

# Organoid brightfield identification-based therapy screening

*Commonly used acronym: Orbits*

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## SCOPE OF THE METHOD

<b>The Method relates to</b>	Human health
<b>The Method is situated in</b>	Basic Research, Translational - Applied Research
<b>Type of method</b>	In vitro - Ex vivo
<b>This method makes use of</b>	Human derived cells / tissues / organs
<b>Specify the type of cells/tissues/organs</b>	Cancer cell lines or primary cells grown as 3D spheroids/organoids

## DESCRIPTION

### Method keywords

live-cell imaging

organoids

spheroids

drug screening  
brightfield imaging  
cytotoxicity assay  
High-throughput  
ex vivo

### **Scientific area keywords**

in vitro 3D modelling  
cancer research  
drug screening  
preclinical drug development

### **Method description**

We developed a high-throughput live-cell imaging-based organoid analysis platform, Organoid Brightfield Identification-based Therapy Screening (Orbits), that allows for kinetic monitoring of organoid growth and drug responses in routine extracellular matrix domes, high-throughput 384-well microplates and advanced microcavity plates, solely based on brightfield imaging. The label-free Orbits deep learning analysis approach was validated against current standard assays for kinetic imaging (fluorescent viability dyes) and high-throughput analysis of organoid viability (CellTiter-Glo 3D assay). By incorporating a fluorescent cell death marker, intra-well normalization for organoid death could be achieved providing further insight into the mechanistic action of the drugs (cytotoxic vs. cytostatic), a feature not achievable with the CellTiter-Glo 3D assay. Our findings validate that Orbits, as a scalable, high-throughput technology, would facilitate the use of patient-derived organoids for drug development and *ex vivo* therapy screening. The developed platform also has broad application potential, from providing a launching point for further brightfield-based assay development to be used for fundamental research, to guiding clinical decisions for personalized medicine.

## **Lab equipment**

Live-cell imaging microscope with widefield and fluorescent imaging functionality (e.g. Tecan Spark Cyto, Sartorius IncuCyte systems)  
Optional: Digital drug dispenser and/or pipetting robot.

## **Method status**

Internally validated

## **PROS, CONS & FUTURE POTENTIAL**

### **Advantages**

Discriminate between cytotoxic and cytostatic drug responses.  
Allows for the use of more accurate growth rate drug response metrics (e.g. GR50 and normalised drug response (NDR)).  
Single-organoid drug response metrics.  
Multiparametric readout.  
Automated, AI-based image analysis which reduces user variability and hands-on analysis time.

### **Challenges**

The plating of the organoids can be challenging due to the use of temperature sensitive extracellular matrix. However, we have established a clear protocol to implement the method in other labs.

### **Modifications**

Identify new parameters that are of interest to study drug responses (e.g. tracking of

organoid movement, merging of organoids,...).

## **Future & Other applications**

The method was developed for tumor organoids or spheroids, but can easily be used for other organoid applications.

## **REFERENCES, ASSOCIATED DOCUMENTS AND OTHER INFORMATION**

### **References**

OrBITS: A High-throughput, time-lapse, and label-free drug screening platform for patient-derived 3D organoids Christophe Deben, Edgar Cardenas De La Hoz, Maxim Le Compte, Paul Van Schil, Jeroen M. Hendriks, Patrick Lauwers, Suresh Krishan Yogeswaran, Filip Lardon, Patrick Pauwels, Annemie Bogaerts, Evelien Smits, Steve Vanlanduit, Abraham Lin bioRxiv 2021.09.09.459656; doi: <https://doi.org/10.1101/2021.09.09.459656>

### **Associated documents**

[2021.09.09.459656v1.full.pdf](#)

### **Links**

[Orbits](#)

## **PARTNERS AND COLLABORATIONS**

### **Organisation**

**Name of the organisation** University of Antwerp (UAntwerpen)

**Department** Center for Oncological Research

**Country** Belgium

**Geographical Area** Flemish Region

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