

# Cellaria and the New Promise for Research

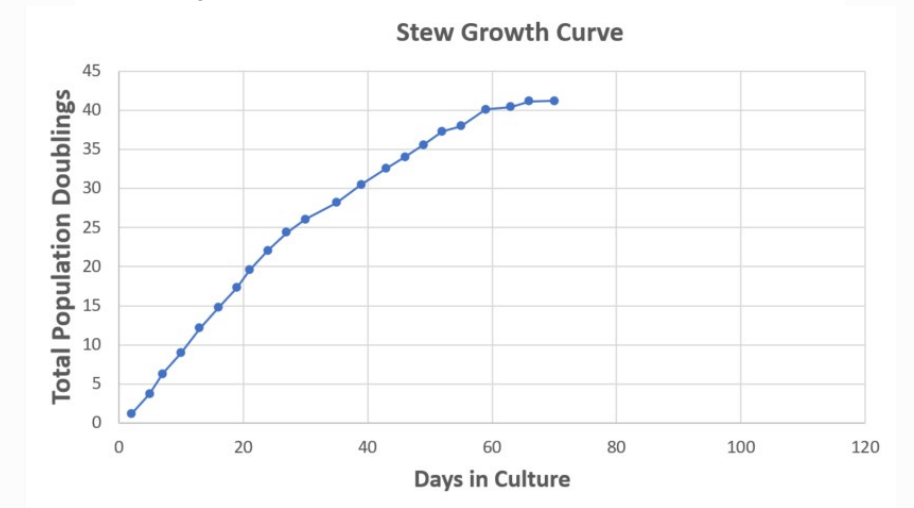


  
Cellaria

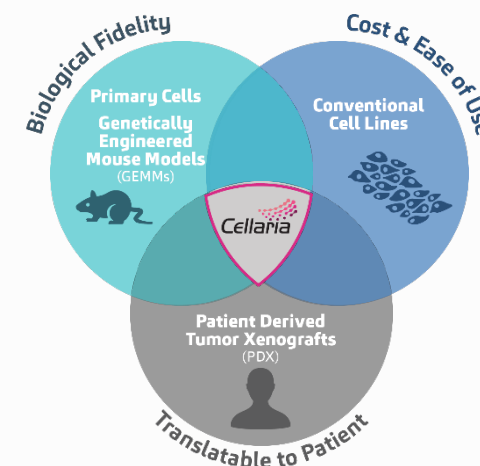
# The Cellaria Advantage

- Cellaria provides next-generation, patient-specific disease models that solve many of the issues of traditional cell line development
- Proprietary formulations used during derivation **increase the success rate from <15% to >95%** for establishing stable, scalable, and heterogeneous cell populations
- Cellaria's technology enables the creation of a broad range of patient cell types, and consequently more thorough investigation of patient response
  - **Cheaper** than genetically engineered cell models and avoids the cost and variability associated with tests conducted in animal models
  - Enables creation of cell models for diseases where researchers previously had limited success (i.e. pancreatic cancer, liver disease)
- Each cell model is characterized using well-controlled, characterization assays to ensure **stable biomarker expression** while enabling easy tracing with **highly detailed lineage and clinical data**
- Cellaria's cell lines are **highly stable** (durable and consistent), especially when compared to many existing cell lines which have changed over the years
- Cellaria's patient cohorts offer a **broad sampling of key population segments** that provide unprecedented insight for disease and treatment investigators

## — Sample Cellaria Cell Line Growth —



## — Cell Line Selection Criteria —



*Cellaria's cell lines outperform conventionally developed cell lines across all selection criteria*

