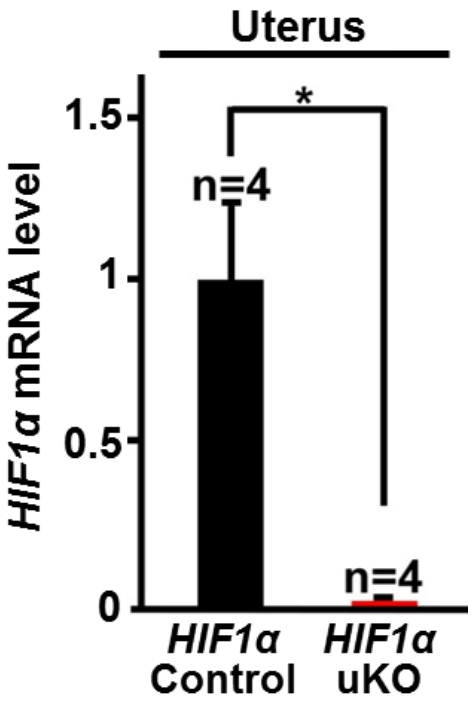
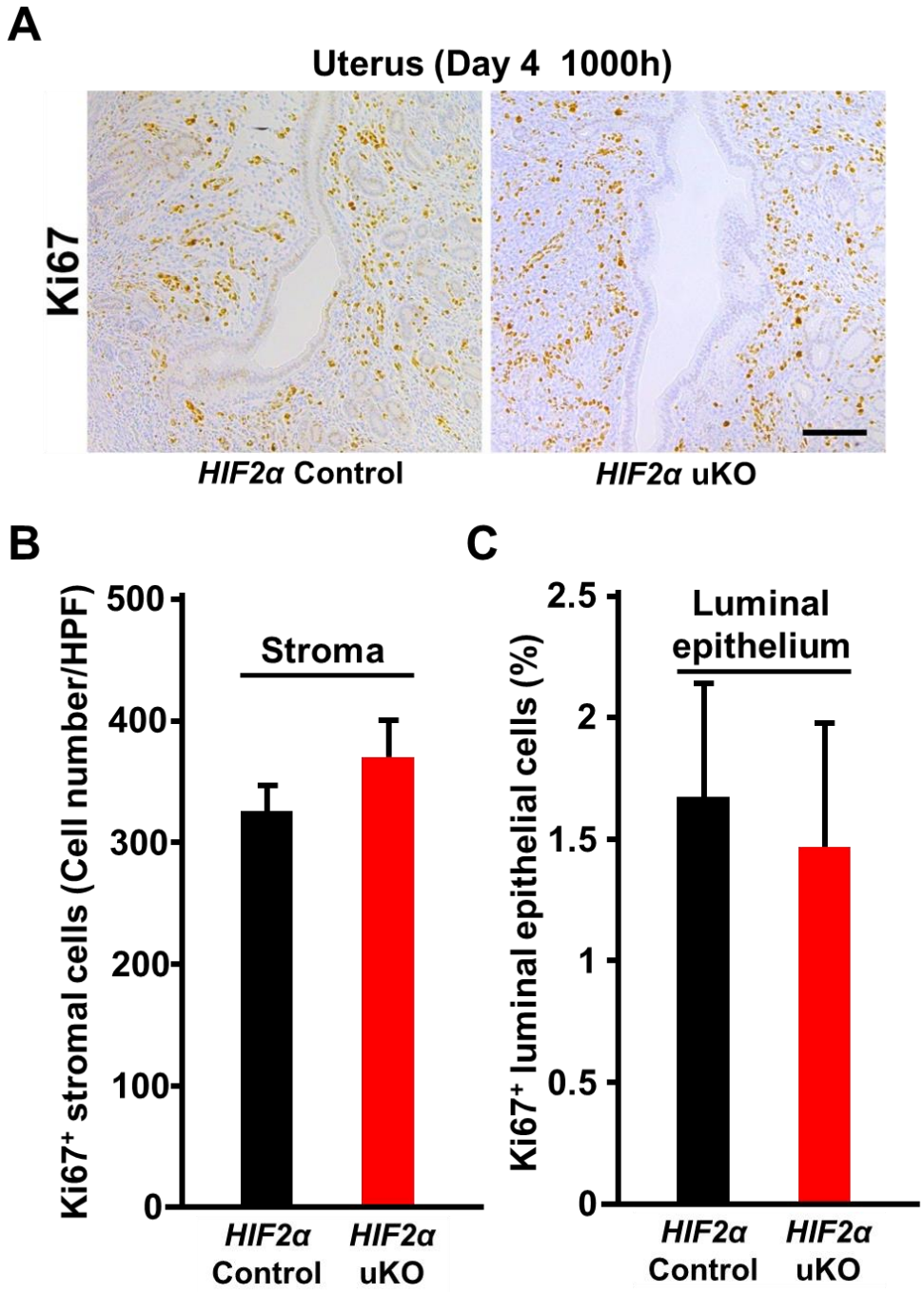
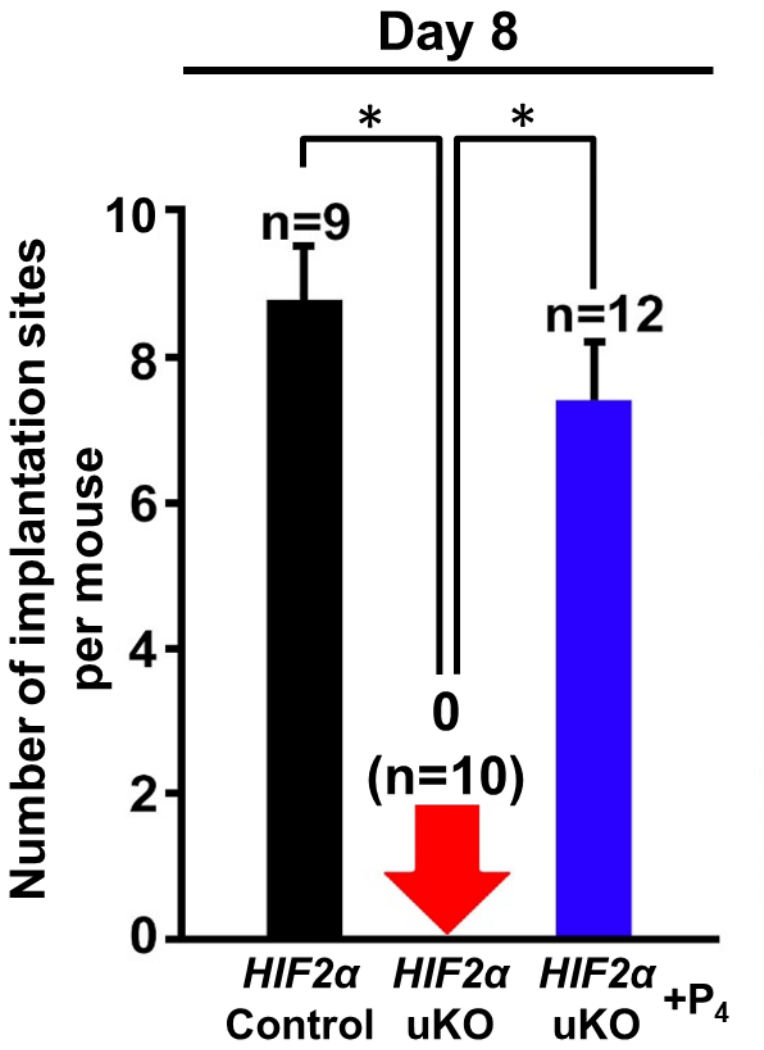


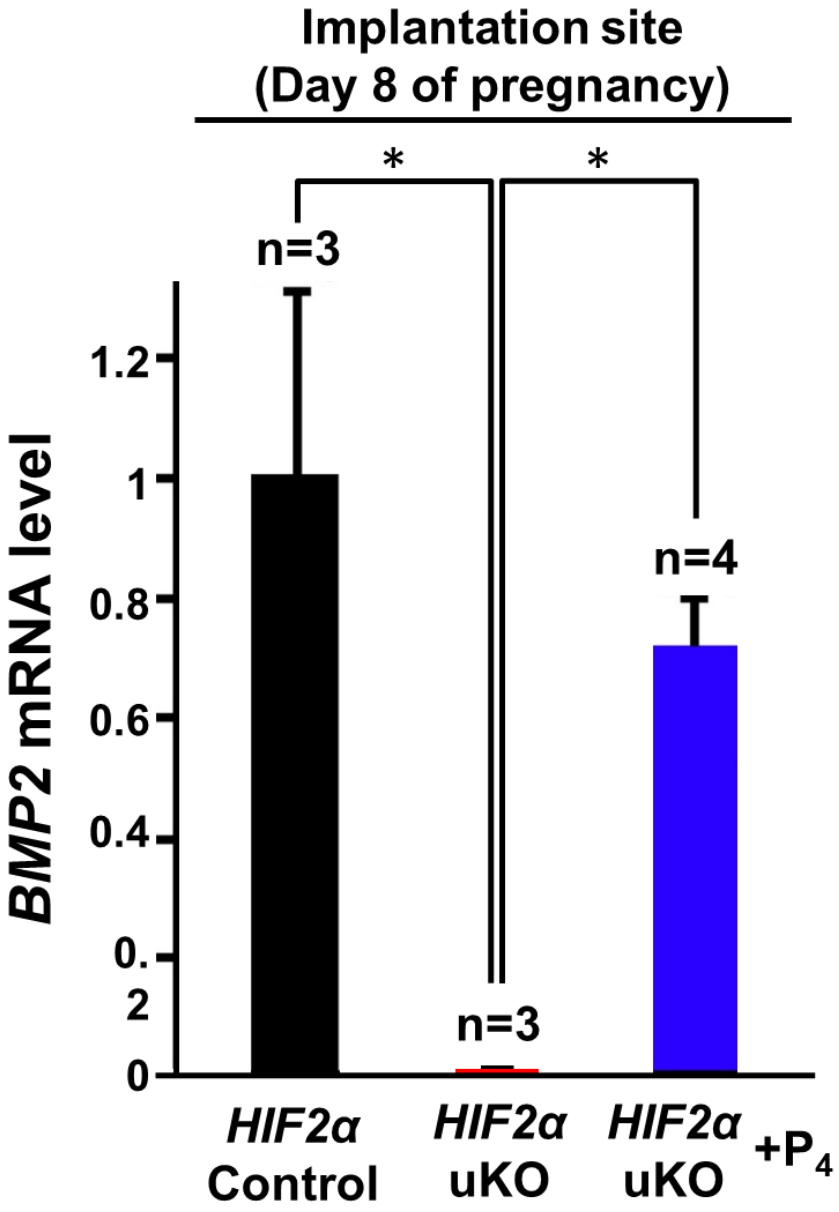
Supplemental Figure 1. *HIF1α* mRNA levels were reduced in the uterine luminal epithelium of *HIF1α* uKO mice. n=4, *$P<0.05$, mean ± SEM, Student's *t* test.



