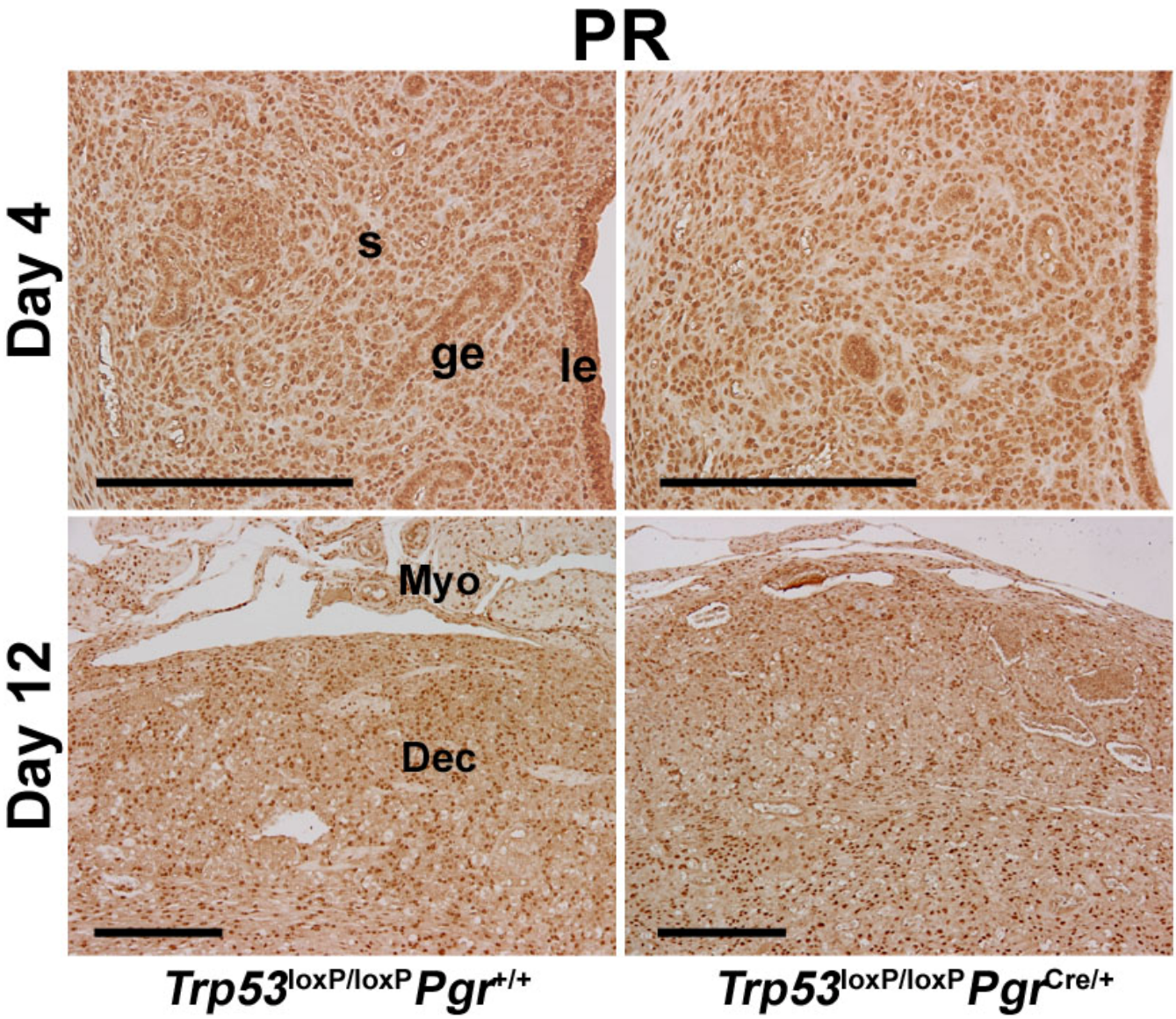
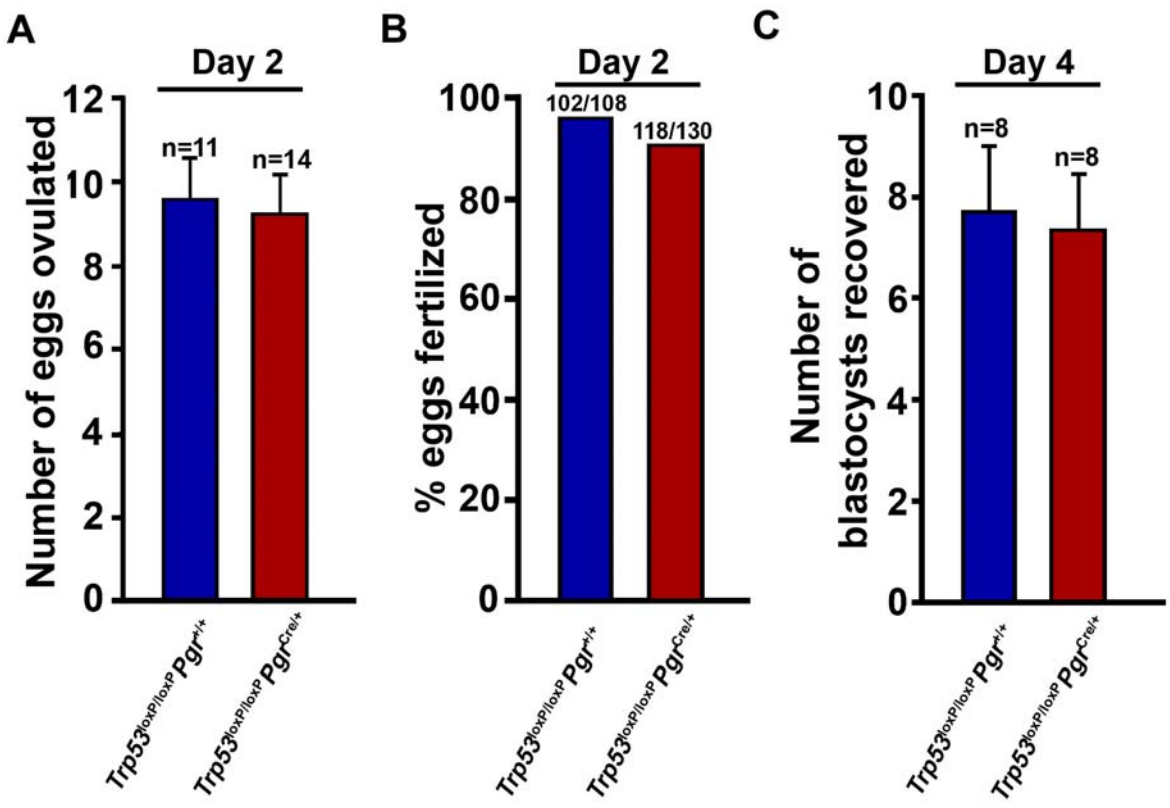


