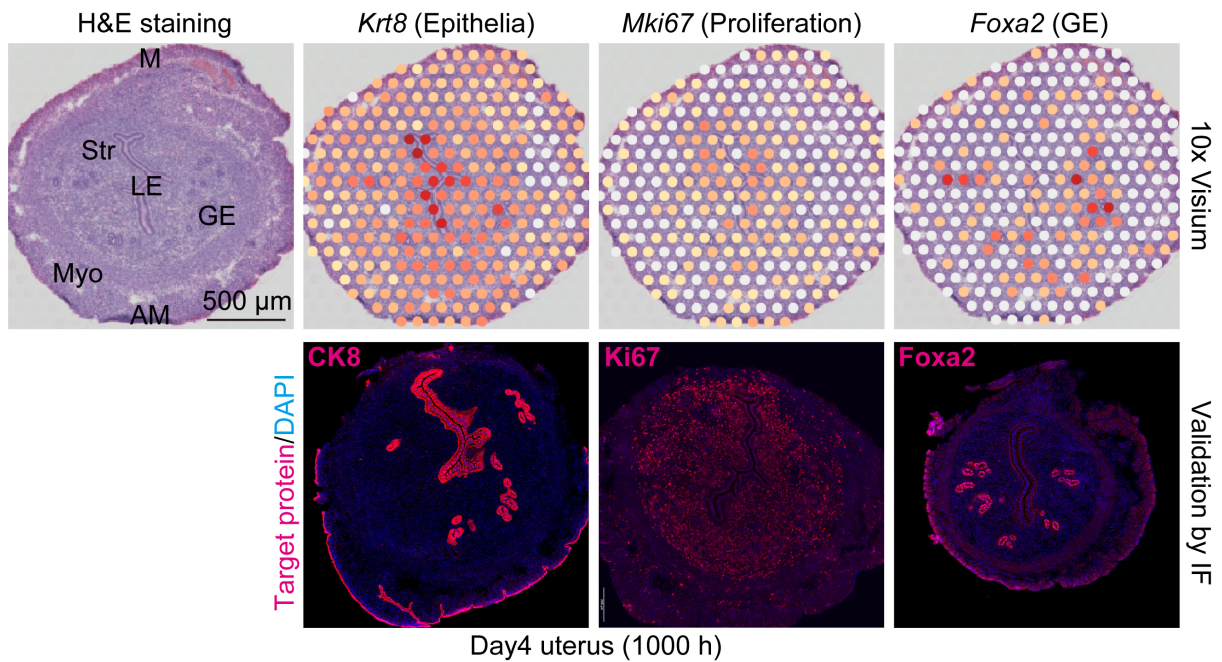
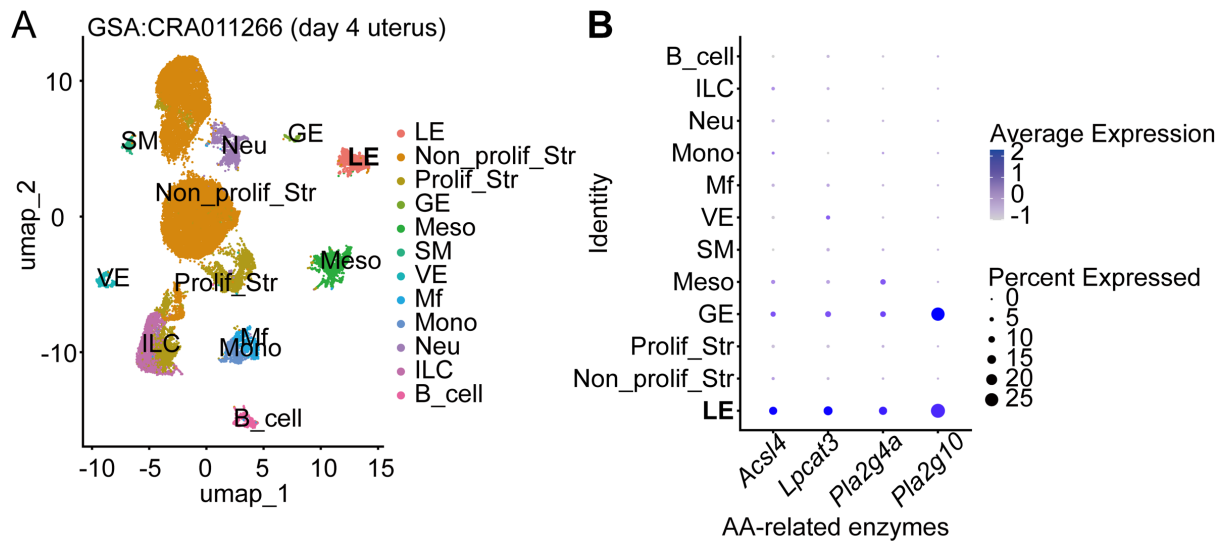


