Metabolic studies in 3D patient-derived tumor organoids

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Contact person

Cyril Corbet

Organisation

Name of the organisation Université Catholique de Louvain (UCL)

Department Institut de Recherche Expérimentale et Clinique

Specific Research Group or Service Pole of Pharmacology and Therapeutics

Country Belgium

Geographical Area Brussels Region

SCOPE OF THE METHOD

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

DESCRIPTION

Method keywords

metabolic profiling

Microenvironment

mammary tumor organoids

spheroids

Scientific area keywords

Cancer metabolism

Nutrient microenvironment

Cancer therapy

3D organoid models

Method description

We have implemented the use of 3D patient-derived tumor organoids, to study metabolic (dys)functions associated with tumor development and progression, including response to anticancer therapies. These sophisticated models allow to better integrate the influence of microenvironmental conditions in the study of tumor cell metabolic phenotypes and to propose novel metabolism-based therapeutic options in precision oncology. Real-time live-cell bioenergetics analysis (with Seahorse XFe96 analyzer) is carried out to assess key parameters related to oxygen consumption and extracellular acidification in patient-derived organoids (PDO) from breast cancer (BC) patients before and after treatment with chemotherapeutic drugs. Absolute amounts of extracellular metabolites (e.g. glucose and lactate) are also assessed to evaluate the overall glycolytic activity in BC PDO.

Lab equipment

- Seahorse XFe96 bioenergetic analyzer,

- ISCUSflex microdialysis system.

Method status

Published in peer reviewed journal

PROS, CONS & FUTURE POTENTIAL

Advantages

Besides genomic, histologic, transcriptomic and proteomic analyses, studies reporting the metabolic characterization of patient-derived organoids (PDO) remain scarce. By applying direct real-time live-cell bioenergetic analyses on PDO from breast cancer patients, we can assess how metabolic phenotypes evolve during a response to anticancer treatments.

Challenges

Such metabolic studies on whole PDO still ignore cellular/metabolic heterogeneity. Fluorescence- and phosphorescence-based lifetime imaging microscopy will also be considered to assess metabolic heterogeneity (i.e. NAD(P)H and oxygenation levels) in PDO.

Modifications

In the near future, similar metabolic analyses will be carried out in PDO models integrating cellular components of the tumor microenvironment (immune cells, cancer-associated fibroblasts), which can metabolically collaborate with cancer cells to resist therapies. Air-liquid-interface method, that is reported to preserve “en bloc” cancer cells with tumor stroma, will be developed in combination with our current metabolic analyses.

Future & Other applications

This method is readily applicable to PDO models established from other tumor tissues (besides breast cancer included in the current study).

REFERENCES, ASSOCIATED DOCUMENTS AND OTHER INFORMATION

Associated documents

Metabolic adaptation towards glycolysis supports resistance to NAC.pdf

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