

Scaling the potential of patient-derived organoids through automation and label-free image analysis of individual organoids

————— **Christophe Deben** —————

UAntwerp Tumoroid Screening lab (TUSC)
Orbits

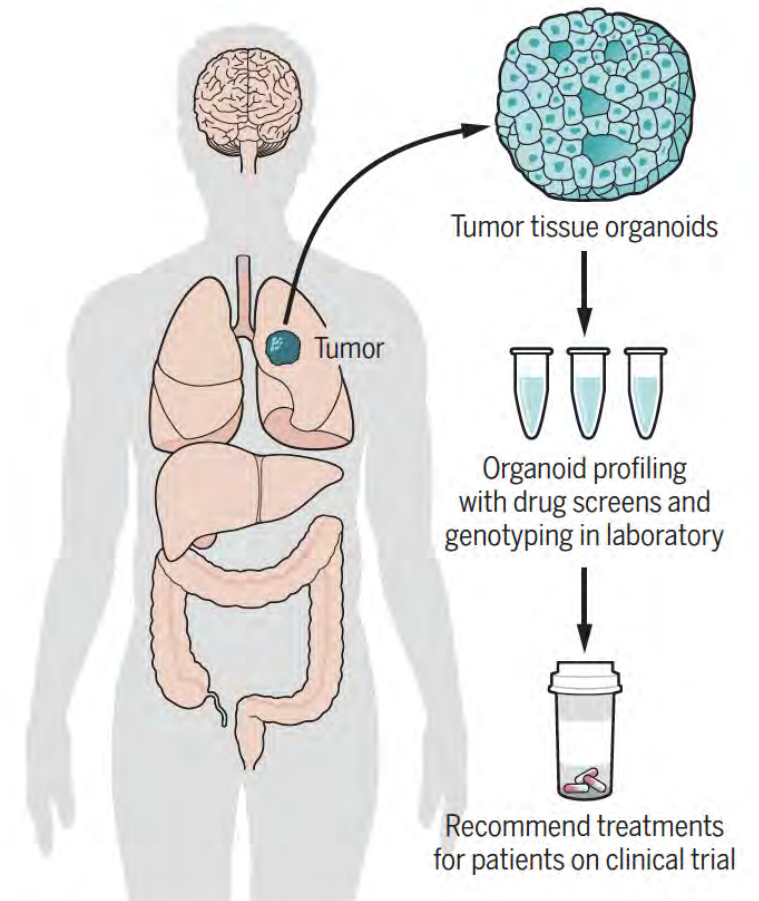
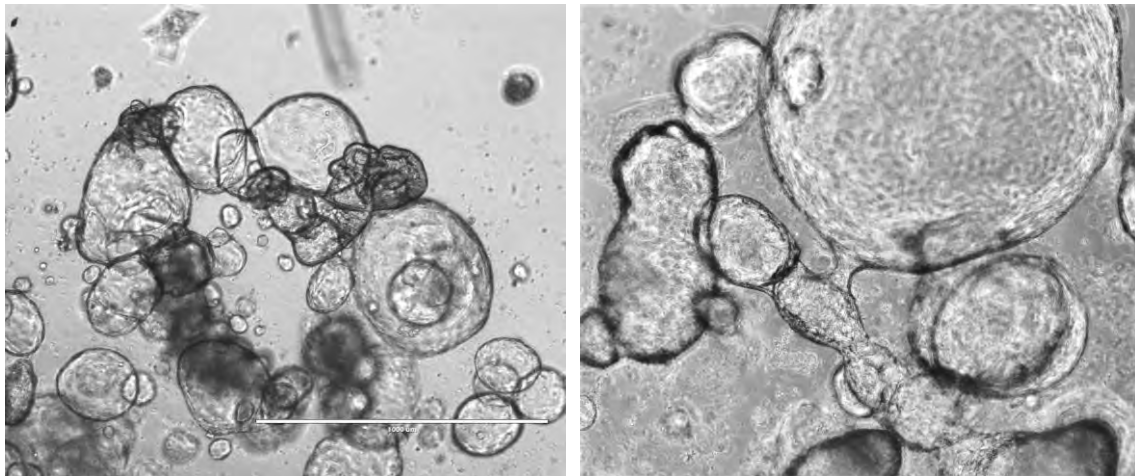


Center for Oncological
Research (CORE)
University of Antwerp



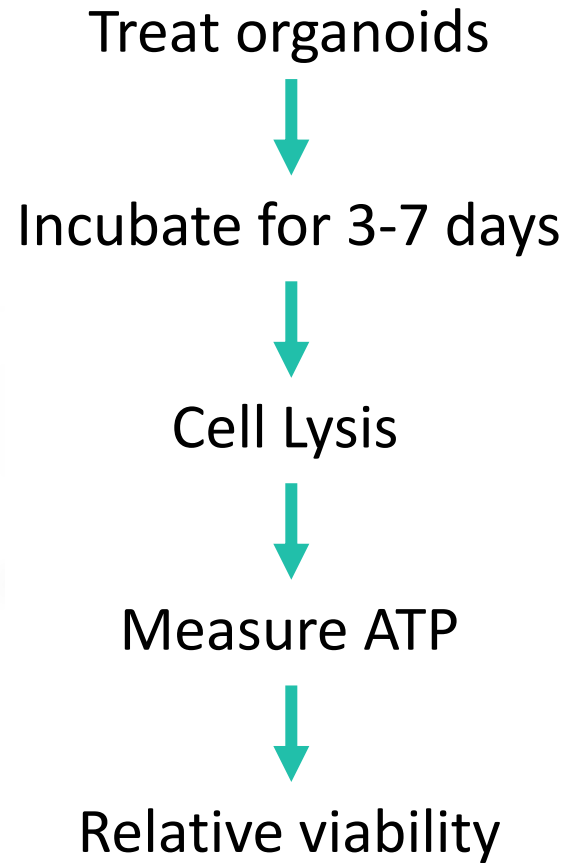
Dawn of the organoid era

- 3D 'micro-tumors' generated directly from patient samples
- Maintain mutational landscape and clonal heterogeneity
- Translational application: predict therapy response
- Preclinical application: accelerated drug development
- Biobanking



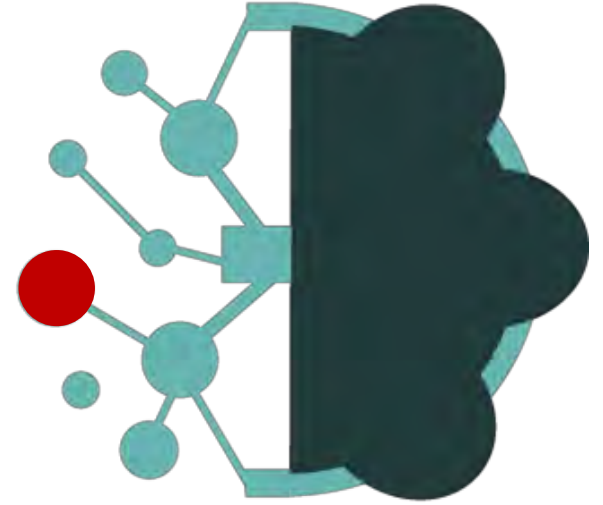
Tuveson et al., Science, 2021

Drug screening **current limitation**

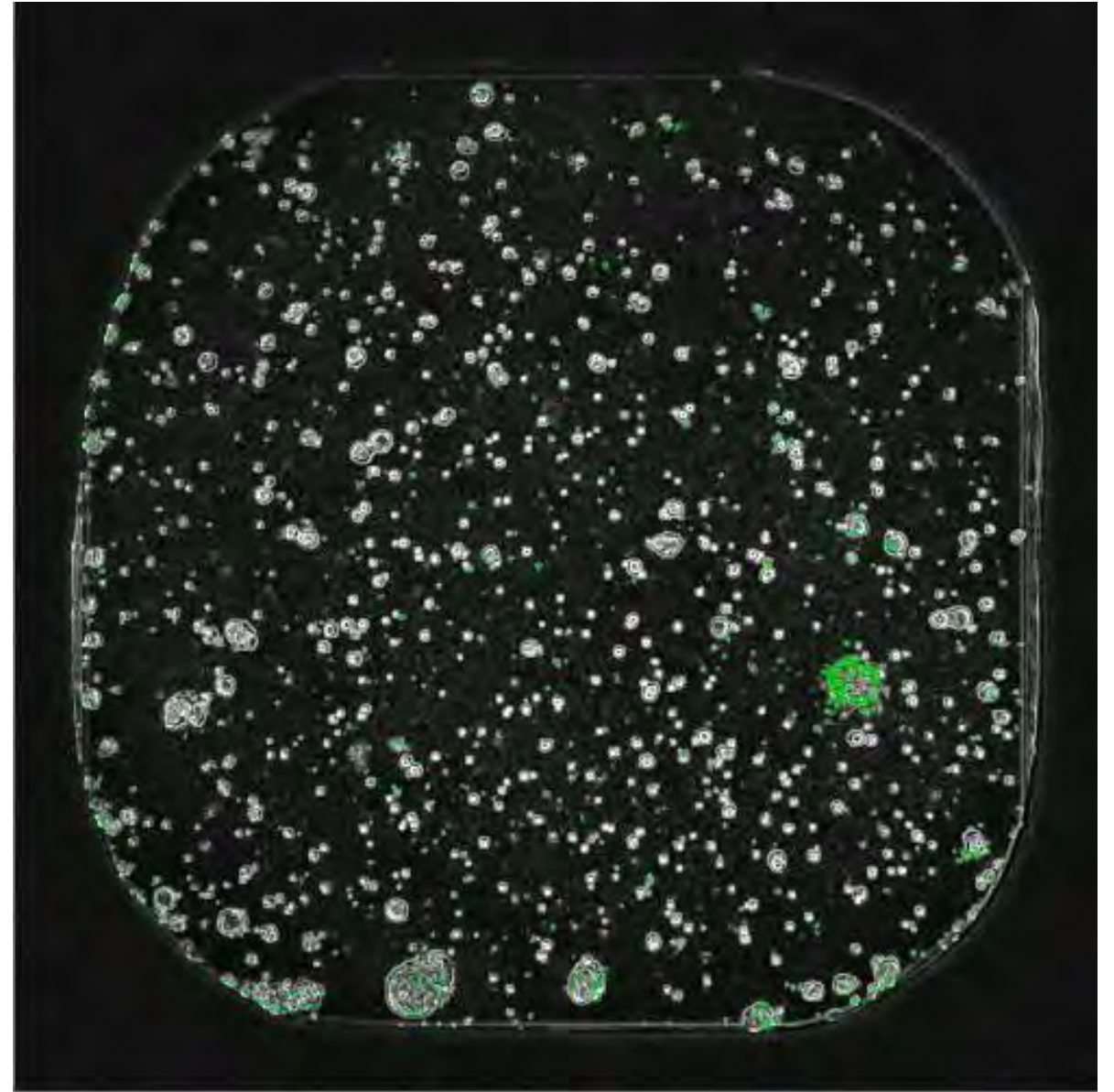


?

Growth arrest?
Cell death?
Homo/heterogeneous response?
Influence metabolic changes?



