



# Encapsulate: Automated Biochips for Personalized Cancer Screening in Microgravity

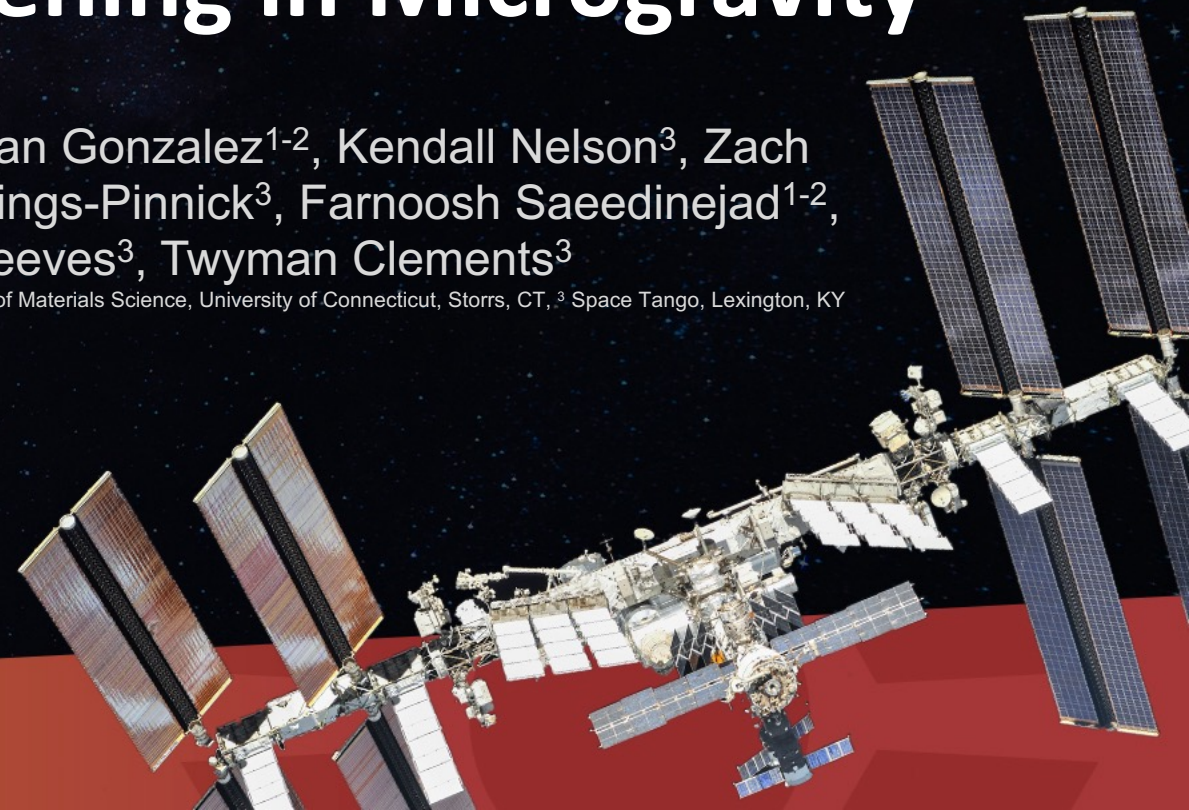
Armin Rad, Ph.D.  
CEO and Co-founder  
Armin@encapsulate.bio

Armin T. Rad<sup>1</sup>, Duran Gonzalez<sup>1-2</sup>, Kendall Nelson<sup>3</sup>, Zach Jacobs<sup>3</sup>, Taylor Stallings-Pinnick<sup>3</sup>, Farnoosh Saeedinejad<sup>1-2</sup>, Mark Reeves<sup>3</sup>, Twyman Clements<sup>3</sup>

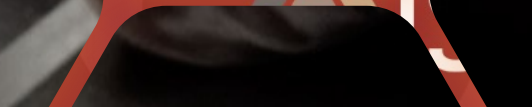
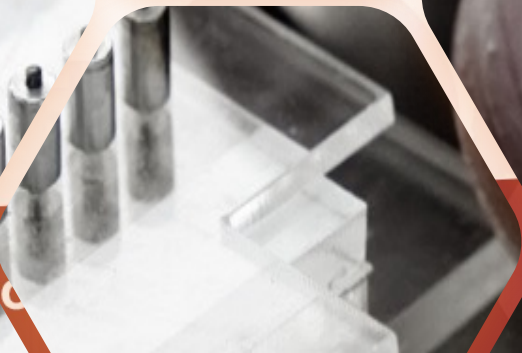
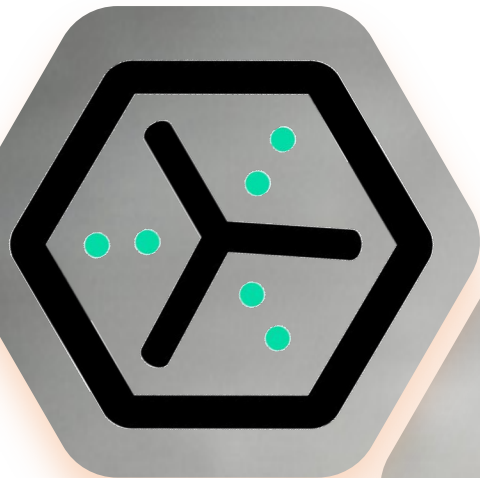
<sup>1</sup> Encapsulate Inc, Farmington, CT, <sup>2</sup> Institute of Materials Science, University of Connecticut, Storrs, CT, <sup>3</sup> Space Tango, Lexington, KY

**AIRBUS**

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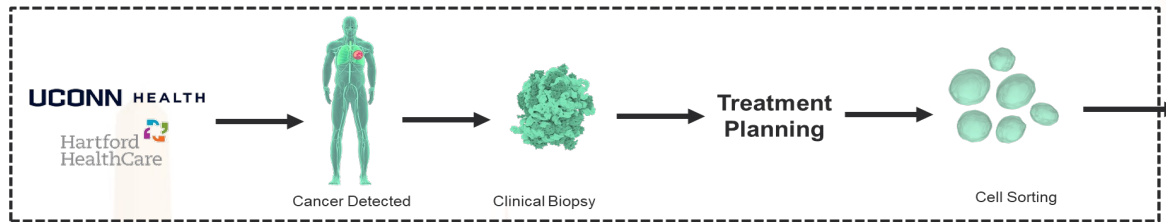






# ISSNL/CASIS Technology in Space Award GA 2019-7750

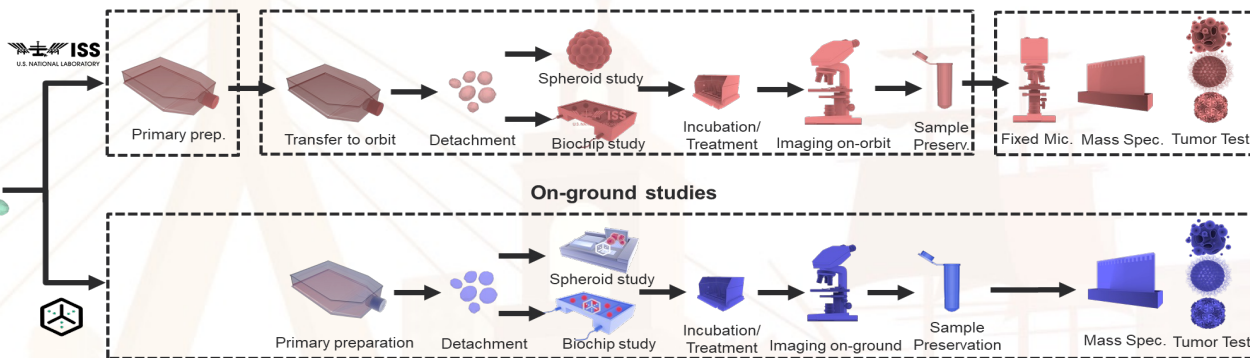
Clinical and ex vivo preparations



Pre-flight preparation

In-flight studies

Post-flight analysis



2024 Technical Sessions





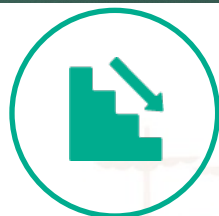
# The conventional process of decision-making has **deficiencies**

Majority of chemotherapy cycles are both ineffective and toxic.



## Ineffective chemotherapy cycles

On average ~**6 cycles**,  
**15 months**, and **\$150K-500K** in  
chemotherapy-related costs <sup>1,2</sup>



## Progressively lower chances for treatment

Ineffective treatment cycles =  
increased risks of  
**drug resistance** ↑  
**metastasis** ↑  
**cancer progression** ↑ <sup>3,4</sup>



## Unsuccessful treatment costs are unbearable

With unsuccessful round,  
cancer patients are **147%** more  
likely to require emergency,  
**75%** more to re-hospitalization,  
and **3X** more costs <sup>5</sup>.



## 25% fatality rate due to chemotherapy toxicity

Only due to side effects of  
chemotherapy, and **not cancer**  
**progression** <sup>6</sup>.

<sup>1</sup> Lancet Oncol. 20.6 (2019): 769-780.

<sup>2</sup> Cancer Research UK. <https://shorturl.at/vzGKv>

<sup>3</sup> Cancer Res 79.18 (2019): 4567-4576.

<sup>4</sup> Adv Pharm Bull. 7.3 (2017): 339-348.

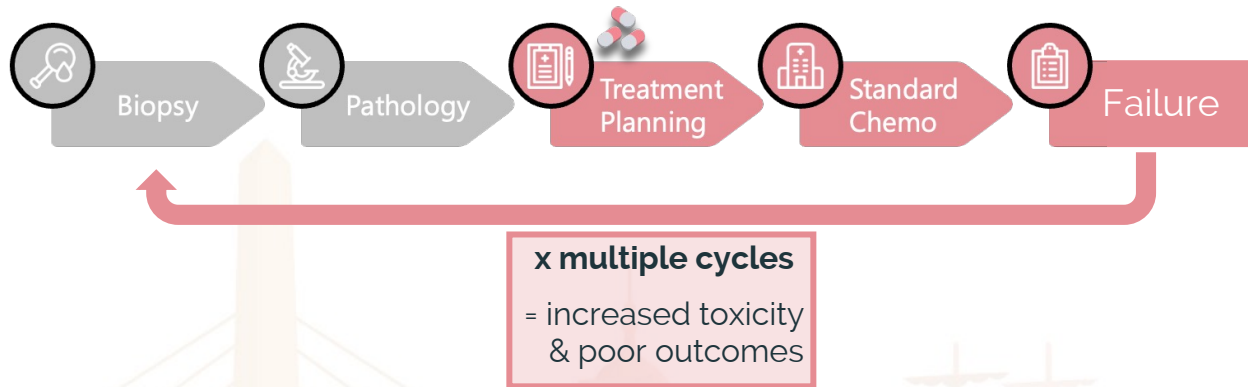
<sup>5</sup> Emergency Cancer Care, 11 (2022): 4.

<sup>6</sup> UK National Confidential Enquiry into Patient Outcome and Death



Multiple cycles = increased mortality, poor outcomes.

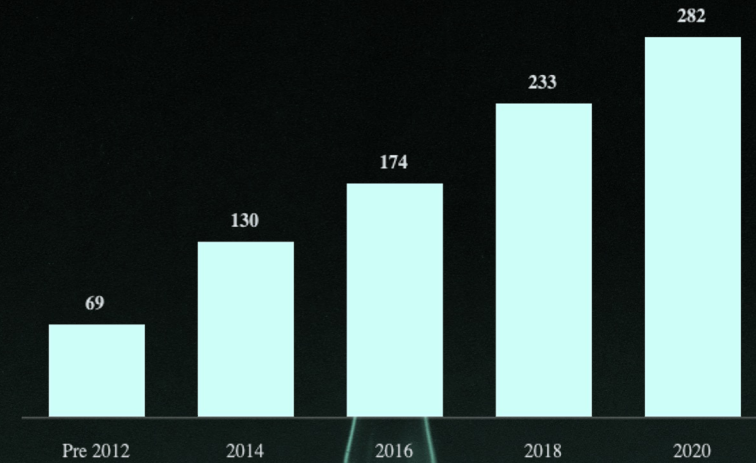
Treatment planning is an **iterative, trial and error**, and **sequential** process



This could be anticipated with a **functional assay**



There is an increase in the number of **approved drugs**





# Solution: Encapsulate

We create **therapeutic response profiles** of patients for oncologists to administer life-saving treatments



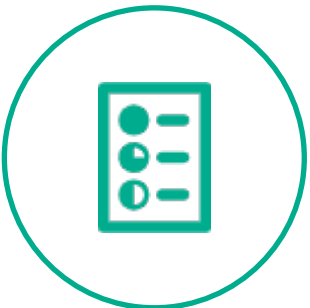
nCapsule

The **biochip** grows patients' cancer cells as **microtumors** outside the body.



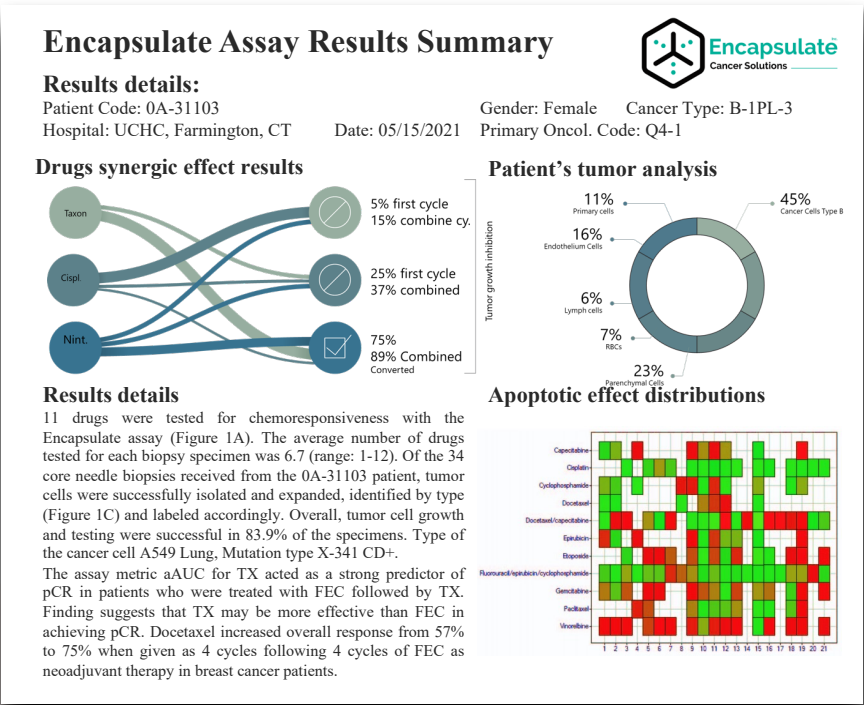
nCapsulizer

Our **automation system**



nVision

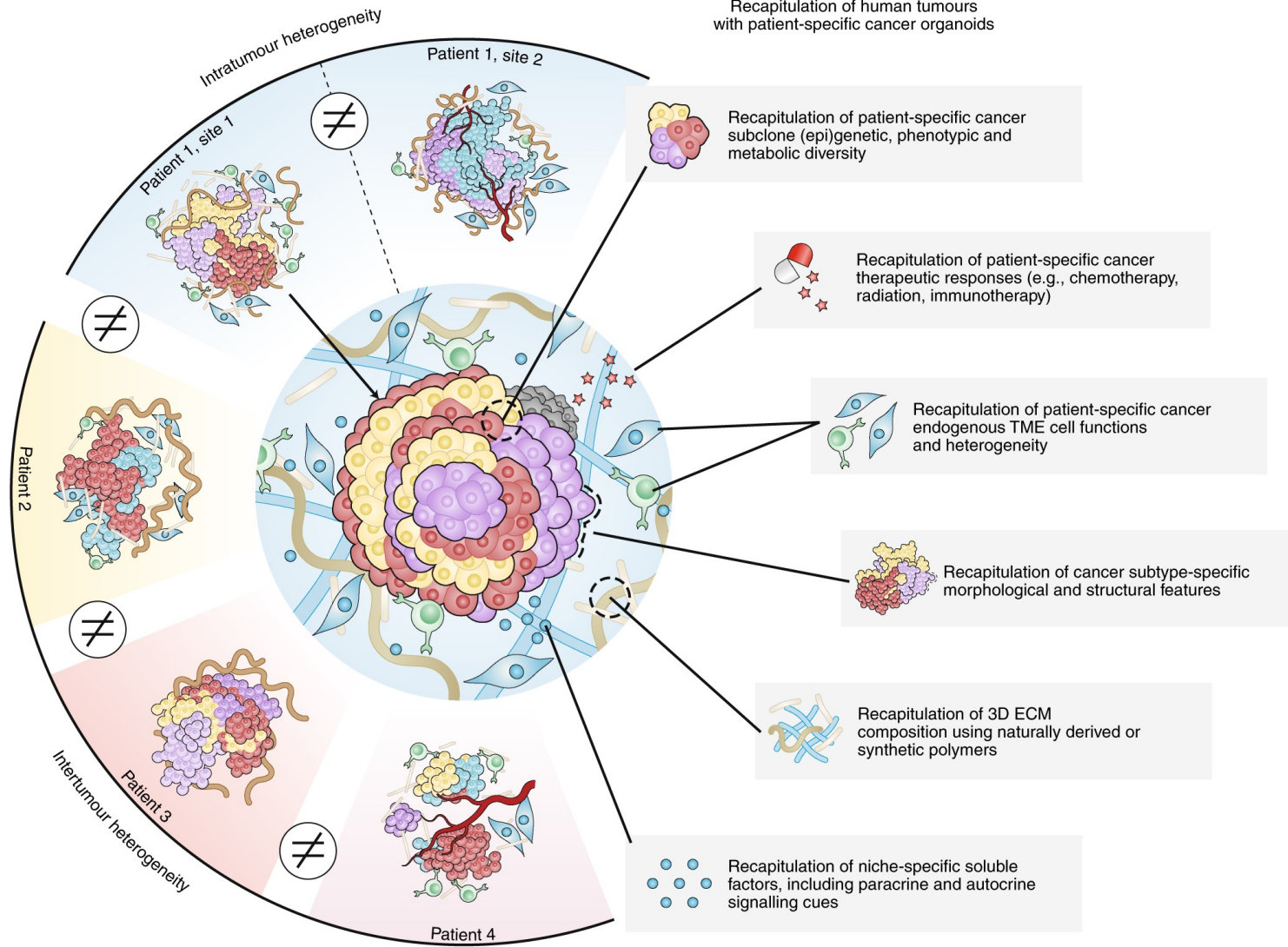
The **report** provides analytical insights **to oncologists** on patients' response profile to potential treatments.



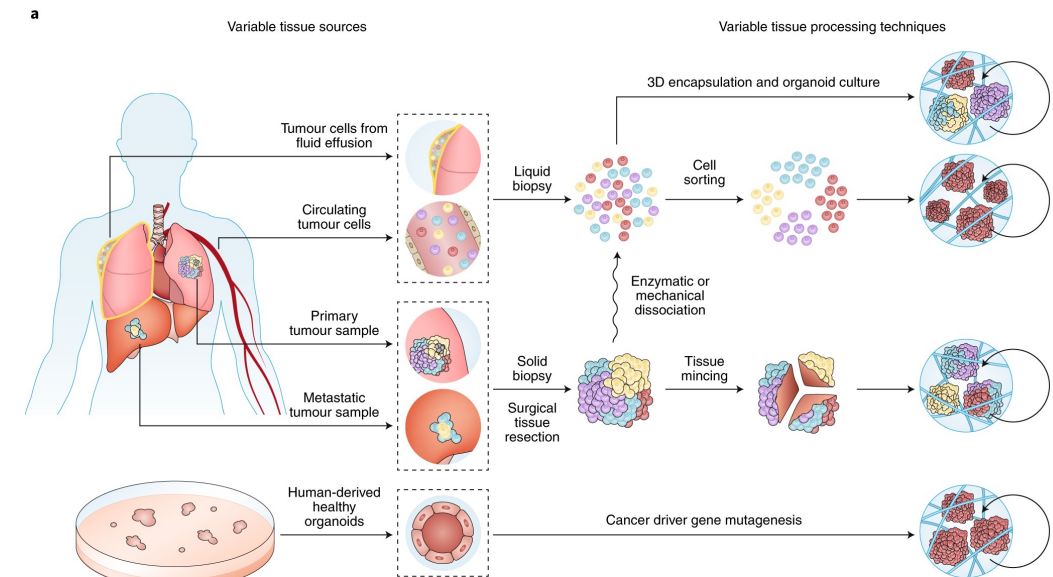
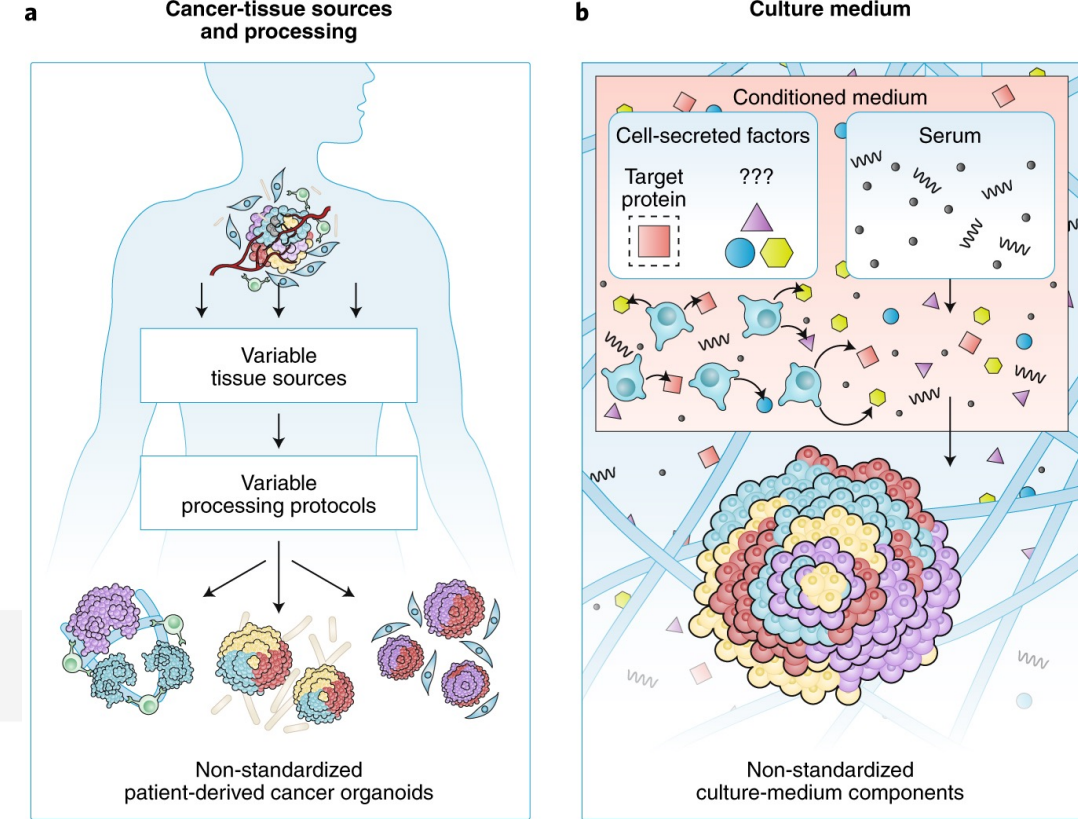