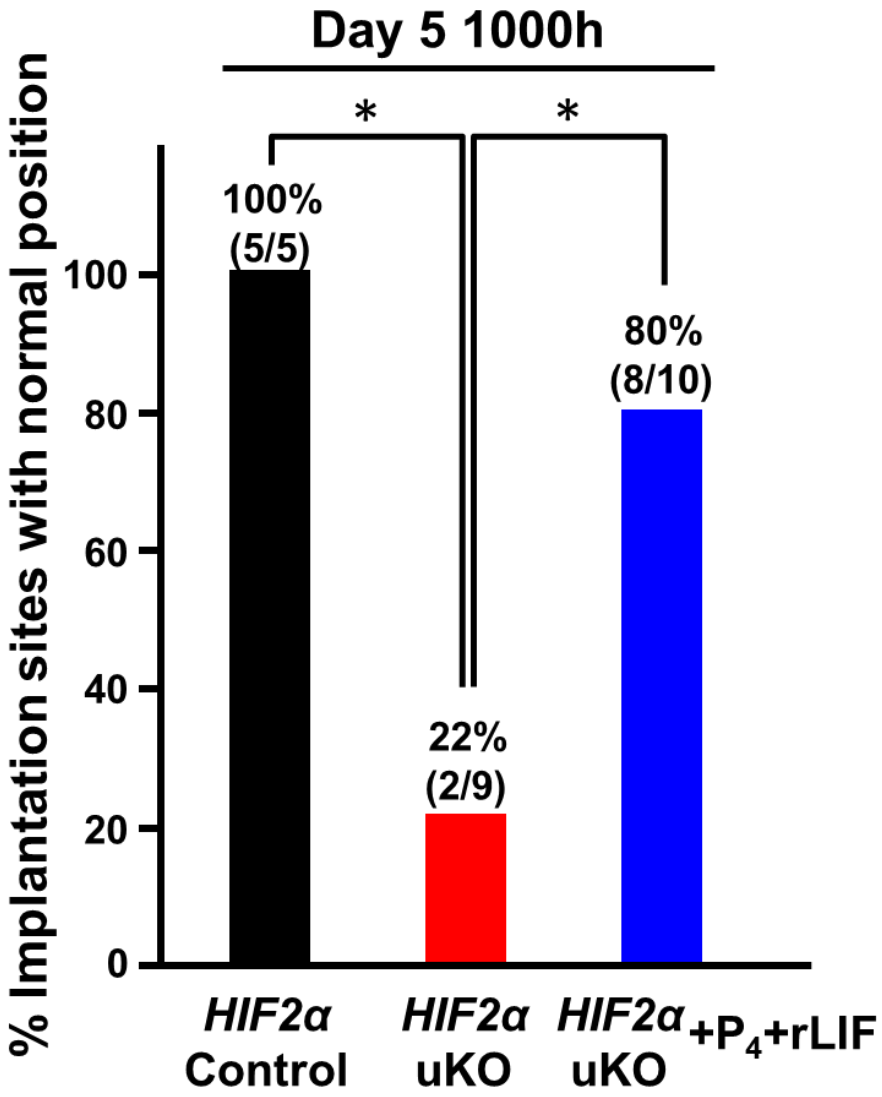
Supplemental Figure 2. Normal proliferation-differentiation switching during implantation, a marker of uterine receptivity, was observed in *HIF2α* uKO uteri on day 4 morning, as evaluated by Ki67 immunostaining. A, Scale bar, 200μm. **B&C**, $Ki67^+$ cell number on 3 randomly selected high-power fields in the uteri obtained from 5 different mice in each group were manually counted. Total number of $Ki67^+$ stromal cells were demonstrated in **B**. Percentage of $Ki67^+$ luminal epithelial