# Broader Applications than Traditional Cell Lines

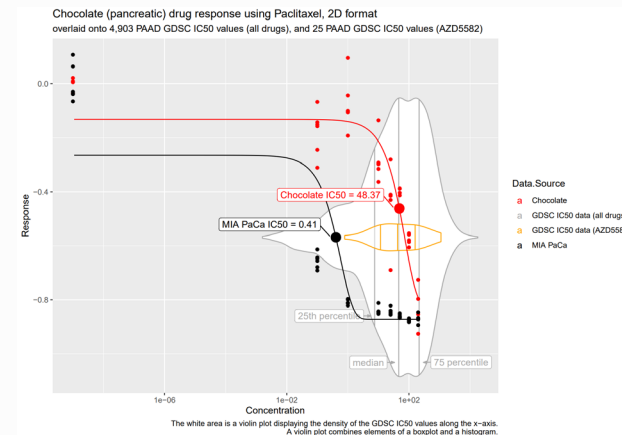
## Traditional Uses of Cell Lines

- **Response screening** of compound libraries to find therapeutic candidates
- **Therapeutic evaluation** by measuring the sensitivity of different cell lines (representing different patient populations) to therapeutic candidates
- **Analysis of the relationship between disease response and genome characteristics**
- **Disease mechanism analysis** to evaluate mechanisms of action in disease development and progression, often using complex assays formats such as spheroid
- **Quality control** to ensure production processes do not alter performance characteristics of the drug

## Expanded Uses of Cellaria's Products

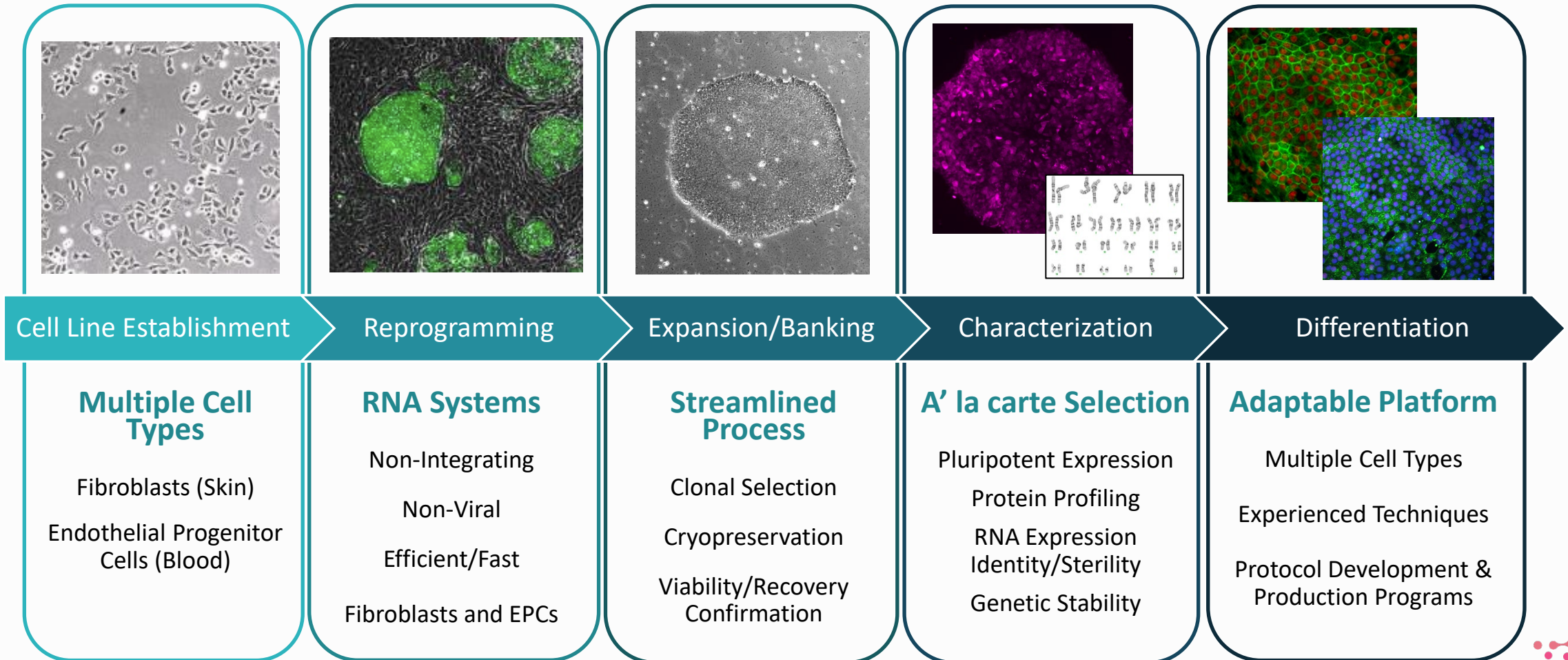
- **Target identification** by creating model systems that better represent the true patient population
- **Therapeutic response analysis** enabling exploration of variations among similar patient populations
- **Metastatic progression** using co-culture assays to investigate mechanism of metastasis
- **Direct clinical models** to analyze the exact patients enrolled in clinical trials