Drug screening **live cell imaging**



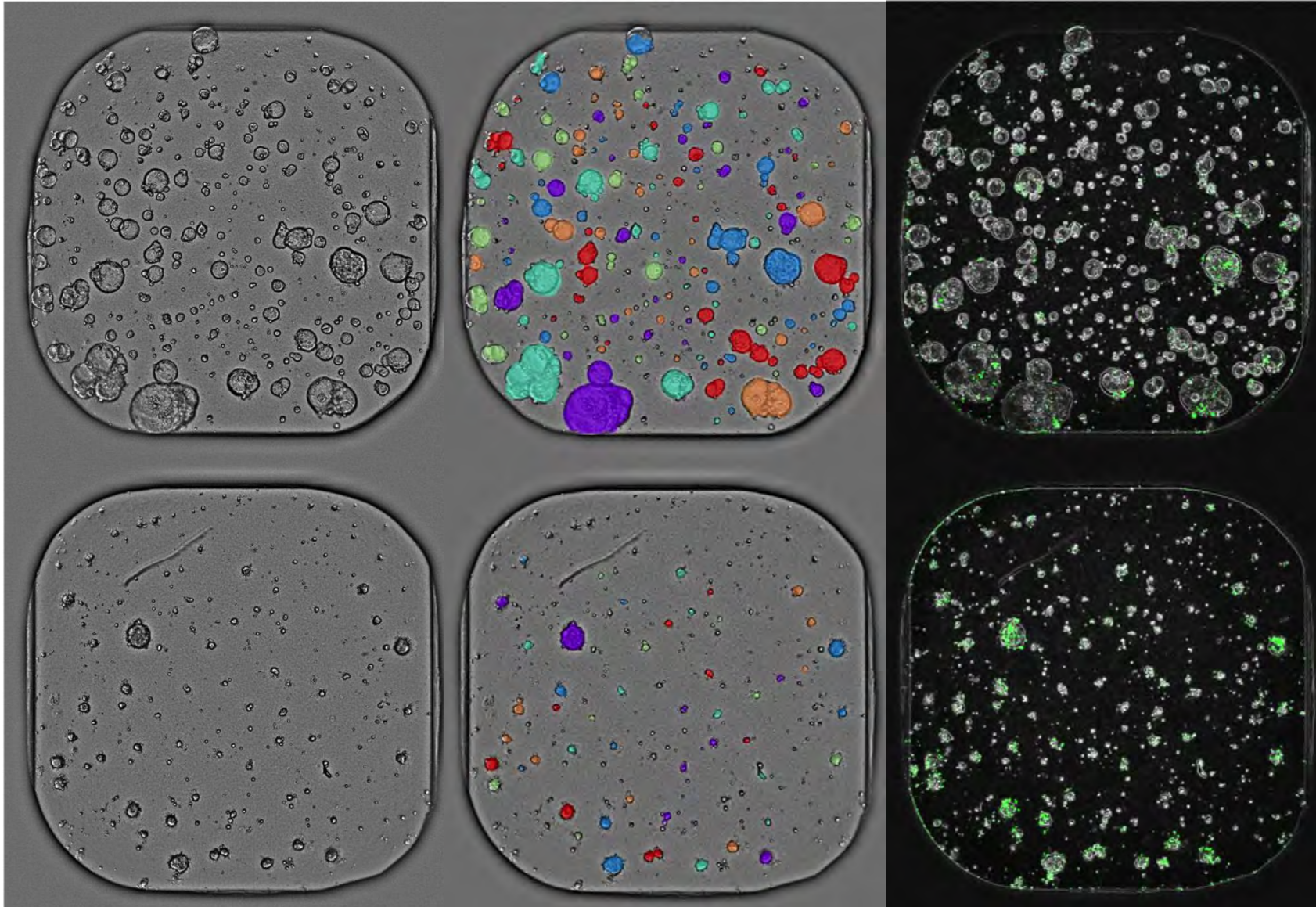
Drug screening **live cell imaging**

Brightfield

Label-free
image segmentation

Cytotox Green

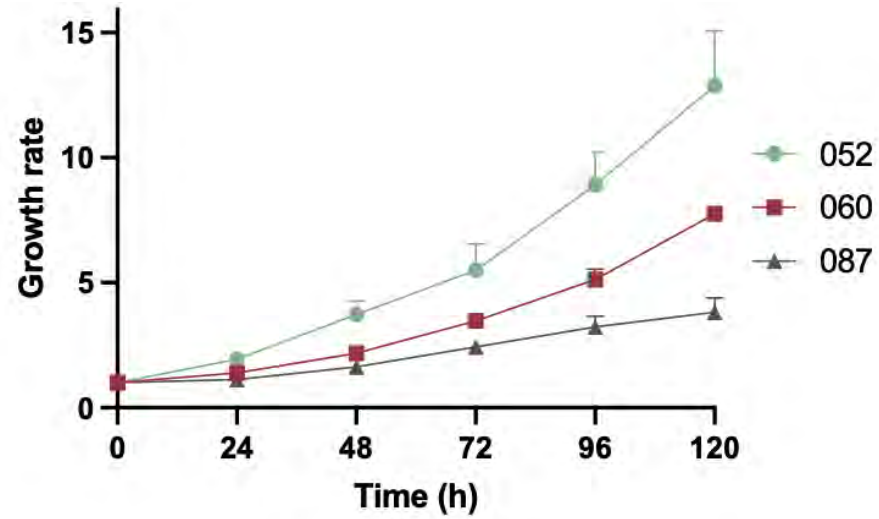
Ctrl-



GemPac



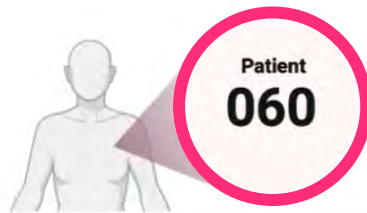
Drug screening growth rate-based drug response metrics



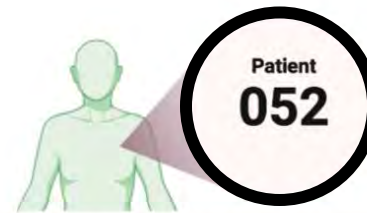
G



Aggressive disease
Tumor growth under FFX
Highly resistant

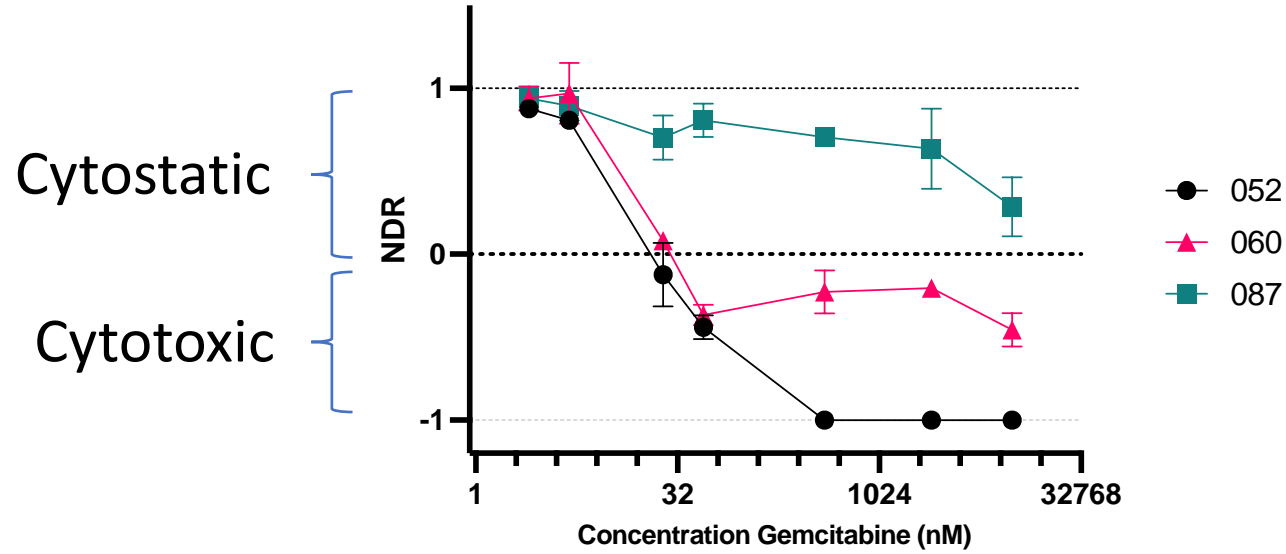


Mixed response
Reduction lymph node activity
But Local relapse (after 4 months)




Good response to GEM-PAC
Disease control (1 year)
Local relapse

Drug screening growth rate-based drug response metrics




G




Patient 087

Aggressive disease
Tumor growth under FFX
Highly resistant



Patient 060

Mixed response
Reduction lymph node activity
But Local relapse (after 4 months)

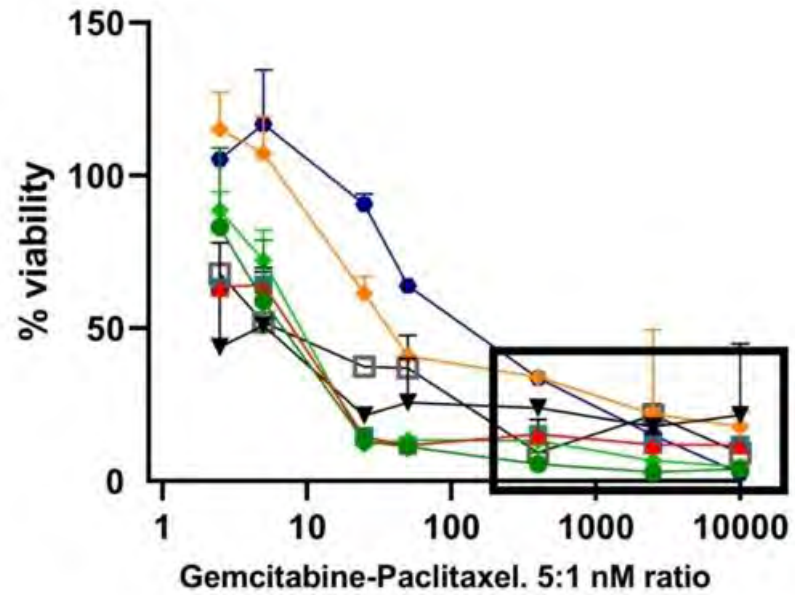


Patient 052

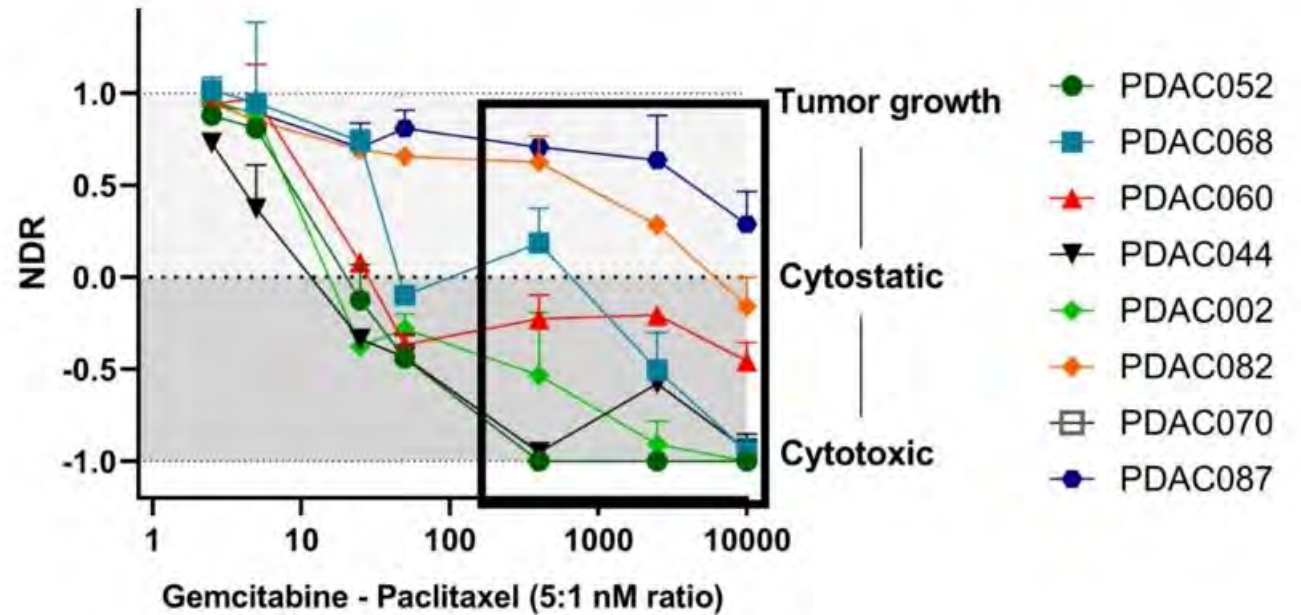
Good response to GEM-PAC
Disease control (1 year)
Local relapse

