

**Abstract Title:** 3D organoid models in human reproductive biology

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**Abstract:** Mammalian/human reproductive development is highly complex and regulated by precise genetic signals to produce testis and ovaries from bipotential gonad followed by concerted genetic and endocrine factors to initiate and maintain development of internal and external genitalia. Because of the relative lack of evolutionary conservation of the genes and signaling pathways in development of mammalian reproductive system, the data from model systems cannot be directly extrapolated to humans. Recent transcriptomic profiling of human fetal gonads provides important insight into somatic lineage specification and development. However, the contribution of any specific cell lineage to the human gonadal architecture and function remains unidentified. Clinical samples have limitations in providing functional or mechanistic understanding and restricted access to human embryonic material has led to the use of animals and short-term primary cell cultures, that have their own limitations.

Human pluripotent stem cells (huPSCs) can self-organize in three-dimensional (3D) cultures and follow intrinsic developmental pathways to form fetal-like tissues under favorable culture conditions. I will highlight the current state of regenerative organoid culture systems in the context of human reproductive biology, emphasizing the shift from clinical samples, which often permit only descriptive studies, to the development of in vitro systems that aim to model key molecular and cellular processes in human reproductive system. I will discuss stem cell-based organoid models of testis and the prostate in male and the ovary, fallopian tube and endometrium in the female.

These organoids provide insights into cellular hierarchies, differentiation, and function- reflecting human physiology and pathophysiology. These provide an unlimited resource for pre-clinical testing of pharmacological molecules for safety and efficacy and have potential for driving personalized medicine in reproductive health.

**Area of expertise:** Development reproductive genetics, 3D organoid and reproductive disorders