Supplemental Figure 1. *Pgr*$^{Cre/+}$ mice have normal reproductive functions and gestational length. **A**, Average litter sizes of WT and *Pgr*$^{Cre/+}$ females. **B**, Gestational length of WT and *Pgr*$^{Cre/+}$ mice. WT and *Pgr*$^{Cre/+}$ females were mated with *Pgr*$^{Cre/+}$ males. All values are mean ± SEM (P>0.05; Student's t test). Numbers above bars indicate number of females examined.

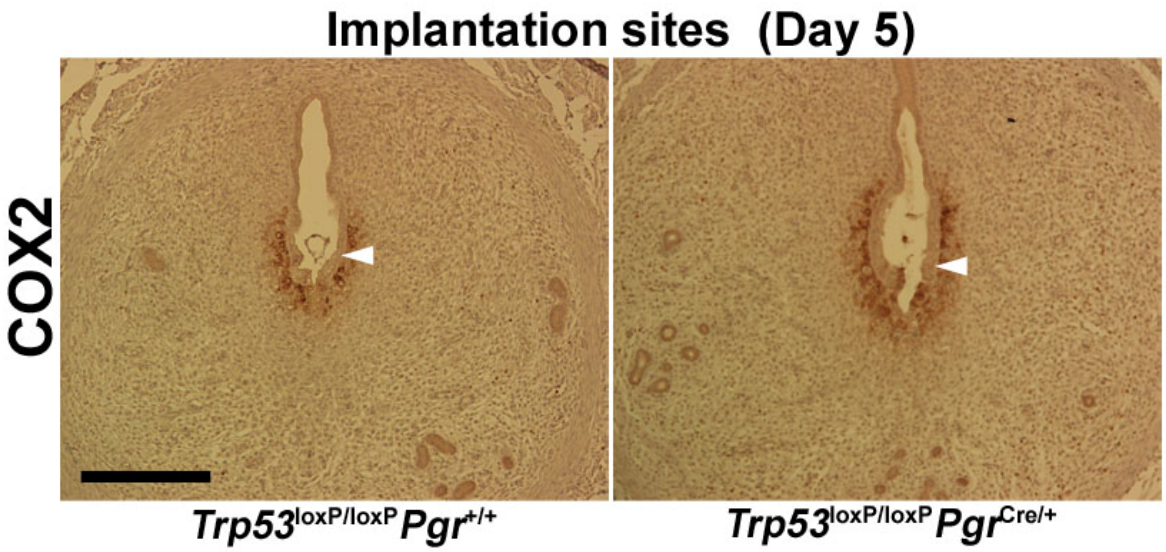


Supplemental Figure 2. Immunolocalization of PR in *Trp53*$^{loxP/loxP}$*Pgr*$^{+/+}$ and *Trp53*$^{loxP/loxP}$*Pgr*$^{Cre/+}$ uteri on days 4 and 12 of pregnancy. Brown deposits indicate nuclear localization of PR. s, stroma; ge, glandular epithelium; le, luminal epithelium; Myo, myometrium; Dec, decidua. Scale bar, 200μm.