Drug screening growth rate-based drug response metrics

Relative viability

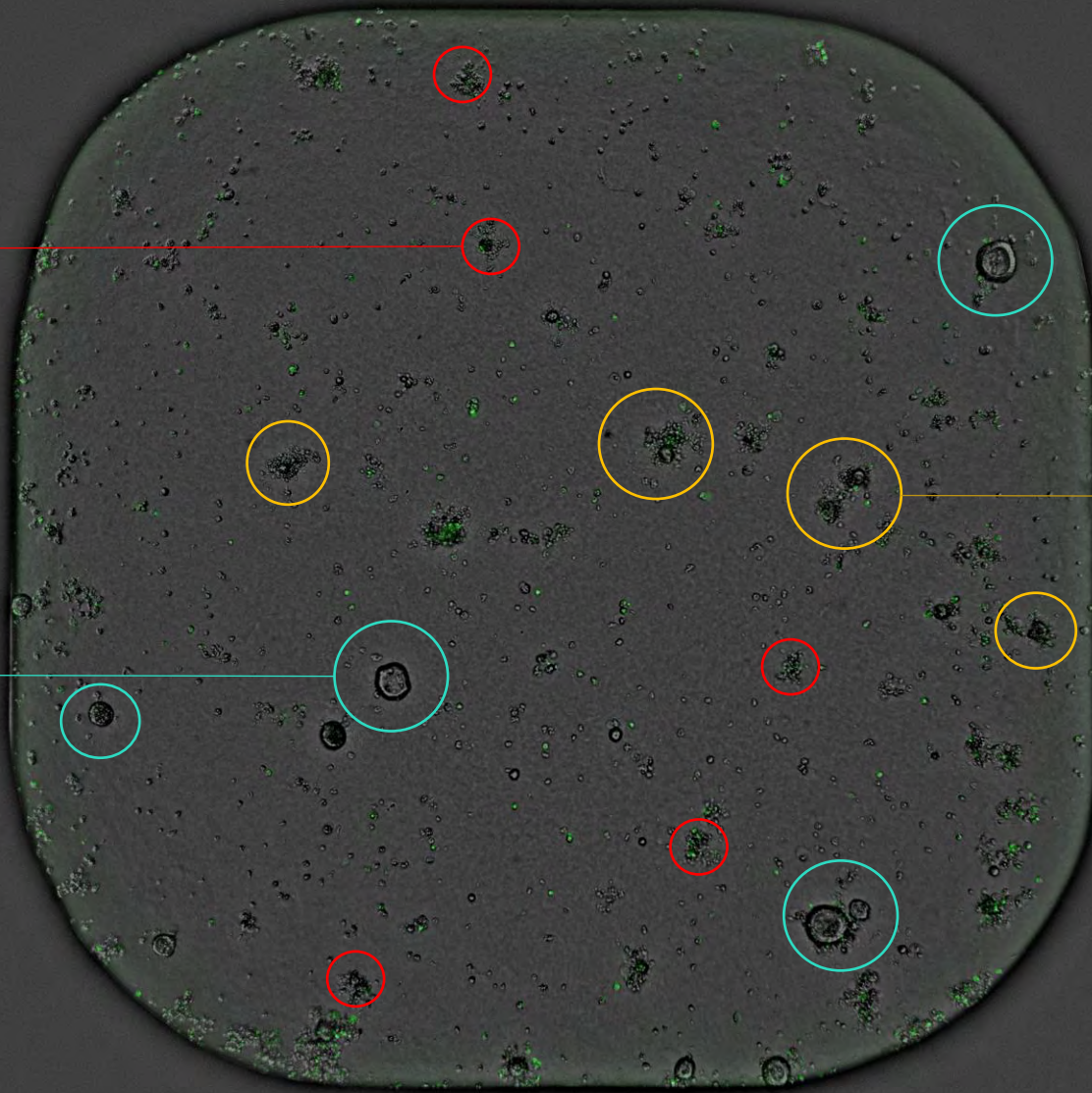


Normalised drug response



Sensitive

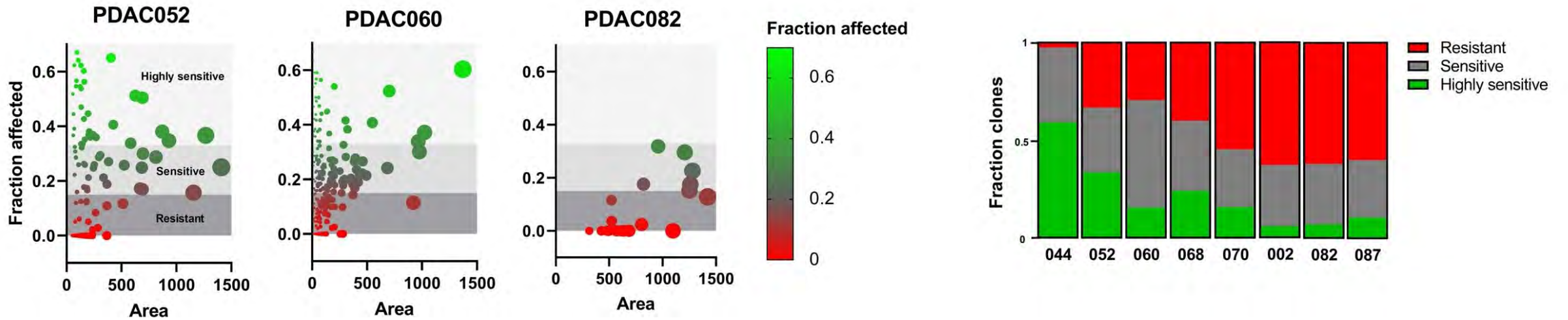
Resistant



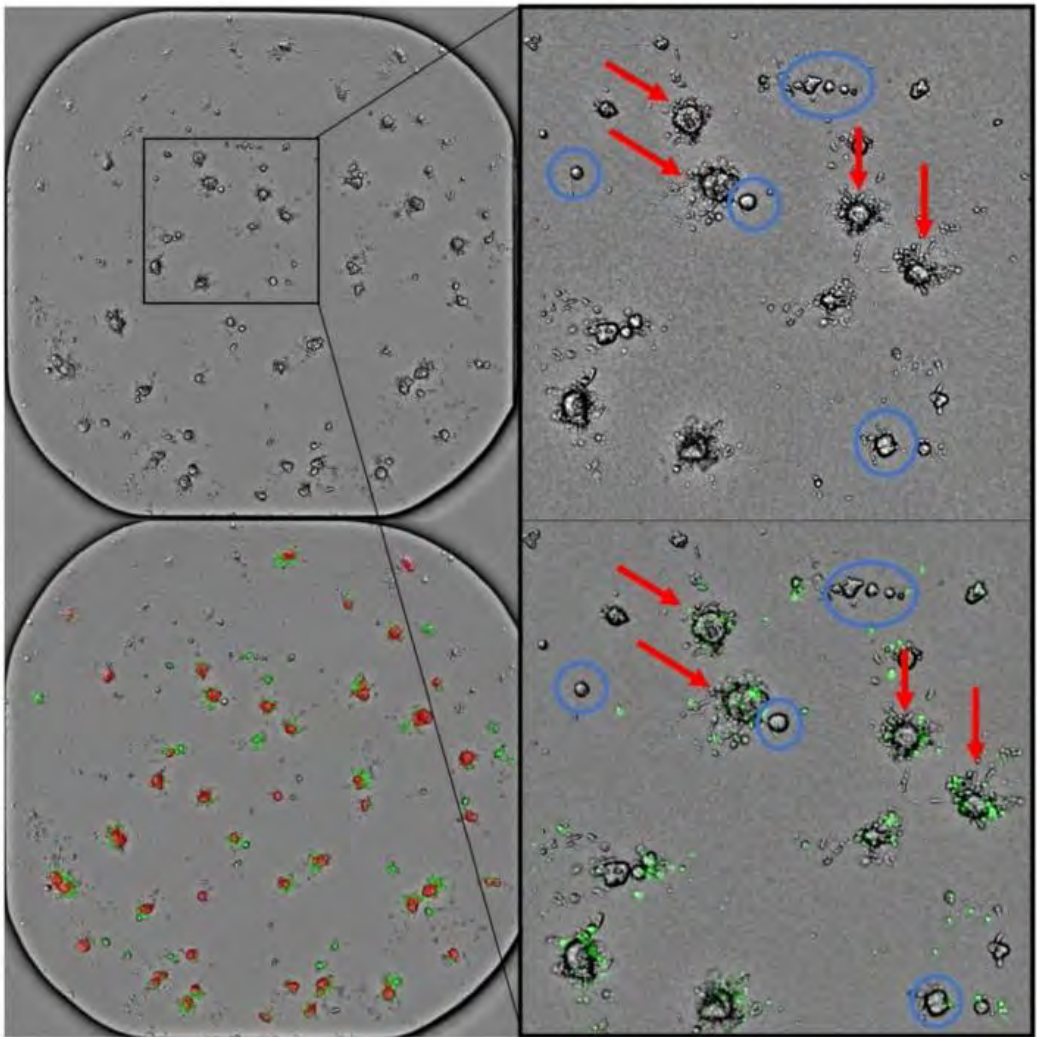
Mixed response
Invading cells?

