

# Metabolic studies in 3D patient-derived tumor organoids

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## Organisation

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**Specific Research Group or Service** Pole of Pharmacology and Therapeutics

**Country** Belgium

**Geographical Area** Brussels Region

## SCOPE OF THE METHOD

<b>The Method relates to</b>	Human health
<b>The Method is situated in</b>	Basic Research
<b>Type of method</b>	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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