SUPPLEMENTAL MATERIALS



Supplemental Figure 1. Validation of 10x Visium analysis on day 4 of pregnancy.

10x Visium data were validated via immunofluorescence of CK8 (*Krt8*; an epithelial marker), Ki67 (*Mki67*; a cell proliferation marker that should be stained in the stroma on day 4), and Foxa2 (a GE marker). M: mesometrium, AM: anti-mesometrium, LE: luminal epithelium, GE: glandular epithelium, Str: stroma, Scale bar: 500 µm. Three independent sections were assessed for each immunofluorescence.

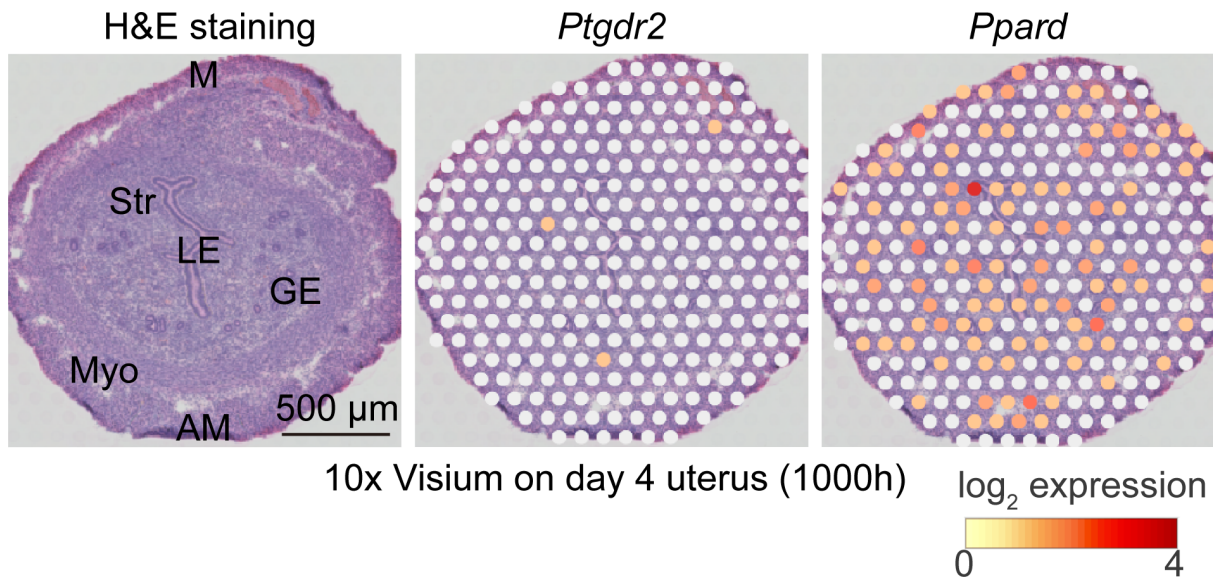


Supplemental Figure 2. Concentrated expression of arachidonic acid (AA)-related genes in the day 4 LE cluster, as revealed by single-cell RNA-seq.