Drug screening **single organoid drug response**

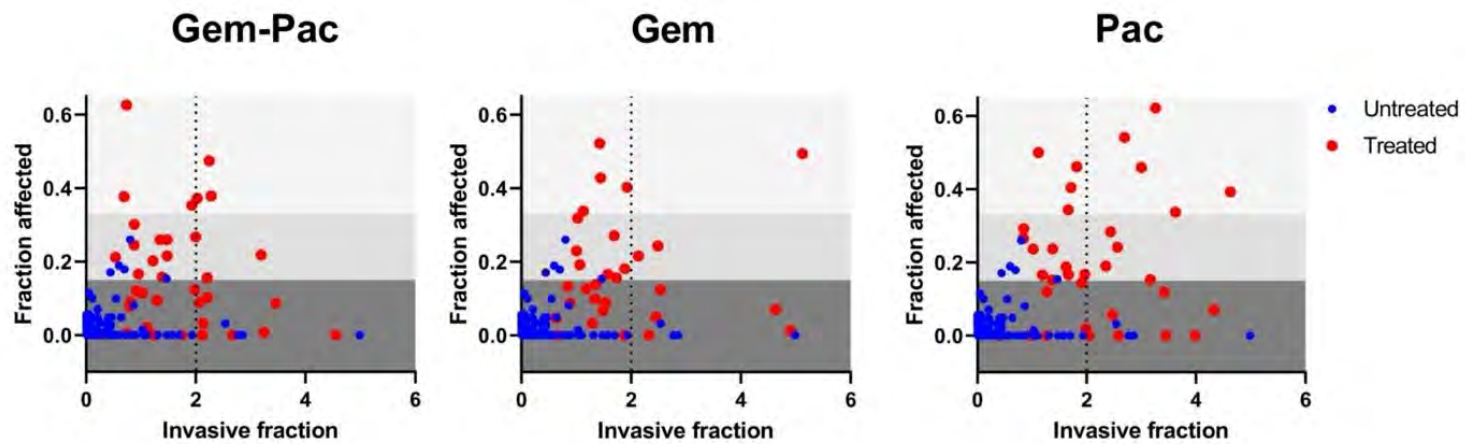
Affected Fraction



Drug screening single organoid drug response

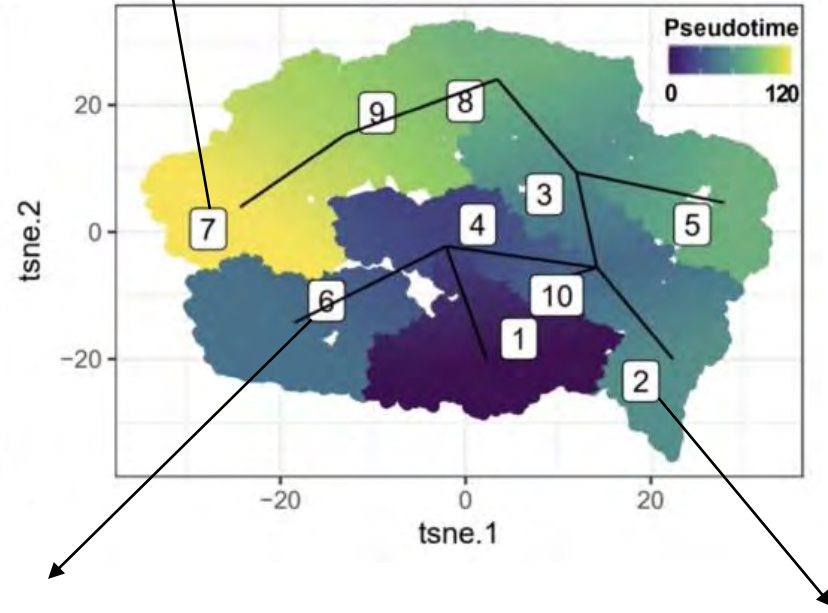
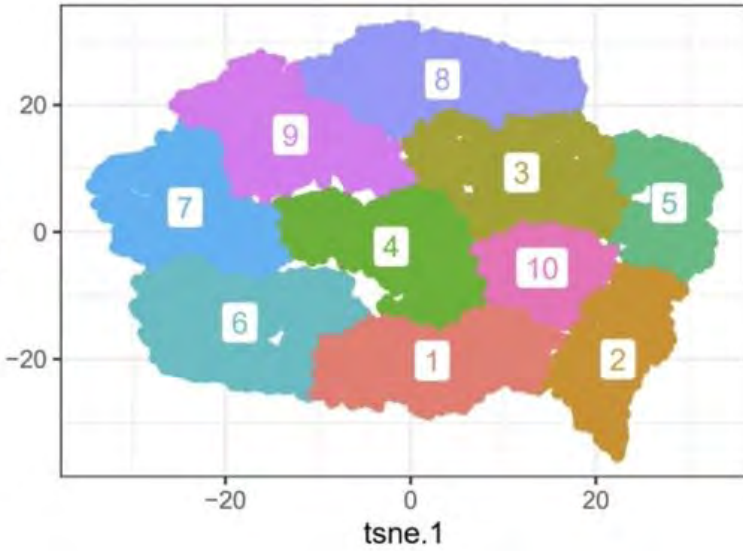


Invasive Fraction



Drug screening **single organoid drug response**

High fraction affected

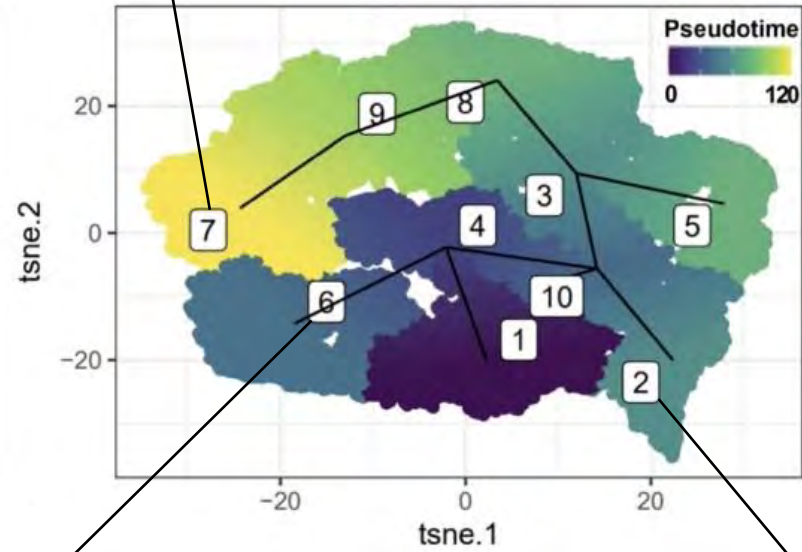
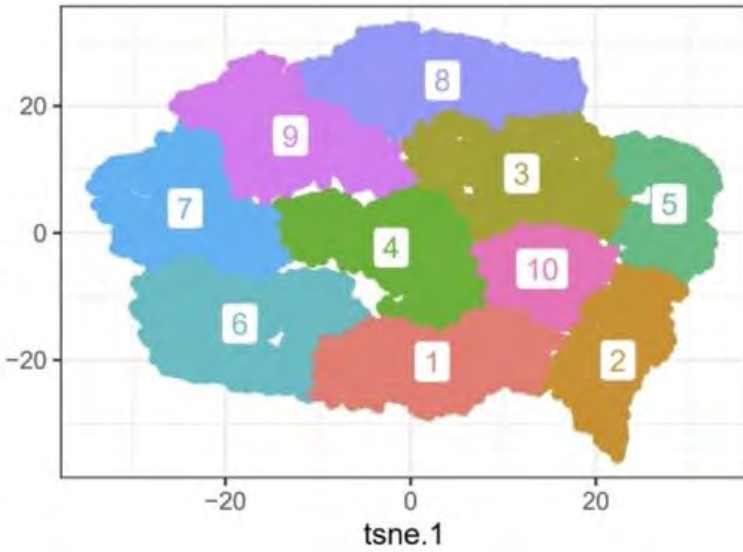


High invasive fraction

Large size
Low fraction affected

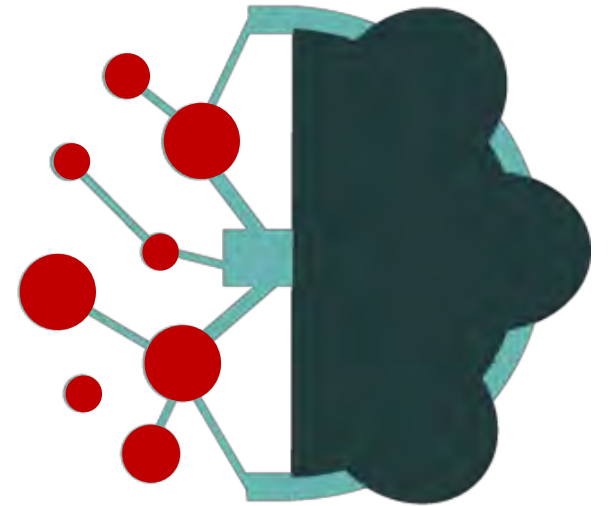
Drug screening **single organoid drug response**