cells were demonstrated in **C**. (*P>0.05,* mean ± SEM, Student's *t* test)



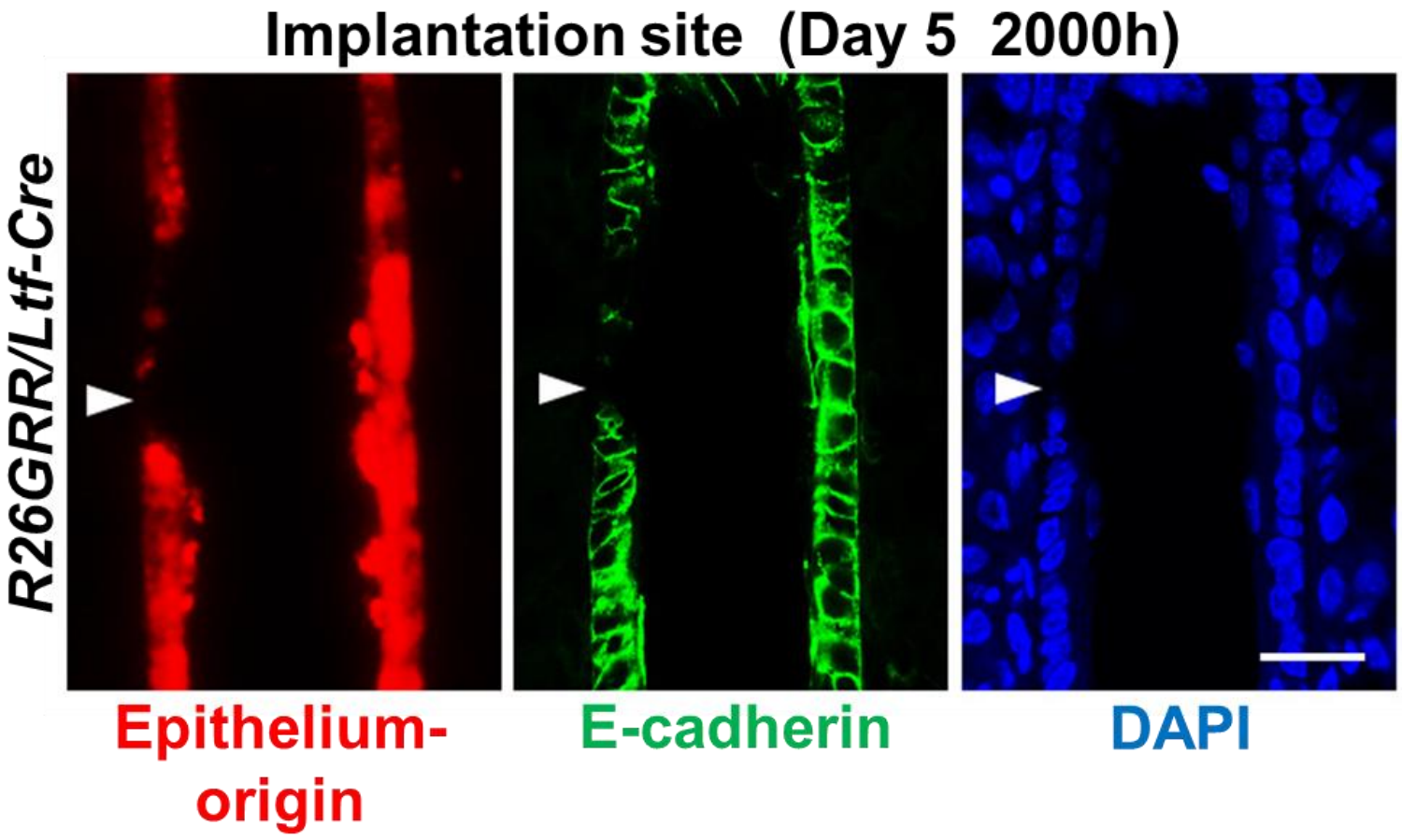
Supplemental Figure 3. P_4 administration restores number of implantation sites in *HIF2α* uKO mice. Daily injection of P_4 from day 2 of pregnancy (2mg/mouse/day) restored number of implantation sites in *HIF2α* uKO mice on day 8 of pregnancy. **P<0.05,* mean ± SEM, Student's *t* test.



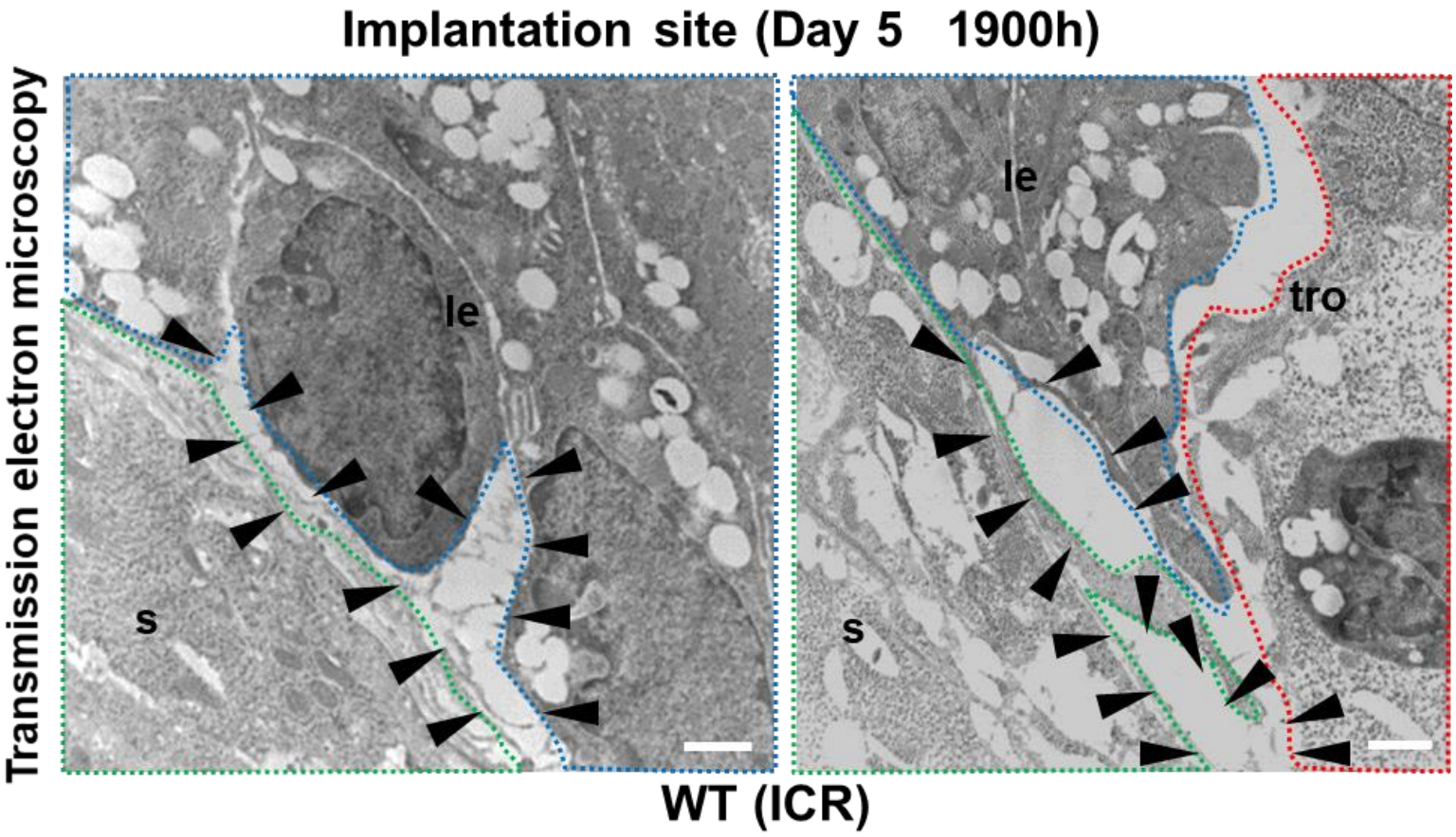
Supplemental Figure 4. Expression of a decidualization marker BMP2 was comparable