Purpose	Transformative precision oncology systems to determine the most effective cancer treatment plan for each patient				
Products Application Readiness Level	<b>nCapsule</b> Best Treatment Clinically Proved	<b>nWell</b> High throughput Data Clinically Proved	<b>nDoser</b> Best Dose In Clinical Tests	<b>nVasive</b> Ultimate tumor fate InSPA/NASA	<b>nCapsulizer</b> Fully Automated InSPA/NASA
A Unique Technology with significant Value Propositions	With our multigel technology, cancer cells are embedded among the natural stromal cells. All microtumors have hypoxic cores that retains resistant cells, and predefined boundaries provides a clear baseline for tumor invasion measurements.				
Markets	Tumor-on-a-chip with multi-gel design				
	Heterogeneous Spheroids with hypoxic core				
	Bioreactor with cyclic flow, controlled CO <sub>2</sub> & humidity				
	Pre-defined shape, size, x-y-z coordination, & automated				
	<b>Clinical Tool</b>  <b>Pharmaceutical Tool</b>  <b>Medical Device</b>  <b>Research Tool</b>	Simple regulatory process with CMS/CLIA clearance   CPT Codes are established Significant social and financial impact in the nation   \$19B+ market   Primary focus: Colon & Pancreas  Encapsulate owns a comprehensive biobank is ready for clinical trial predictions No regulatory is required   Faster revenue generation path   \$7B+ market  Class II FDA Approval required Larger market with a nationwide and international expansion through partnership with chain labs  Sales as a research tool, through licensing/direct sales, Space cancer research   Academic laboratories   Private biotech companies			

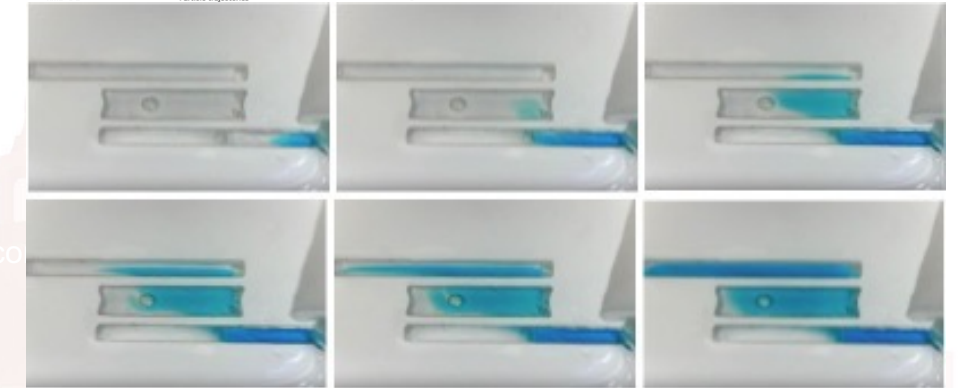
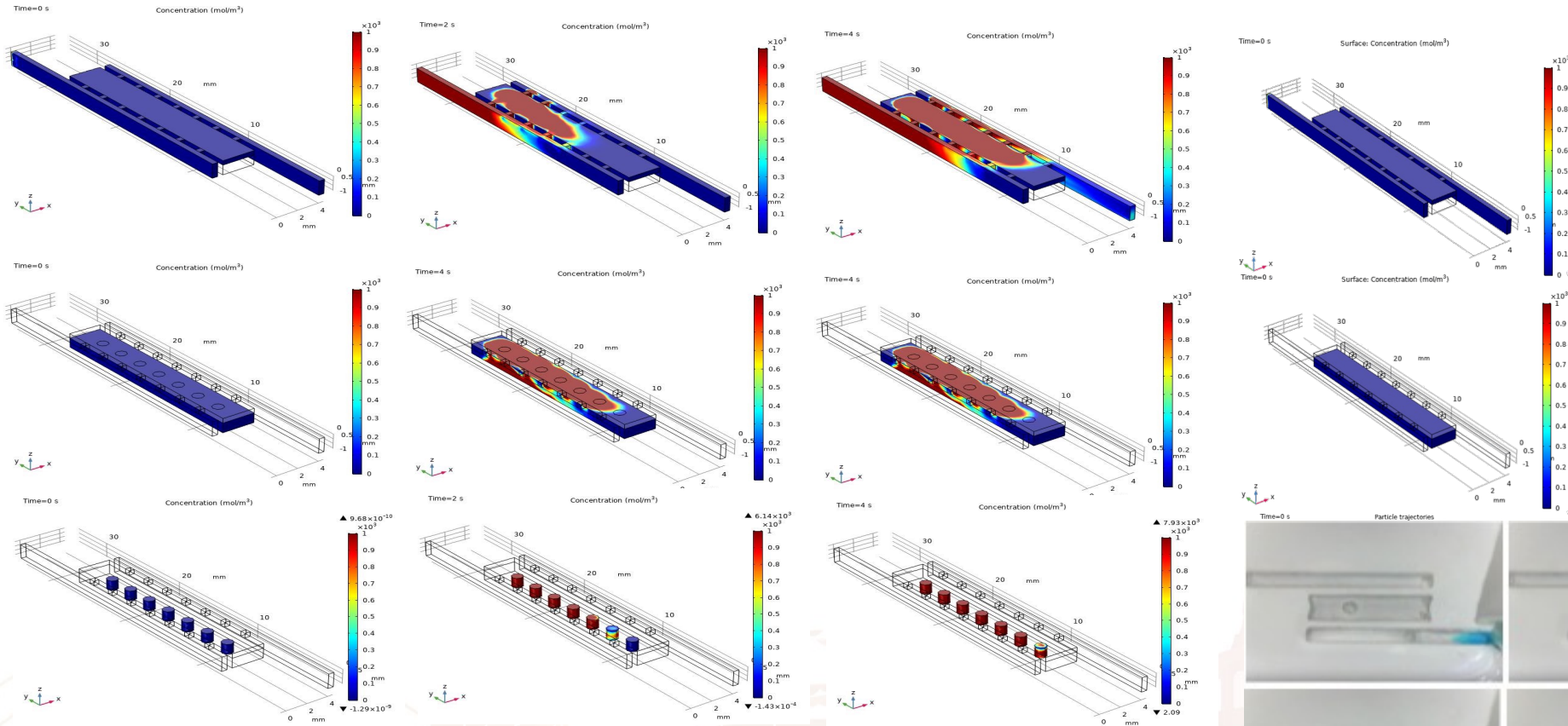




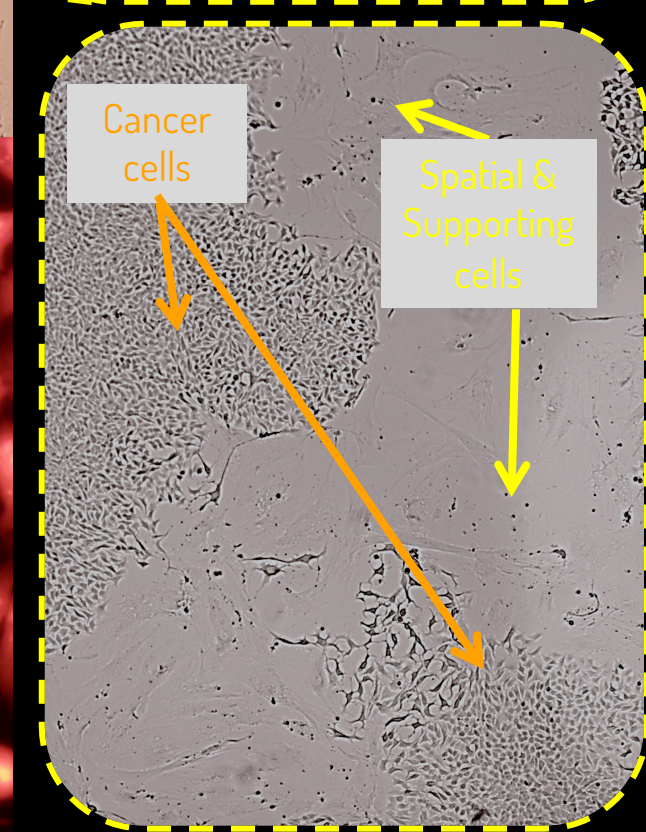
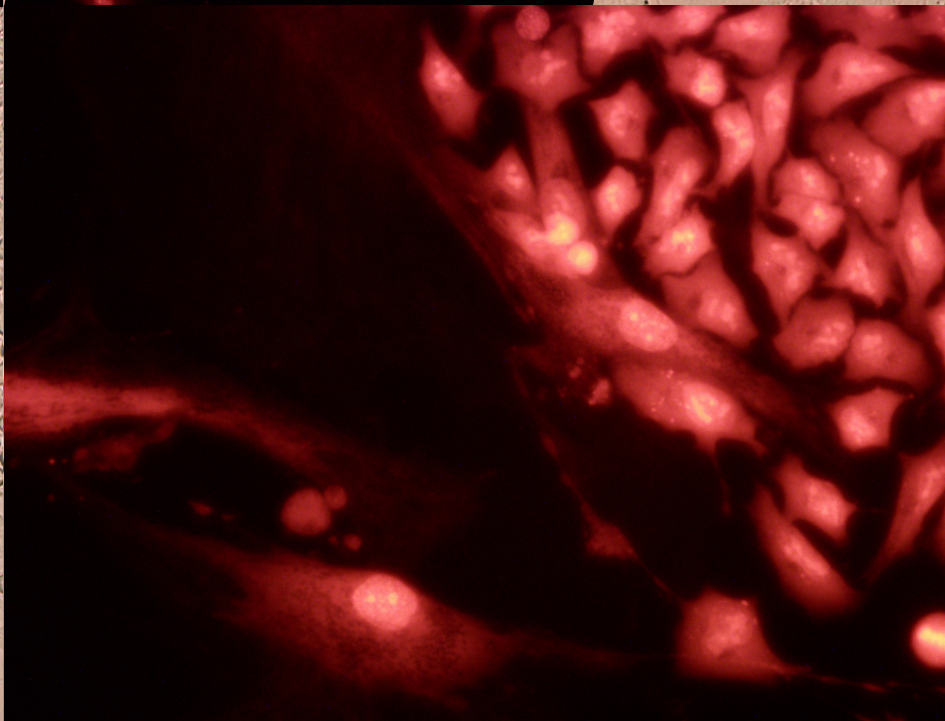
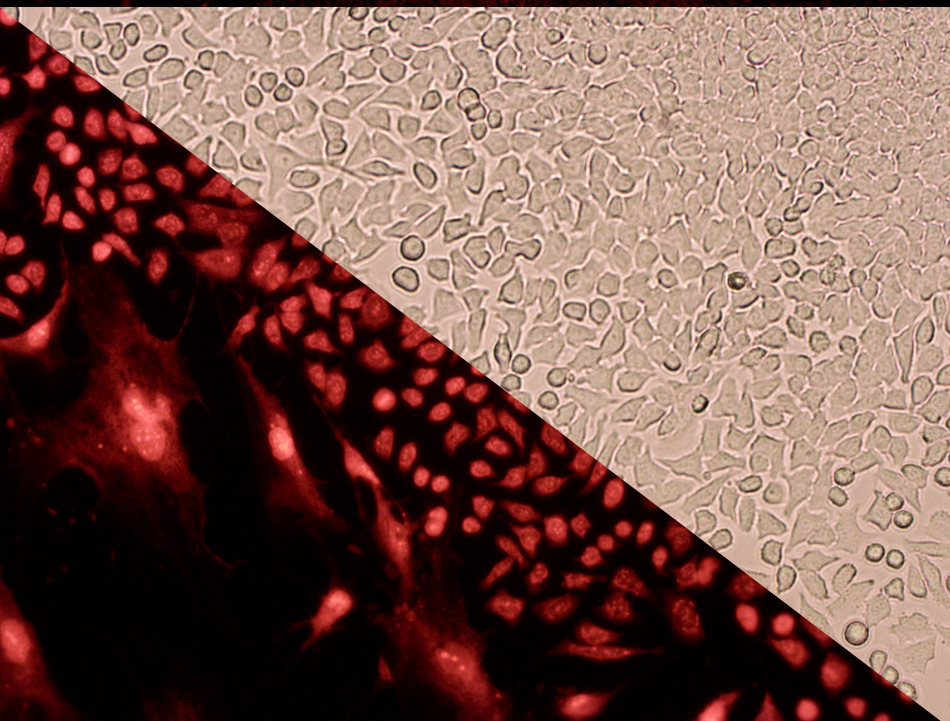
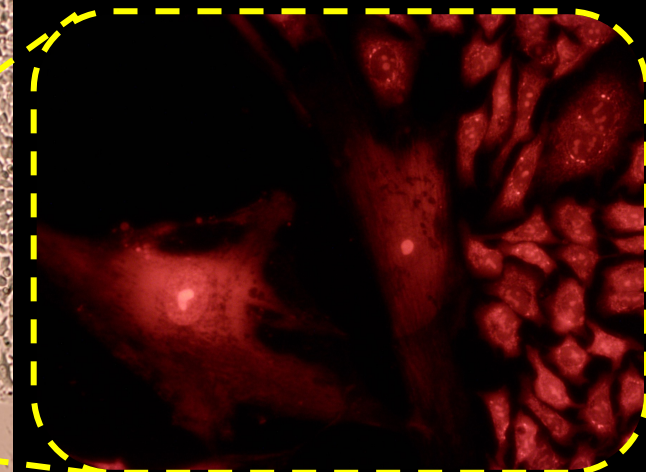
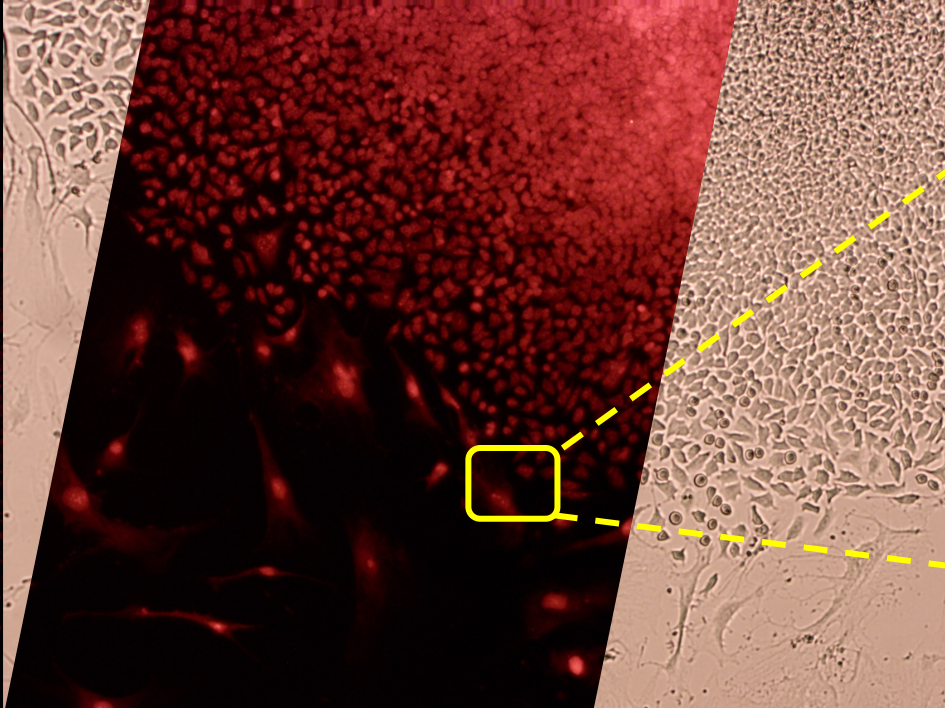
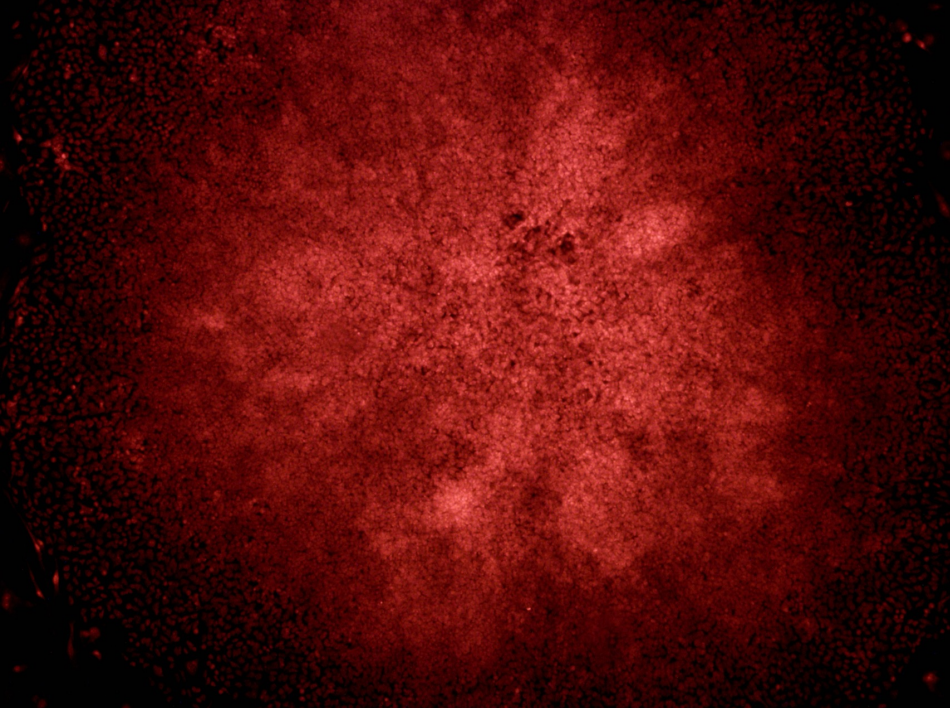
Bauer L. LeSavage et al, Nature Materials, 2022



# Mass Transfer and Diffusion Simulations

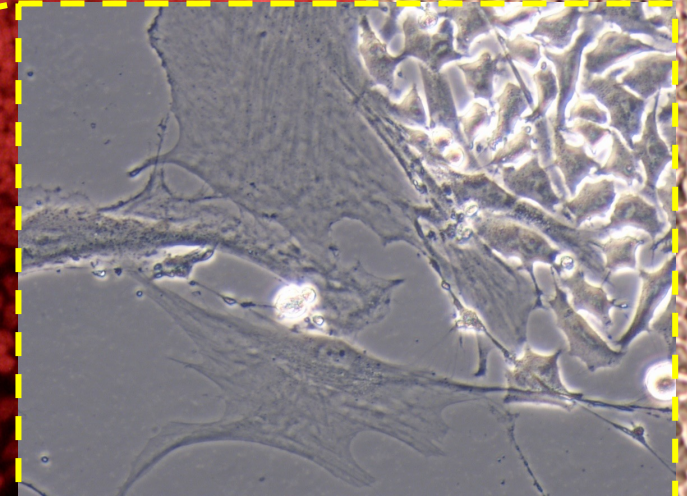








Patient tumor grown in a microtumor form, labeled by our NanoNest® fluorescence tag (pre-chemo).



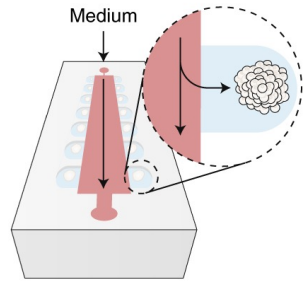
Cancer cells

CAF cells  
(supporting)

- Our optimized protocol for tumor dissociation, along with our optimized enzymatic cocktail enable us to preserve high cell viability and grow patients' specimens in their innate biological status.
- In long-term studies (50 days+), the cells can create their own natural tumors in our system.
- Heterogeneous tumor cells reorient themselves with a cancerous core surrounded by supporting stromal-like cells.