High fraction affected

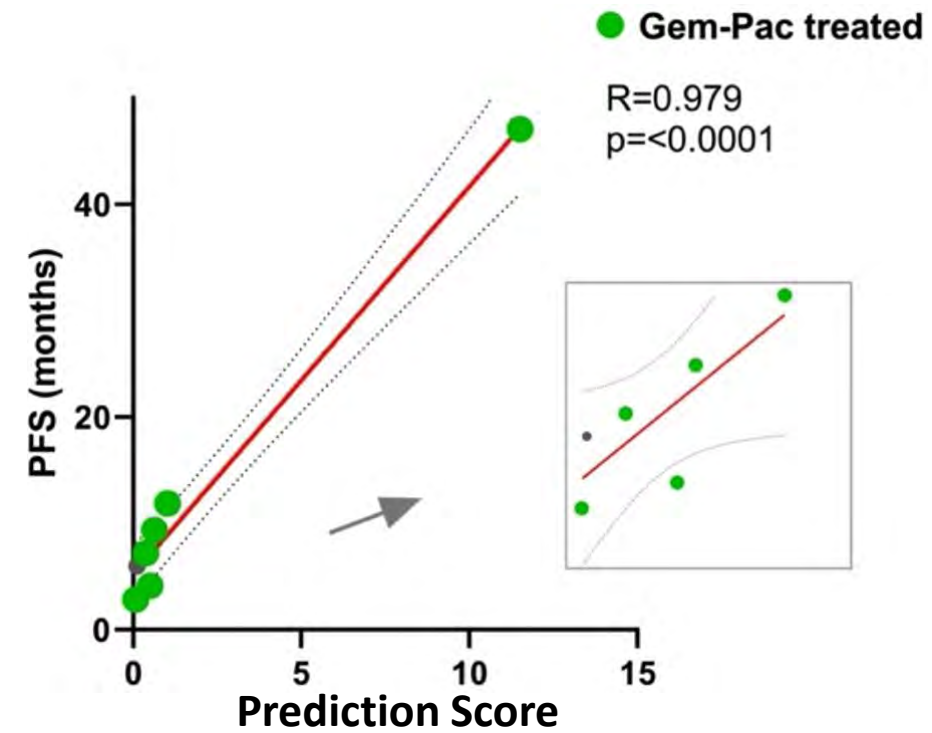


High invasive fraction

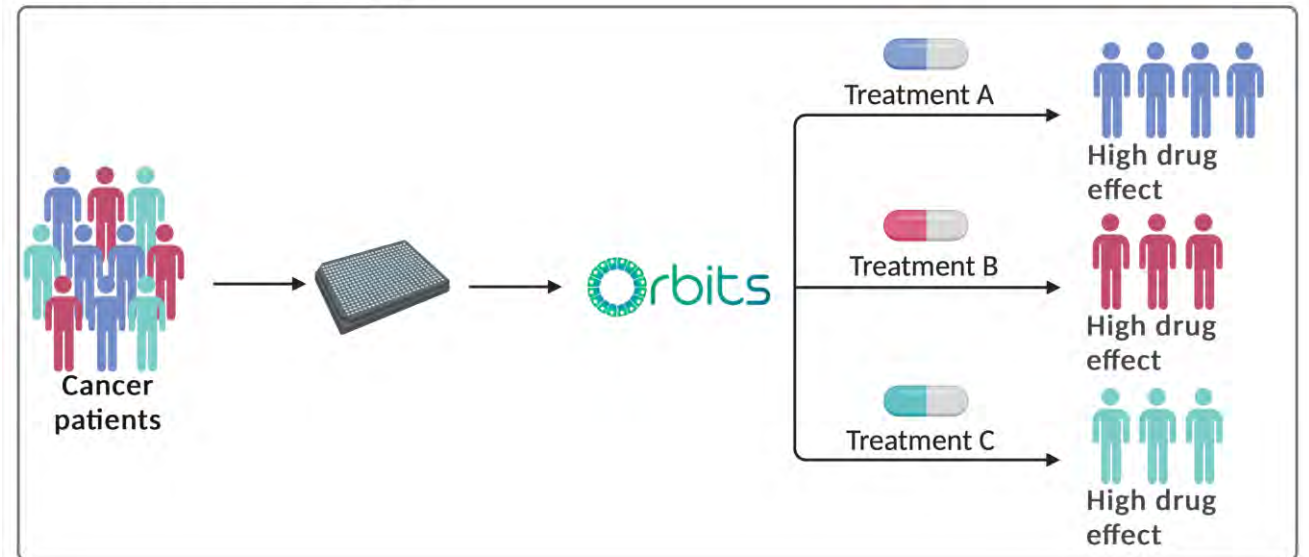
Large size
Low fraction affected



Drug screening **Orbits** prediction score

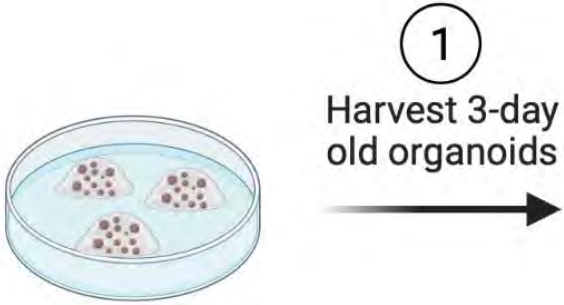


Precision cancer therapy



Drug screening workflow

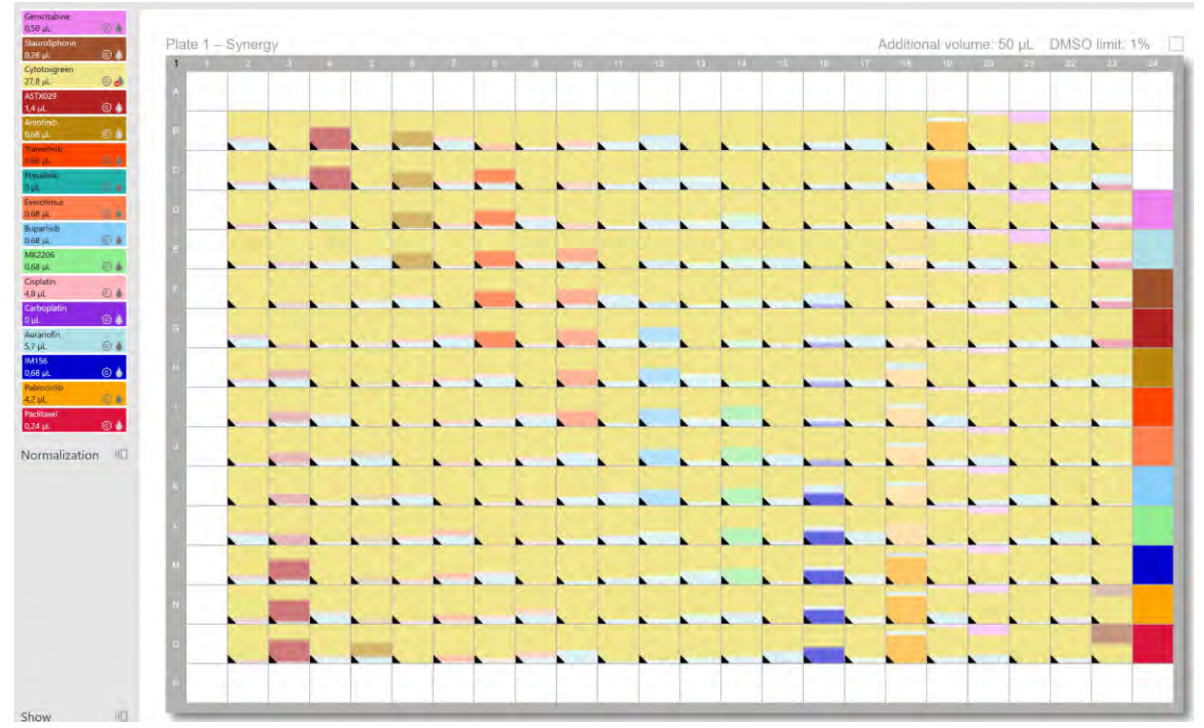
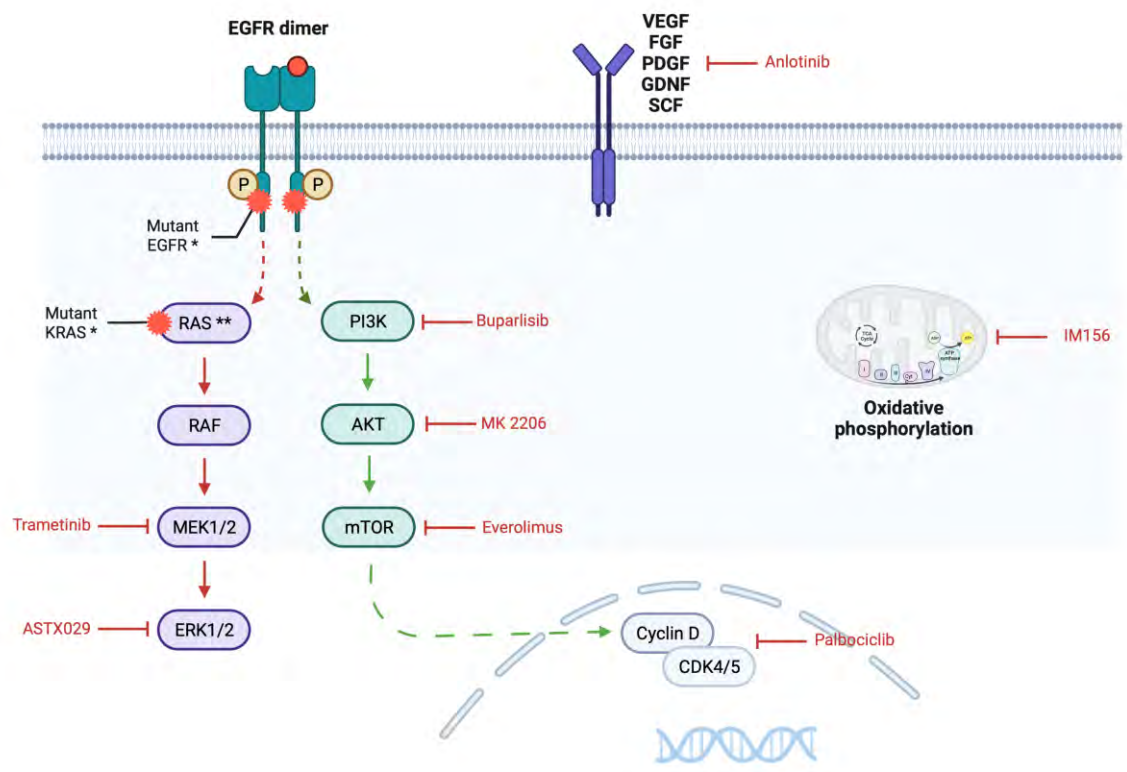
Multiparametric Tumor Organoid Drug Screening Using Widefield Live-Cell Imaging for Bulk and Single-Organoid Analysis



Drug screening synergy



Auranofin (TrxRi, drug repurposing)



Created with BioRender.com

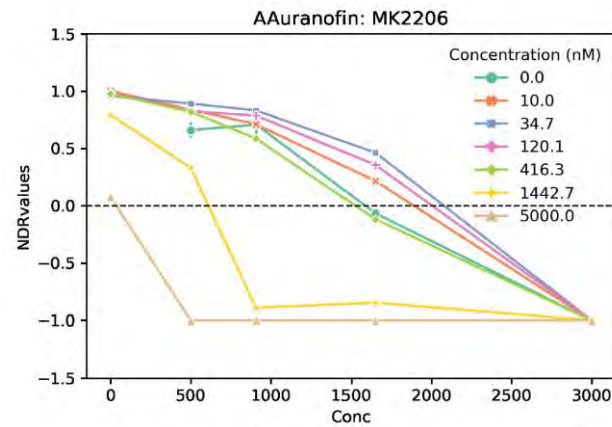
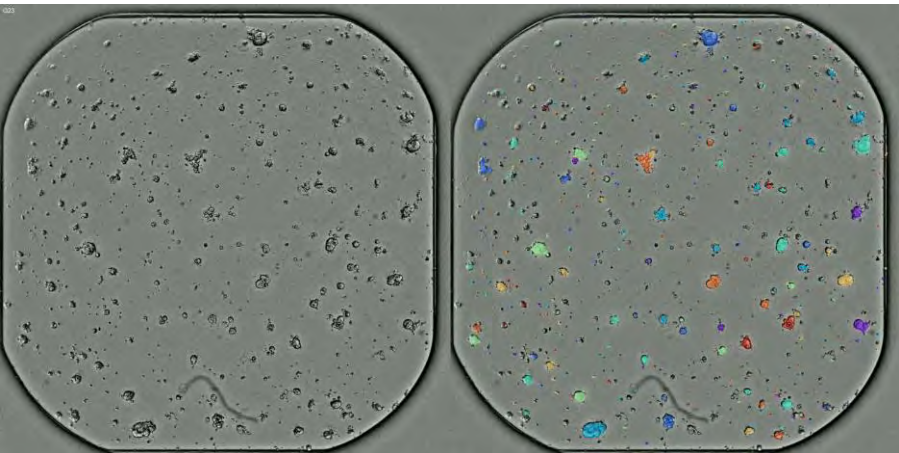
Tecan D300e Digital Dispenser is for research use only. Not for use in diagnostic procedures. Tecan D300e Digital Dispenser is a product of HP Inc. CA, USA.