(A) UMAP projections of day 4 mouse uteri.

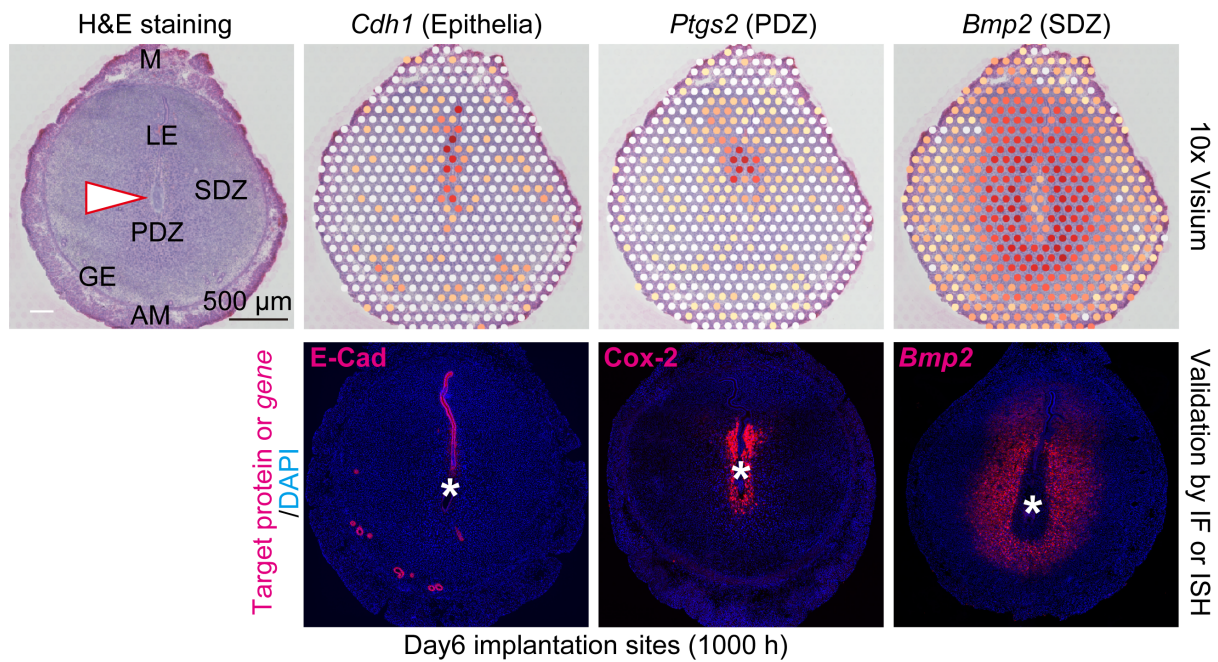
(B) Dot plot showing the log₂ expression of AA-related genes characteristic of each cluster.

LE: luminal epithelia, Non_prolif_Str: non-proliferative stroma, Prolif-Str: proliferative stroma, GE: glandular epithelia, Meso: mesothelia, SM: smooth muscle, VE: vascular endothelia, Mf: macrophage, Mono: monocytes, Neu: neutrophil, ILC: innate lymphoid cell, B_cell: B cell.