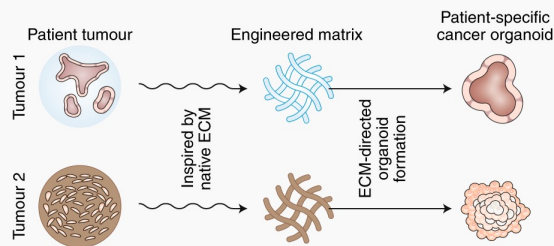
## Bacteria Spheroids for antibiotic evaluation



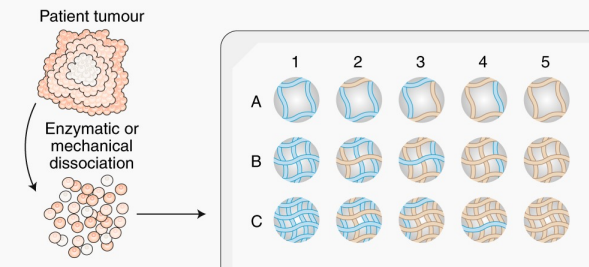
Organoid-on-a-chip and microwell culture

- Enhances control of nutrient transport to organoids
- Enables standardization of organoid size
- Enables modular assay and cell-type integration

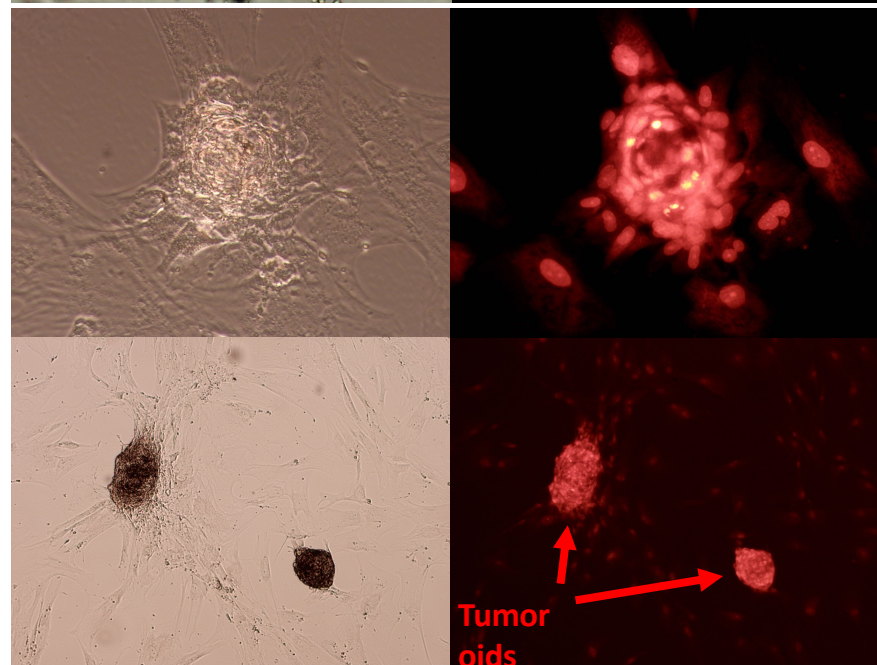
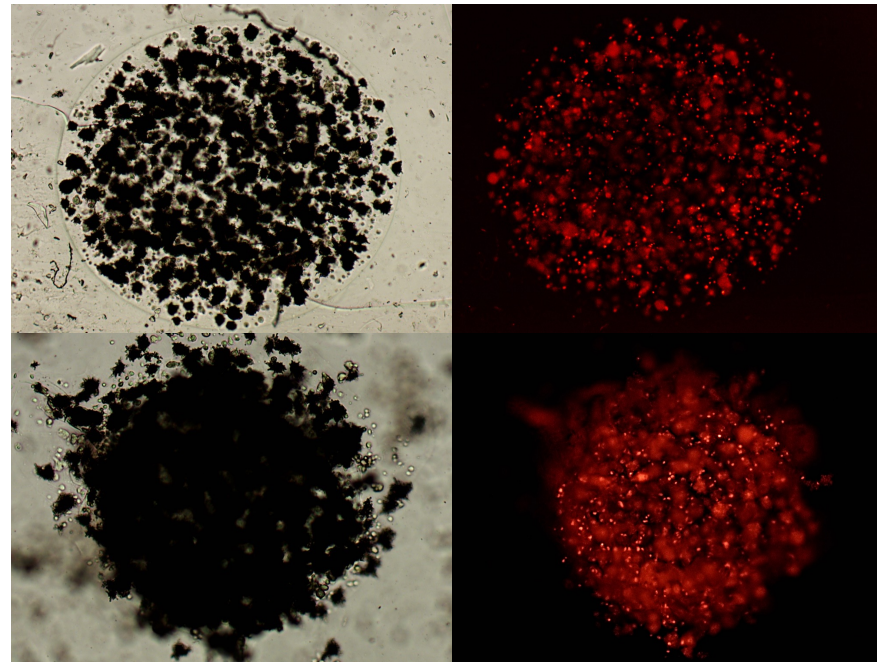
### b Patient- and disease-specific modelling



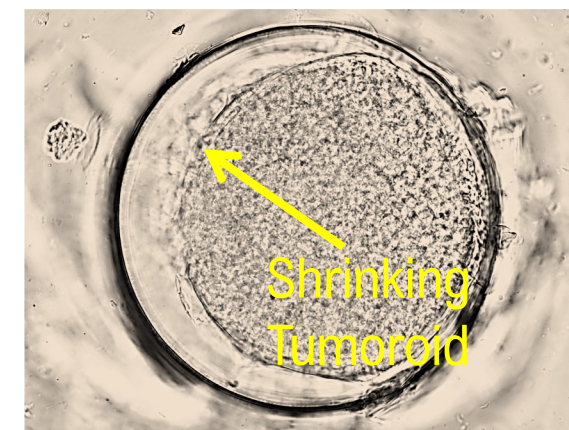
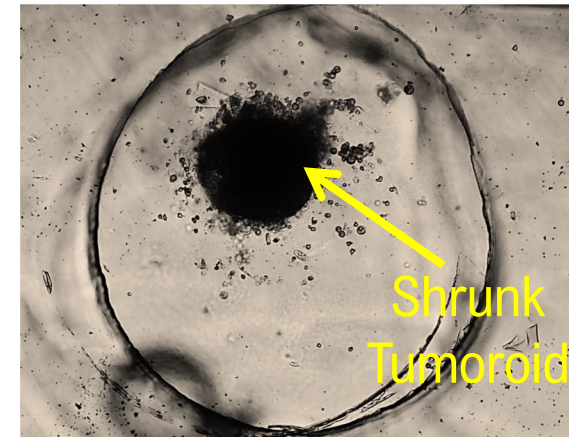
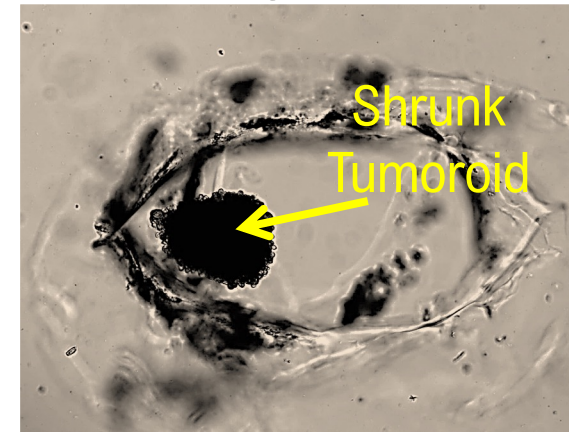
### c Screening ECM parameters



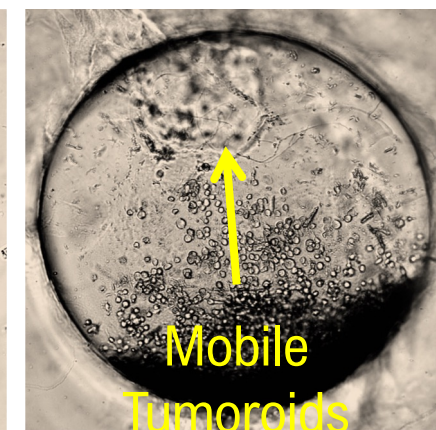
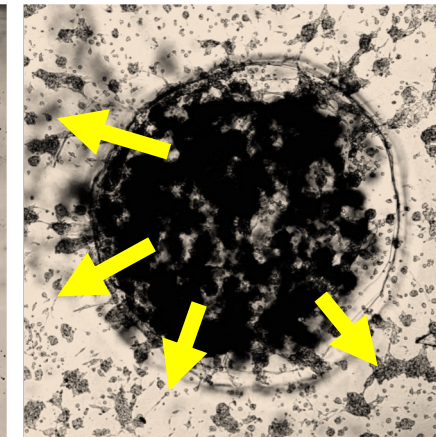
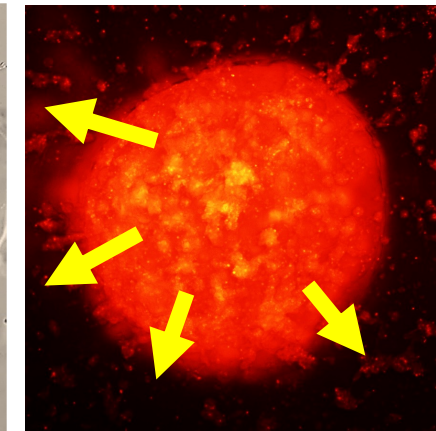
Next-generation cancer organoids, Bauer L. LeSavage et al, Nature Materials, 2022



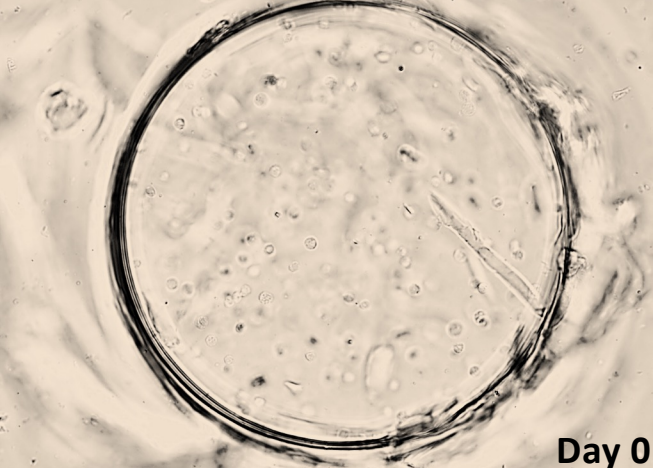
## Shrinking Tumoroids



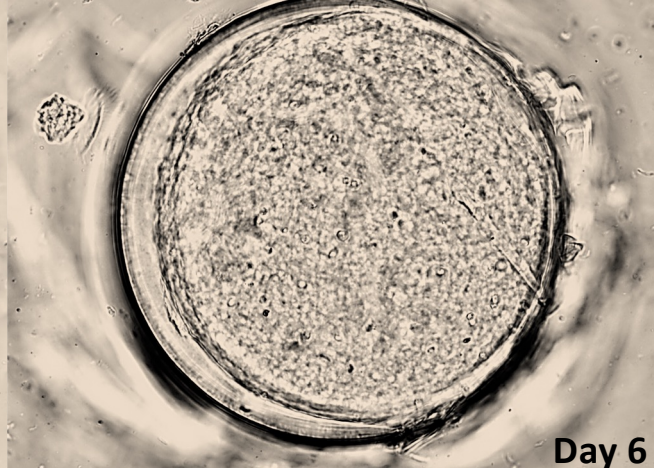
## Aggressive tumoroids







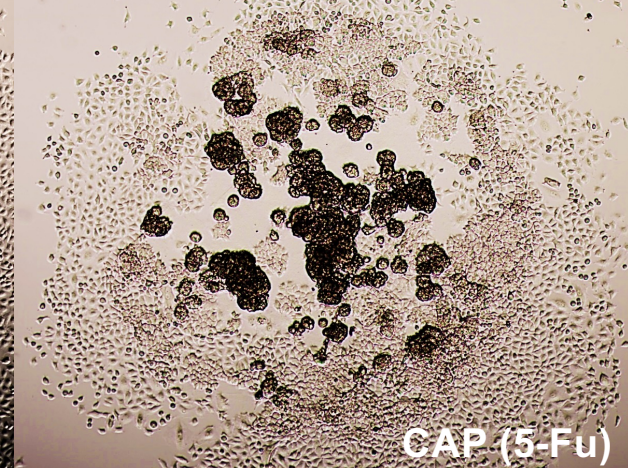
Day 0



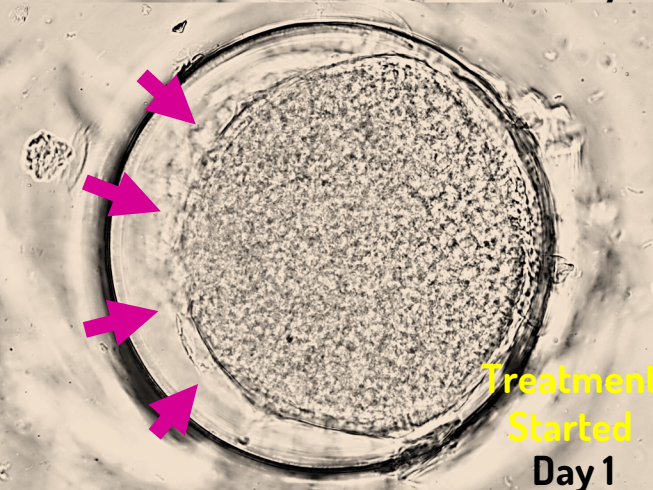
Day 6



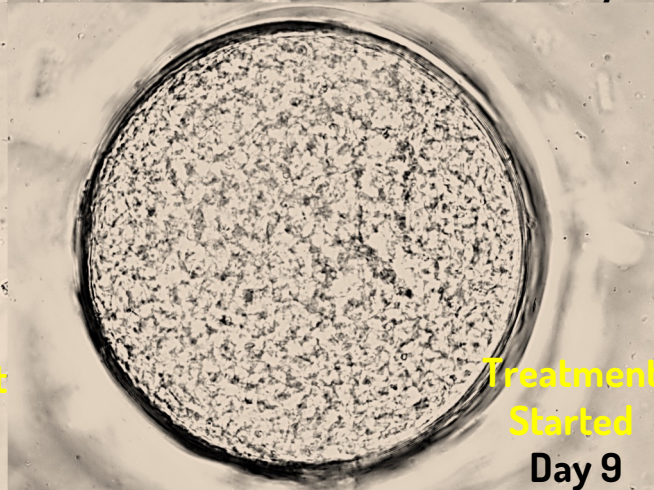
No treatment



CAP (5-Fu)