Drug screening synergy

Orbits



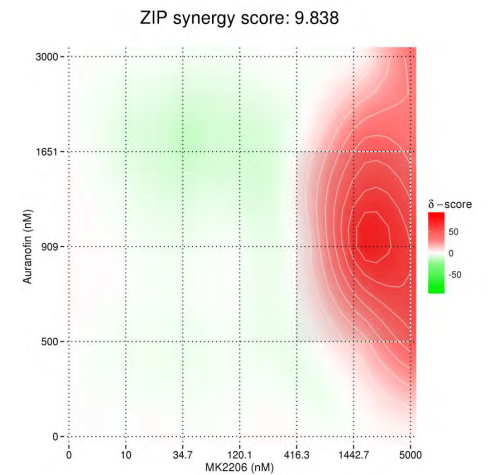
Orbits



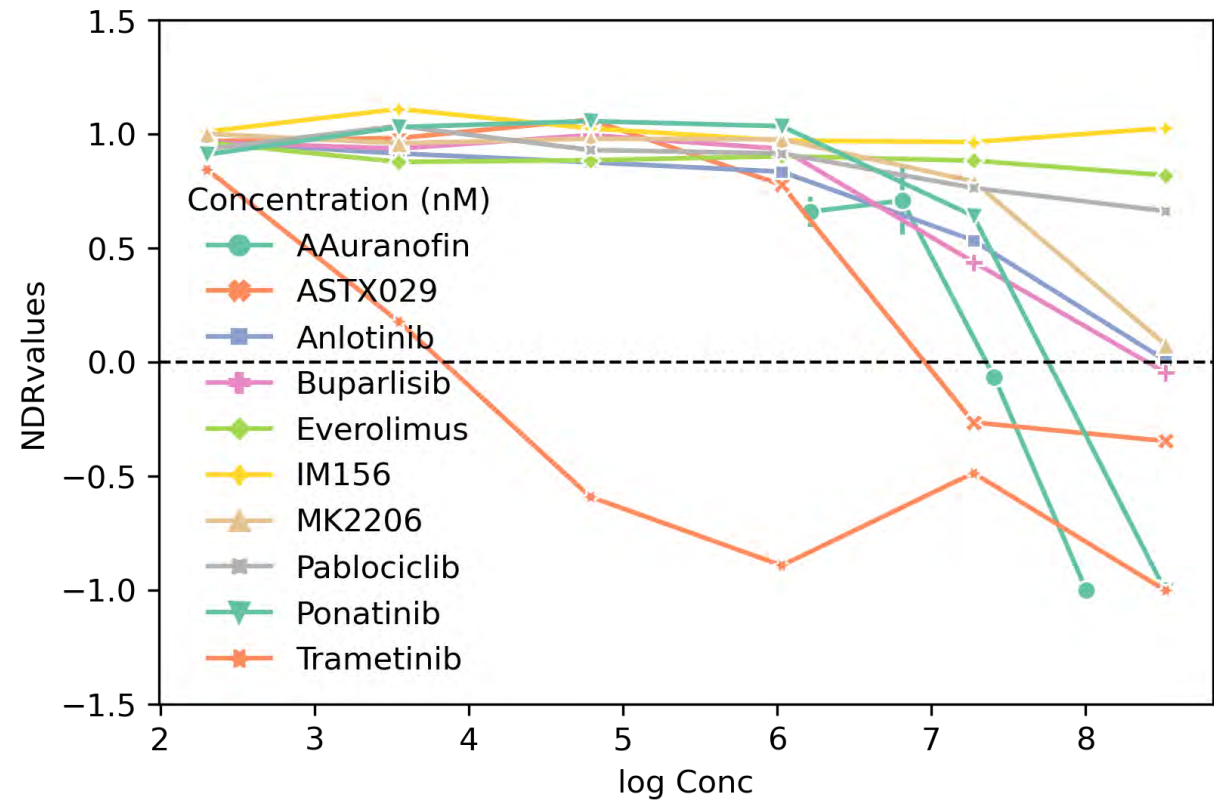
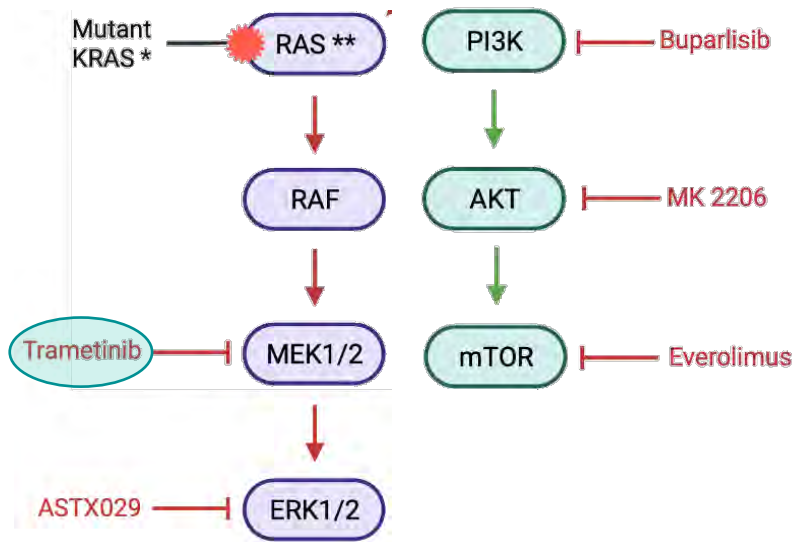
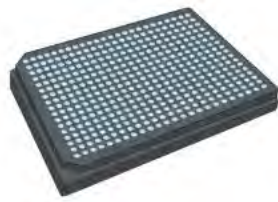
<https://synergyfinder.fimm.fi/>

SynergyFinder web application (version 3.0)
an interactive analysis of multi-drug combination data.

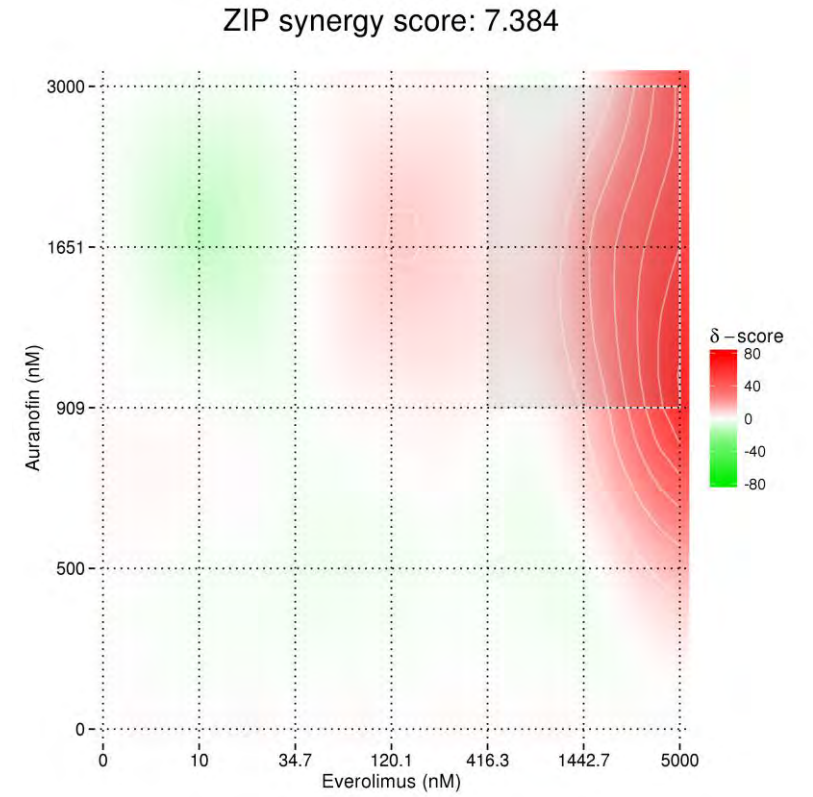
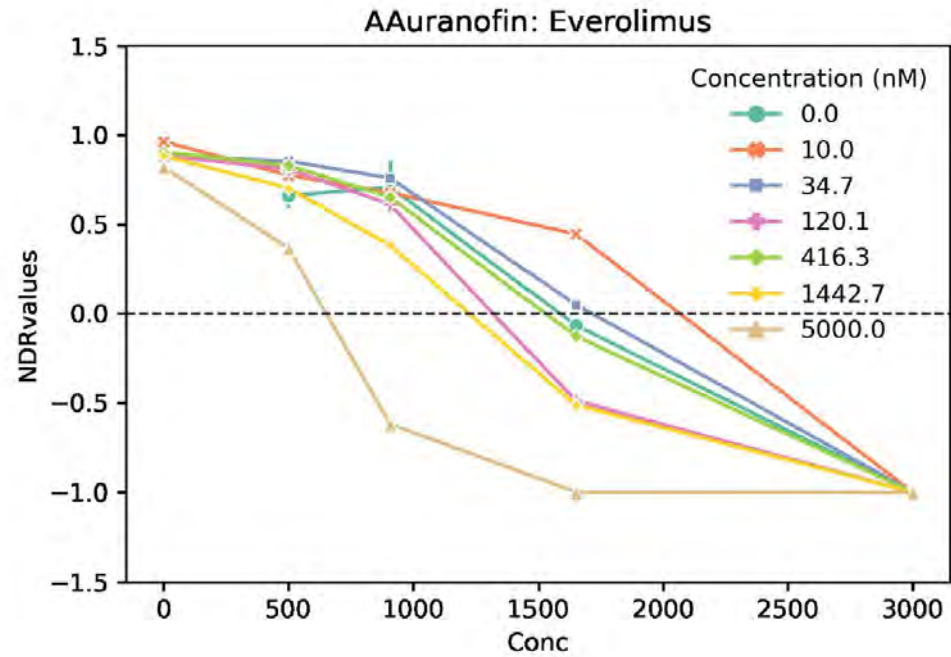
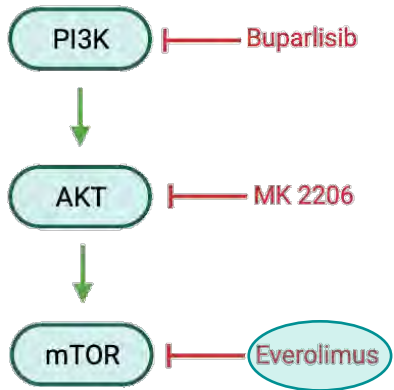
▶ Start the tour



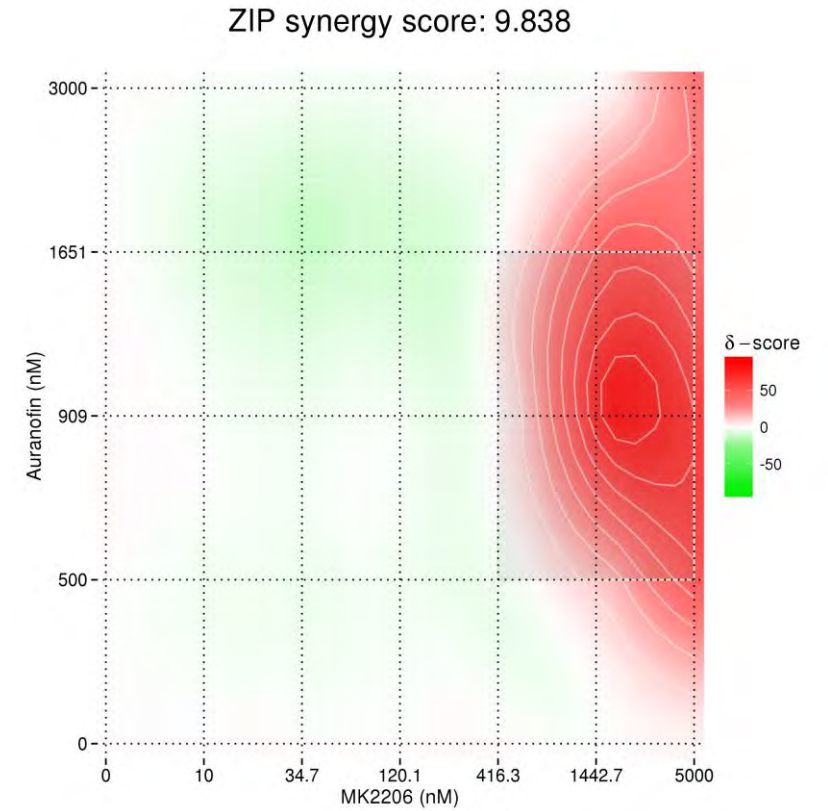
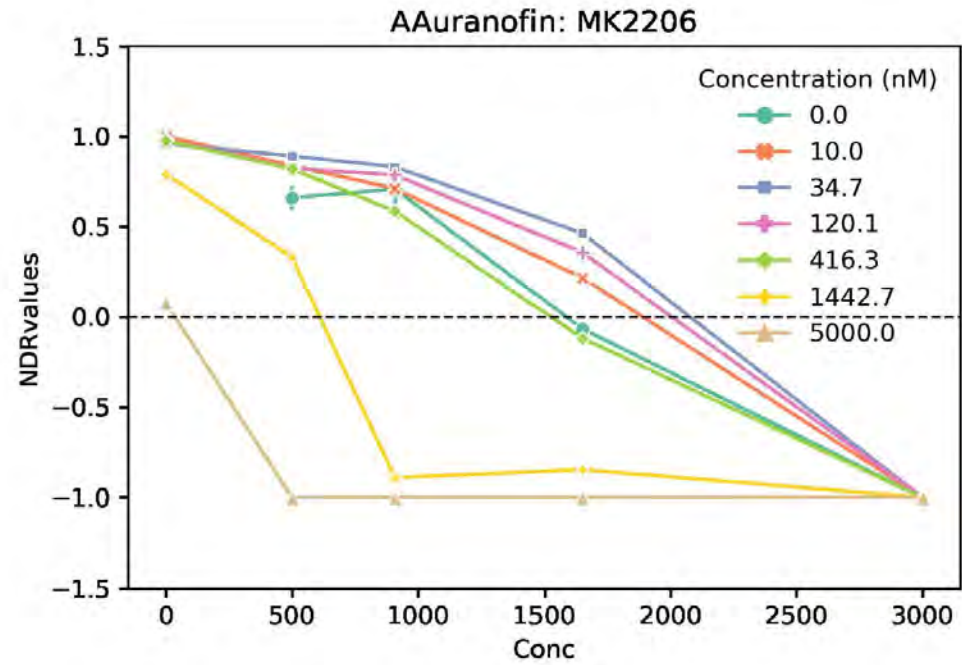
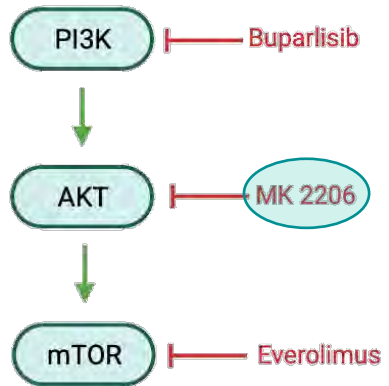
Drug screening synergy