between *HIF2α* uKO mice with P_4 treatment and control mice on day 8 of pregnancy. n≥3, *$P<0.05$, mean ± SEM, Student's *t* test.



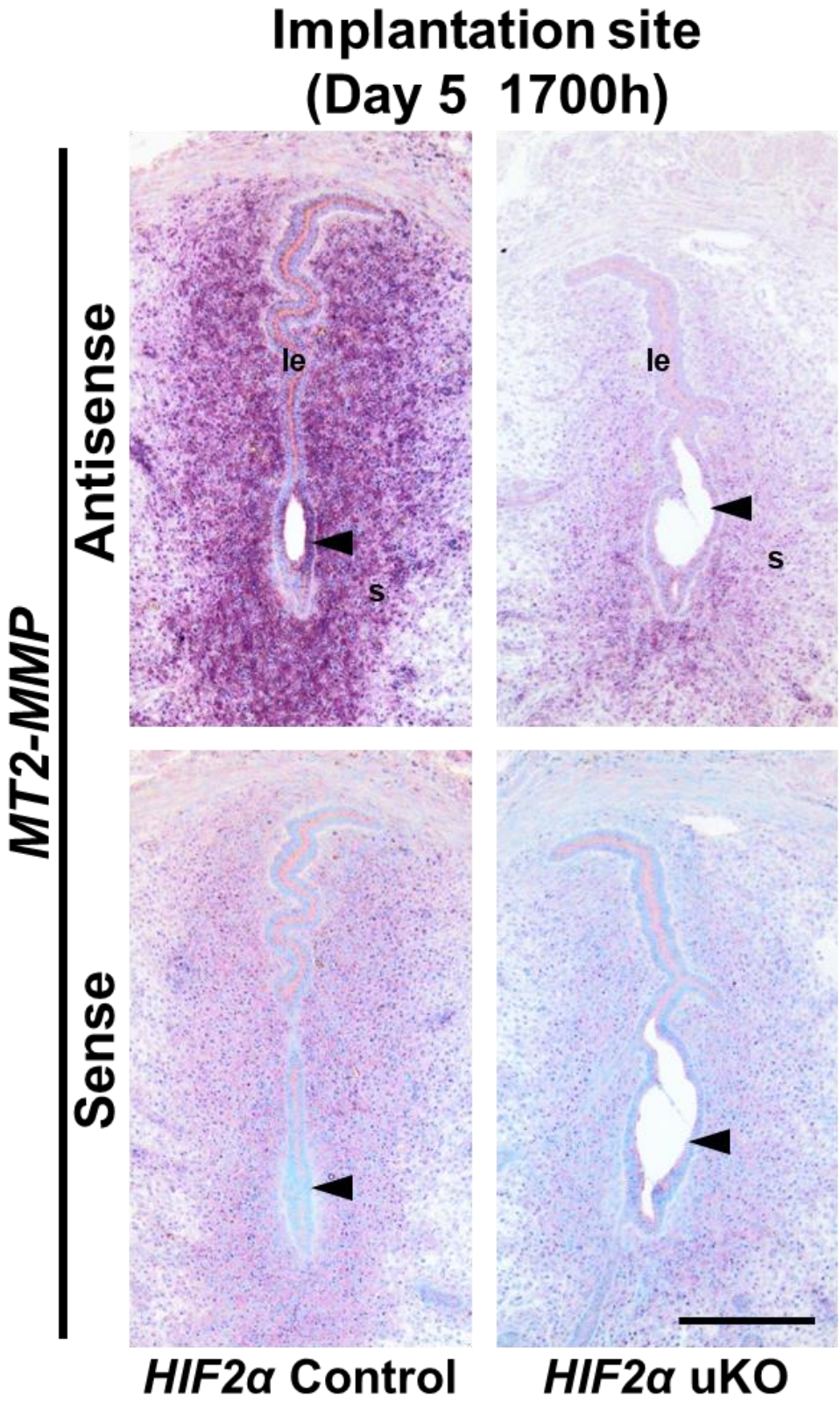
Supplemental Figure 5. Injection of recombinant LIF into *HIF2α* uKO mice in addition to P_4 injection normalizes the position of embryo attachment to the bottom of endometrial crypt on day 5 morning. The position of embryo was evaluated by H&E staining. Percentage of normal position of embryo was calculated. n≥5, *$P<0.05$, Fisher's exact probability test.