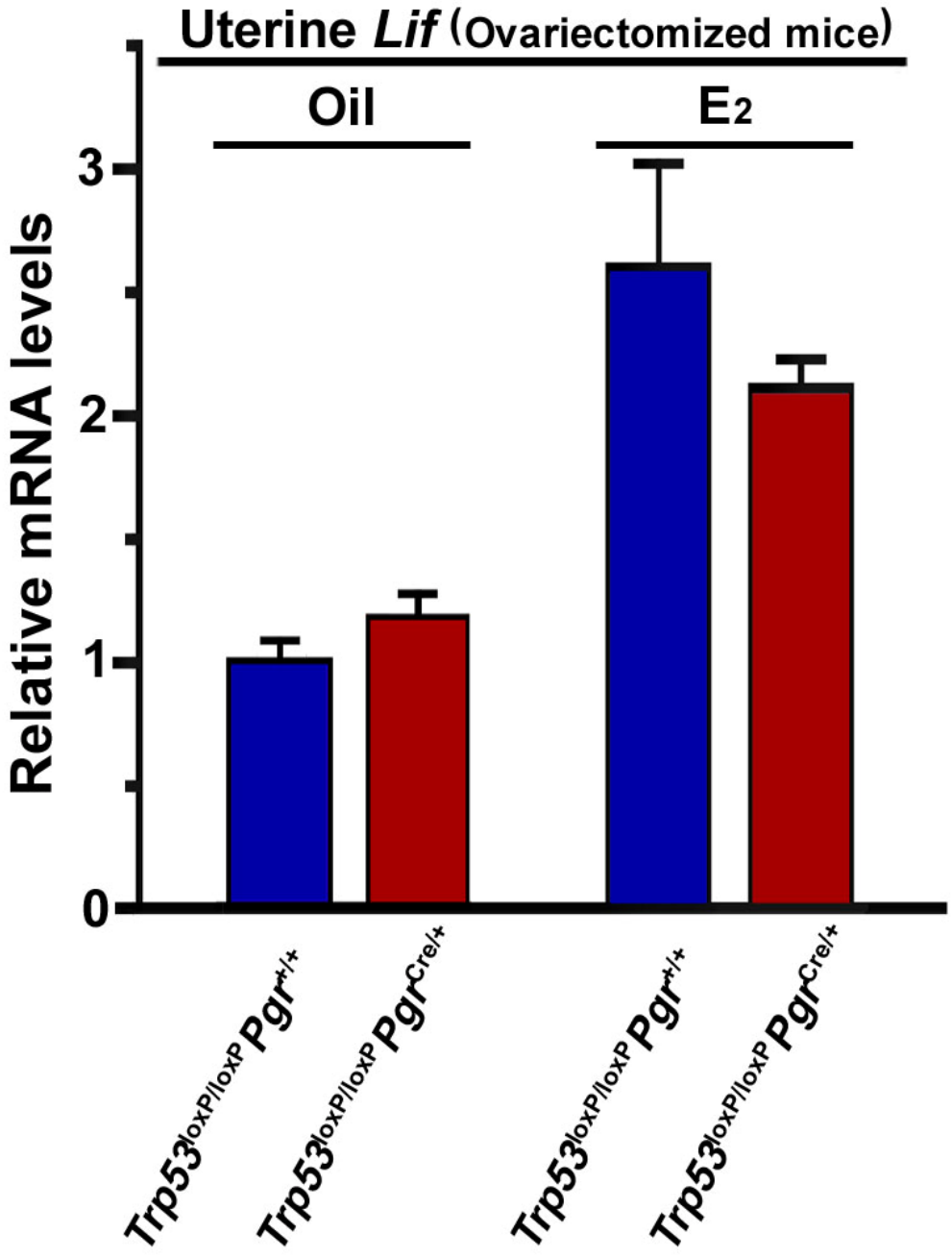


Supplemental Figure 3. Mice with conditional deletion of uterine *Trp53* show normal ovulation and fertilization. **A**, The number of ovulated eggs on day 2 of pregnancy is not significantly different between *Trp53*$^{loxP/loxP}$*Pgr*$^{+/+}$ and *Trp53*$^{loxP/loxP}$*Pgr*$^{Cre/+}$ females. Numbers above bars indicate number of mice examined. Values are mean ± SEM (P>0.05, Student's t test). **B**, Fertilization rate, as determined by the number of 2-cell embryos recovered after flushing oviducts on day 2, is comparable between *Trp53*$^{loxP/loxP}$*Pgr*$^{+/+}$ and *Trp53*$^{loxP/loxP}$*Pgr*$^{Cre/+}$ females (P>0.05, Fisher's exact probability test). Numbers above bars indicate number of fertilized eggs per total number of ovulated eggs. **C**, Development of preimplantation embryos and their oviductal-uterine transport, as determined by the recovery of blastocysts from uteri on day 4 of pregnancy, are similar in

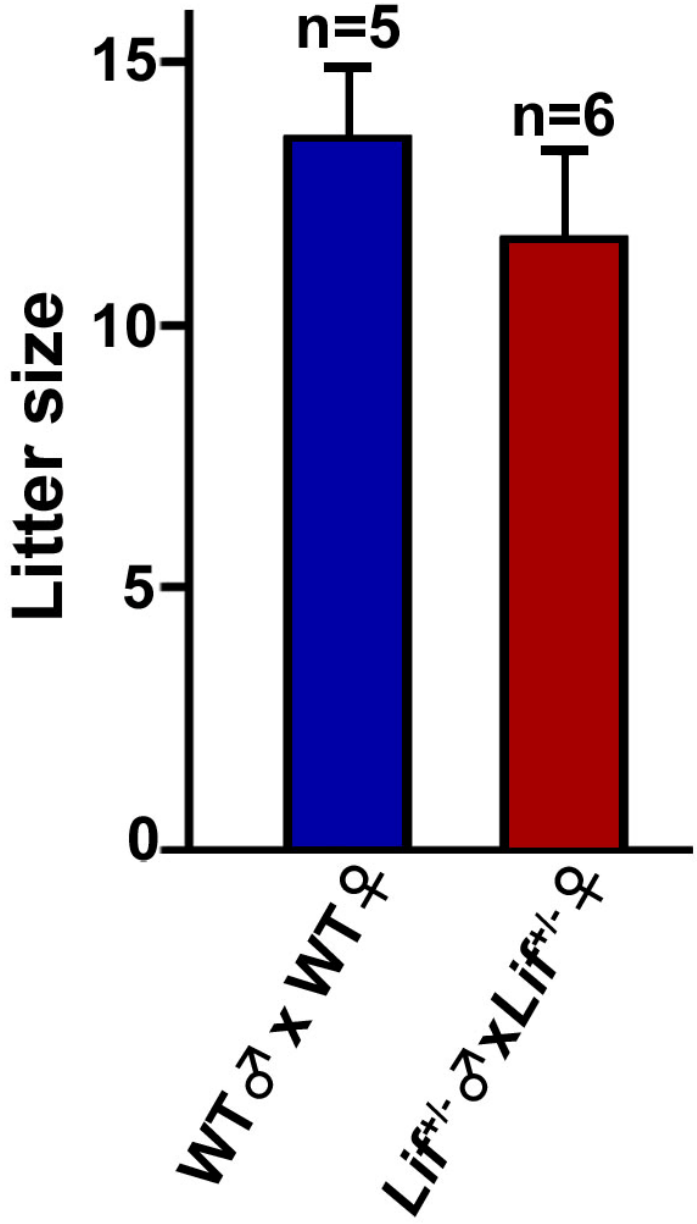
Trp53$^{loxP/loxP}$*Pgr*$^{+/+}$ and *Trp53*$^{loxP/loxP}$*Pgr*$^{Cre/+}$ females. Numbers above bars indicate number of mice examined. Values are mean ± SEM (P>0.05, Student's t test).