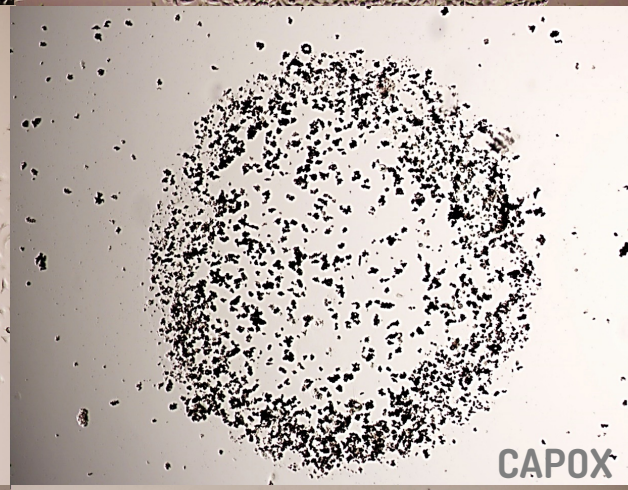
Treatment  
Started  
Day 1



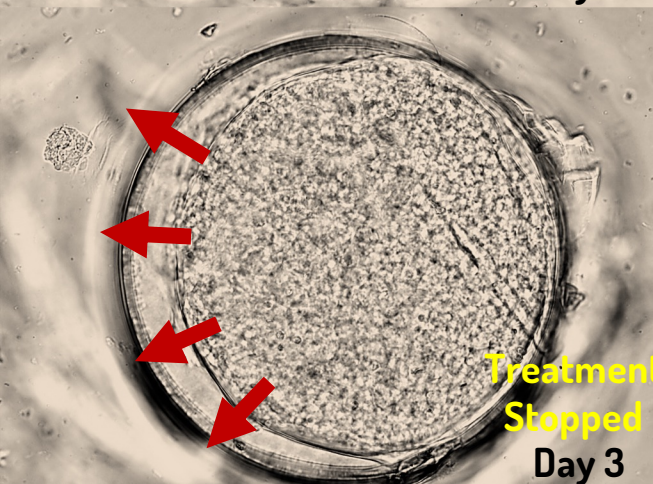
Treatment  
Started  
Day 9



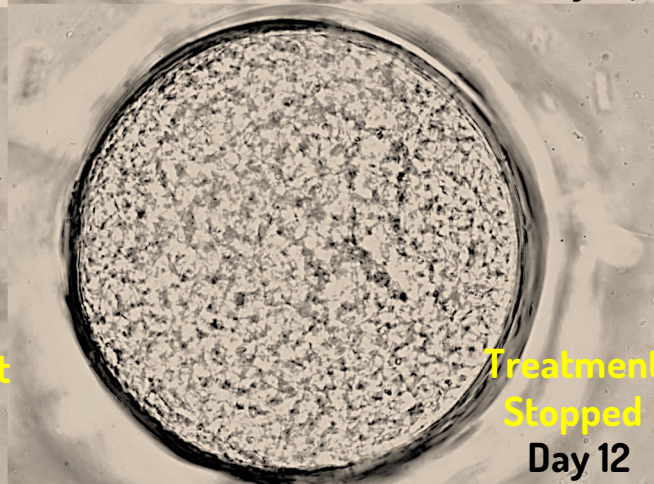
GEM



CAPOX



Treatment  
Stopped  
Day 3



Treatment  
Stopped  
Day 12



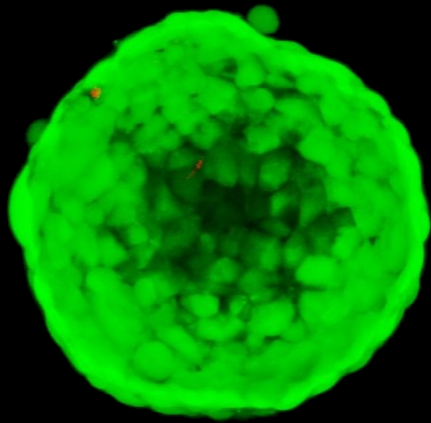
FOLFIRI



FOLFOX

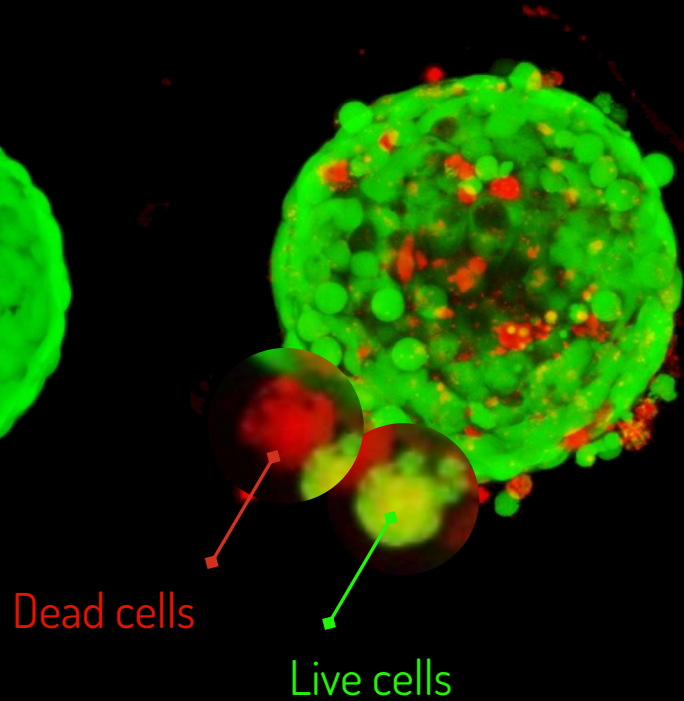


Human lung cancer



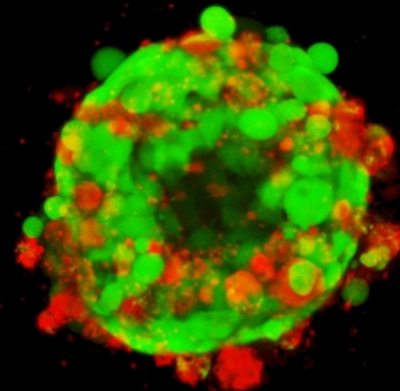
DRUG A

*(low concentration)*



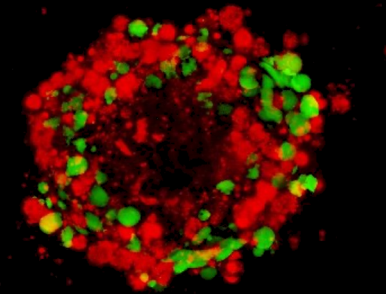
DRUG A

*(high concentration)*



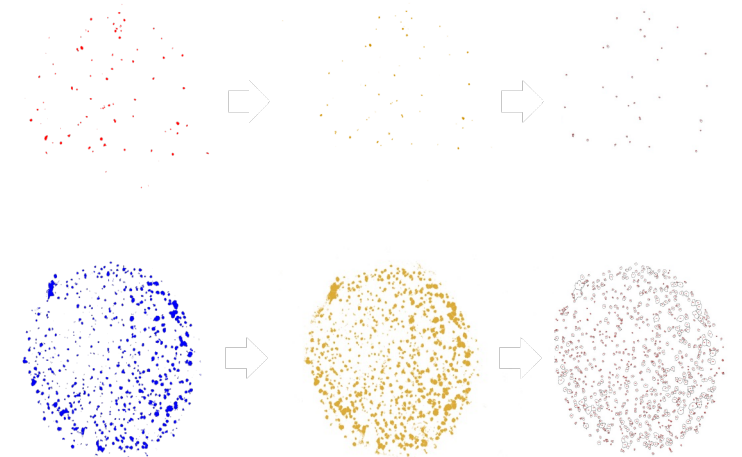
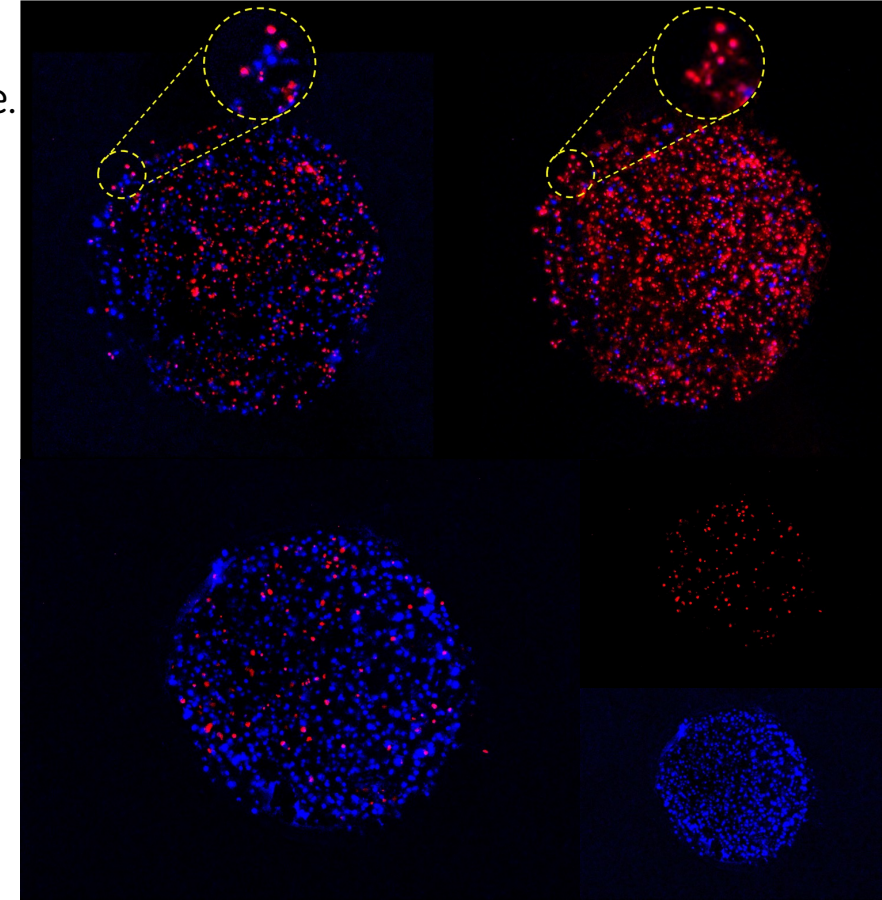
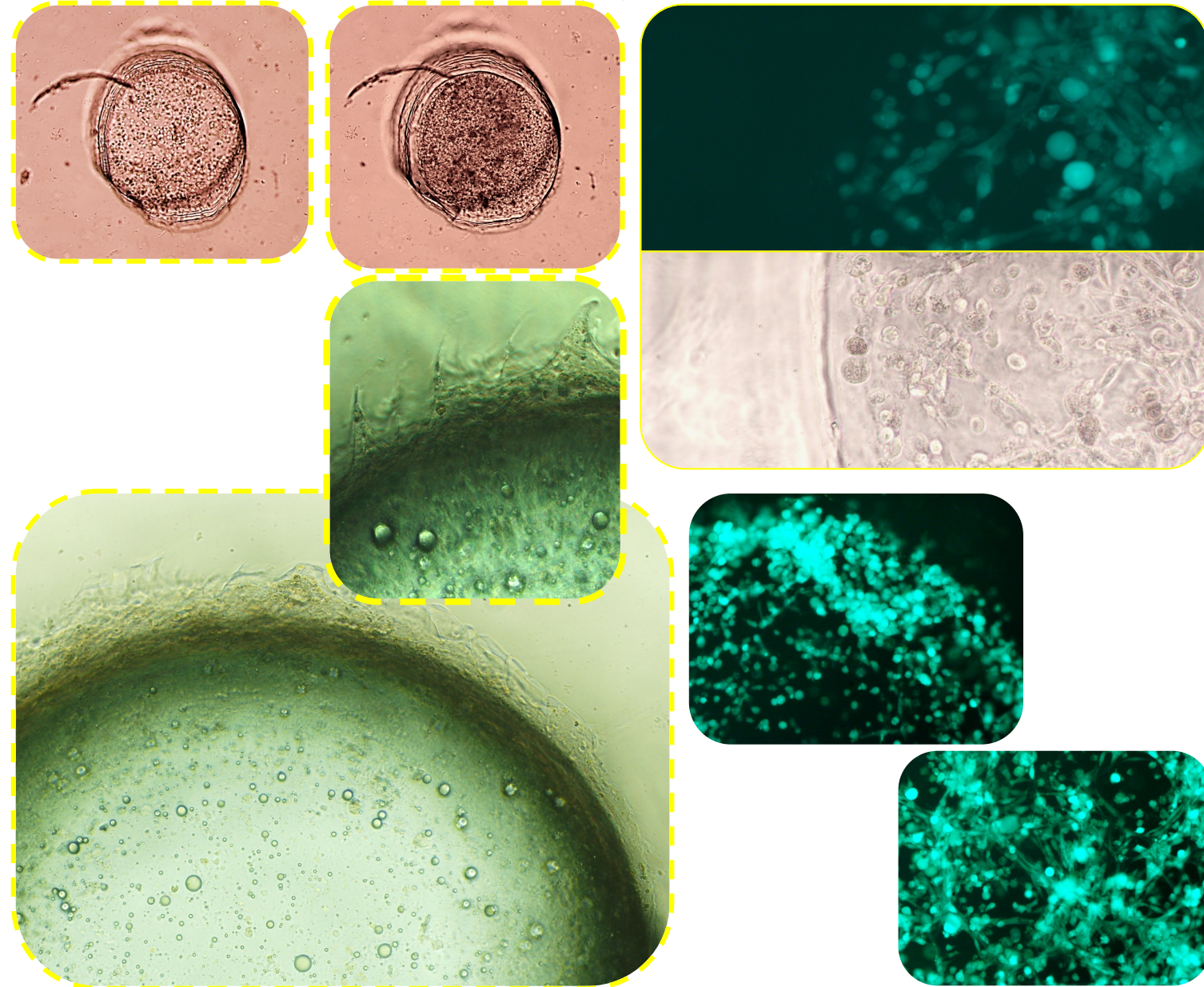
DRUG B

*(low concentration)*



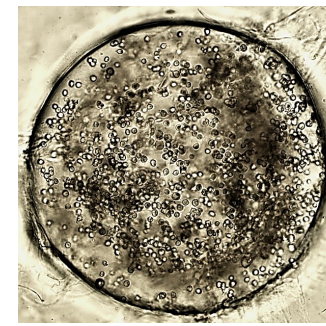
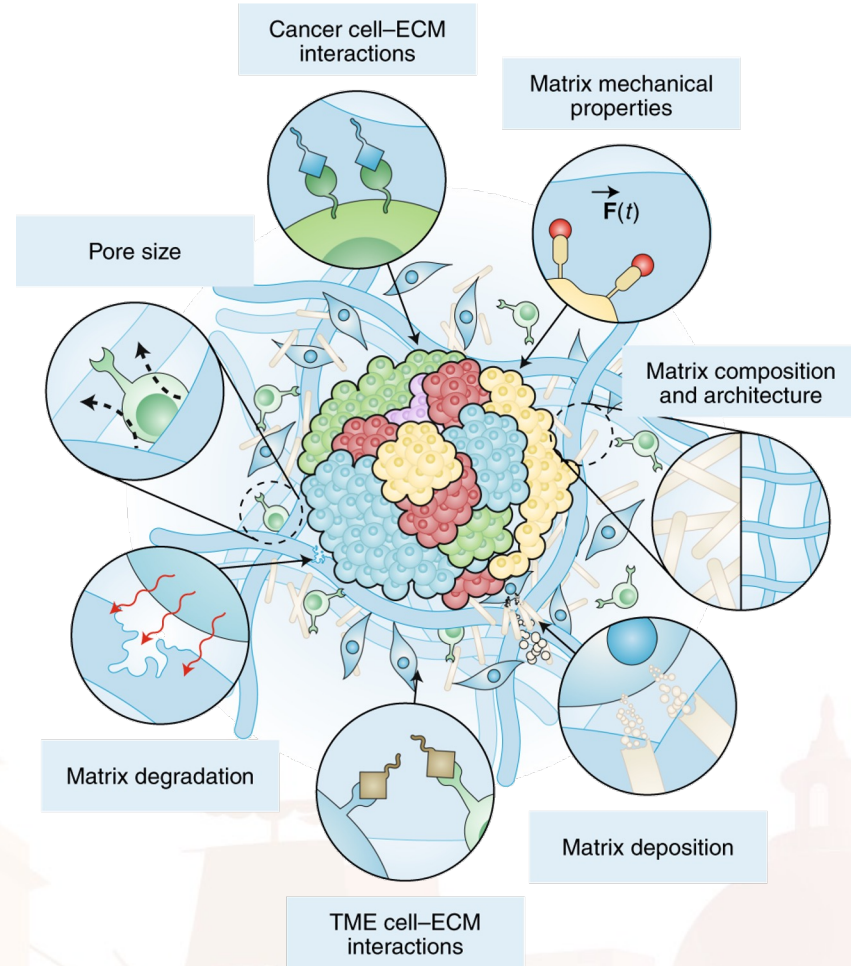
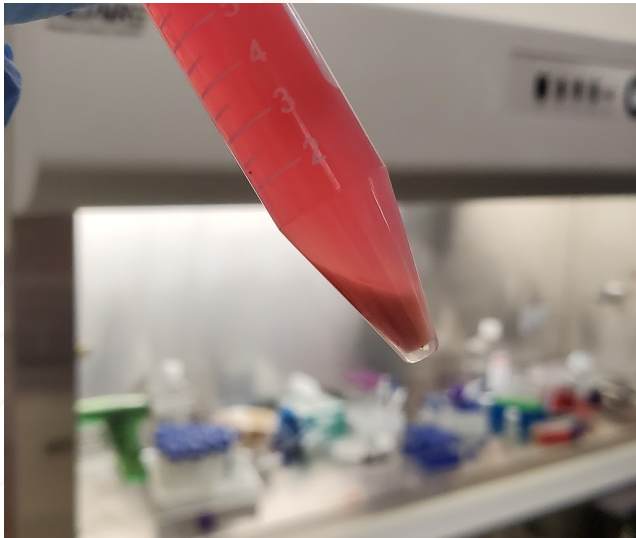
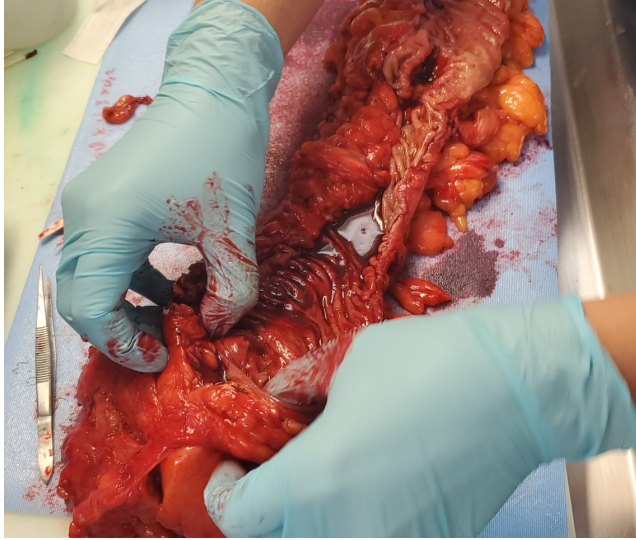


- nCapsule microtumors can be treated in 2 hours and start to proliferate within 24 hours.
- The size, the shape, and the density of these tumors are reproducible and easily modifiable.
- Tumor invasion can take place in 7 days post microtumor fabrication.

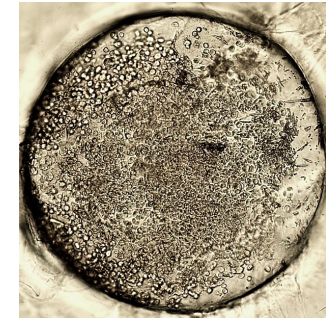




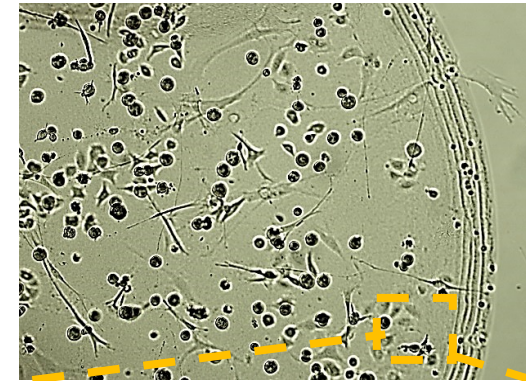
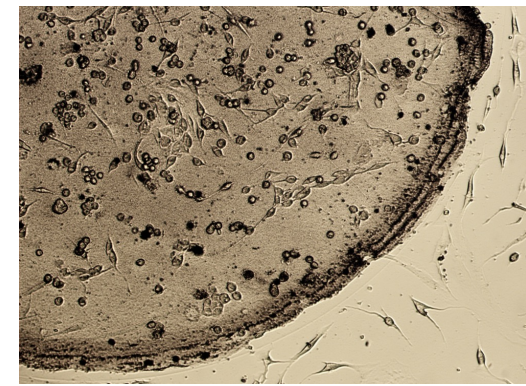
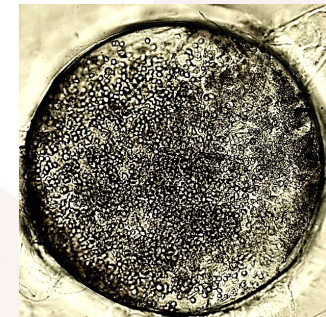
# Tumoroids Heterogeneity and Growth



After 24 hours



After 48 hours





## First round response:

Complete: 8

Partial: 7

Non-responder: 15

Whole  
treatment  
success  
(5-year  
survival):  
Failed: 19  
Success: 11

II: 4  
III: 8  
IV: 18

30 Bio-banked  
patient samples  
21 Cell lines

Total  
of 74  
rounds

CR: 28  
PR: 15  
SD: 6  
PD: 25

20 White  
5 African-  
American  
4 Latino  
1 Asian

14  
Women /  
16 Men

Biopsies  
from:  
Colon,  
Rectum,  
Sigmoid,  
Lung, &  
Ovary

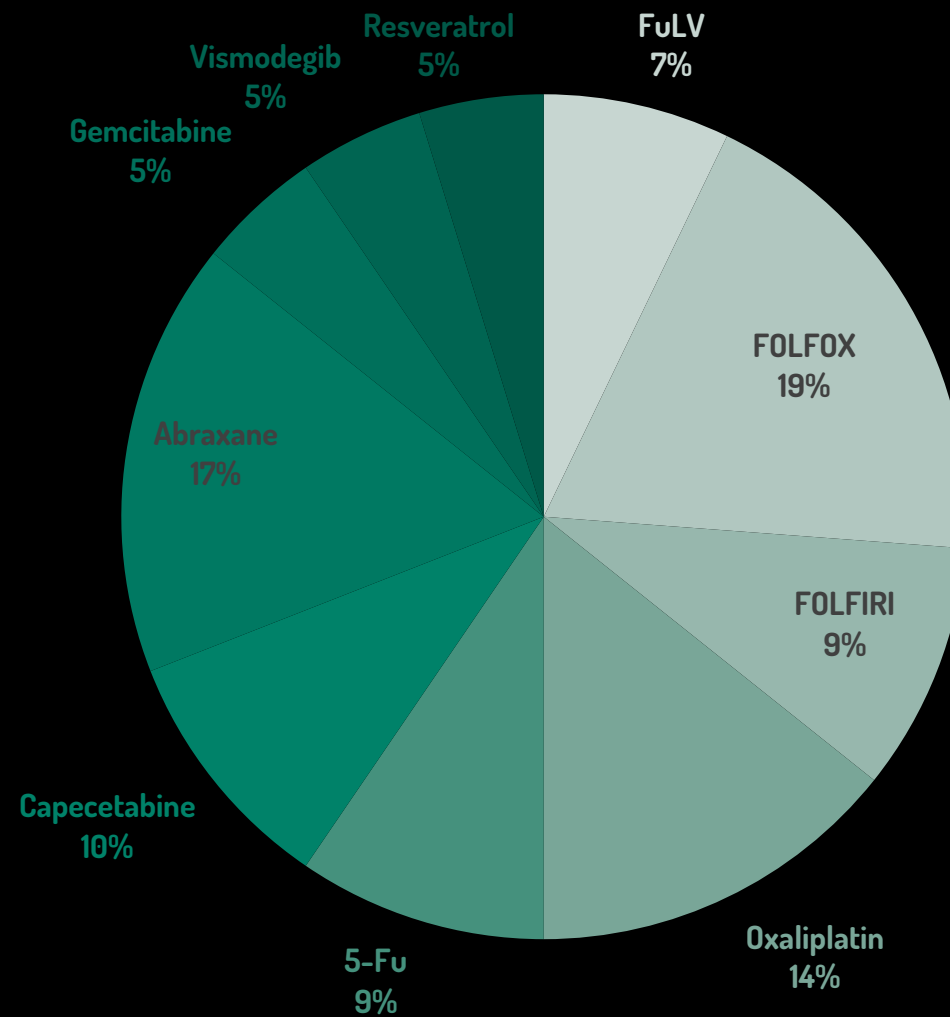
Total of  
30  
Prospecti  
ve  
30  
Retrospe  
ctive

More  
than  
7000  
µTumors  
to date

Ages: 38-  
82

1 Current  
Smoker  
8 Previous  
Smoker  
21 Non-  
smoker

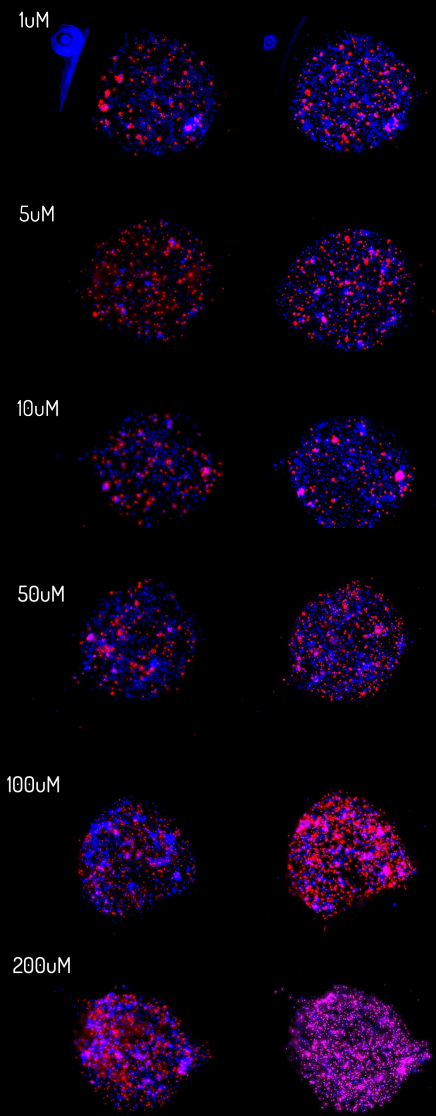
Number of responders in the first 30 patients



