Female & Male gonad organoid models

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FIELD OF ACTIVITY
Endocrinology, Developmental Biology

KEY WORDS
#sex development #sex determination #gonadal fate #testicular and ovary identity #hormons

OVERVIEW OF APPLICATION AND MARKET NEEDS

The Human Developmental Genetics Laboratory developed an Innovative organ-on-chip models of testis and ovary to study gonadal development in vitro. This project addresses a critical gap in biomedical research: there is no reliable models for gonadal development and sex determination, especially because they are poorly conserved across evolution, making it hard to translate form animal models to human.
These gonad-on-chip technologies offer numerous applications, including:

- Modeling reproductive disorders, which affect nearly 15% of the global population.
- Screening for endocrine disruptors, environmental toxins, and chemical compounds, supporting regulatory and toxicological assessments.
- Genetic diagnosis in assisted reproductive technologies (ART) to improve fertility treatments.
- Studying Disorders of Sex Development (DSDs) with a dedicated platform for research and drug screening.
- Providing a platform for in vitro gametogenesis, opening new possibilities in reproductive medicine.

These models present a unique opportunity for pharmaceutical, biotech, and reproductive health industries to develop novel therapeutic, diagnostic, and screening tools. They can be cultivated in 96 wells plates, allowing for high-throughput screening.

Human iPSCs can be easily sourced in repositories, compared to ovary or testis cells that are complex to source and use. The protocol of differentiation of iPSCs into gonadal cells allows this model to be used widely.

TECHNOLOGY DESCRIPTION

The research team developed protocols for differentiation of human pluripotent cells towards gonadal progenitors. Transcriptomic analysis reveals that the in vitro–derived murine gonadal cells are equivalent to embryonic day 11.5 in vivo progenitors. Using similar conditions, Sertoli-like cells derived from 46,XY human induced pluripotent stem cells (hiPSCs) exhibit sustained expression of testis-specific genes, secrete anti-Müllerian hormone, migrate, and form tubular structures.
Granulosa-like cells exhibit typical organization and development of such structure and secrete progesterone.

MARKET OUTLOOK

- Infertility and reproductive disorders treatment market size is estimated at 1.7B$ in 2024, with a CAGR of about 8% until 2034, reaching 3.8B$. This substantial growth allows for investments in screening technologies for drugs, modelling such diseases for R&D.
- Endocrine disruptors market size was estimated to be between 150M$ and 200M$ in 2023.

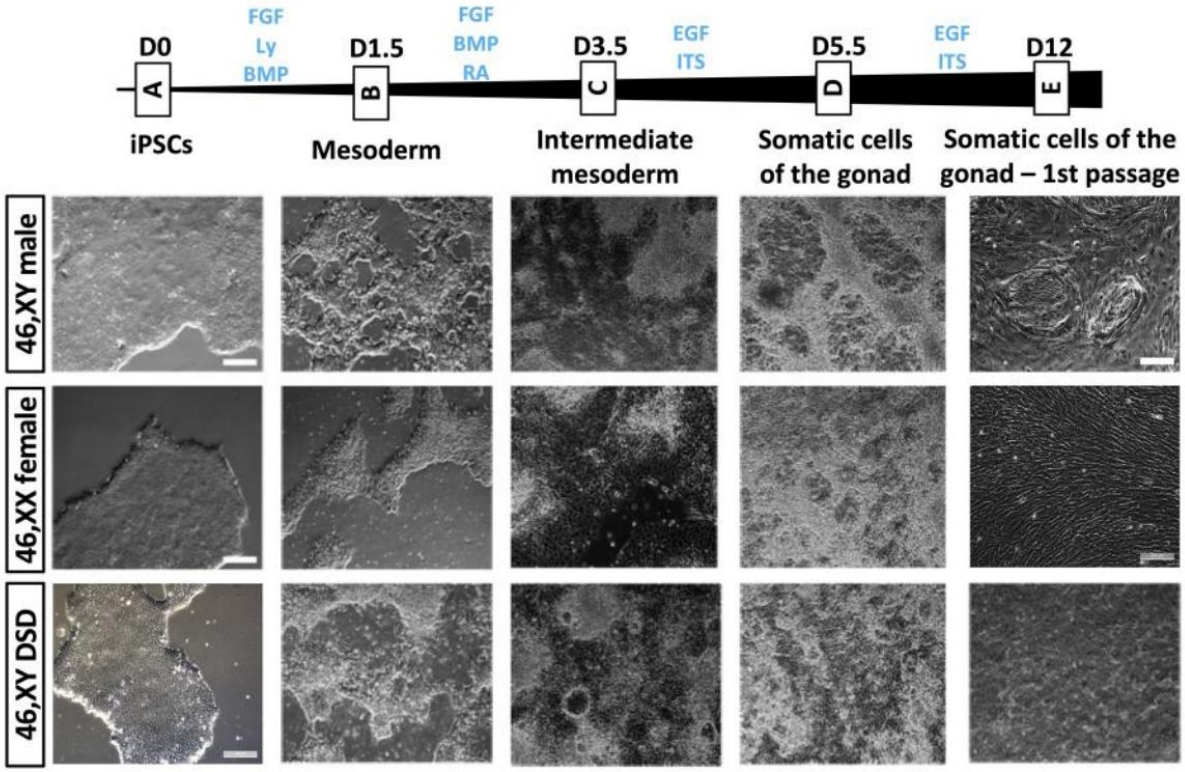
PUBLICATIONS

Nitzan Gonen et al. In vitro cellular reprogramming to model gonad development and its disorders. ScienceAdvances 9, eabn9793 (2023). DOI: 10.1126/sciadv.abn9793

PATENTS

Patent application submitted.

DIFFERENTIATION OF HUMAN IPSCS INTO SOMATIC CELLS OF THE GONADS



Differentiation of human iPSCs derived from healthy 46,XY male, 46,XX female, and a patient with 46,XY DSD with a pathogenic variant in NR5A1. Differentiation time points are indicated together with BF images of the cells at each stage of the differentiation process. iPSC derived from the 46,XY healthy male are the only cells to self-aggregate and form tubule-like structures. D, days; scale bars, 200 µm. EGF, epidermal growth factor; ITS, Insulin-Transferrin-Selenium.

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