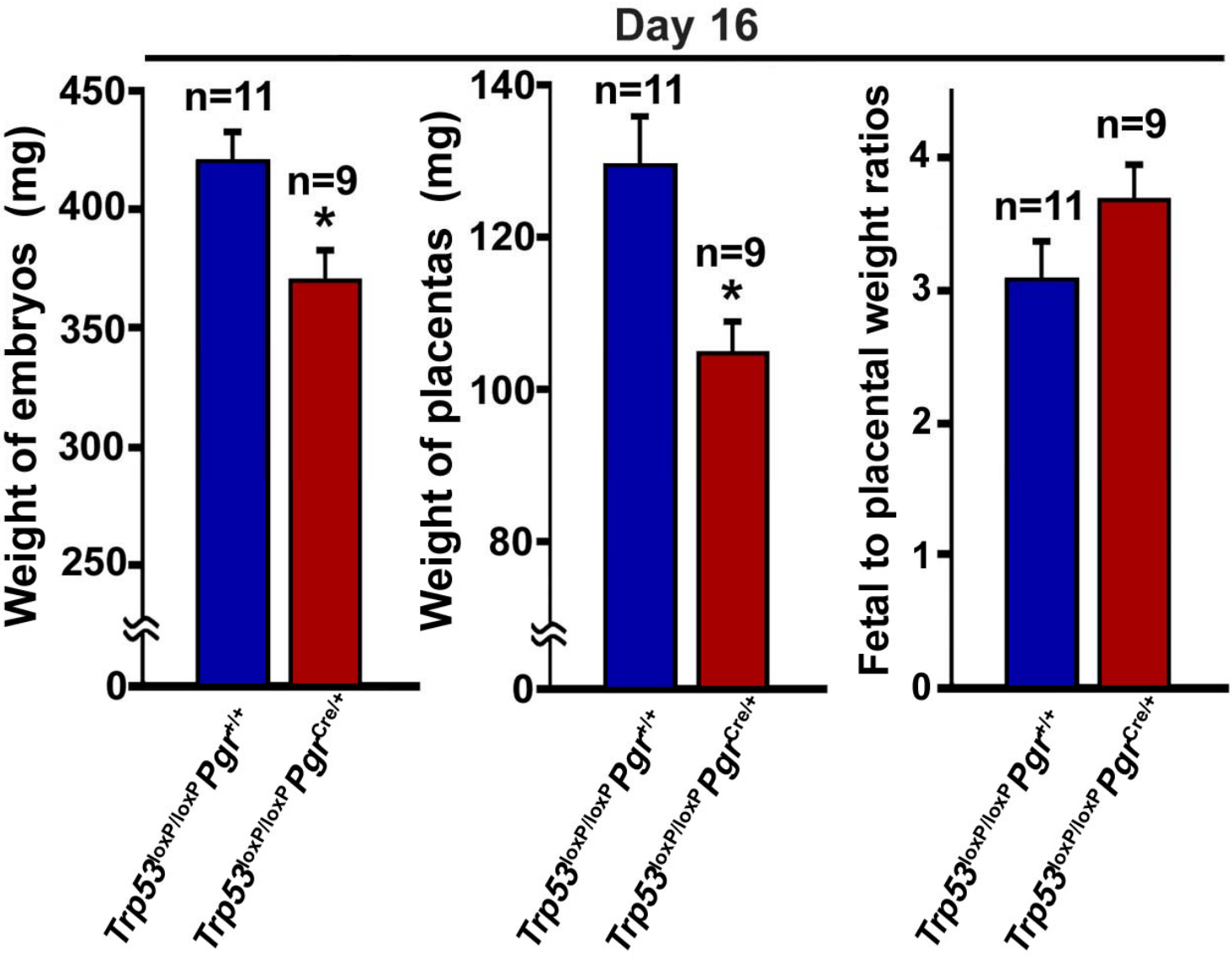
Supplemental Figure 4. Immunostaining of COX2 in implantation sites of *Trp53*$^{loxP/loxP}$*Pgr*$^{+/+}$ and *Trp53*$^{loxP/loxP}$*Pgr*$^{Cre/+}$ mice on day 5 of pregnancy. Dark brown deposits indicate the site of COX2 immunostaining. Arrowheads indicate the location of implanting blastocysts. Scale bar, 200μm.



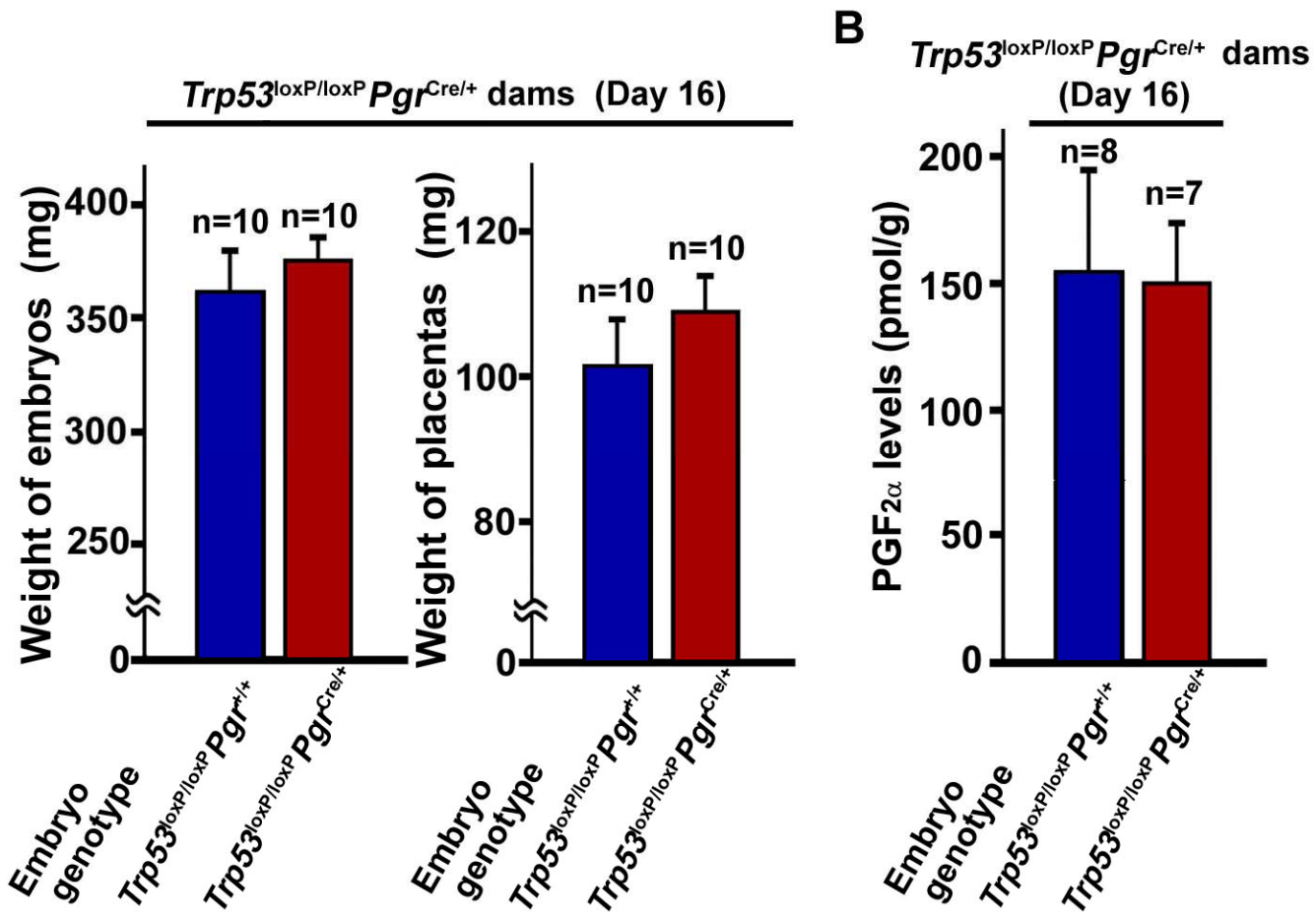
Supplemental Figure 5. *Lif* mRNA levels in estrogen-treated uteri of ovariectomized mice as determined by Northern hybridization. *Lif* mRNA levels are similar in ovariectomized *Trp53*$^{loxP/loxP}$*Pgr*$^{+/+}$ and *Trp53*$^{loxP/loxP}$*Pgr*$^{Cre/+}$ uteri treated with E_2. Oil-treated uteri were used as controls. All values are mean ± SEM of 3 independent samples (P>0.05, Student's t tests).