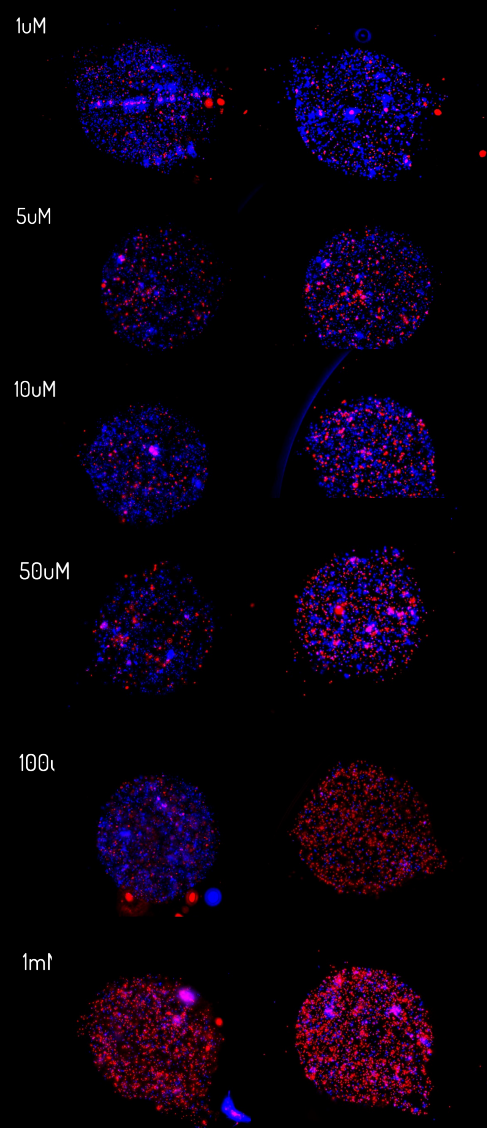




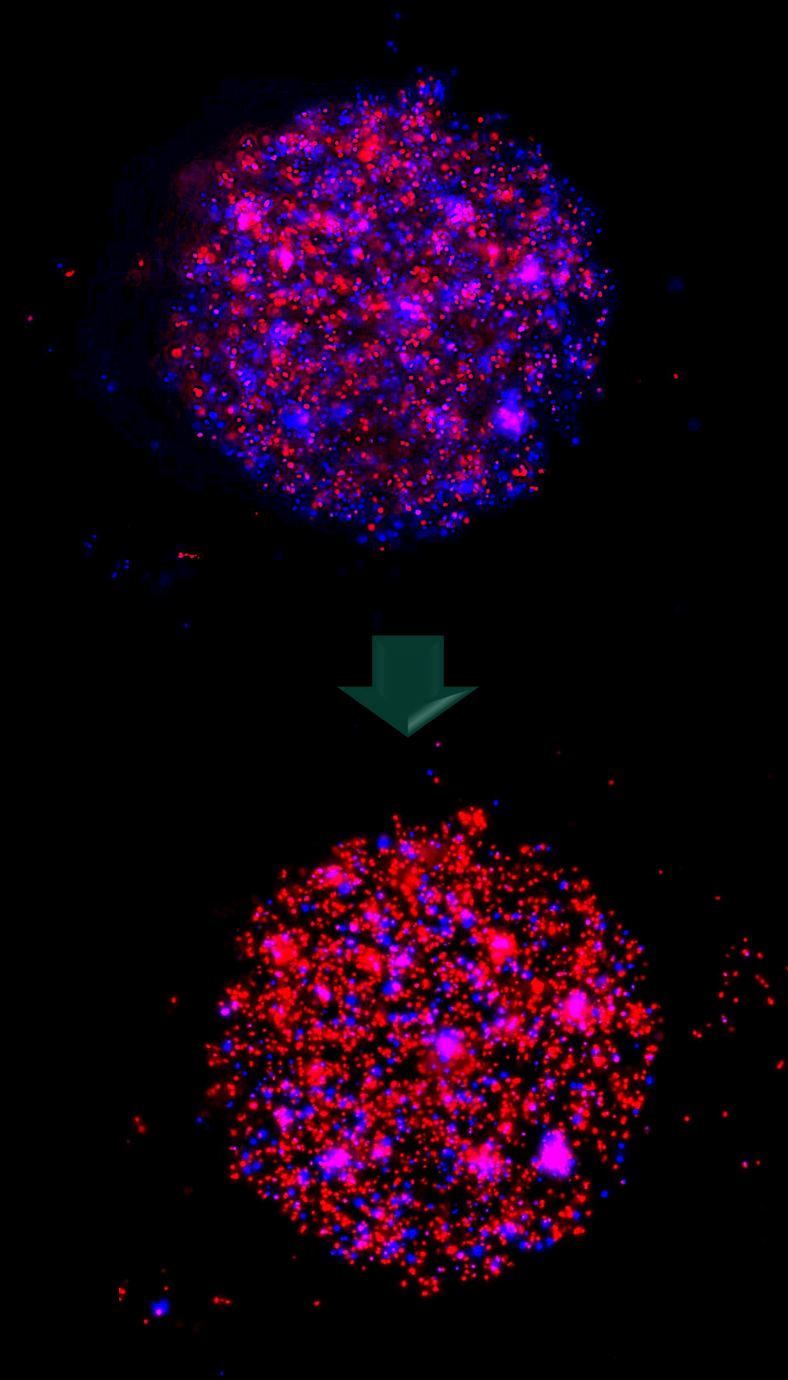
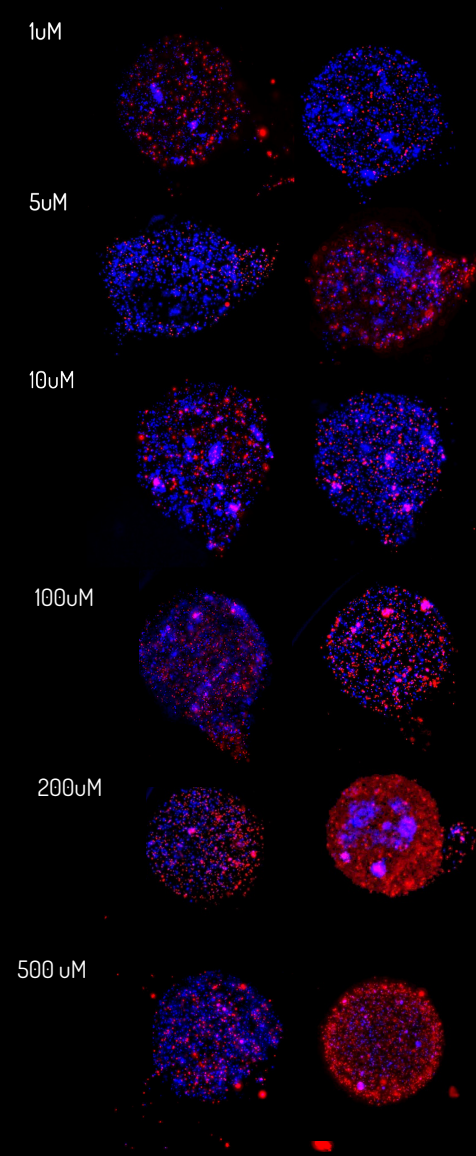
OX: Day 3 → day 7



FOLFOX: Day 3 → day 7



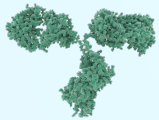
FOLFIRI: Day 3 → day 7



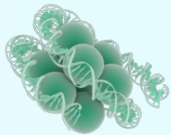


- ✓ Best combination with other drugs
- ✓ Minimal effective dose
- ✓ Resistance development
- ✓ Genetic mutations after treatment
- ✓ Microbiome alterations
- ✓ Tumor metastatic response
- ✓ Pre- & post- treatment mutations
- ✓ RNA/DNA seq
- ✓ Proteomics and metabolomics
- ✓ Drug diffusion model within ECM

Proteomics



Metabolomics



Direct Toxicity



Follow-up mutations



Dose

- ✓ Continuous Viability Decrease
- ✓ <20% Viability

Time

- ✓ No increase in cell #
- ✓ <100 Alive per tumoroid

Resistance

- ✓ Genetic Mutations
- ✓ Slope of the size measurements
- ✓ No z-axis variation

Single Agents

- ✓ Combinational Therapies
- ✓ Single Agent Therapies
- ✓ Consecutive therapies

## A translational tool to screen compounds

Cancer types

6

# of cell lines available

25

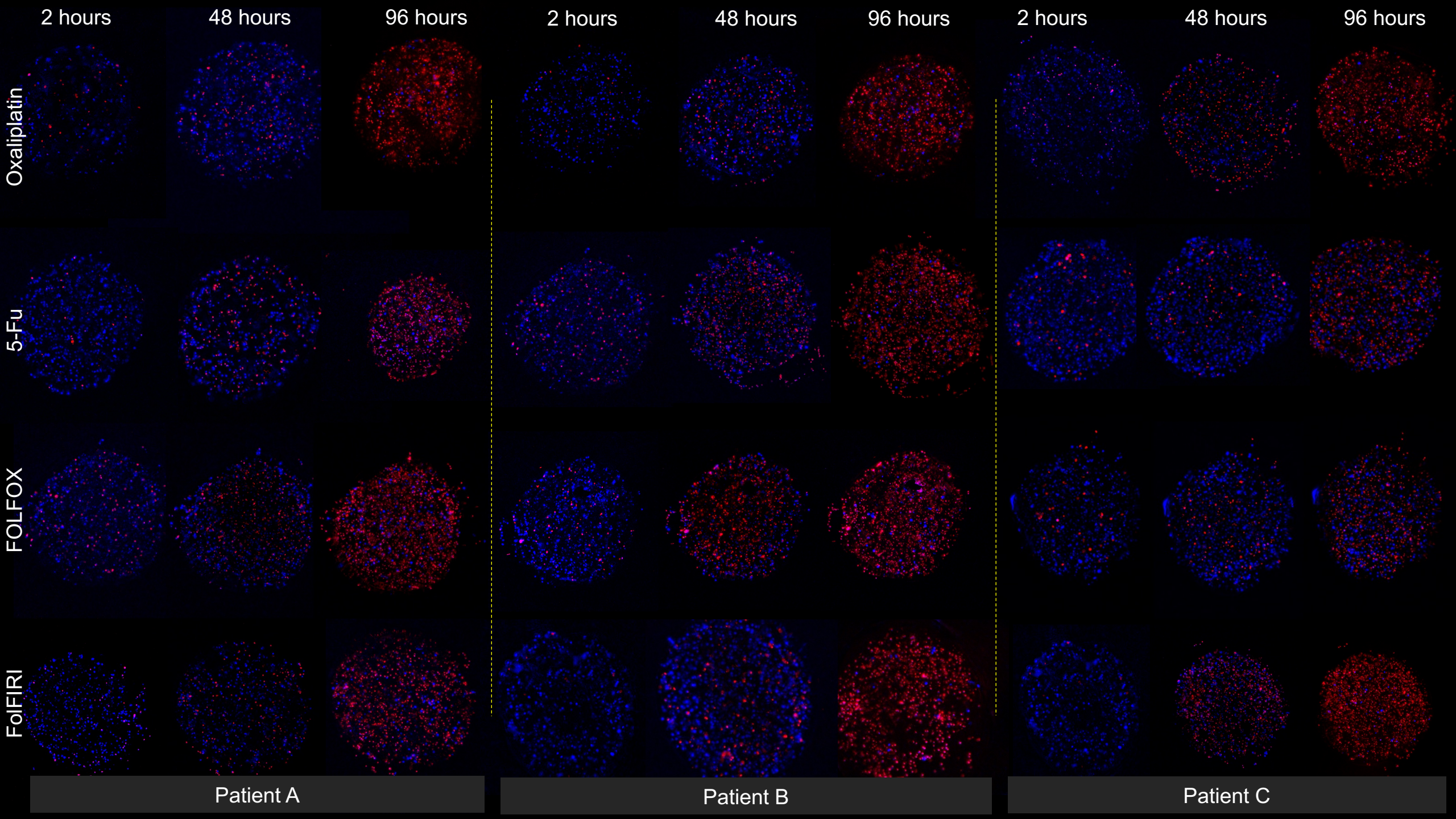
# of patient samples

45

## Patients can be sorted by:

- Demography (gender, age, ethnicity, etc.)
- Cancer stage (II to IVB)
- Metastatic vs. Non-Metastatic
- Chemo-sensitive vs. Resistant
- Pre-op chemo vs. naïve
- Genetic mutations
  - We have a 50-gene mutation panel including APC, BRAF, CDKN2A, EGFR, ERBBs, FGFR, GNAS, JAKs, KDR, KRAS, PIK3CA, RBI, PTEN, SMAD4, TP53, dMMR, ...







# Clinical Results

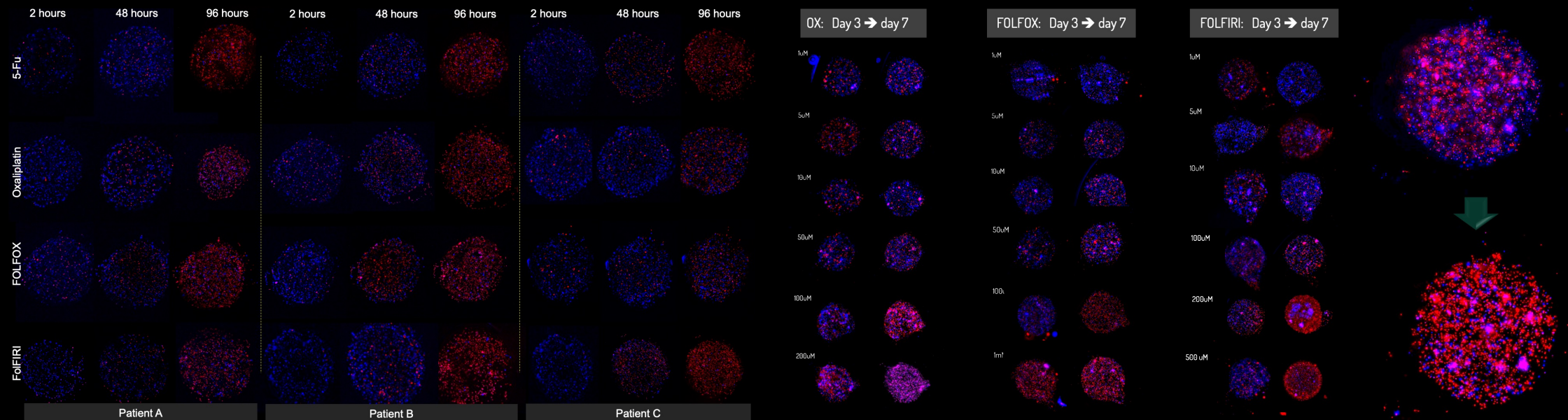
	# of rounds	F05LFOX	5-FU	Oxaliplatin	FOLFIRI	XELOX	Other	Final Fate
BC1	2							
BC2	3						Bev	
BC3	3							
BC4	3							
BC5	7						CET	
BC6	7						Avastatin	
BC7	3							
BC8	3							
BC9	3							
BC10	3							
BC11	3							
BC12	4		?					
BC13	3						MVASI	
BC14	3							
BC15	5						Avastatin	
BC16	3						Zaltrap	
BC17	4						Stivarga	
BC18	11						MVASI	
BC19	4							
BC20	3						MVASI	

# Encapsulate Predictions

[illegible]



## Pre/Post treatment Mutations

[illegible]



# Completed two rounds of **clinical validation** (colon and pancreatic)

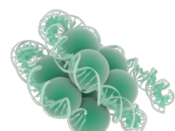
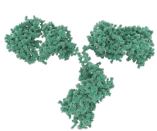
## Clinical Outcomes

In **2022-2023** Encapsulate performed retrospective clinical studies on colorectal and pancreatic cases.

**94 out of 98** RECIST outcome predictions precisely matched the clinical outcome. **100%** of survival predictions were accurate. The technology was effective in forming tumoroid for all the cancer patients tested.

## Assays included

Proteomics Metabolomics Mutations Toxicity

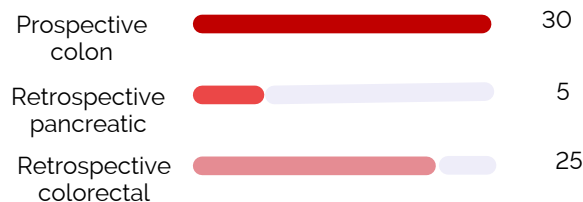


We **proved the accuracy** of our platform for predicting:

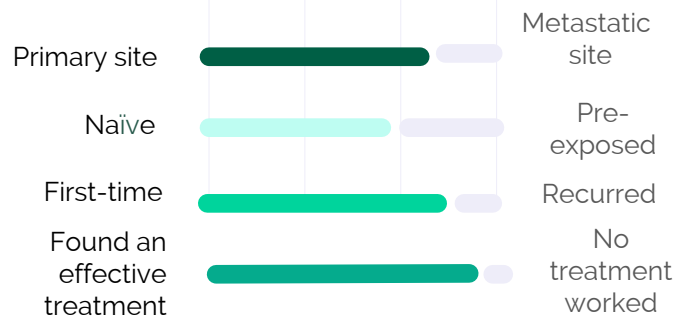
- Effective treatment(s)
- Drug elimination
- Minimal effective dose
- Resistance development

## Successfully tested

30+30 samples in different conditions, stages, and tumor locations have been tested.



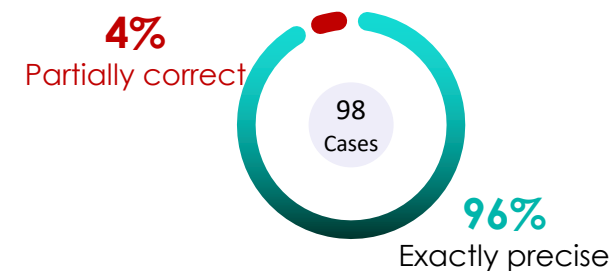
Patients with tumors at stage II, III, and IV, Naïve or pre-exposed to chemo/radiation, and resected from primary tumor location or secondary sites such as abdomen, lung, ovary, and liver, have been tested successfully and shown to be predicted precisely.



## Response rate in clinical samples



## Accuracy of clinical predictions



## Tumoroid formation success rate



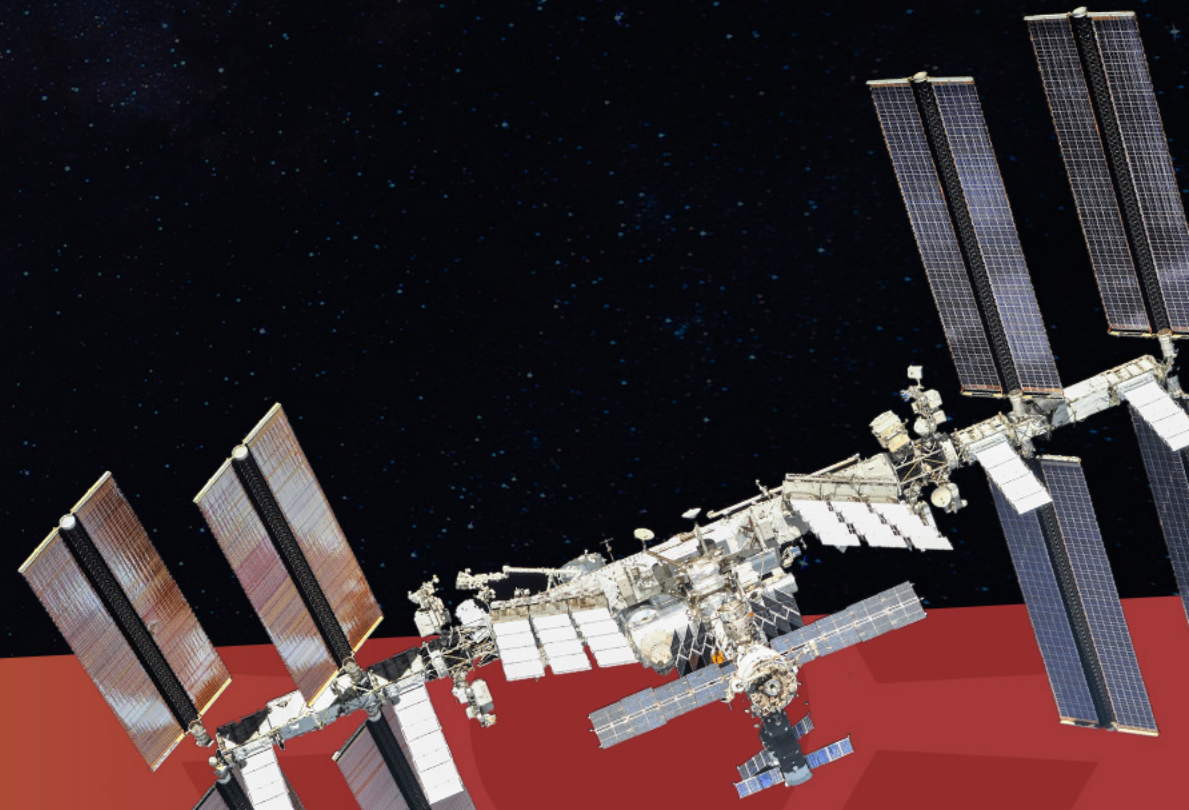




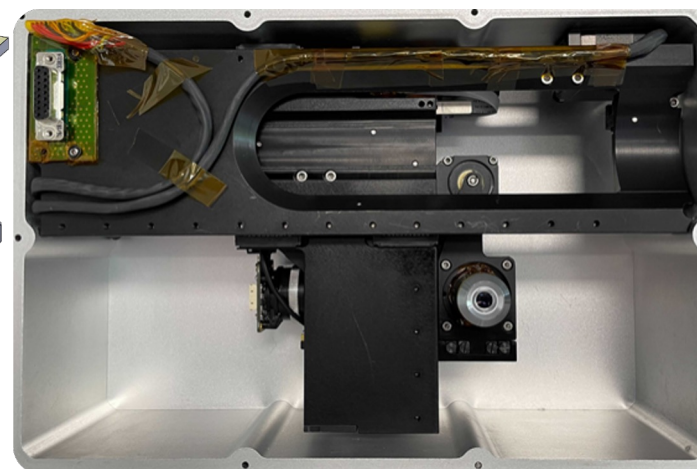
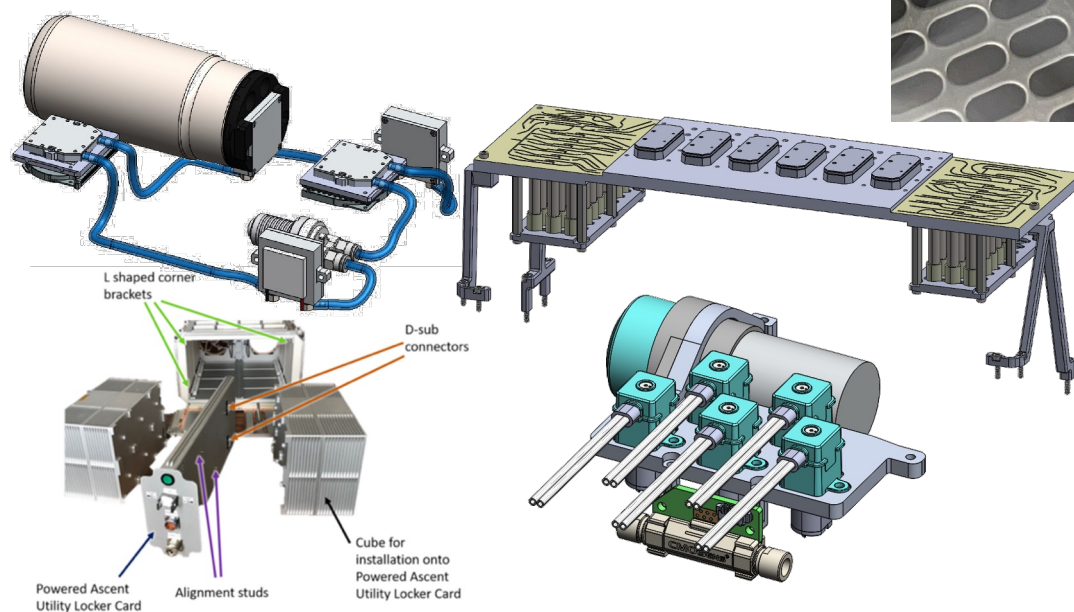
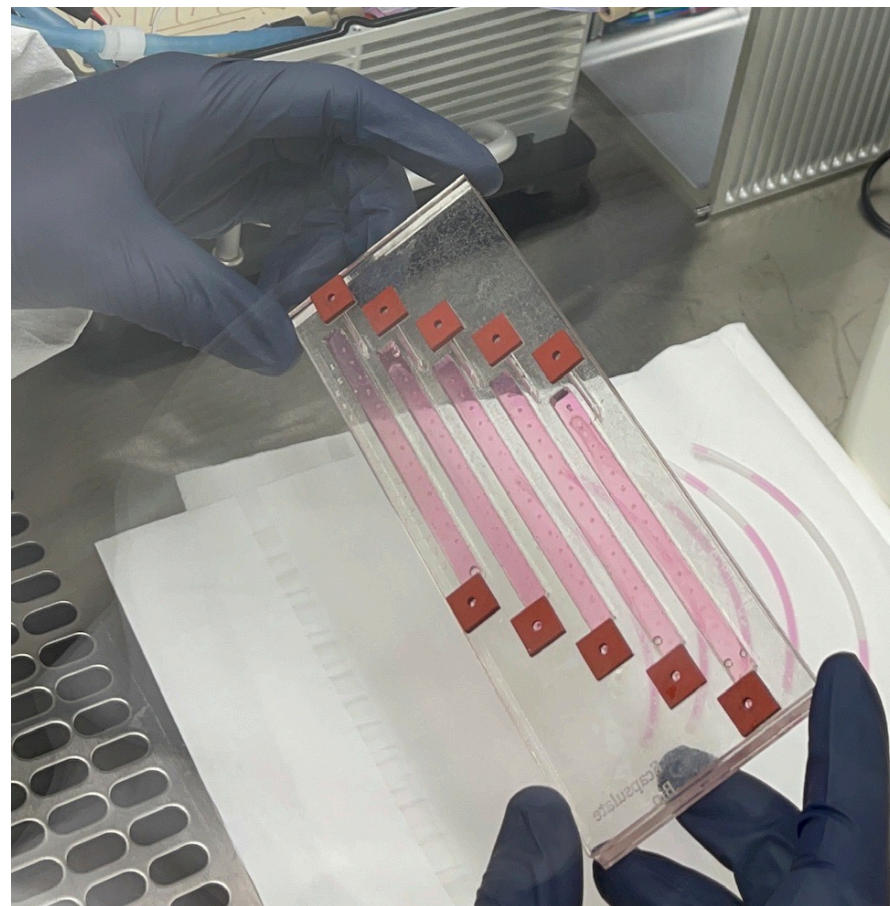
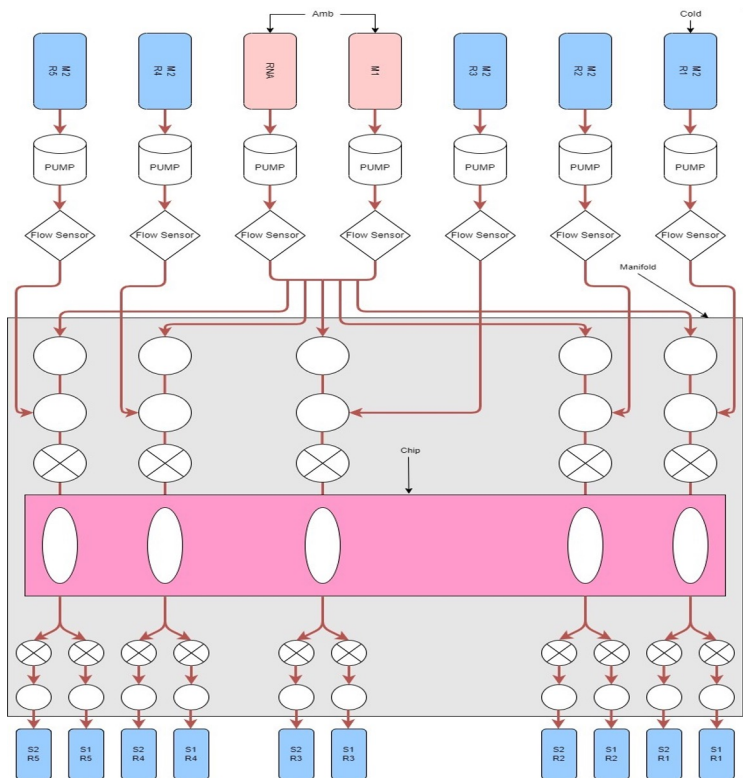
# SpaceX CRS 30 Flight Results