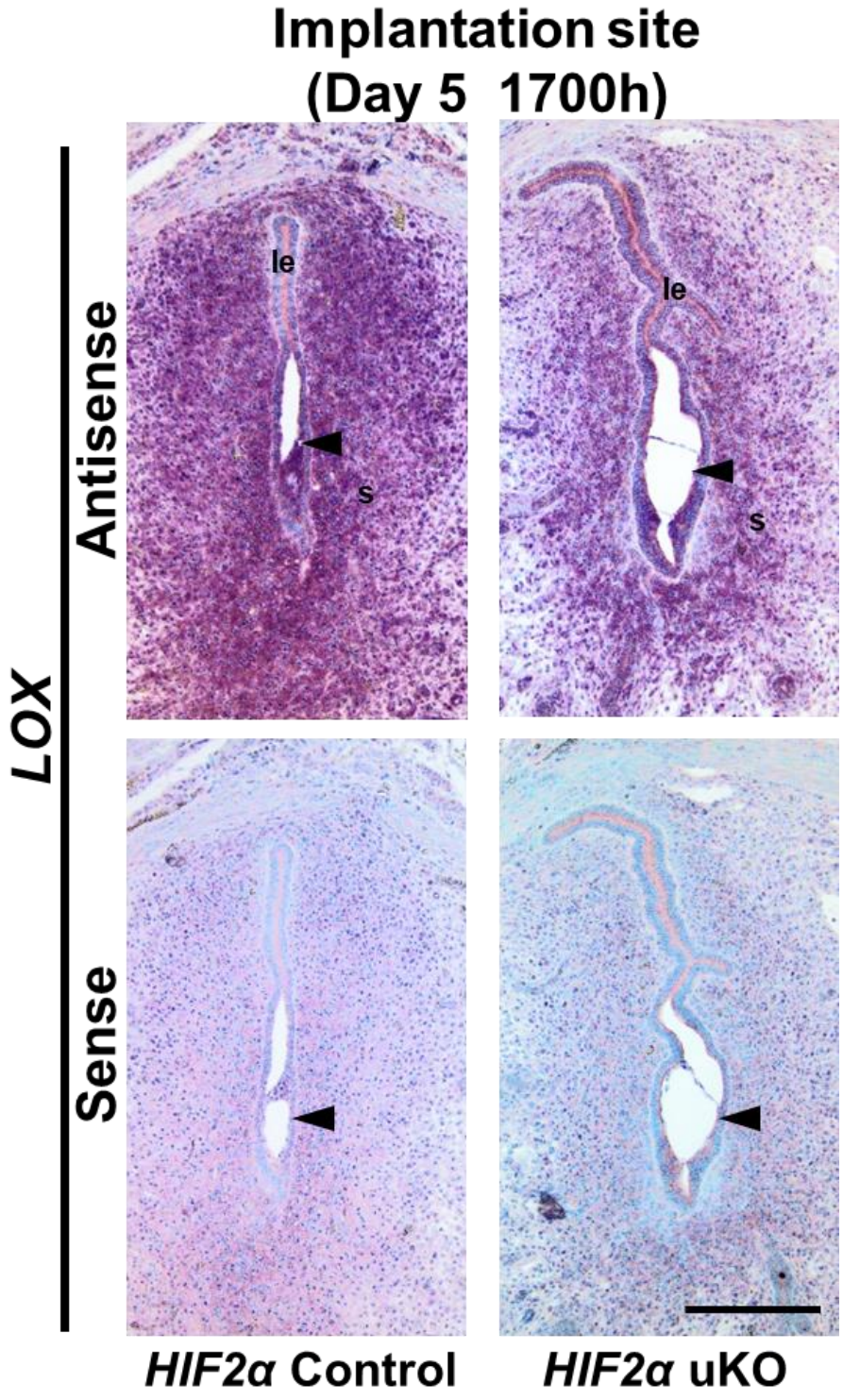
Supplemental Figure 6. EMT is not involved in vanishment of luminal epithelium around embryo. EMT at the implantation site was investigated using R26GRR/Ltf-Cre mice which can be used for tracing of the cells with uterine epithelium origin. Epithelium-derived cells were not apparently observed in the uterine stroma surrounding the invading embryo at 2000h on day 5 of pregnancy. Scale bar, 100μm.