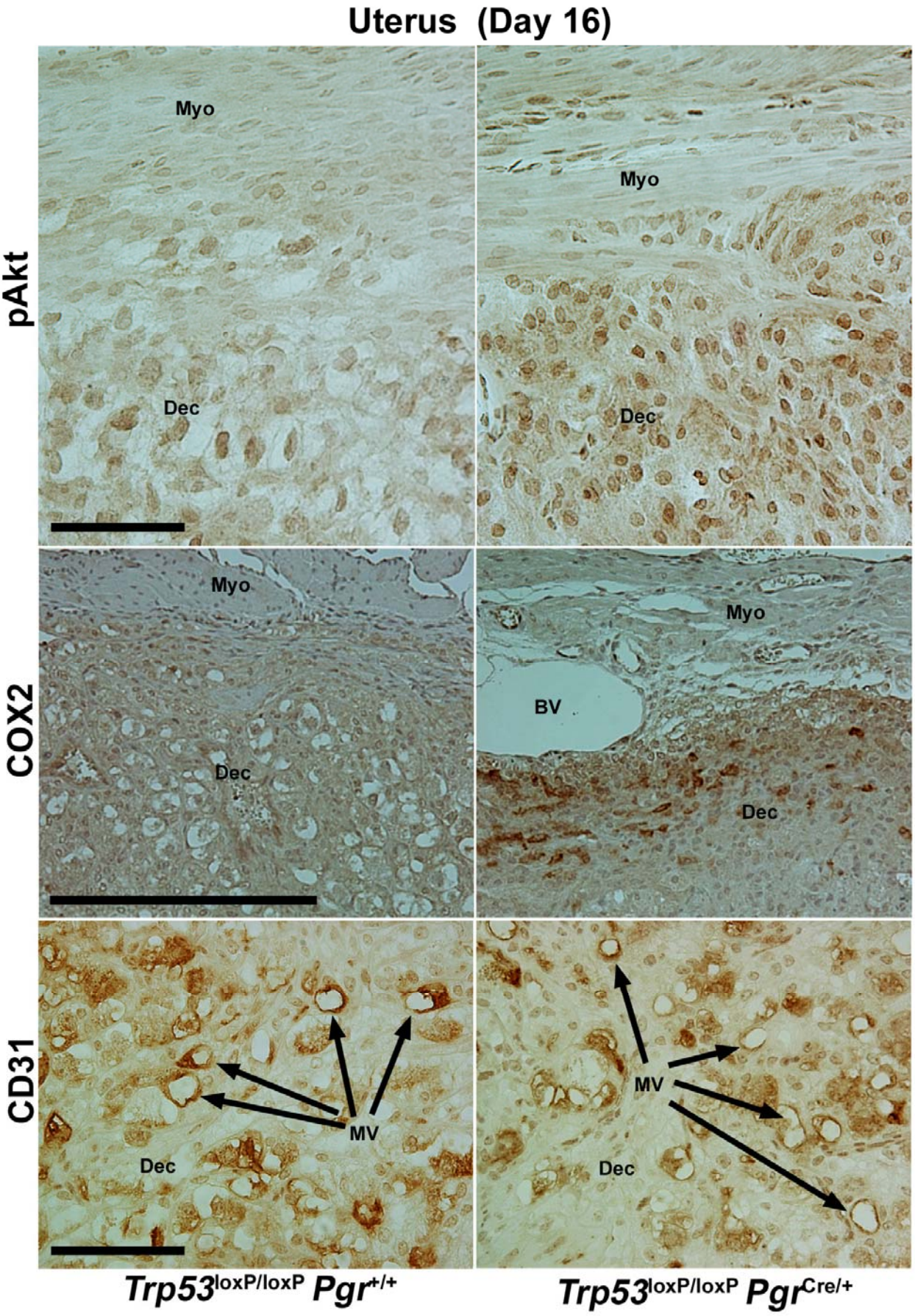
Supplemental Figure 6. *Lif*$^{+/-}$ mice have normal reproductive functions. Average litter sizes of WT and *Lif*$^{+/-}$ females. WT and *Lif*$^{+/-}$ females were mated with WT and *Lif*$^{+/-}$ males, respectively. Numbers above bars indicate number of females examined. Values are mean ± SEM (P>0.05, Student's t tests).