**AIRBUS**

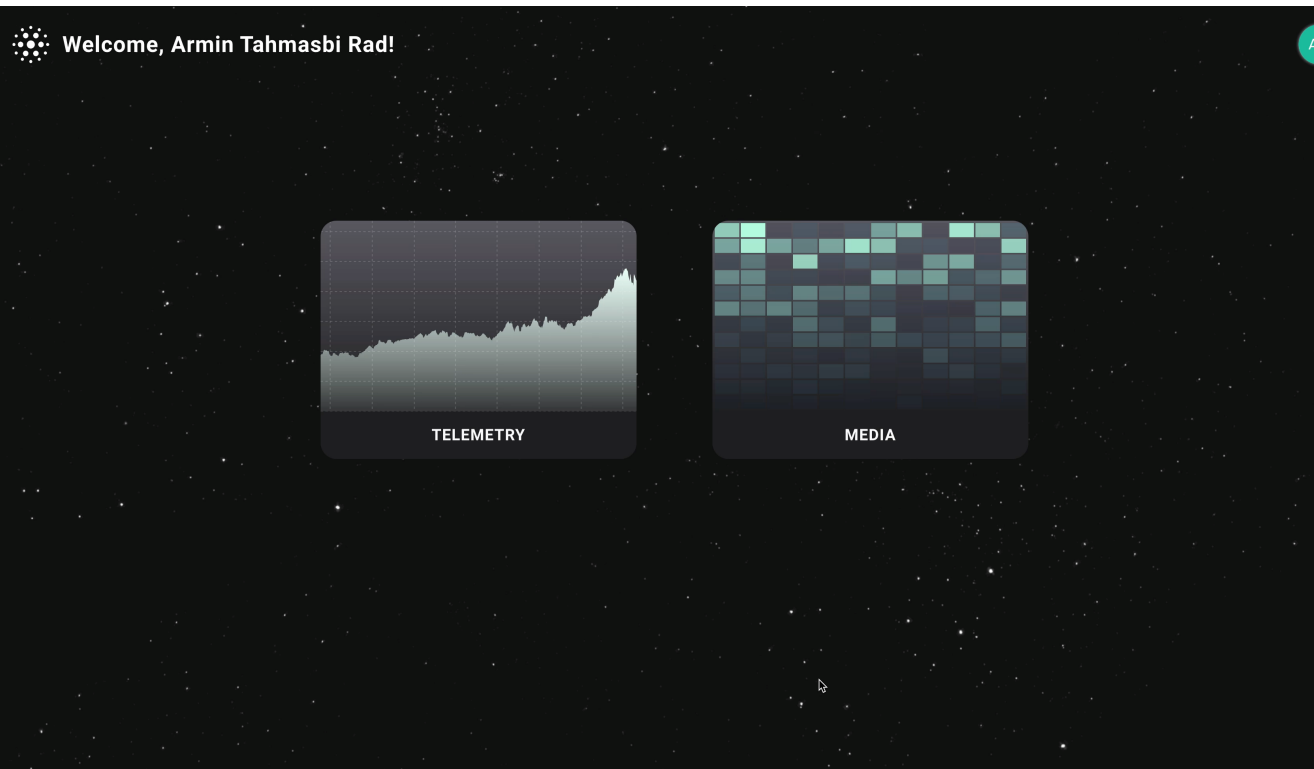
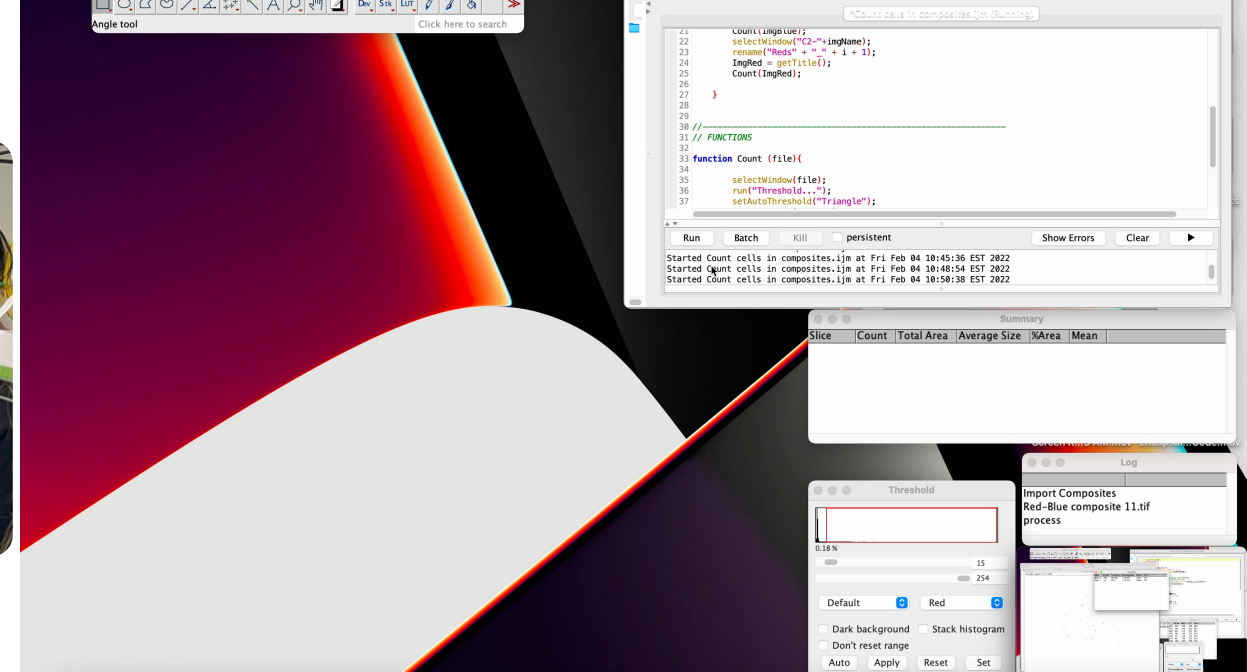
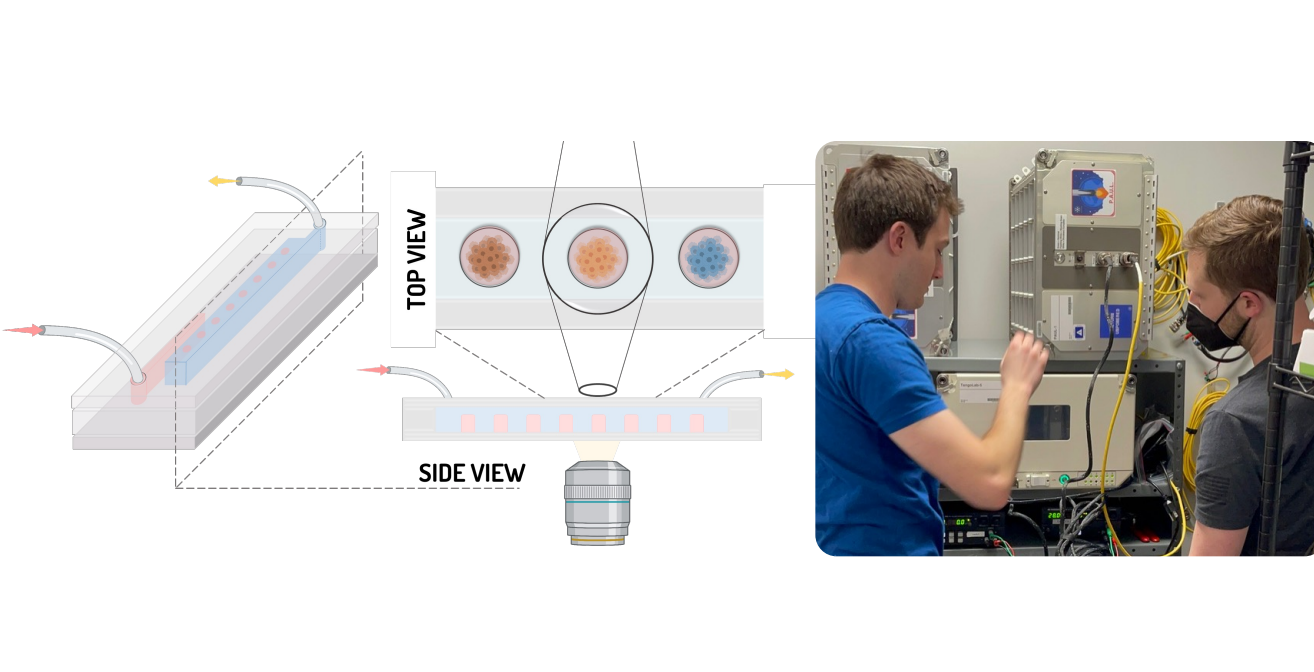
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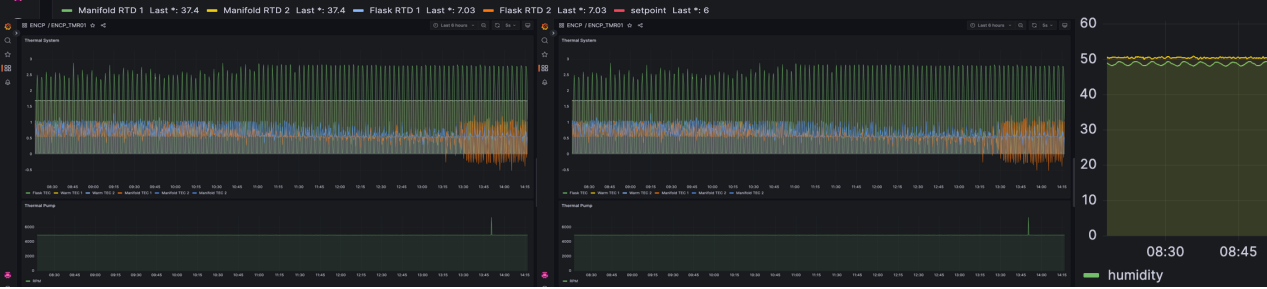






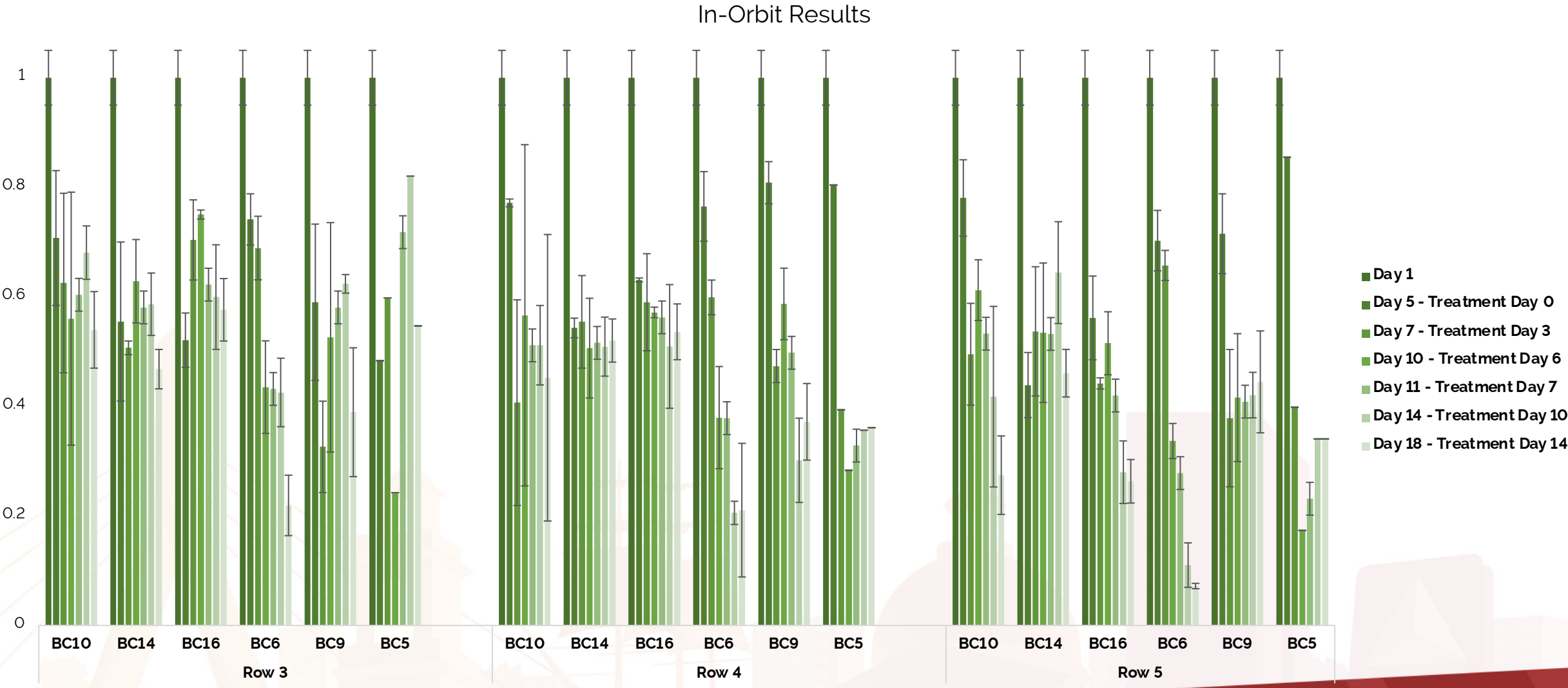




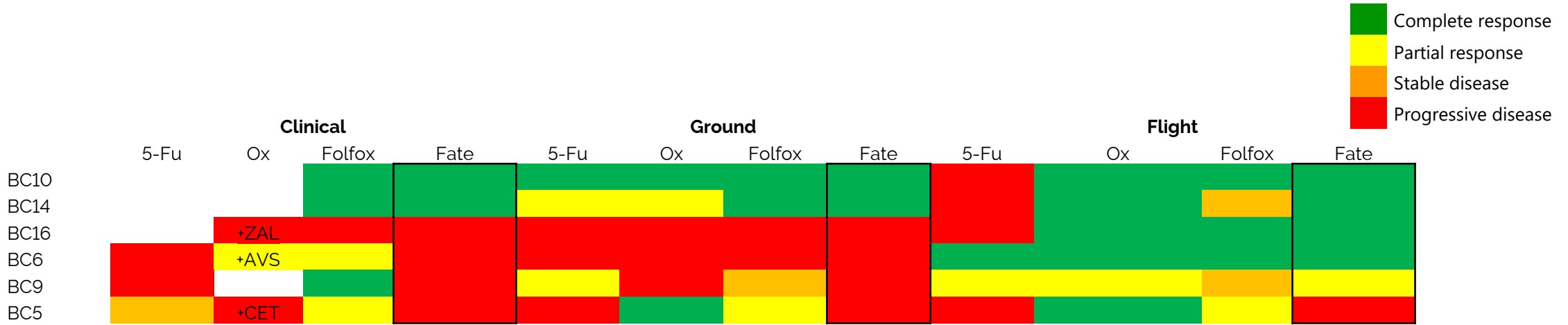




# In-Orbit Studies







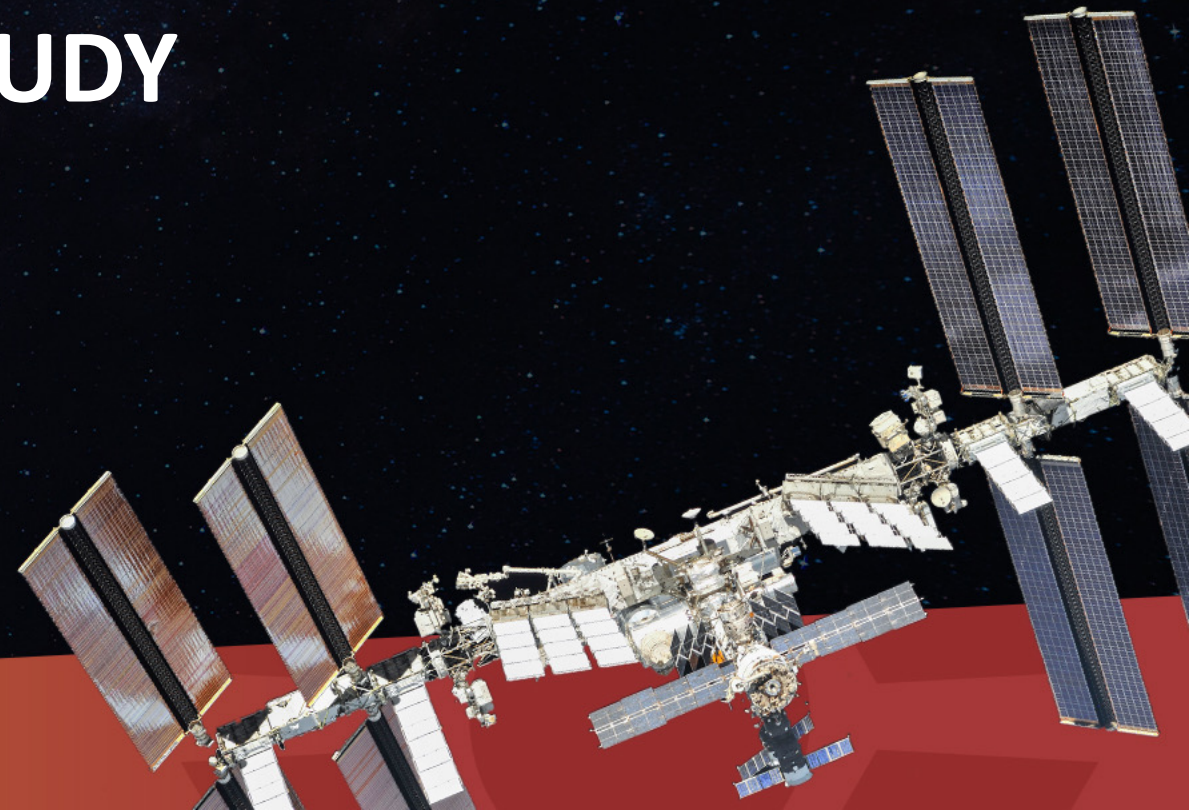
	Primary Mutations	Chemo-response based on genes			uG effect expected?		Stage	Gender	Race	Age	# of rounds
		5-Fu	Ox	Folfox							
BC10	APC, CDKN2A, PIK3CA, dMMR	APC, dMMR	dMMR	PIK3CA	APC	dMMR	III B	F	White	50	3
BC14	APC	APC			APC		III A	M	White	55	3
BC16	APC	APC			APC		II	F	White	69	3
BC6	KDR, KRAS, TP53				KRAS	TP53	IV C	F	White	53	7
BC9	APC, ERBB2, FGFR, GNAS, KRAS, MET, TP53	APC	KRAS		APC	TP53	III A	F	White	38	3
BC5	EGFR, PIK3CA, TP53	EGFR		PIK3CA	PIK3CA	TP53	IV B	M	Latino	61	8