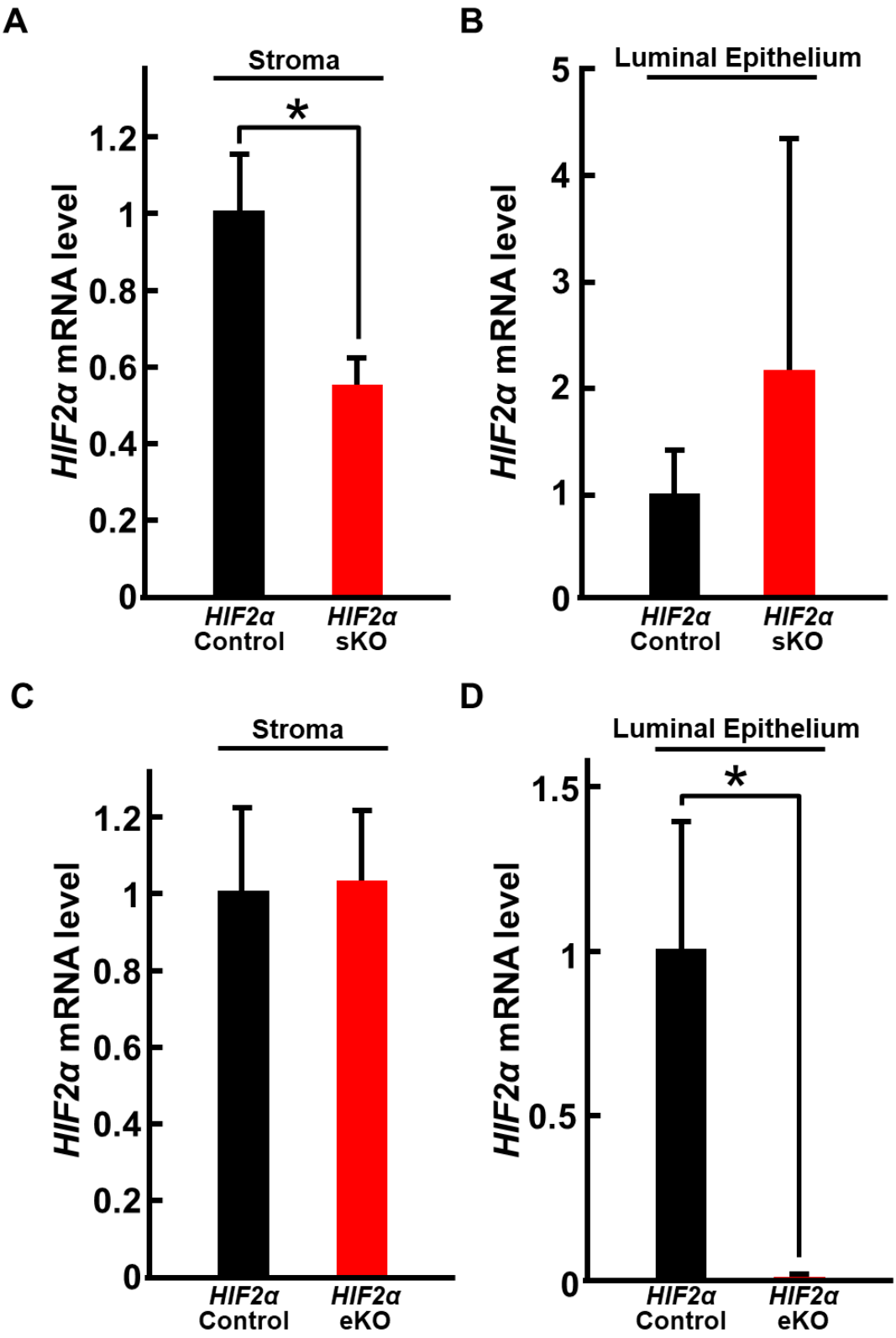
Supplemental Figure 7. Detachment of luminal epithelium from stroma occurs in WT mice on ICR background. Transmission electron microscopic analyses of embryo-uterine interface at 1900h on day 5 demonstrated the newly-formed gaps between the stroma and the luminal epithelium (arrowhead) and the invading trophoblast into these gaps in WT mice on ICR background. Scale bar, 1μm; s, stroma; tro, trophoblast; le, luminal epithelium.