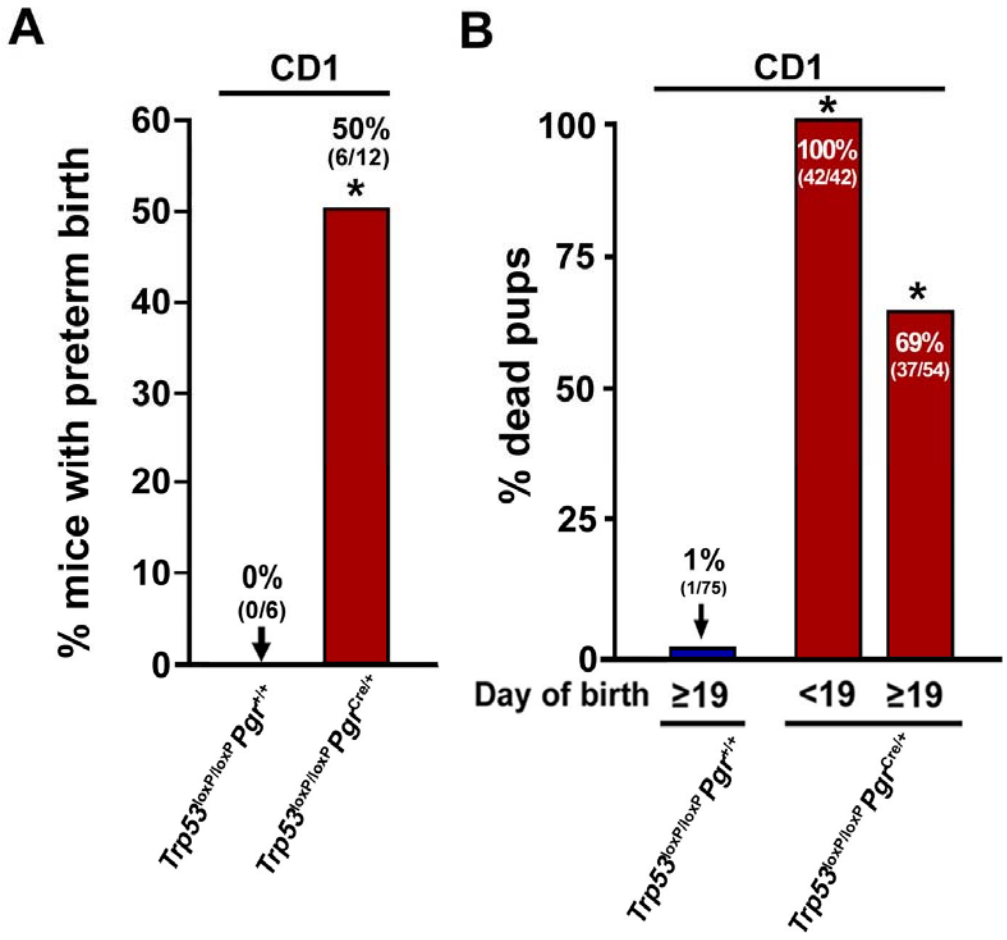
Supplemental Figure 7. Embryos and placentas are smaller in day 16 pregnant mice with uterine deletion of *Trp53*. Weights of embryos and placentas as well as fetal to placental weight ratios in *Trp53*$^{loxP/loxP}$*Pgr*$^{+/+}$ and *Trp53*$^{loxP/loxP}$*Pgr*$^{Cre/+}$ uteri on day 16 of pregnancy are shown. Numbers above bars indicate number of females examined. Values are mean ± SEM (**P*<0.05, Student's *t* test).



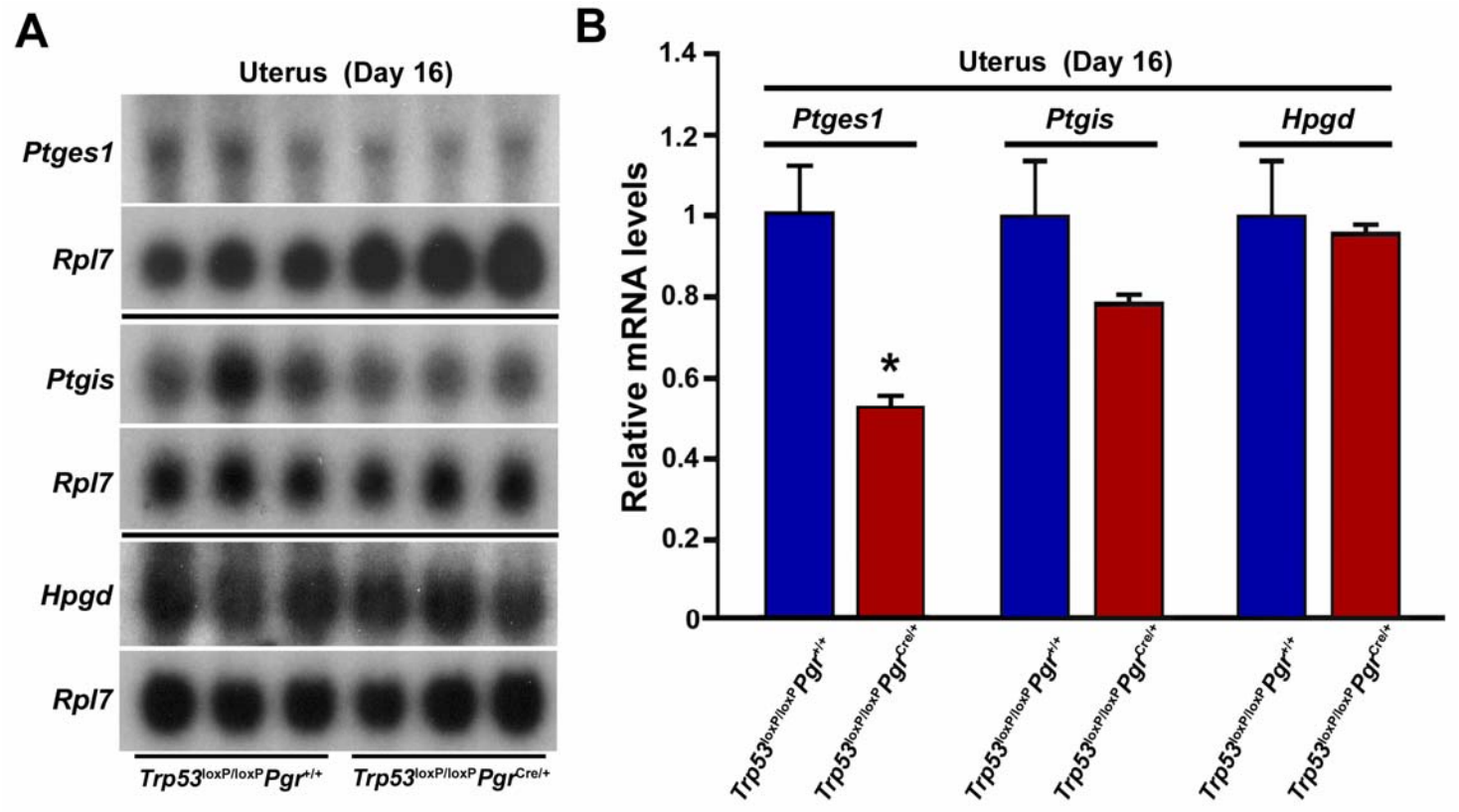
Supplemental Figure 8. Failure of embryo genotypes to influence maternal environment affecting embryonic or placental growth or $PGF_{2\alpha}$ levels in uteri lacking p53 on day 16 of pregnancy. **A**, Weights of *Trp53*$^{loxP/loxP}$*Pgr*$^{+/+}$ and *Trp53*$^{loxP/loxP}$*Pgr*$^{Cre/+}$ embryos and placentas in *Trp53*$^{loxP/loxP}$*Pgr*$^{Cre/+}$ uteri on day 16 of pregnancy are comparable. Numbers above bars indicate number of embryos and placentas examined. **B**, In *Trp53*$^{loxP/loxP}$*Pgr*$^{Cre/+}$ mothers on day 16, $PGF_{2\alpha}$ levels are comparable at implantation sites carrying *Trp53*$^{loxP/loxP}$*Pgr*$^{+/+}$ and *Trp53*$^{loxP/loxP}$*Pgr*$^{Cre/+}$ embryos. Implantation sites from which placentas and fetuses had been removed were used for PG assays. Numbers above bars indicate number of implantation sites examined. All values are mean ± SEM (P>0.05, Student's *t* test).