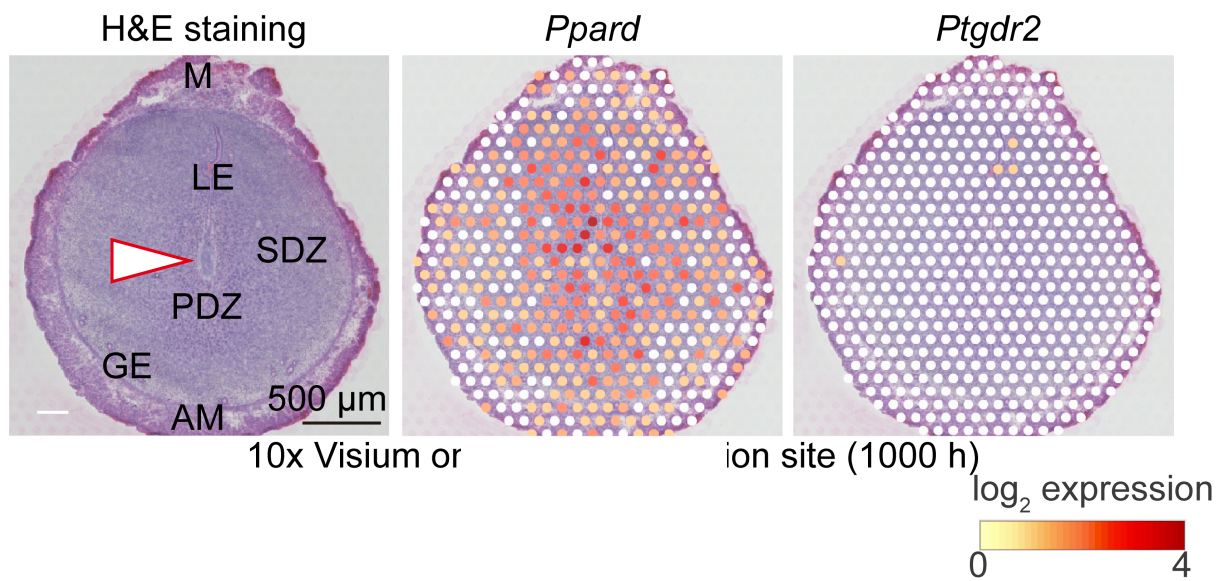
Supplemental Figure 3. Expression of *Ptgdr2* (the second PGD₂ receptor) and *Ppard* (a possible PGI₂ receptor) in day 4 uterus.

M: mesometrium, AM: anti-mesometrium, LE: luminal epithelium, GE: glandular epithelium, Str: stroma, Scale bar: 500 μm .



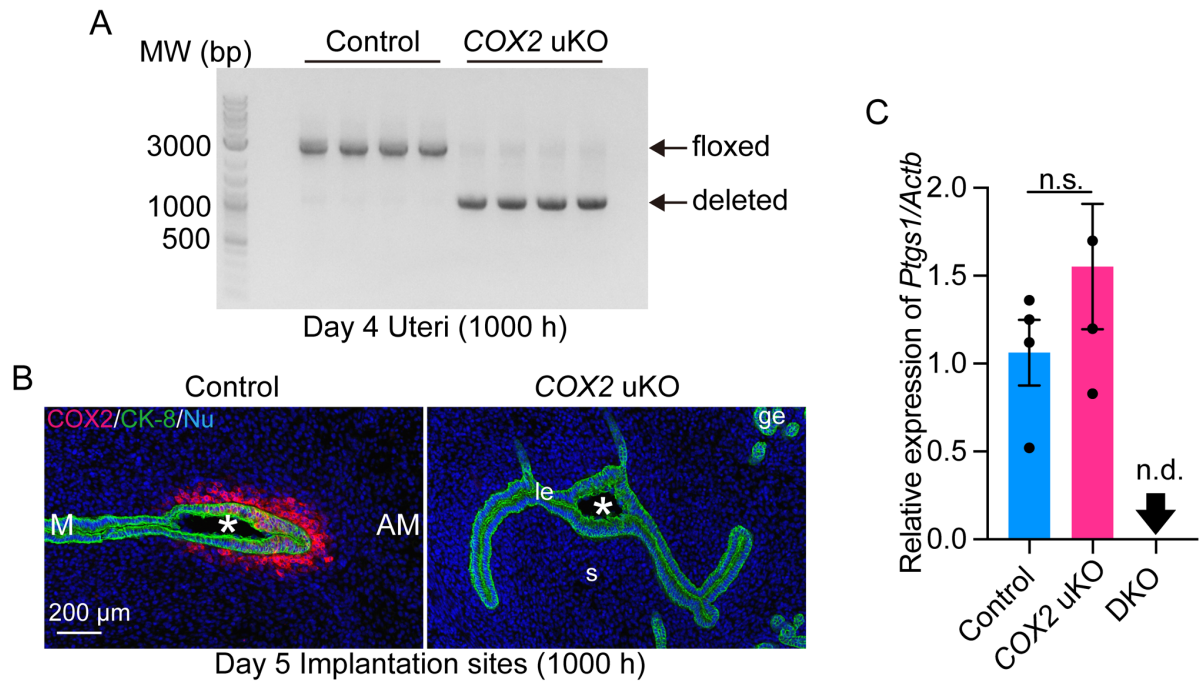
Supplemental Figure 4. Validation of 10x Visium analysis on day 6 of pregnancy.