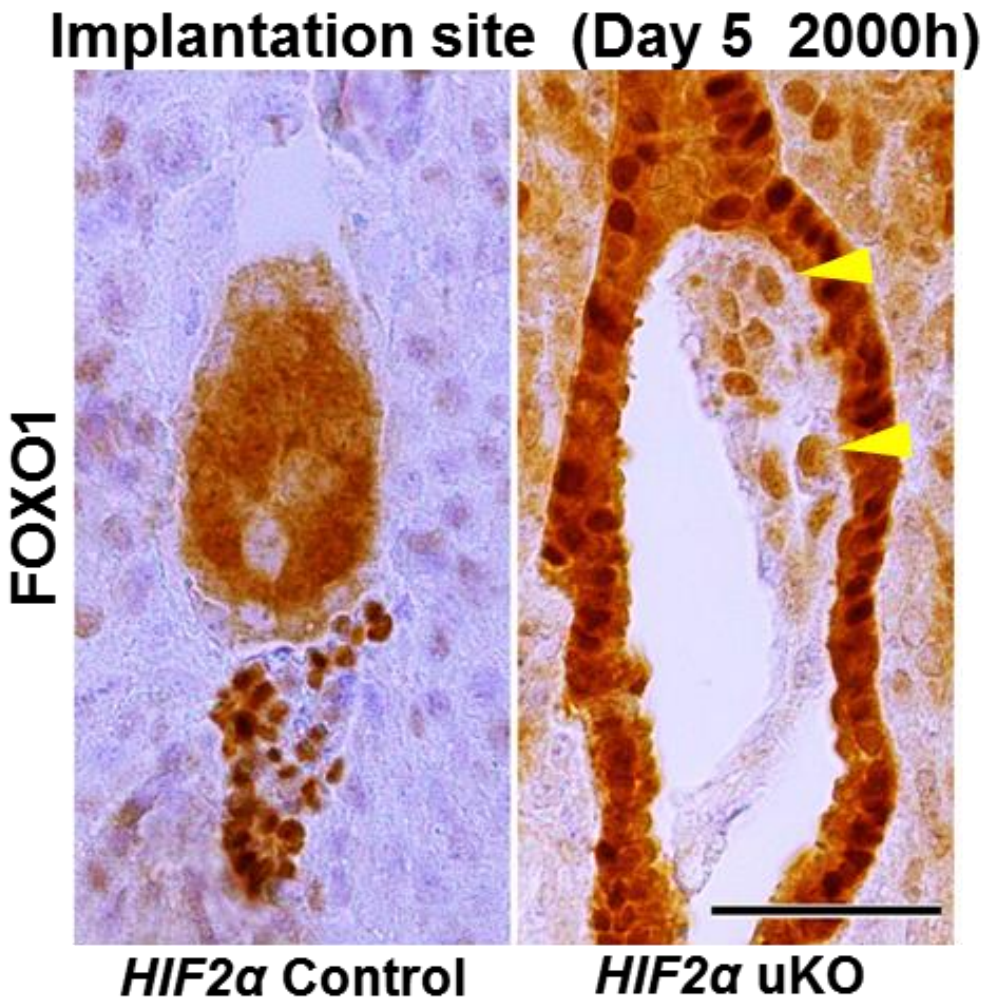
Supplemental Figure 8. MT2-MMP expression is downregulated in *HIF2α* uKO uterus on day 5 evening. Scale bar, 200μm; arrowhead, an embryo; le, luminal epithelium; s, stroma.



Supplemental Figure 9. LOX expression is downregulated in *HIF2α* uKO uterus on day 5 evening. Scale bar, 200μm; arrowhead, an embryo; le, luminal epithelium; s, stroma.



Supplemental Figure 10. *HIF2α* sKO and eKO mice show effective downregulation of *HIF2α* mRNA in uterine stroma and luminal epithelium, respectively. Stroma and luminal epithelium were collected by laser capture microdissection. *HIF2α* mRNA levels were reduced in the uterine stroma and luminal epithelium of *HIF2α* sKO and eKO mice, respectively. n≥3, **P<0.05,* mean ± SEM, Student's *t* test.



Supplemental Figure 11. Nuclear accumulation of FOXO1 was observed in the embryo of *HIF2α* uKO mice, while its cytosol staining was observed in those of control mice during embryo invasion (day 5, 2000h). Scale bar, 200μm; arrowhead, nuclear staining of FOXO1 in the embryo attached to the uterus of *HIF2α* uKO mice.

Supplemental Table 1. **Primer sequences for qPCR.**

Gene	Strand	Sequence
mouse *Hif1a*	Forward	TCGGCGAAGCAAAGAGTCTG
	Reverse	CACTGTCTAGACCACCGGC
mouse *Hif2a (Epas1)*	Forward	TGAGGAAGGAGAAATCCCGTG
	Reverse	GGCAACTCATGAGCCAACTC
mouse *Prl3c1*	Forward	ACCTTTCCTGAGCTGGAGGC
	Reverse	GAACAGACCCTTCCAGGTGC
mouse *Prlr*	Forward	TTCTTCTCAGAGACACGCGG
	Reverse	GCGTTCTTTAGTTCTGCTGGA
mouse *Cox2 (Ptgs2)*	Forward	AGAACCGCATTGCCTCTGAA
	Reverse	AGAAGCGTTTGCGGTACTCA
mouse *Lif*	Forward	GCTATGTGCGCCTAACATGA
	Reverse	AGTGGGGTTCAGGACCTTCT
mouse *Vegf (Vegfa)*	Forward	CGATTGAGACCCTGGTGGAC
	Reverse	GCTGGCTTTGGTGAGGTTTG
mouse *Adm*	Forward	CATCCAGCAGCTACCCTACG
	Reverse	TTCGCTCTGATTGCTGGCTT
mouse *Lox*	Forward	TTACACTAACAACGGCCGTGAAGA
	Reverse	CTAGACCACGGTCCCACTGAAGA
mouse *Mt2-mmp (Mmp15)*	Forward	CTTGTACGCTCAGACCCAAGCA
	Reverse	TTCCTGGACTCCATCCCAAAG
mouse *Bmp2*	Forward	TGGAAAAGGACATCCGCTCC
	Reverse	TGCCACGATCCAGTCATTCC
mouse *Actb*	Forward	TGTTACCAACTGGGACGACA
	Reverse	GGGGTGTTGAAGGTCTCAAA