Organoid brightfield identification-based therapy screening

Commonly used acronym: *Orbits*

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Contact person

Christophe Deben

Organisation

Name of the organisation University of Antwerp (UAntwerpen)

Department Center for Oncological Research

Country Belgium

Geographical Area Flemish Region

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	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 respons.
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