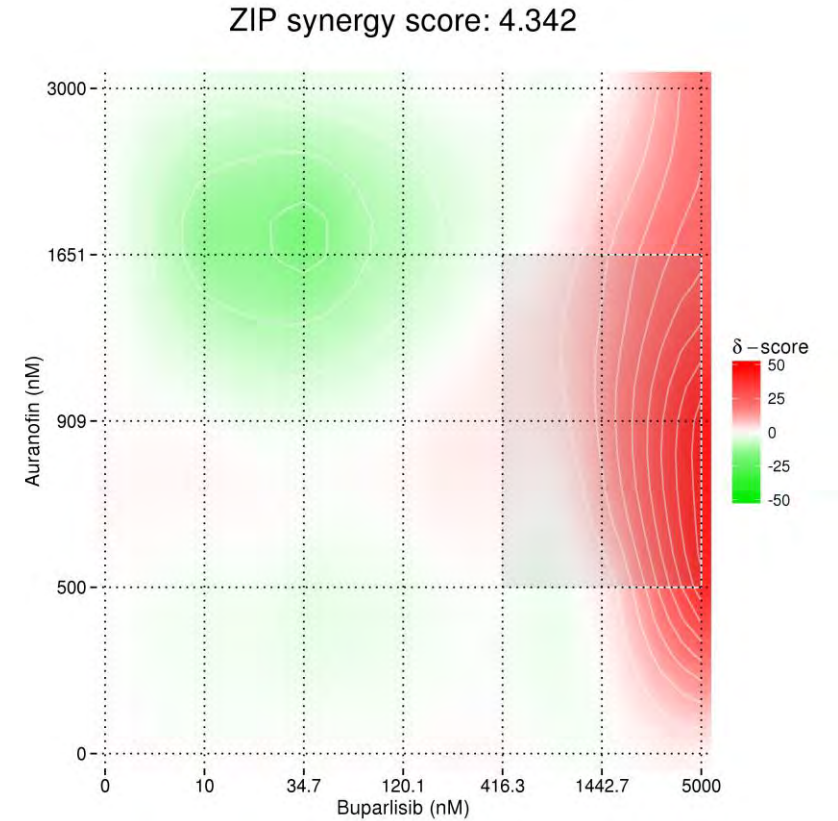
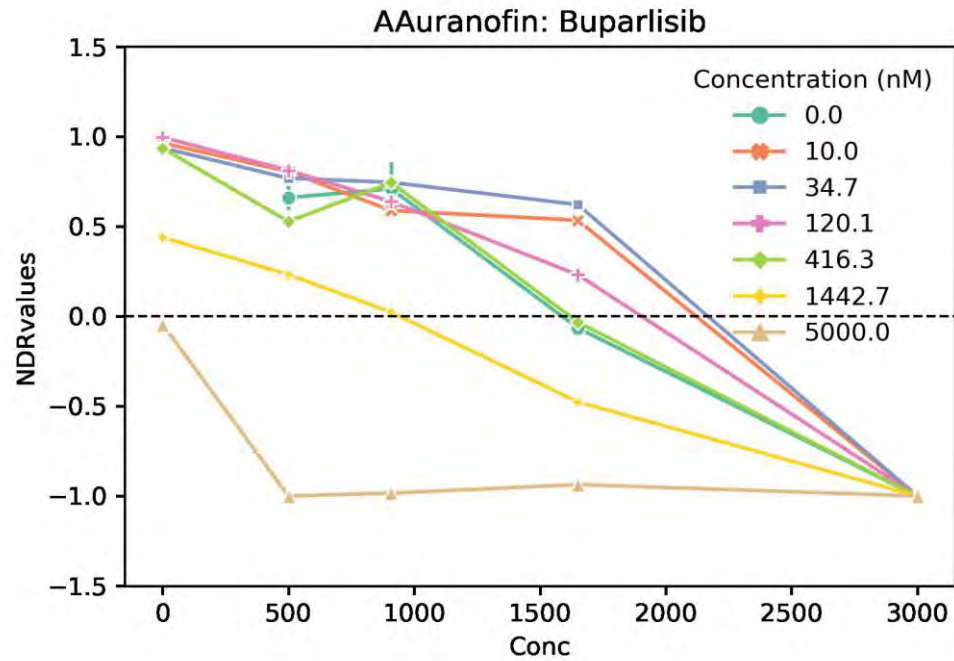
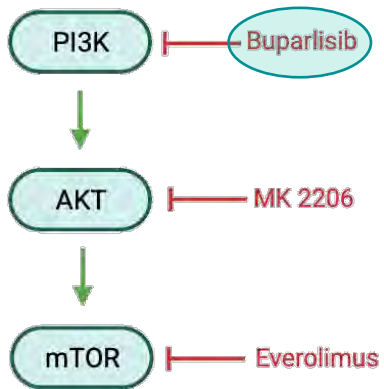
Drug screening synergy



