Combining Lab Automation with Data Analysis Automation to Enable High-Throughput Screening of Patient-Derived Organoids

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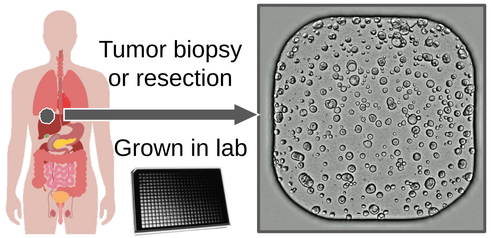
Introduction



Patient-Derived Organoids

- Generated from patient tumors
- Retain patient characteristics
- Can be stored and re-used in the lab for drug screening
- Potential to represent human tumors better than any in vitro model

Current organoid analysis methods fall short in at least 1 of 2 major criteria:

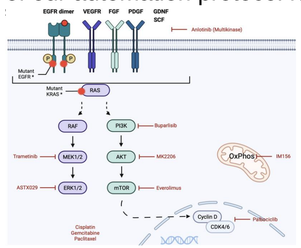
1) Low recapitulation of patient tumor response

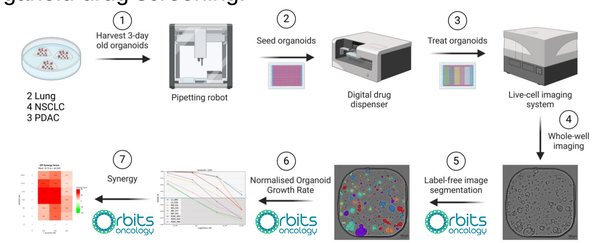
2) Low throughput and scalability

We hypothesized that leveraging live-cell imaging techniques with computer vision and lab/data automation will capture the dynamic organoid drug responses in a high-throughput compatible solution.

Aims & Methods

The aim of our study was to test the sophistication and high-throughput compatibility of our automation protocol for organoid drug screening.



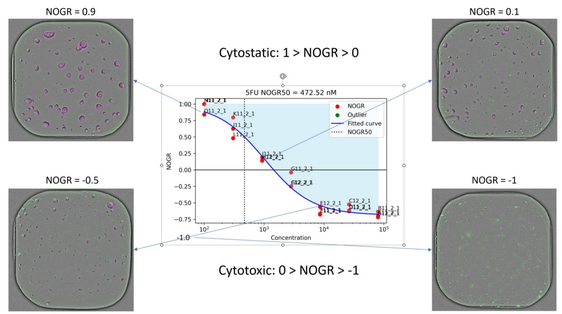


Drug combinations: 11 distinct drug combinations were chosen with Auranofin, a rheumatoid arthritis drug repurposed for cancer treatment, to target multiple redox pathways

Drug screening: 9 organoids were harvested and used for drug screening experiments (2 non-cancerous pulmonary organoids–lung, 4 non-small cell lung cancer–NSCLC, 3 Pancreatic ductal adenocarcinoma–PDAC). Lab automation was complimented with image and data analysis automation, using the Orbits Oncology digital platform.

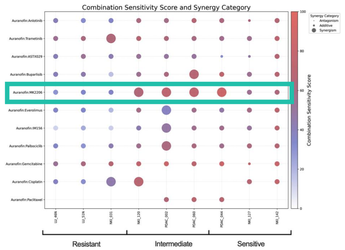
Results

1. Delineating Cytotoxic vs Cytostatic Drug Effects



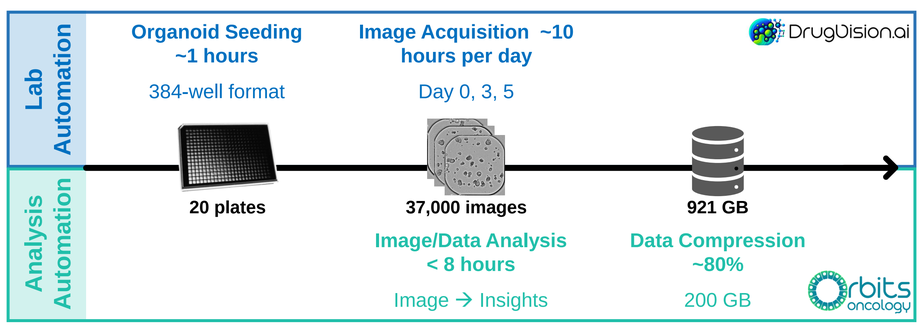
Normalized Organoid Growth Rate (NOGR) metrics were calculated and provided drug response insights most representative of visual organoid responses to Fluorouracil (5FU), chemotherapy. Cytotoxic drug effects (NOGR < 0) were delineated from cytostatic effects (0 < NOGR < 1). Blue area is the area-over-the-curve, used to compare drug effects.

2. Determining Optimal Drug Combination



ZIP synergy scores and combination sensitivity scores (based on NOGR) were calculated for the combination of Auranofin with 11 therapies. ZIP Bubble size: small = antagonism; large = synergism. Sensitivity Color: white = no drug effect; red = high drug effect. Organoids were categorized as resistant, intermediate, and sensitive to therapy. Lung (LU), NSCLC (NKI).

3. Evaluating High-Throughput Compatibility



Conclusions

Auranofin:

- Highly synergistic with AKT inhibitor MK2206 in multiple tumor organoid lines
- Additional organoid dependent additive and synergistic interactions

Automation Protocol for Organoid Screening:

- Highly recapitulates patient tumor response & is high-throughput compatible
- NOGR metrics improves organoid drug response & synergistic calculations
- Analysis automation must compliment lab automation for a complete screening solution

Related references:

https://doi.org/10.1186/s13046-024-03012-z

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