10x Visium data were validated by either immunofluorescence of E-Cad (*Cdh1*; an epithelial marker) and COX2 (*Ptgs2*; a PDZ gene) or *in situ* hybridization (ISH) of *Bmp2* (an SDZ gene). M: mesometrium, AM: anti-mesometrium, LE: luminal epithelium, GE: glandular epithelium, PDZ: primary decidual zone, SDZ: secondary decidual zone. The arrowhead and asterisks indicate embryos. Scale bar: 500 μ m. Three independent sections were assessed for each immunofluorescence or ISH.



Supplemental Figure 5. Expression of *Ptgdr2* (the second PGD₂ receptor) and *Ppard* (a possible PGI₂ receptor) in day 6 implantation site.

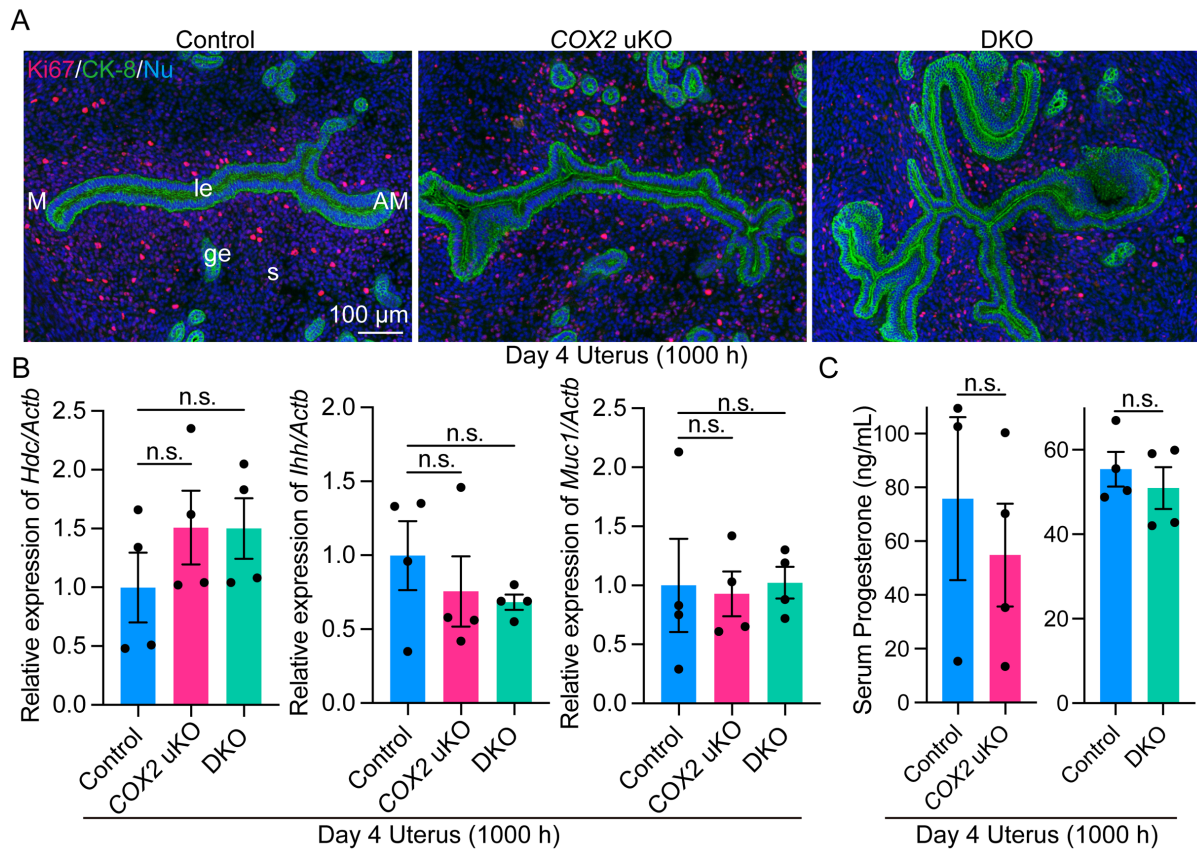
M: mesometrium, AM: anti-mesometrium, LE: luminal epithelium, GE: glandular epithelium, PDZ: primary decidual zone, SDZ: secondary decidual zone. The arrowhead indicates the attached embryo. Scale bar: 500 μm .