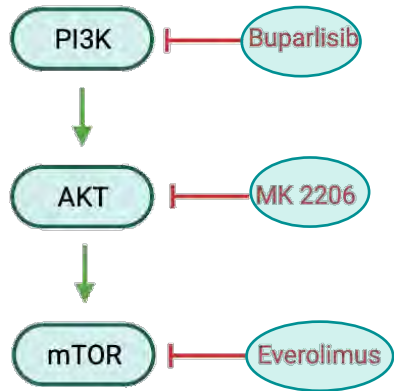
Drug screening synergy



Drug screening synergy

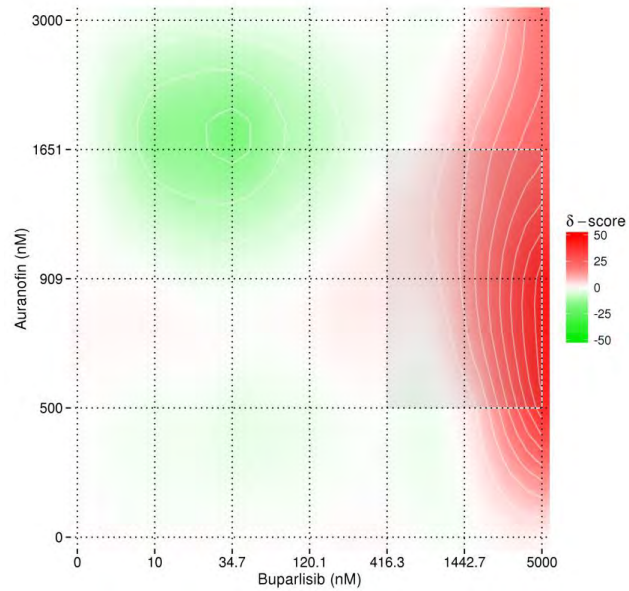


Drug screening synergy



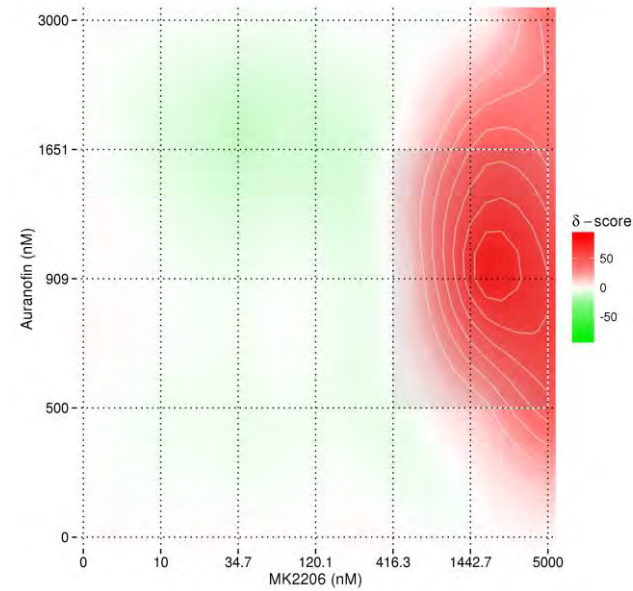
Buparlisib

ZIP synergy score: 4.342



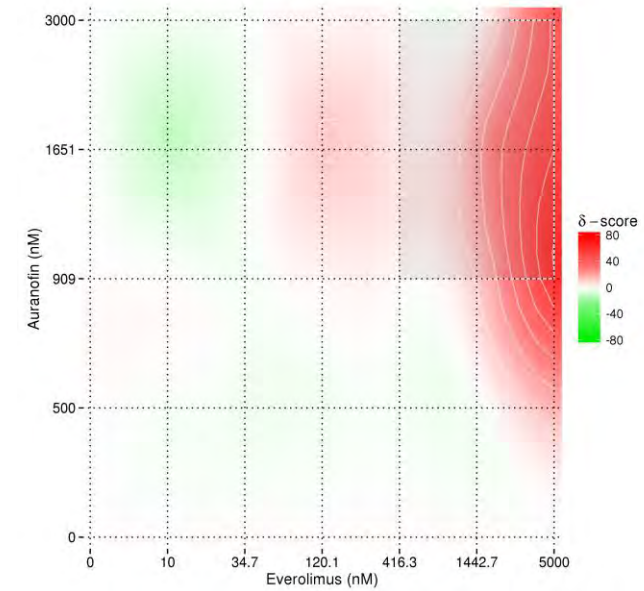
MK2206

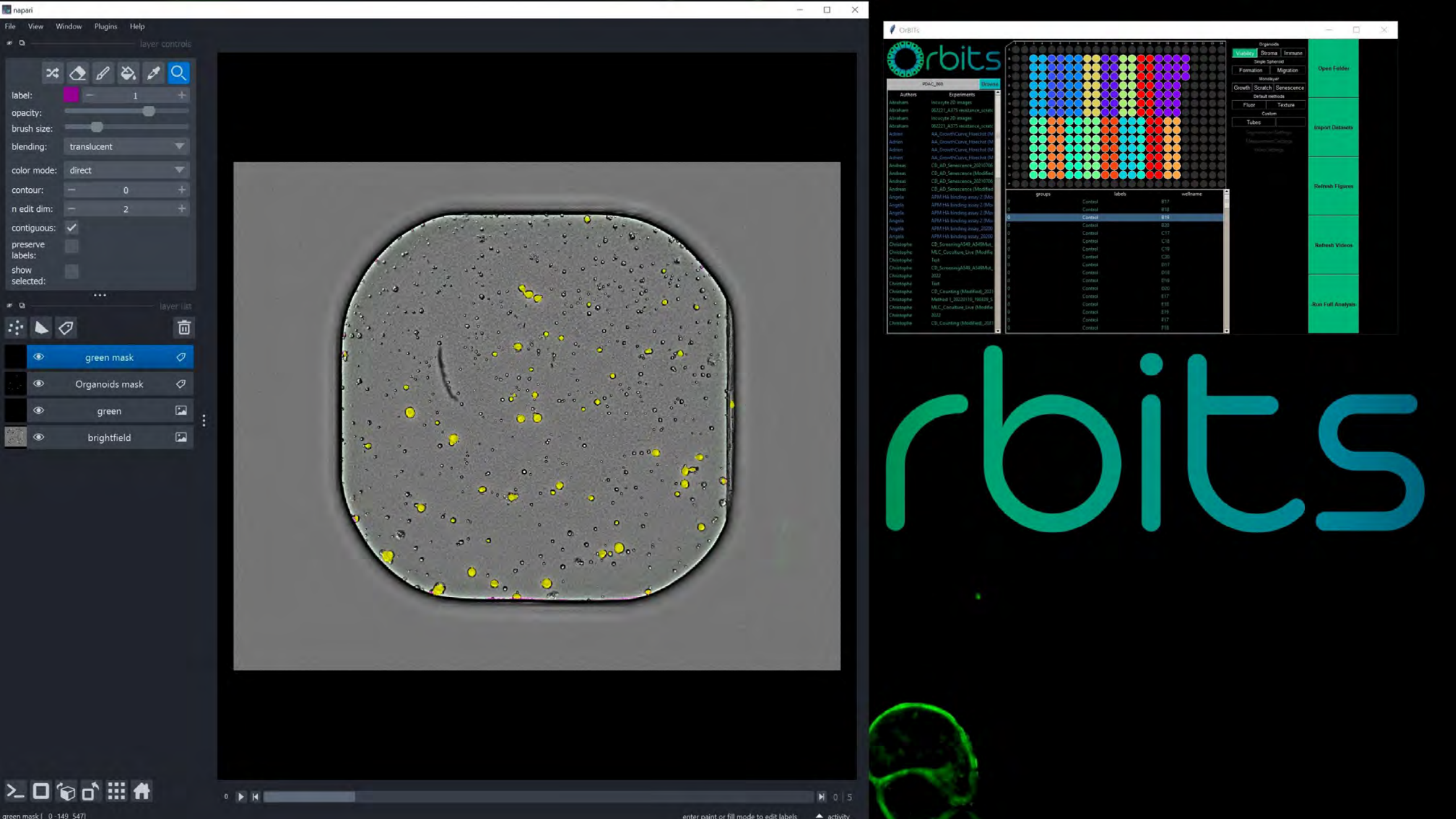
ZIP synergy score: 9.838



Everolimus

ZIP synergy score: 7.384





layer controls

label: 1

opacity: [slider]

brush size: [slider]

blending: translucent

color mode: direct

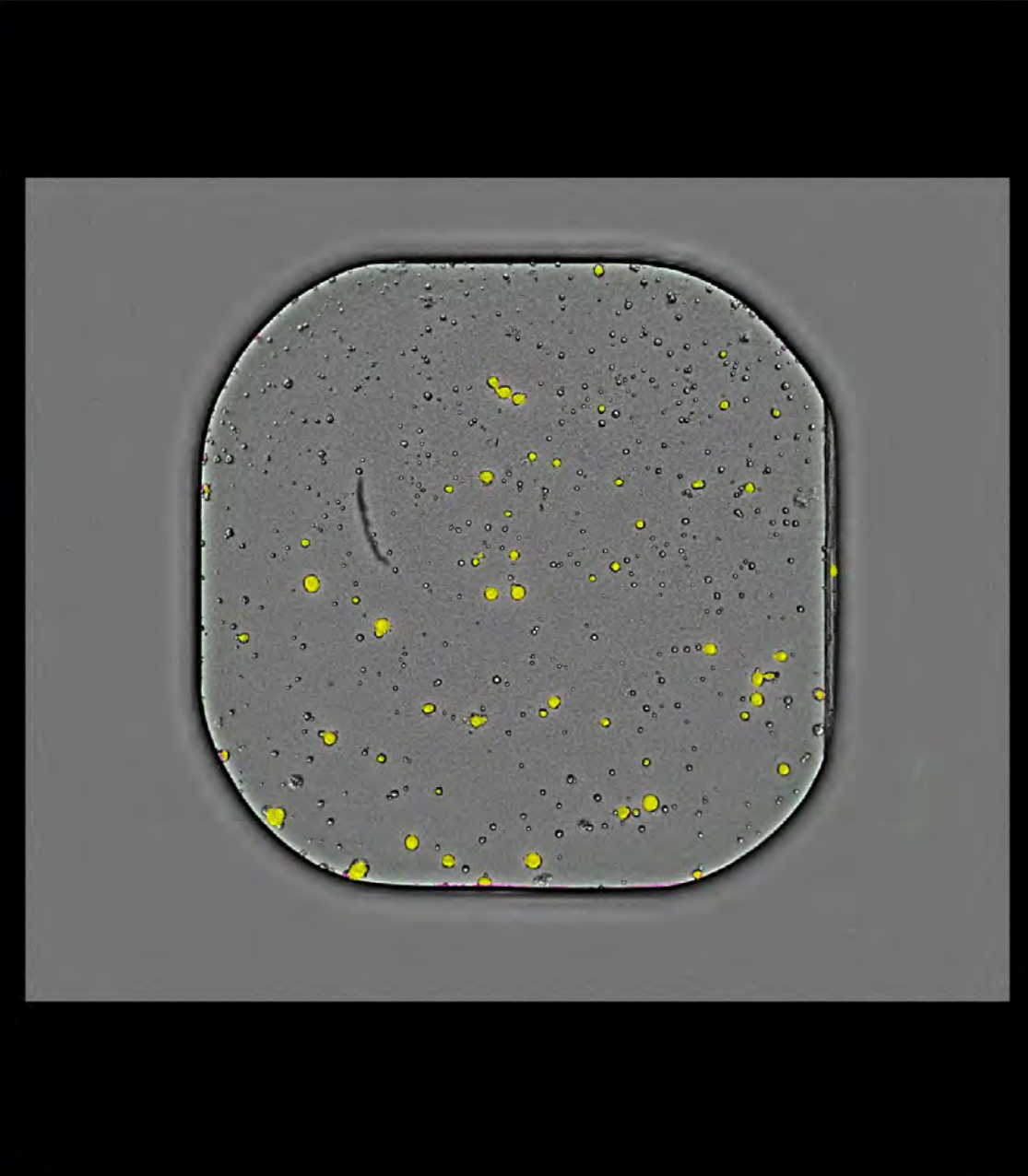
contour: 0

n edit dim: 2

contiguous:

preserve labels:

show selected:



layer list

- green mask
- Organoids mask
- green
- brightfield

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Experiments

groups	labels	wellname
Control		B17
Control		B18
Control		B19
Control		B20
Control		C17
Control		C18
Control		C19
Control		C20
Control		D17
Control		D18
Control		D19
Control		D20
Control		E17
Control		E18
Control		E19
Control		E20

Open folders

Import Datasets

Refresh Figures

Refresh Videos

Run Full Analysis

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




User Storage

0.21/10.00 GB



◀ 1/1 ▶

Name	Size (GB)	Experiments	Last Modified (Europe/Brussels)	Progress
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JoVE Run 1     	0.104 GB		Thu Dec 15 2022 10:02:33	 ANALYZED 
<input type="checkbox"/> PDAC_060		1	Thu Oct 27 2022 21:12:11	

User Storage

0.21/10.00 GB

Analysis

JoVE Run 1

Organoids

Multi-Organoid

Stroma

Immune

Single Spheroid

Formation

Migration

Monolayer

Growth

Scratch

Senescence

Default Methods

Fluor

Texture

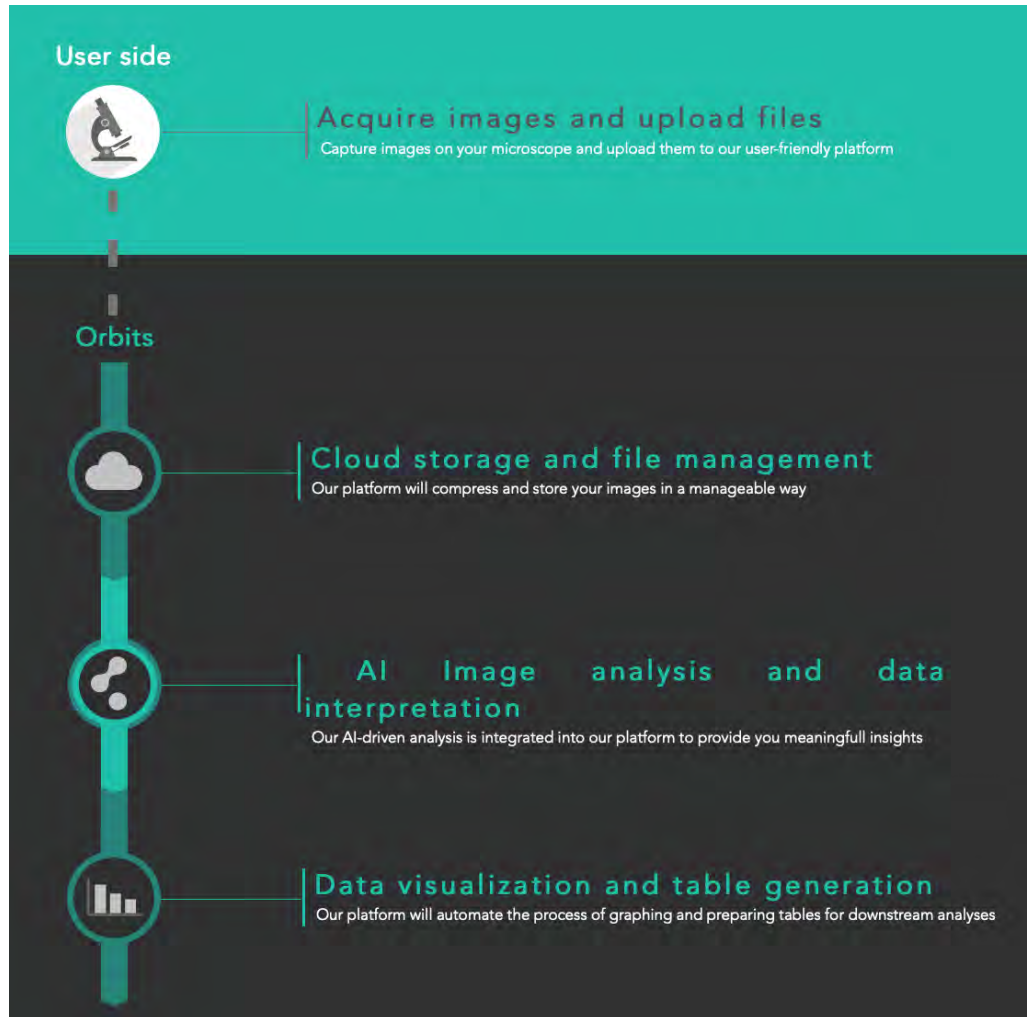
Custom

Tubes

Default Parameters

< Back

Analyze



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Tumoroid Screening Lab

- ✓ Tumoroid Biobank
- ✓ High-throughput Spark Cyto System
- ✓ Confocal imaging
- ✓ Complex microtumor models
- ✓ Orbits integration
- ✓ Proprietary image analysis modules and co-culture screening assays

christophe.deben@uantwerpen.be

For research use only. Not for use in diagnostic procedures

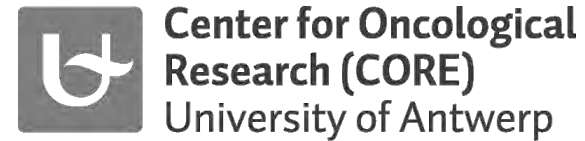


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