

# Ovarian cancer-derived organoid models for experimental and preclinical studies

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### **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
This method makes use of	Human derived cells / tissues / organs
Specify the type of cells/tissues/organs	ovarian cancer tissues

## **DESCRIPTION**

# **Method keywords**

organoids
Preclinical study models
drug screening
Neuregulin-1

High-grade serous ovarian cancer

#### Scientific area keywords

Disease modeling
Ovarian cancer
Experimental model
Preclinical model
Tumour-derived
Organoid biobank.

## **Method description**

We have established organoid cultures from patient-derived ovarian cancer (OC), in particular from the most prevalent high-grade serous ovarian cancer (HGSOC). Testing multiple culture medium components identified neuregulin-1 (NRG1) as key factor in maximizing OC organoid development and growth, although overall derivation efficiency remained moderate (36% for HGSOC patients, 44% for all patients together). Established organoid lines showed patient tumor-dependent morphology and disease characteristics, and recapitulated the parent tumor's marker expression and mutational landscape. Moreover, the organoids displayed tumor-specific sensitivity to clinical HGSOC chemotherapeutic drugs. Patient-derived OC organoids provide powerful tools for the study of the cancer's pathobiology (such as importance of the NRG1/ERBB pathway) as well as advanced preclinical tools for (personalized) drug screening and discovery.

## Lab equipment

- Cell incubator;
- Biosafety cabinet;
- Cell culture ;
- Epifluorescence;

- Confocal microscopes.

#### **Method status**

Published in peer reviewed journal

#### PROS, CONS & FUTURE POTENTIAL

#### **Advantages**

- Established epithelial OC-derived organoids capture disease cellular characteristics and molecular phenotype.
- Epithelial OC-derived organoids are amenable to drug screening and show differential sensitivity of individual patient organoid lines to the chemotherapeutic agents tested.
- 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**

More studies are required to enhance the derivation efficiency (as is also true for other cancer-derived organoids). Developing more complex organoid models containing the different cell types of a tissue.

## **Future & Other applications**

- Epithelial OC organoid models can be highly instrumental in moving into the field of immunotherapy (e.g., using CAR-T and natural killer cells).
- 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.
- Strong potential as an experimental and preclinical research model, and in particular as impetus to revive NRG1/ERBB research in OC, which may eventually identify response-predictive biomarkers, assist in clinical decision making, and provide personalized therapeutic options, particularly for patients in whom standard clinical routes have been exhausted.

#### REFERENCES, ASSOCIATED DOCUMENTS AND OTHER INFORMATION

#### References

Maenhoudt N., Defraye C., Boretto M., Jan Z., Heremans R., Boeckx B., Hermans F., Arijs I., Cox B., Van Nieuwenhuysen E., Vergote I., Van Rompuy A., Lambrechts D., Timmerman D., Vankelecom H. Developing Organoids from Ovarian Cancer as Experimental and Preclinical Models Stem Cell Reports, Vol. 14, 717–729, (2020) https://doi.org/10.1016/j.stemcr.2020.03.004

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.I, 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

#### **Associated documents**

#### Links

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#### PARTNERS AND COLLABORATIONS

# Organisation

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Coordinated by