Supplemental Figure 6. Efficient deletion of COX1 and COX2 in uterine tissues.

(A)(B) *COX2* deletion in the uterus was confirmed via RT-qPCR on day 4 (A) and immunostaining on day 5 (B). In (B), epithelial cells were co-stained with an anti-CK-8 antibody. M: mesometrium, AM: anti-mesometrium, LE: luminal epithelium, GE: glandular epithelium, S: stroma, *: embryo. Scale bar: 200 μ m. Three independent sections were assessed for each genotype in (B).

(C) RT-qPCR confirmed *COX1* deletion (*Ptgs1*) in DKO uteri on day 4 of pregnancy. n = 4 per genotype. Mean \pm SEM, n.d.: not detected. n.s.: not significant (Student's *t*-test).

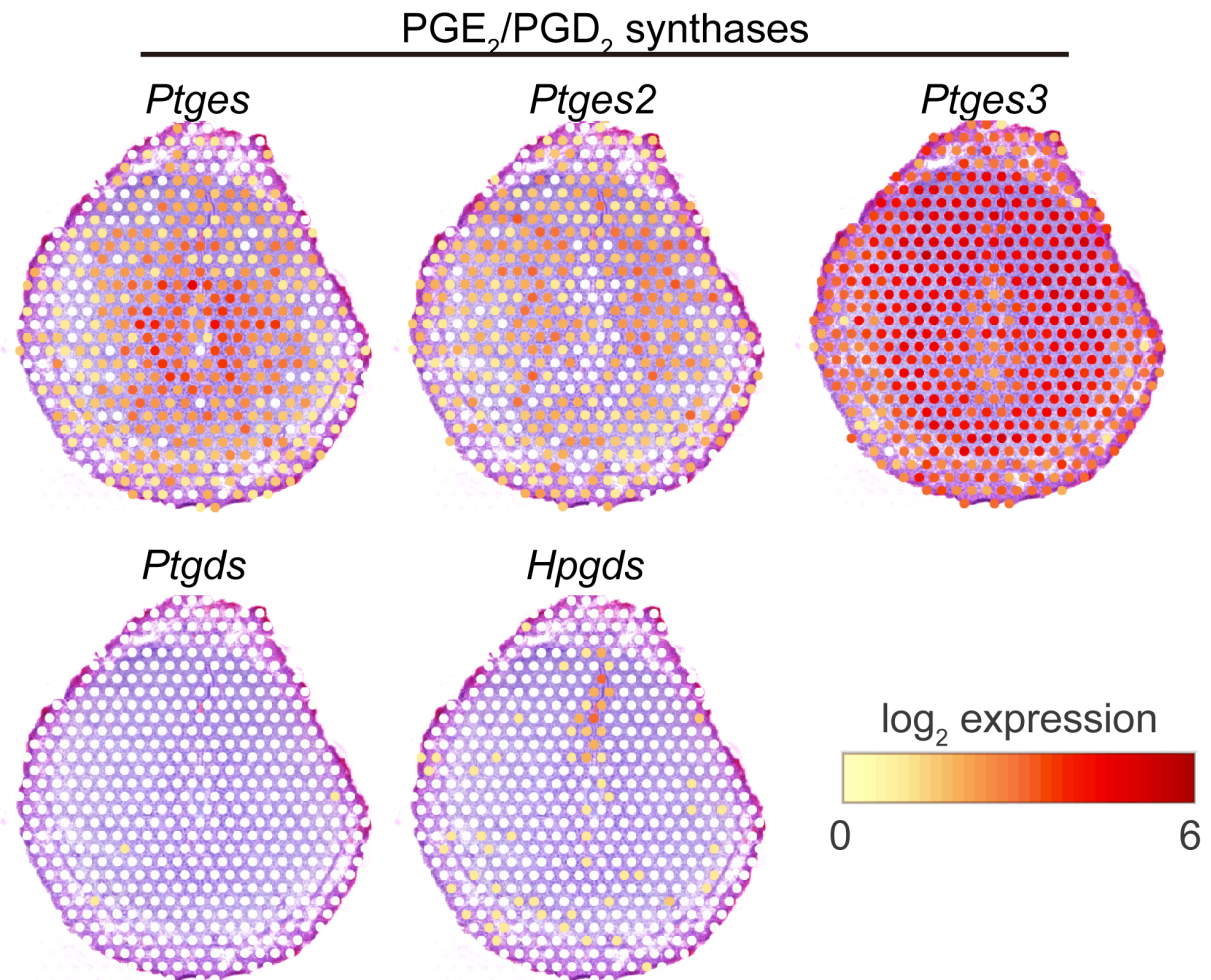


Supplemental Figure 7. *COX1/COX2* DKO does not impair uterine receptivity and ovarian function.

(A) Representative images of the immunostaining of Ki67 (a proliferation marker) and CK-8 showing comparable PDS in each genotype on day 4 of pregnancy. M: mesometrium, AM: anti-mesometrium, LE: luminal epithelium, GE: glandular epithelium, S: stroma. Scale bar: 100 μ m. Three independent sections were assessed for each genotype.