## CASE STUDY

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96 hours

5-Fu

FOLFOX

PTX

## Patient BC05

Gender	Race	Diagnosis	T	N	M	Stage	Specimen Type	Spec Considered	Site	Specimen age in years	Patient Birth Year	Patient Age at Collection	Smoking History	Chemo Tissue Exposure	Rad Tissue Exposure
Male	Latino	Colon Cancer	T3	N2a	M1	IVB	LC Malignant	Primary	Colon	4	1958	61	Previous smoker	No	No
Mismatch Repair			KRAS Mutation			EGFR Mutation			BRAF mutations		HER2 Mutations		ROS1 rearrangement		ALK rearrangement
Intact			Negative			Negative			Negative		Negative		Negative		
	# of rounds	FOLFOX		5-FU		Oxaliplatin		FOLFIRI		XELOX		Other		Final Fate	
BC05	7	1		2-3				5-6				CET - 4			

# Encapsulate Predictions

[illegible]

BC	GC	MUTATIONS
		ABL1, AKT, ALK
		APC (may be NR: 5FU)
		ATM
		BRAF (Check V600E)
		CDH1
		CDKN2A
		CSF1R
		CTNNB1
		EGFR
		ERBB2 (R: Ner, Lap, Tr)
		ERBB4
		EZH2
		FBXw7 (NR: Ox, Tr)
		FGFR1,2,3
		FLT3
		GNAI1,GNA
		GNAS
		HNFA
		HRAS
		IDH1, 2
		JAK2
		JAK3
		KDR
		KIT
		KRAS (NR: CET/ R: Ox)
		MET
		NOTCH1, MPL, NPM1
		NRAS
		PDGFRA
		PIK3CA (NR: Cet, X, D)
		PTEN
		PTPN11
		RBI
		RET
		SMAD4
		SMARCB1
		SMO
		SRC
		STK11
		TP53
		VHL
		dMMR: PMS2



KRAS mutation is a predictor of oxaliplatin sensitivity by the mechanism of ERCC1 downregulation

EGFR contributes 5-FU resistance in colon cancer cells through autophagy induction

KRAS and BRAF Mutations in Advanced Colorectal Cancer Are Associated With Poor Prognosis but Do Not Preclude Benefit From Oxaliplatin or Irinotecan

No correlation

Supposed not to respond to Oxaliplatin (KRAS negative), and respond to 5-Fu (EGFR negative)

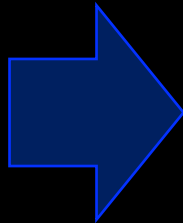
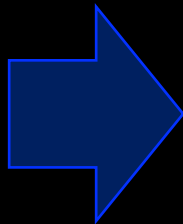
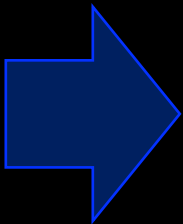
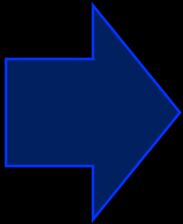
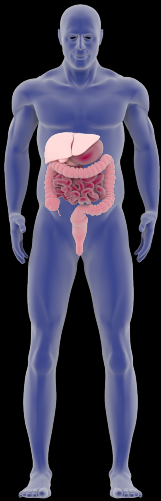
DNA Mismatch Repair	KRAS Mutation	EGFR Mutation	BRAF mutations	HER2 Mutations	ROS1 rearrangement	ALK rearangmen	Code
Intact							BC1
Intact							BC2
Intact							BC3
Intact							BC4
Intact	Negative	Negative			Negative	Negative	BC5
Intact	Positive		Negative	Negative			BC6
Intact							BC7
Intact	Negative						BC8

Expected to respond to Oxaliplatin (KRAS positive),

Expected not to respond to Oxaliplatin (KRAS negative),

FWID	Unique Aliquot ID	Gender	Ethnicity	Race	Diagnosis	T	N	M	Stage	Specimen Type	Spec Considered	Site	Specimen age in years	Specimen Collection Year	Patient Birth Year	Patient Age at Collection	Smoking History	Chemo Tissue Exposure	Rad Tissue Exposure
106203	164152	Male	Spanish; Hispanic	Latino	Colon Cancer	T3	N2a	M1	IVB	LC Malignant	Primary	Colon	3	2018	1958	61	Previous smoker	No	No

Course 1	Course 1 Start	Course 1 Chemo	Response to Chemo Course 1	Course 2	Course 2 Start	Course 2 Chemo	Response to Course 2	Course 3	Course 3 Start	Course 3 Chemo	Response to Course 3	Course 4	Course 4 Chemo Start	Course 4 Considered	Response to Course 4
Folfox Modified	11/2018	Palliative	PR - Partial Response	Adrucil/Fluorouracil	5/2019	Palliative	PR - Partial Response	Erbix/Cetuximab	10/2019	Palliative	PD - Progressive Disease	Folfiri	10/2019	Palliative	PD - Progressive Disease



Folfox: PR

5-Fu: PR

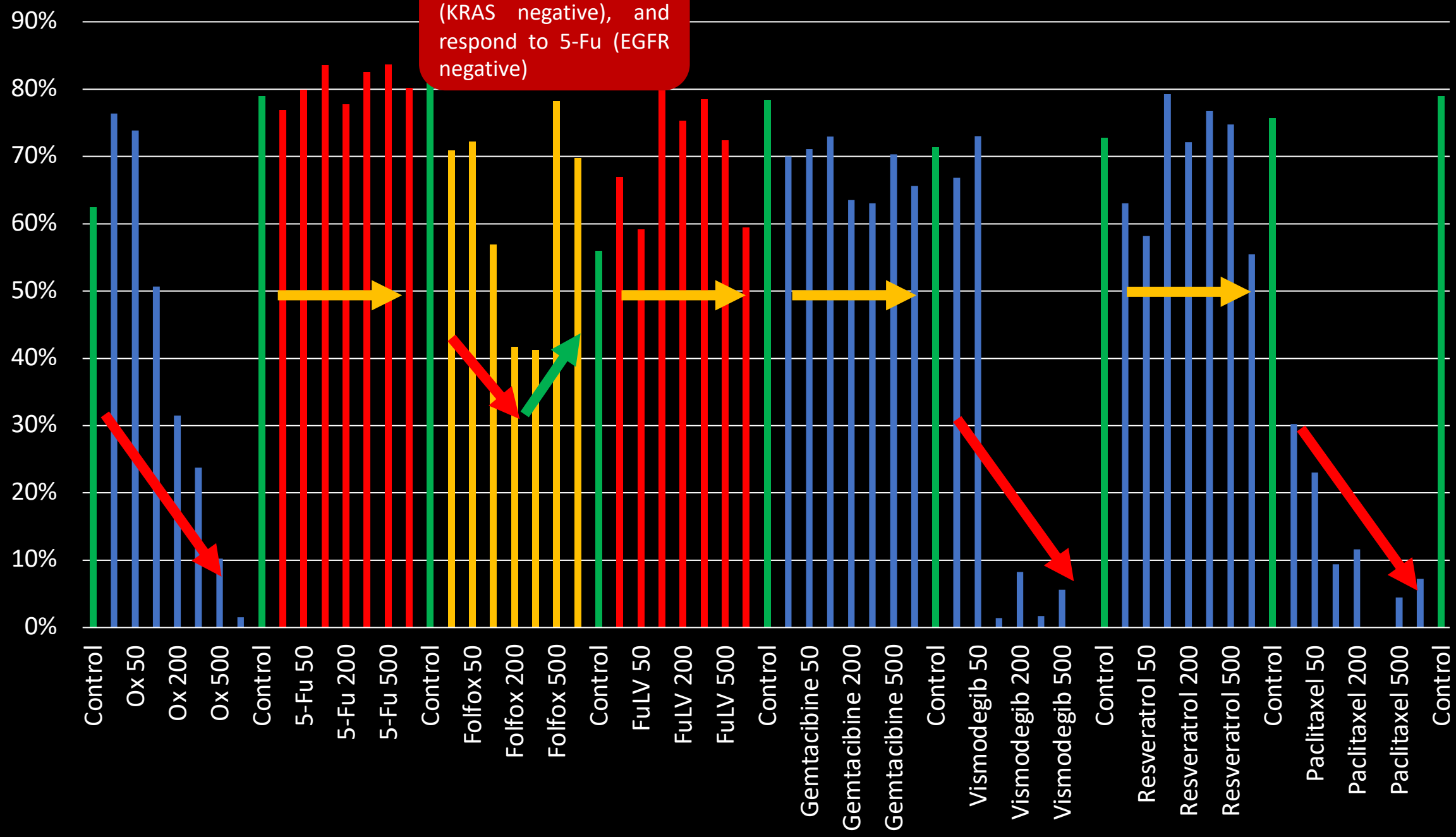
Cet: PD

FolFIRI:  
PD

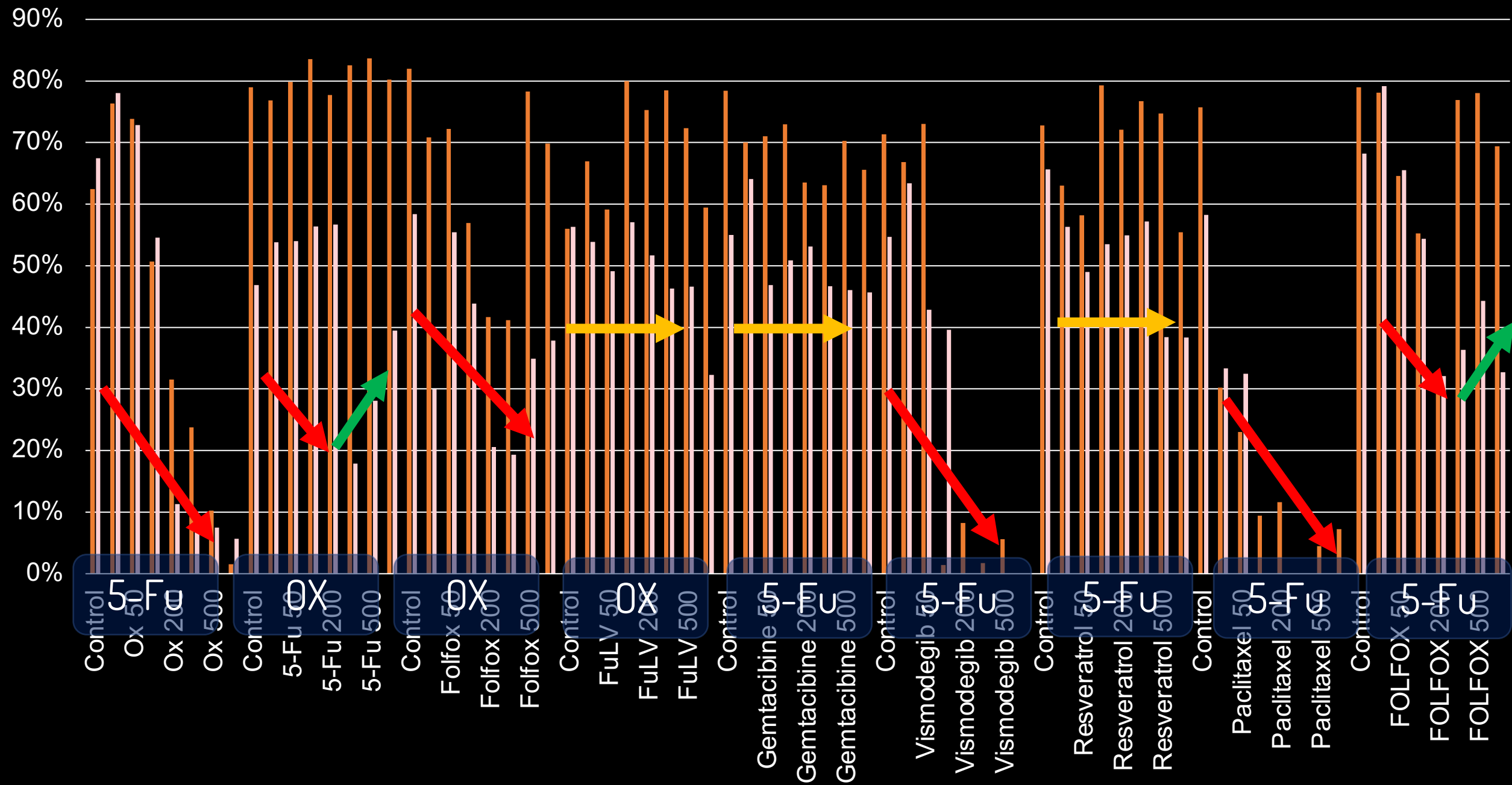


BC5

Supposed not to respond to Oxaliplatin (KRAS negative), and respond to 5-Fu (EGFR negative)

