Human testicular organoids

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Organisation

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In Vitro Toxicology and Dermato-Cosmetology (IVTD)

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SCOPE OF THE METHOD

The Method relates to	Human health
The Method is situated in	Basic Research
Type of method	In vitro - Ex vivo

Specify the type of cells/tissues/organs	Testicular cells from trans women testes

DESCRIPTION

Method keywords

testicular organoids

testicular tissue of transgender women

in vitro testis model

testosterone production

3D Cell culture

human-based model

Scientific area keywords

new approach methodologies (NAMs)

Endocrine disruption

alternative to animal testing

reproductive toxicology

Method description

Testicular organoids are a promising tool for studying testicular function and the effects of toxicants. Immature testicular cells are currently the most efficient at forming organoids that closely recapitulate seminiferous tubule-like architecture and functions. However, the scarcity of human immature testicular tissue limits its use in high-throughput applications. This study explores the potential of using testicular tissue from trans women (trans tissue), mostly discarded as medical waste and characterised by an immature phenotype, to create human testicular organoids (trans organoids). These organoids were histologically and androgenically compared to reference organoids derived from prepubertal, pubertal, and adult cisgender testicular tissues. The results demonstrate that trans organoids form compartmentalised, cytotypic *de novo* tissues similar to those from pubertal testicular tissue. Additionally, trans organoids exhibit significant testosterone production, sustain this function

over extended culture periods, and respond to gonadotrophic stimulation. Deconvolved bulk RNAseq data indicates that cell population proportions within these organoids are close to prepubertal and pubertal testicular tissues, with gene expression clustering them alongside prepubertal and trans tissues. Functional analysis reveals that trans organoids share with prepubertal, pubertal, and trans tissues varied cellular processes. Factors such as the duration of hormone therapy, the expression of anti-Müllerian hormone – an immaturity marker – within the tubules, and the proportion of peritubular myoid cells in the donor tissue were found to predict the success of trans organoid formation. This study highlights the potential of trans organoids as a sustainable and scalable human testicular model for high-throughput toxicological testing and reproductive research. While trans tissue is a valuable replacement for immature tissue, further research should focus on optimising organoid architecture, evaluating their utility in reprotoxicity testing, and promoting germ cell differentiation.

Method status

Still in development

Published in peer reviewed journal

PROS, CONS & FUTURE POTENTIAL

Future & Other applications

https://doi.org/10.1093/hropen/hoaf043 - This study highlights the potential of trans organoids as a novel and ethically sustainable human-based model for male reproductive health research, reproductive toxicology, and endocrine disruption studies. While trans tissue is a valuable replacement for immature tissue, further research should focus on optimizing organoid architecture, evaluating their utility in reprotoxicity testing, and promoting germ cell differentiation.

REFERENCES, ASSOCIATED DOCUMENTS AND OTHER INFORMATION

Associated documents

hoaf043.pdf

Links

Original publication

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