(B) RT-qPCR revealed comparable levels of the receptive markers *Hdc* (left), *Ihh* (middle), and *Muc1* (right) in day 4 uteri from each genotype. $n = 3$ per genotype. Mean \pm SEM, n.s.: not significant (one-way ANOVA).

(C) Serum P₄ concentrations on day 4 were not affected by *COX2* uKO (left) or *COX1/COX2* DKO (right). $n = 3$ per genotype. Mean \pm SEM, n.s.: not significant (Student's *t*-test).



10x Visium on day 6 implantation site (1000 h)

Supplemental Figure 8. Spatial expression of PGE₂/PGD₂-specific synthesis-related enzymes during the invasion phase.

Spatial transcriptomics of day 6 implantation sites showing expression patterns of specific PGE₂ and PGD₂ synthases. PDZ is encircled by a dashed line.

Supplemental Table 1. Differentially expressed genes in each cell cluster in day 4 uteri, as revealed by 10× Visium transcriptomics analysis.

Supplemental Table 2. Summary of GO enrichment analysis of LE-specific genes on day 4, as revealed by Metascape.

Supplemental Table 3. Differentially expressed genes in each cell cluster in day 4 uteri, as revealed by 10× Visium transcriptomics analysis.

Supplemental Table 4. Summary of GO enrichment analysis of PDZ-specific genes, as revealed by Metascape.