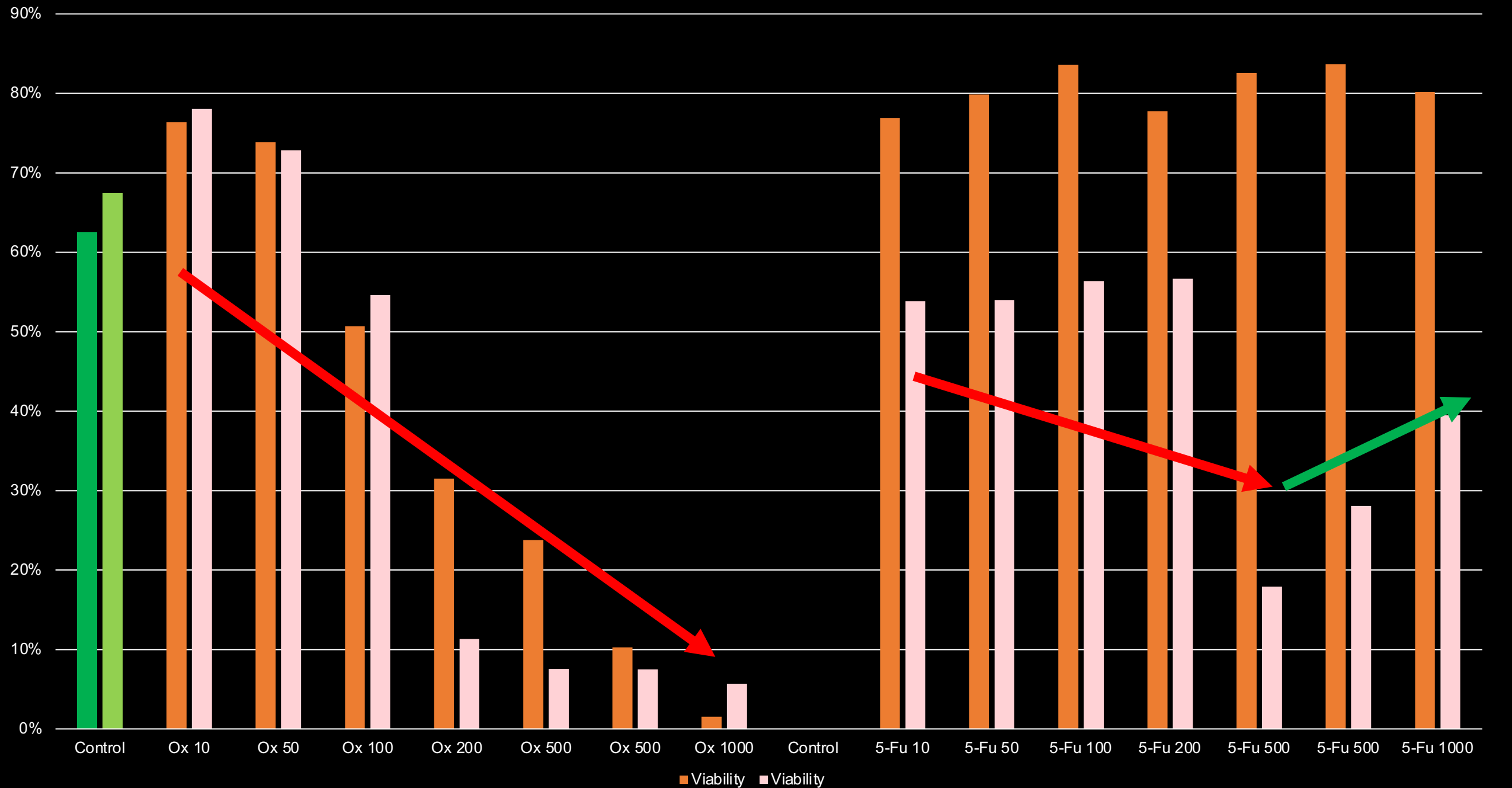


Round 1 & Round 2

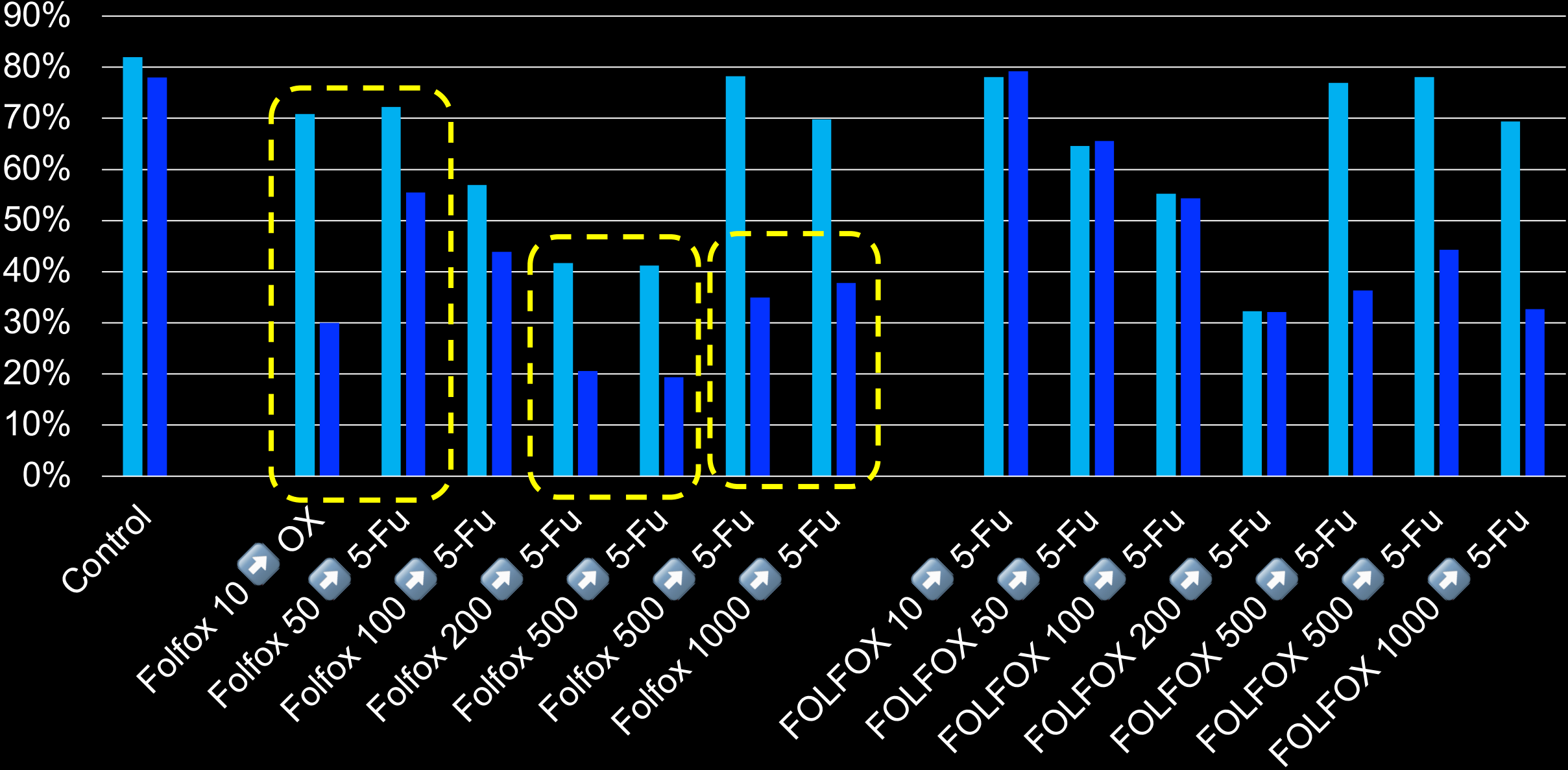




# 5Fu-OX vs OX-5Fu

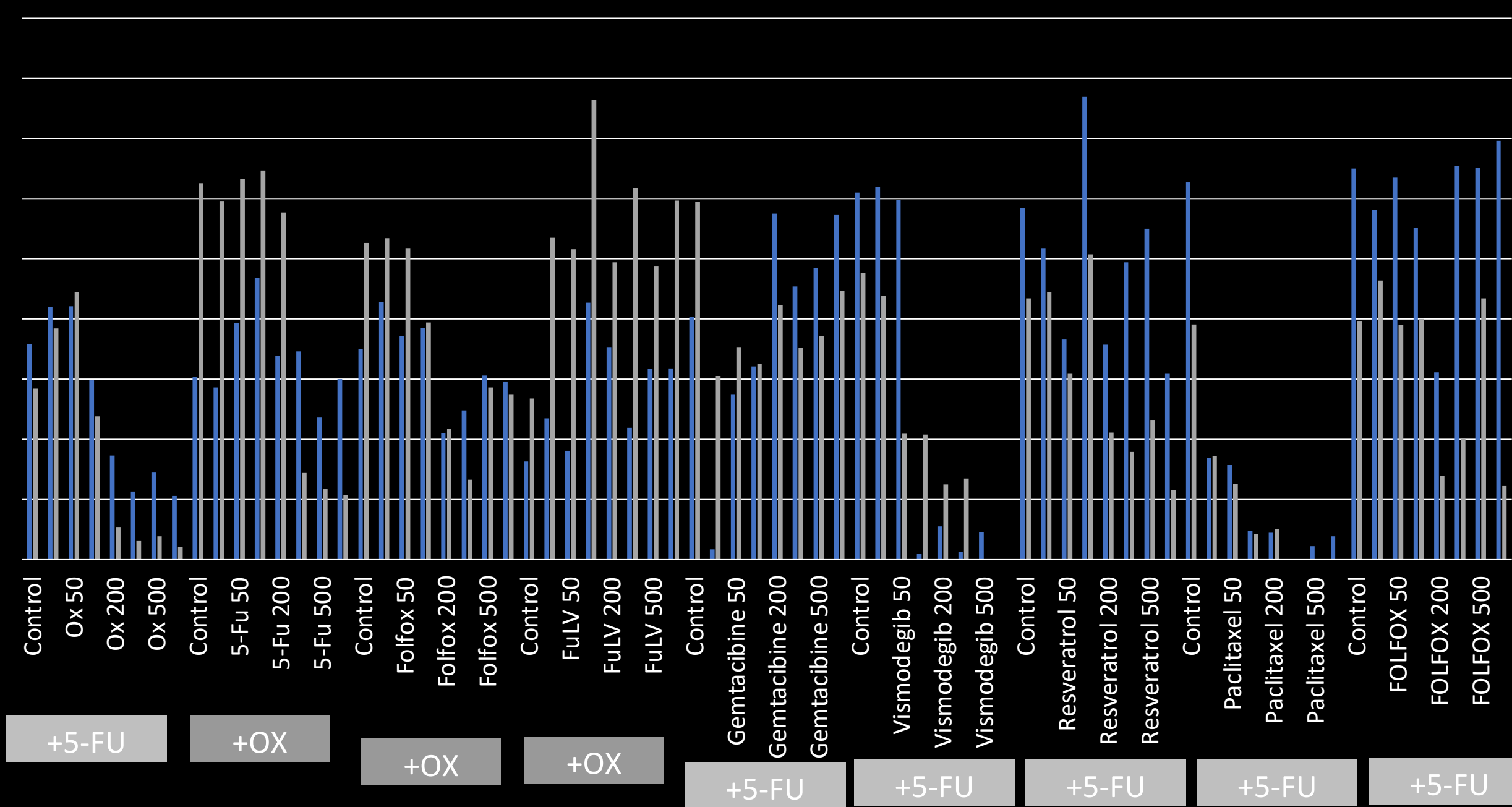


After Folfox





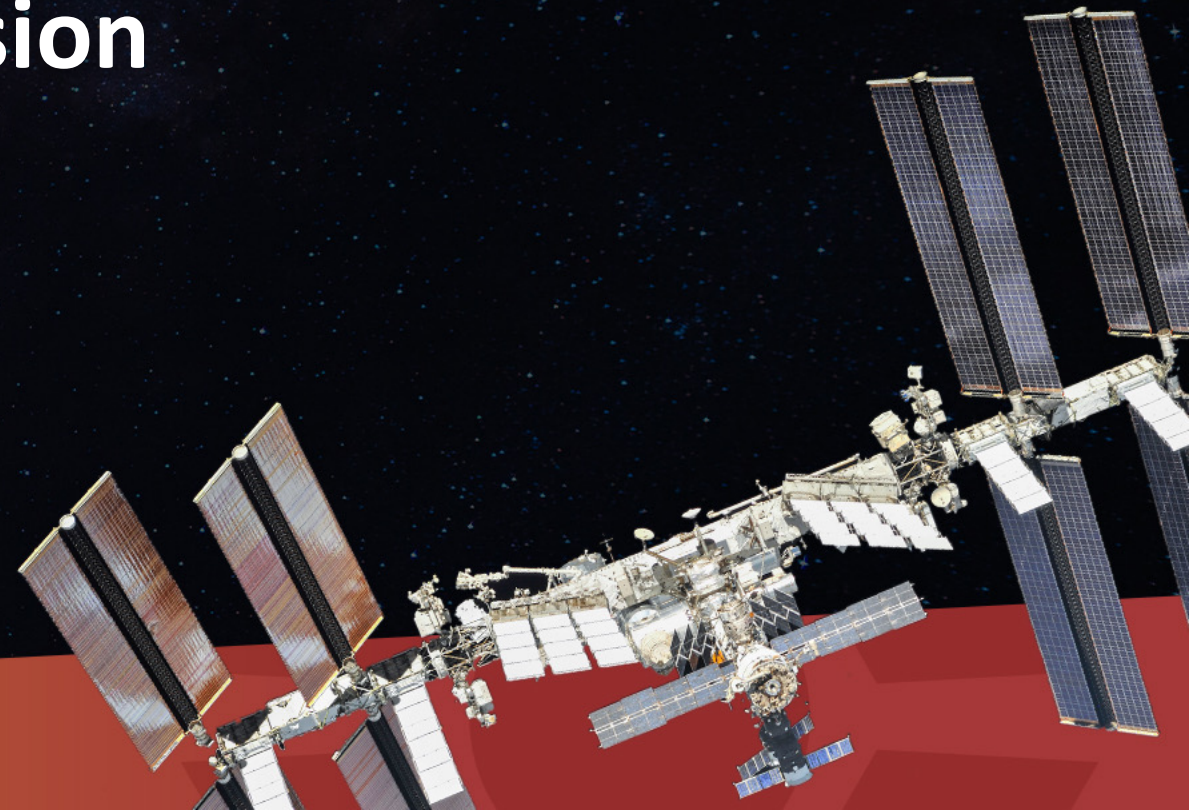
# Alive cells trend



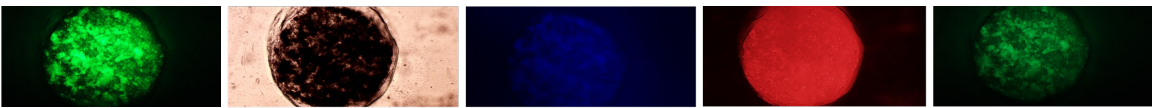


# Conclusion

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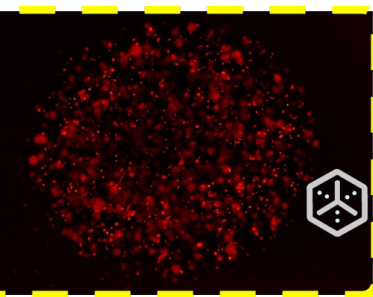
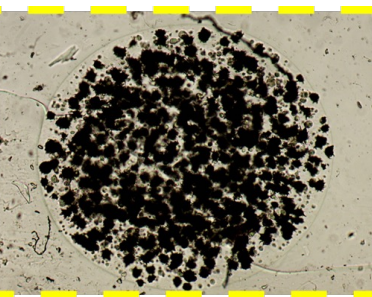
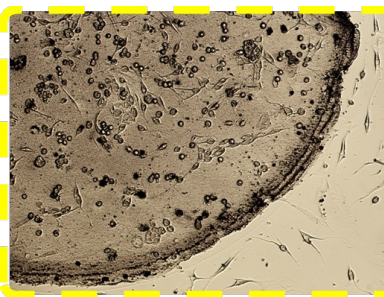
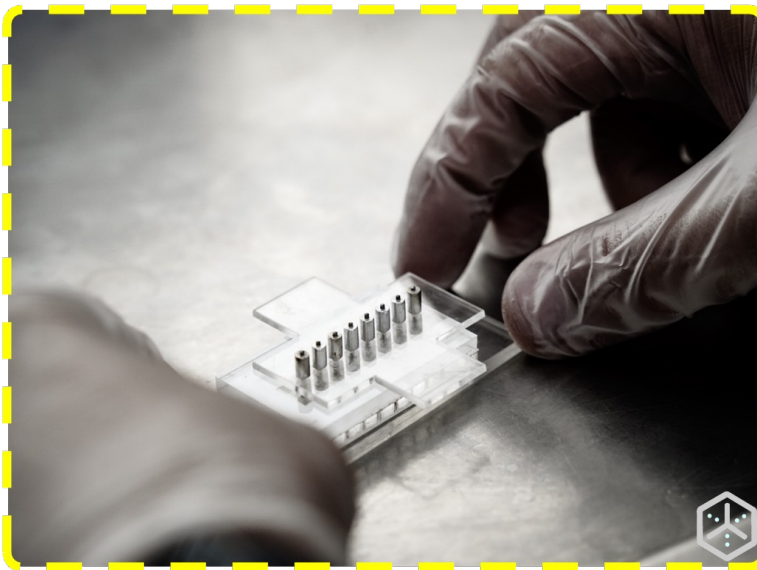
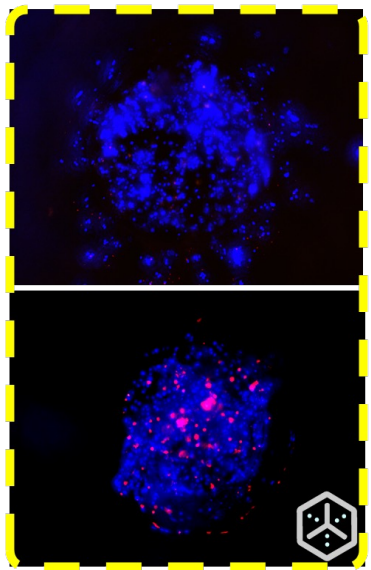




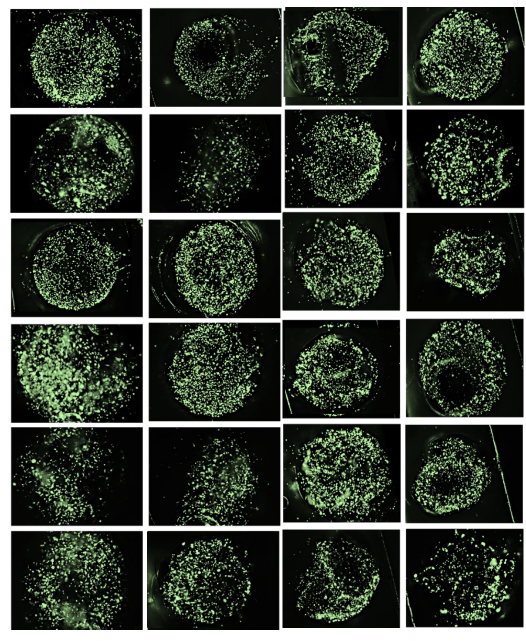
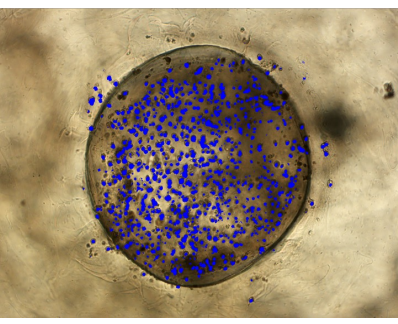
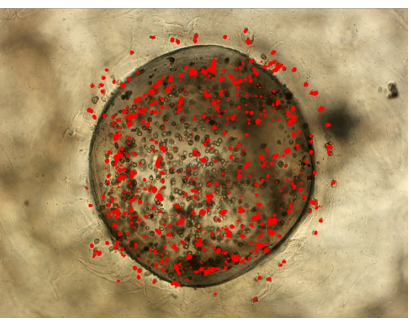
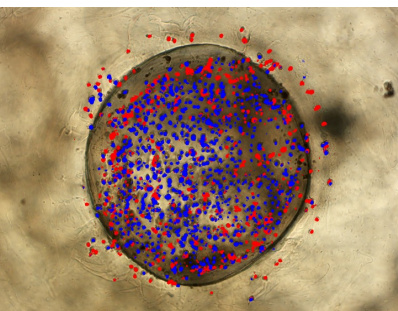
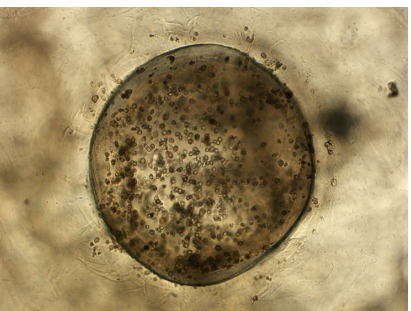
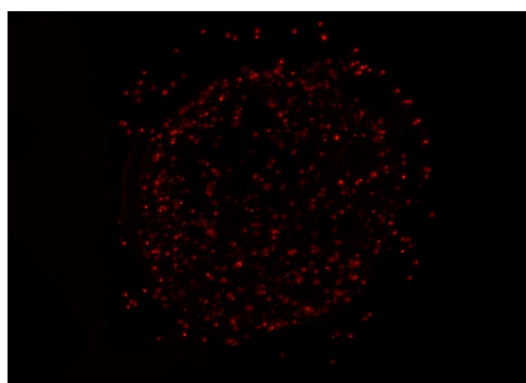
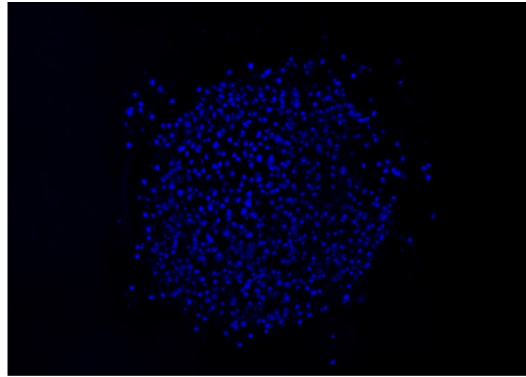
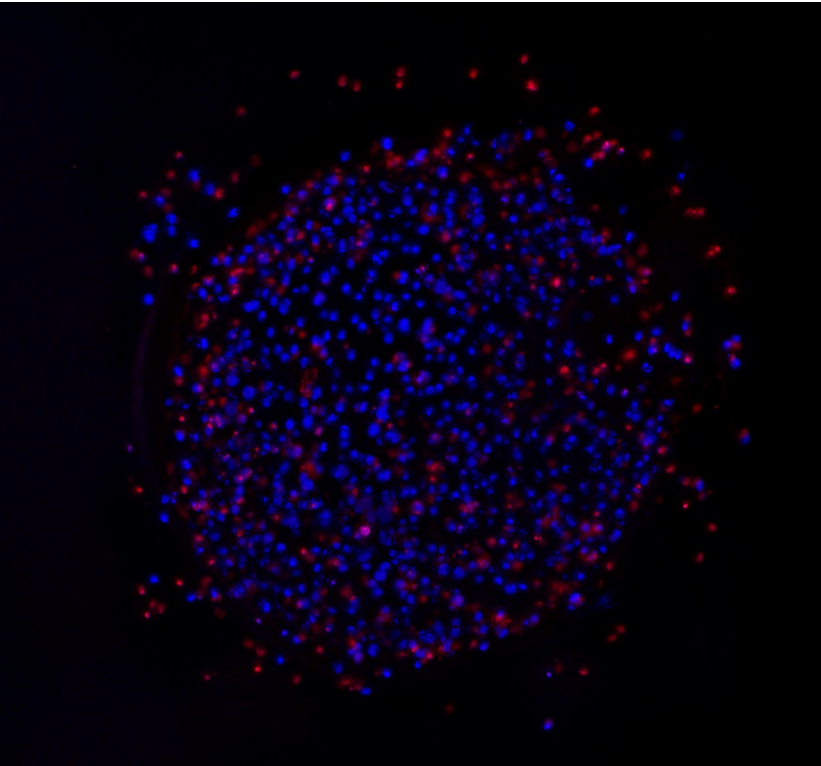
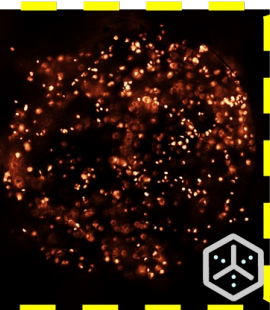
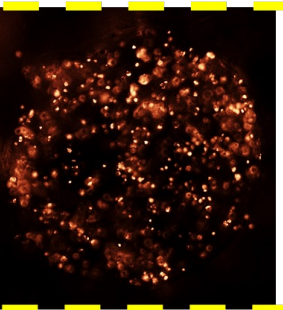
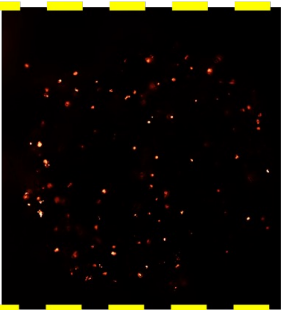
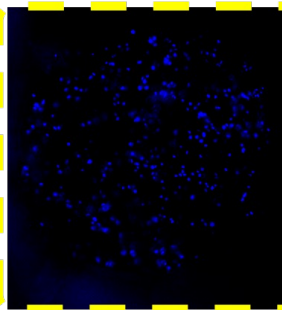


Our novel synthesized hydrogel has on-demand shape, high transparency & biocompatibility

With only \$6.20 to fabricate, easy to load, with 16 distinct tumoroids per each device, it takes only 1 hour to have a patient-derived microtumor ready to test.



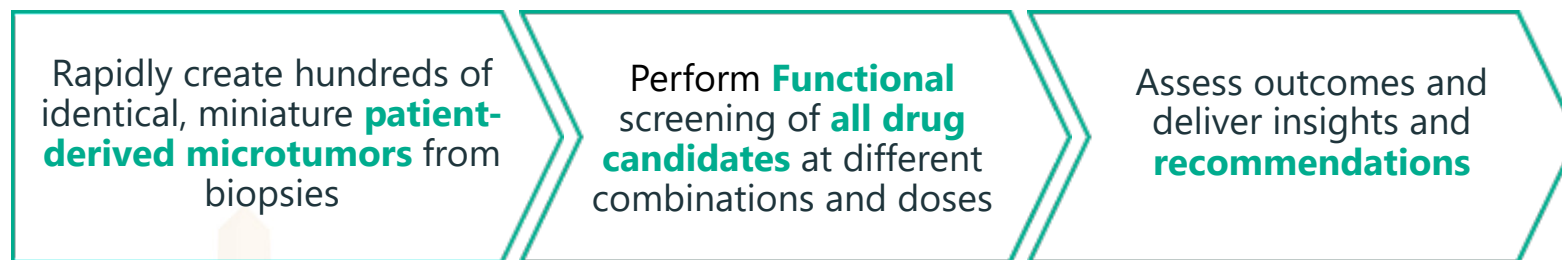
A timeline on the long-term multiple chemo rounds (Blue: alive cells, Red: dead cells)



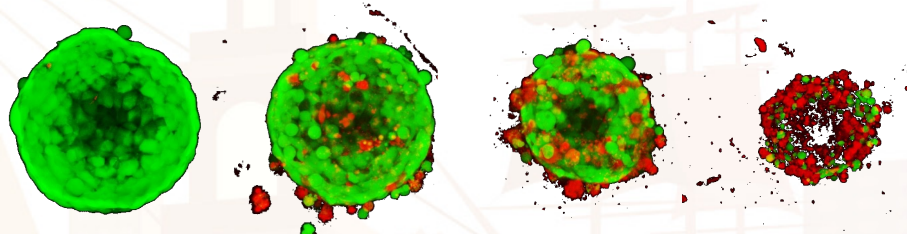


# A patient **tumor-specific treatment** has potential to save lives

## OUR SOLUTION



in seven days



## THE OUTCOME

Treatment time reduced by **10+ months** (avg time = 15 months)

Chemotherapy-related treatment costs reduced by **\$100K+ per patient** in addition to chemotherapy-related comorbidities

**Saving lives**





	Cell Line	Primary Cell	Spheroid	Organoid	OTSC	OOAC	Syngeneic Model	GEMM	Carcinogen Model	PDX/CDX	Humanized Mouse	Encapsulate
Relative Cost	\$	\$	\$	\$\$	\$	\$\$	\$\$\$	\$\$\$	\$\$\$	\$\$\$	\$\$\$	\$
Preparation Time	🕒	🕒	🕒	🕒	🕒	🕒	🕒🕒	🕒🕒🕒	🕒🕒	🕒🕒	🕒🕒🕒	🕒
Ease of establishing	✔️	✔️	✔️	✔️	✔️	✔️	✔️	✔️	✔️	✔️	✔️	✔️
Ease of long-term maintenance	✔️	✔️	✔️	✔️	❌	❌	✔️	✔️	✔️	✔️	✔️	✔️
Ease of use	✔️	✔️	✔️	✔️	✔️	✔️	✔️	✔️	✔️	✔️	✔️	✔️
Ease of passage	✔️	✔️	❌	✔️	❌	❌	❌	✔️	❌	✔️	✔️	✔️
Ease of genetic modification	✔️	✔️	✔️	✔️	✔️	✔️	✔️	✔️	✔️	❌	❌	✔️
Success rate of establishment	❌	✔️	✔️	✔️	✔️	✔️	✔️	✔️	✔️	✔️	✔️	✔️
Physiologic representation	❌	✔️	✔️	✔️	✔️	✔️	✔️	✔️	✔️	✔️	✔️	✔️
Similarity to original tumor	❌	❌	❌	✔️	✔️	✔️	❌	❌	❌	✔️	✔️	✔️
Vascularization	❌	❌	❌	✔️	✔️	✔️	✔️	✔️	✔️	✔️	✔️	✔️
Cell diversity	❌	✔️	❌	✔️	✔️	✔️	✔️	✔️	✔️	✔️	✔️	✔️
Preservation of heterogeneity	❌	❌	❌	✔️	✔️	✔️	❌	❌	❌	✔️	✔️	✔️
Preservation of tumor morphology	❌	❌	❌	✔️	✔️	❌	❌	❌	❌	✔️	✔️	✔️
Preservation of microenvironment	❌	❌	❌	❌	✔️	✔️	✔️	✔️	✔️	✔️	✔️	✔️
Scalability	✔️	✔️	✔️	✔️	✔️	✔️	✔️	✔️	✔️	✔️	✔️	✔️
Clinical response prediction	✔️	✔️	✔️	✔️	✔️	✔️	❌	❌	❌	✔️	✔️	✔️
High-throughput drug screening	✔️	✔️	❌	✔️	✔️	✔️	❌	❌	❌	✔️	✔️	✔️
Genome-wide screening	✔️	✔️	✔️	✔️	❌	❌	✔️	❌	❌	❌	❌	✔️
Biobanking	✔️	✔️	❌	✔️	❌	❌	❌	❌	❌	✔️	❌	✔️

\$ Cheap    \$\$ Expensive    \$\$\$ Quite Expensive    🕒 Time Efficient    🕒🕒 Less Time Consuming    🕒🕒🕒 Time Consuming    ✔️ Well-suited    ✔️ Suited    ✔️ Partially-suited    ❌ Unsuitable



# We are grateful for the supports by:

ISS National Lab

Boeing Space

Space Tango team

Jennifer Read

Bret Schipper

John Catechis

Alain Berinstain

Ben Lump

Isabel Moore

Shelby Giza

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[info@encapsulate.bio](mailto:info@encapsulate.bio)



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## 2024 Technical Sessions