Uterus (Day 16)
pAkt
COX2
CD31
Myo
Dec
BV
MV
Trp53loxP/loxP Pgr+/+
Trp53loxP/loxP PgrCre/+

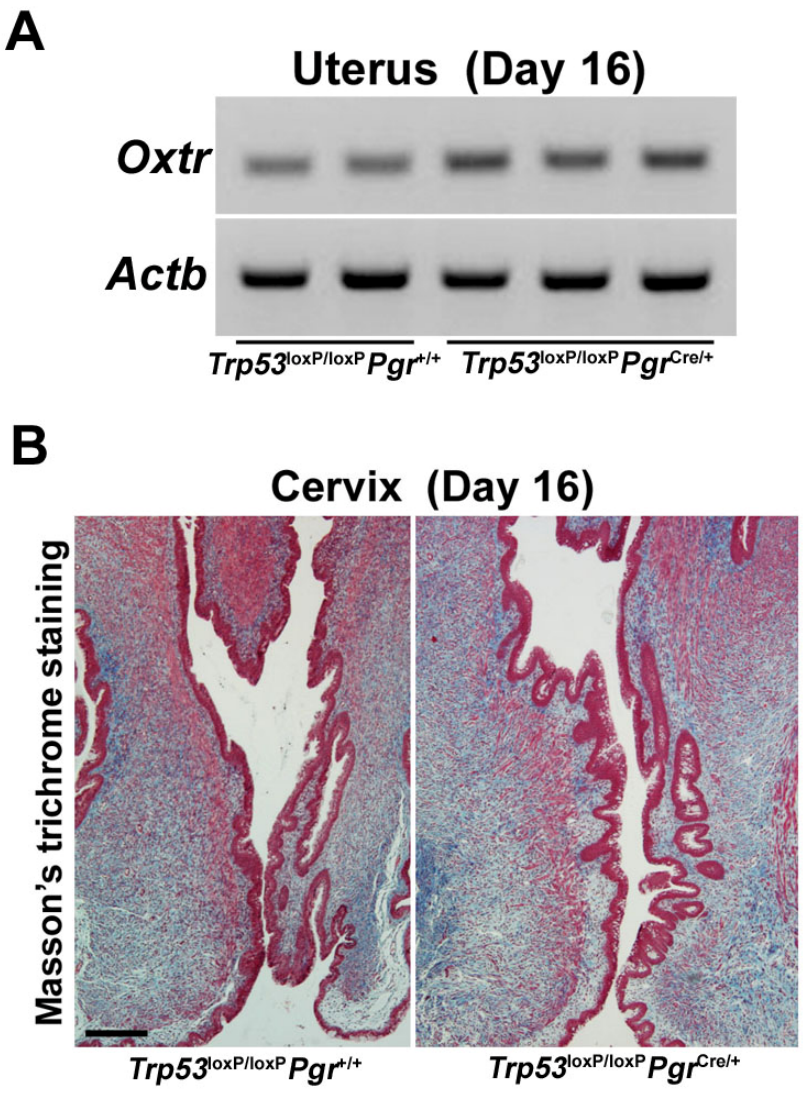
Supplemental Figure 9. Immunostaining of pAkt, COX2 and CD31 in *Trp53*$^{loxP/loxP}$*Pgr*$^{+/+}$ *and* *Trp53*$^{loxP/loxP}$*Pgr*$^{Cre/+}$ uteri on day 16 of pregnancy. Uterine loss of p53 enhances intensity of pAkt and COX2 immunostaining in decidual cells. **The distribution of CD31-positive cells is comparable in *Trp53*$^{loxP/loxP}$*Pgr*$^{+/+}$ *and* *Trp53*$^{loxP/loxP}$*Pgr*$^{Cre/+}$ decidual layers.** Brown deposits indicate sites of positive immunostaining. Myo, myometrium; Dec, decidua; BV, blood vessel; MV, microvessel. Scale bar, 200μm.



