Development of organoids from human endometrial diseased tissues for mechanistic pathogenic research and (personalized) drug screening

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Contact person

Hugo Vankelecom

Organisation

Name of the organisation Katholieke Universiteit Leuven (KUL)

Department Development and Regeneration

Country Belgium

Geographical Area Flemish Region

SCOPE OF THE METHOD

The Method relates to	Human health
The Method is situated in	Basic Research, Translational - Applied Research
Type of method	In vitro - Ex vivo
Specify the type of cells/tissues/organs	healthy and diseased endometrial and endometriotic tissues

DESCRIPTION

Method keywords

organoids

Preclinical study models

drug screening

Hormone responsiveness

WNT

RSPO

LGR

Scientific area keywords

Endometriosis

Endometrial disease

Tumour-derived

Organoid biobank

Method description

We have developed multiple organoid models from a broad spectrum of endometrial pathologies that capture endometrial disease diversity and will provide powerful research models and drug screening and discovery tools. Organoids from endometriosis show disease-associated traits and cancer-linked mutations. Endometrial cancer-derived organoids accurately capture cancer subtypes, replicate the mutational landscape of the tumours and display patient-specific drug responses. Organoids were also established from precancerous pathologies encompassing endometrial hyperplasia and Lynch syndrome, and inherited gene mutations were maintained. Endometrial disease organoids reproduced the original lesion when transplanted *in vivo*. This represents the start of an extended biobank across healthy and pathological endometrium providing promising research models and drug screening and discovery tools.

Lab equipment

- Cell incubator ;
- Biosafety cabinet ;
- Cell culture ;
- Epifluorescence ;
- Confocal microscopes.

Method status

Published in peer reviewed journal

PROS, CONS & FUTURE POTENTIAL

Advantages

- Organoid models capture disease heterogeneity, maintain key features of the primary tissue, including the genetic background, and reproduce the lesion after *in vivo* transplantation.
- Organoids show strong expandability thereby overcoming the hurdle of limiting quantities of primary biopsies.
- Endometrial cancer-organoids show patient-specific drug responses, thereby providing conceptual evidence that the organoids are amenable to (personalized) drug screenings.
- Organoids are state-of-the-art research models that bridge the gap between bench and bedside, more reliably than animal models do, and may thus in the future gradually substitute for the latter.

Challenges

Typical organoids reproduce the epithelial compartment of a (diseased) tissue. Hence, more advanced models, also incorporating other cells (such as stromal, endothelial and immune cells), are still needed to fully replicate the original tissue.

Modifications

Developing more complex organoid models containing the different cell types of a tissue.

Future & Other applications

- The endometriosis organoid biobank can be valuable in deciphering disease (and type-specific) pathogenesis, especially if epithelial and stromal compartments are (re)combined in future studies, and in the search for drug targets that provide an alternative to current hormonal suppression therapy.
- Organoids developed from hyperplastic endometrium (including Lynch syndrome) faithfully reproduce the disease genotype and can be valuable in the search for molecular mechanisms underlying the hyperplastic phenotype and its progression toward cancer.

- Since organoids are typically composed of the epithelial compartment of the original tissue, further perfecting the model by adding stromal and immune components of the tumor/tissue microenvironment will eventually be needed to reach the organoid model's full potential.

REFERENCES, ASSOCIATED DOCUMENTS AND OTHER INFORMATION

References

Boretto, M., Maenhoudt, N., Luo, X. et al. Patient-derived organoids from endometrial disease capture clinical heterogeneity and are amenable to drug screening. Nat Cell Biol 21, 1041–1051 (2019). https://doi.org/10.1038/s41556-019-0360-z

Boretto M., Cox B., Noben M.l, Hendriks N., Fassbender A., Roose H., Amant F., Timmerman D., Tomassetti C., Vanhie A., Meuleman C., Ferrante M., Vankelecom H. Development of organoids from mouse and human endometrium showing endometrial epithelium physiology and long-term expandability. Development (2017) 144, 1775-1786 doi:10.1242/dev.148478

Links

Prof. dr. Hugo Vankelecom, Department of Development and Regeneration, Cluster ...