

## Developing a Mammalian Uterus from Stem Cells

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### ABOUT THE STUDY

The uterus' principle job is to provide an appropriate environment for the embryo to implant and gestate to full term. Recent single-cell transcriptional atlases of the human uterus during the menstrual cycle and the maternal-foetal interface during the first trimester of pregnancy provide complete roadmaps for the advancement of stem cell-based models. The purpose of stem cell-based uterine models is to provide a defined, adaptable, and scalable system to answer fundamental reproductive biology concerns.

Major subjects include embryo implantation processes and diseases, embryogenesis, interaction between the developing embryo and the mother, and disorders of the female reproductive system [1].

The first trimester of pregnancy is a particularly active and crucial period during which the embryo organizes the body plan prior to the foetal growth phase in the second and third trimesters.

Although complex *in vitro* models capable of complete recapitulation of the structure and function of the uterus may be required in a clinical setting to improve the chances of survival of premature fetuses, such models would lack the scalability and experimental flexibility required for drug discovery and genetic screening [2].

We cover the development of stem cell-based uterine models to provide light on the early phases of human embryogenesis and related diseases in this study. We discuss the uterus's developmental origins as well as its architecture, function, and disorders. We emphasise the essential components from which a stem cell-based uterus might be created and offer a modular strategy to constructing uterine models based on recent advances in organoid culture.

We explore techniques based on self-organization as well as controlled assembly, either *via* microfluidic or print-based procedures, and conclude how these technologies might be leveraged to address implantation failure and important uterine diseases [3].

### Developmental origin of the uterus

The uterus in mammals develops from the intermediate mesoderm, which is located after gastrulation between the paraxial and lateral plate mesoderm. The embryo folds at Carnegie Stage (CS) 10 to generate intraembryonic coeloms, which are bordered by lateral plate mesoderm and intermediate mesoderm, with the coelomic epithelium as the inner lining. To generate the nephric duct, a fraction of intermediate mesoderm cells undergoes mesenchymal-to-epithelial transformation. This transformation necessitates the expression of *Lhx*, an essential transcription factor of the urogenital system in both mice and humans. The development of adult kidneys, the ureter, and the genital tract is dependent on the nephric ducts. The Wolffian (mesonephric) ducts are the first central section of the nephric duct [4].

Morphogenetic changes at CS12-16 result in the implantation of the Wolffian ducts into the cloaca, the bladder's precursor. Coelomic epithelial cells generated from the intermediate mesoderm invaginate to create the Müllerian (paramesonephric) ducts at CS14-17, which lengthen caudally along the Wolffian ducts at CS18-23. *Lhx1* is expressed in the Müllerian and Wolffian ducts of mice, and *Wnt* signaling is essential for Wolffian duct elongation. Human embryo histological investigations indicate that this morphogenetic mechanism is preserved. Wolffian and Müllerian ducts join to create the bipotential genital tract at CS23. The Müllerian ducts degenerate in men, but the Wolffian ducts continue to develop male reproductive organs. The Müllerian ducts evolve into the female reproductive system in females, whereas the Wolffian ducts degenerate. In any scenario, sex is determined by gene expression from the X and Y chromosomes. At week 8-9, the Müllerian ducts fuse to produce the uterus, fallopian tubes, cervix, and upper vaginal tract, which will undergo morphogenesis to form the uterus, fallopian tubes, cervix, and upper vaginal tract.

### CONCLUSION

In humans, Müllerian duct fusion occurs in one central uterine cavity, but in rats, Müllerian duct fusion is less widespread,

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allowing the creation of two separated uterine horns. The growing human uterus begins to generate glands in the endometrium around week 16. Until birth, endometrial glands progressively expand in complexity and form branches inside the stroma, and they will continue to develop postnatally until adolescence. This is in contrast to mouse development, in which glands arise primarily after birth. Nonetheless, WNT signalling is required for the development of endometrial glands in both humans and mice. The production of myometrium at week 22 marks the end of prenatal uterine development, and the uterus takes on its adult structure. The last stages of human uterine development take place during adolescence, when the uterus grows further under the effect of sex steroid activation and commences the menstrual cycle.

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