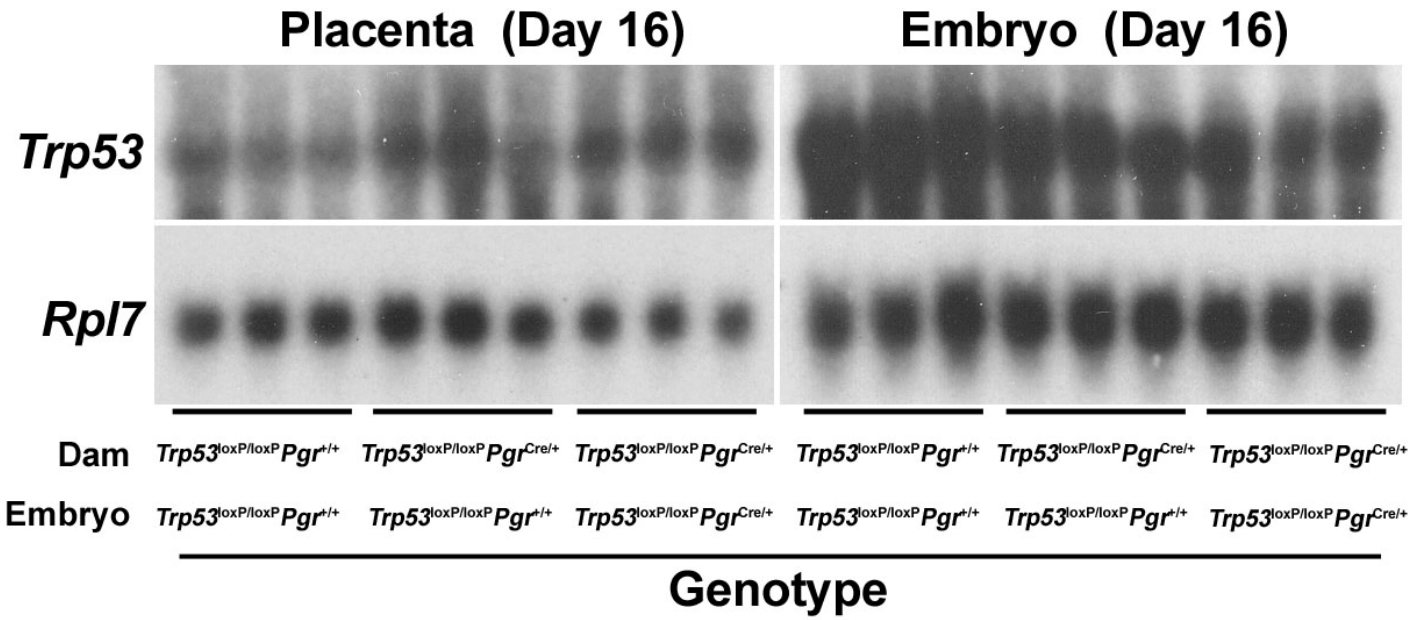
Supplemental Figure 10. Uterine deletion of *Trp53* promotes preterm birth in *Trp53*$^{loxP/loxP}$*Pgr*$^{Cre/+}$ mice on a CD1 background. **A**, Preterm birth occurred in 50% of CD1 *Trp53*$^{loxP/loxP}$*Pgr*$^{Cre/+}$ dams. Preterm birth is defined as deliveries on day 17 or 18. All CD1 *Trp53*$^{loxP/loxP}$*Pgr*$^{+/+}$ dams delivered between day 19 evening and day 20 morning. Numbers in parentheses indicate number of dams with preterm birth per total number of dams examined. *P<0.05, Fisher's exact probability test. **B**, All pups born on day 17 or 18 were dead around delivery or died immediately after birth. Numbers in parentheses indicate number of dead pups per total number of pups examined. *P<0.05 compared to *Trp53*$^{loxP/loxP}$*Pgr*$^{+/+}$ mice, Fisher's exact probability test.



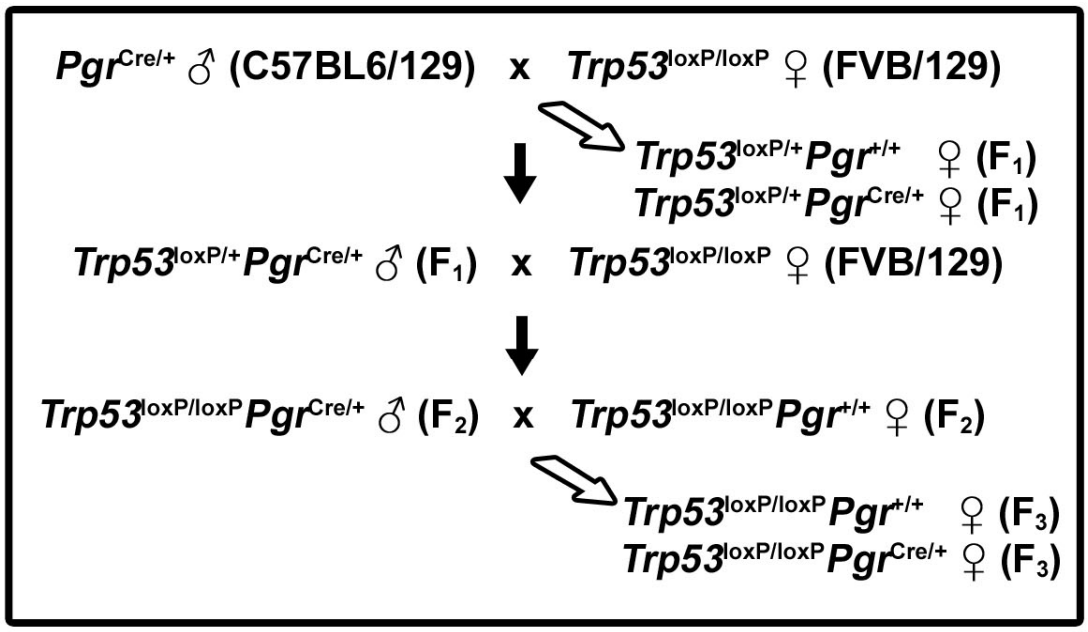
Supplemental Figure 11. Relative mRNA levels of *Ptges1*, *Ptgis* and *Hpgd* in day 16 uteri of *Trp53*$^{loxP/loxP}$*Pgr*$^{+/+}$ and *Trp53*$^{loxP/loxP}$*Pgr*$^{Cre/+}$ females. **A**, Northern hybridization. **B**, Relative mRNA levels normalized against *Rpl7.* All values are mean ± SEM of 3 independent samples (*P<0.05, Student's t test).



Supplemental Figure 12. Status of uterine oxytocin receptor (*Oxtr*) and cervical ripening in *Trp53*$^{loxP/loxP}$*Pgr*$^{Cre/+}$ mothers on day 16 of pregnancy. A, Semi-quantitative RT-PCR results show modest increases in *Oxtr* mRNA levels in *Trp53*$^{loxP/loxP}$*Pgr*$^{Cre/+}$ uteri. **B**, Representative photomicrographs of cervical sections stained with Masson's trichrome. Collagen fibrils are depicted by blue staining. Signs of cervical ripening were not evident in *Trp53*$^{loxP/loxP}$*Pgr*$^{+/+}$ and *Trp53*$^{loxP/loxP}$*Pgr*$^{Cre/+}$ females as depicted by the presence of compacted stroma and collagen fibrils. Scale bar, 200μm.



Supplemental Figure 13. *Trp53* mRNA is present in placentas and embryos developing in *Trp53*$^{loxP/loxP}$*Pgr*$^{Cre/+}$ uteri on day 16 of pregnancy. Three independent samples with indicated genotypes were evaluated in each group by Northern hybridization.



Littermate *Trp53*$^{loxP/loxP}$*Pgr*$^{+/+}$ and *Trp53*$^{loxP/loxP}$*Pgr*$^{Cre/+}$ mice from the F_3 generation and littermate *Trp53*$^{loxP/+}$*Pgr*$^{+/+}$ and *Trp53*$^{loxP/+}$*Pgr*$^{Cre/+}$ mice from the F_1 generation were used for specific experiments.

Supplemental Figure 14. Breeding scheme to generate mice with uterine deletion of *Trp53*.