Ovarian cancer-derived organoid models for experimental and preclinical studies

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Organisation

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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
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

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