## Cellaria's Cell Line Outperforms Standard



# Cellaria Custom Model Services

- Customers rely on Cellaria to develop the model, perform certain elements of characterization and perform preliminary drug screening
- Modular and milestone driven services, allowing customers to select the project components that fit best with their needs



# Cellaria's Commercial Products

- Cellaria provides a broad range of disease media and models that encompass historically challenging disease areas
- Increasing demand for well-controlled characterization assays: gene expression, protein profiling, and mutation identification
- Planned new product launches include models for triple negative breast cancer, cholangiocarcinoma, serous ovarian cancer, and non-small cell lung cancer
- All in-house manufacturing with process development underway to increase the company's lot size from 100 to 500 vials per lot

## Breast Cancer Model

**Product:**  
**Wood**



Infiltrating ductal and lobular carcinoma of the breast

## Colon Cancer Model

**Product:**  
**Ferry**



Adenocarcinoma of the large intestine

## Ovarian Cancer Models

**Product:**  
**Carousel**



Endometrioid adenocarcinoma of the ovary

**Product:**  
**Powder**



Serious carcinoma of the ovary

## Tumor Medium



Renaissance

## Lung Cancer Model

**Product:**  
**Jacket**



Adenocarcinoma of the lung non-small cell lung cancer

## Pancreatic Cancer Models

**Stew**



**Products:**  
**Chocolate**



**Basket**



Adenocarcinoma of the pancreas  
Cellaria's pancreatic products are differentiated based on the underlying patient population

## Customizable Cell Media



OMNI

# Cellaria's Commercial Assays

## **3D Spheroid and 3D Co-Culture (MINT™ Assay)**

- Characterization of disease progression and response to drug candidates in standard spheroid, and co-culture environments that mimic the tumor microenvironment and the metastatic niche.

## **Drug Response**

- Using standard techniques, including XTT, CellTiterGlo, Cyquant, CellToxGreen, to evaluate drug candidates and determine drug response of various patient cohorts, and comparisons to clinically approved drugs for the disease of interest.

## **Migration, Growth and Kinetic Assays**

- Using various luminescent and fluorescent imaging techniques, general characteristics of growth, cell migration and calcium mobilization are measured.

## **Flow Cytometry Analysis and IHC**

- Standard flow cytometric and IHC assays for multiplex cell surface marker identification, apoptosis, and cell cycle analysis.

## **Identity (Cell Line Authentication)**

- STR-analysis for at least 10 microsatellite loci including sex determination, report to include details of results, any evidence of contamination with other cell lines, match to original cell line (if iPSC and provided by customer) and information if sample matched to repositories (ATCC, NIH).

## **Custom Differentiation**

- Custom differentiation protocol optimized for specific cell types

## **Trilineage Differentiation**

- Differentiation towards all three lineages using the STEMDiff™ Trilineage Differentiation Kit (7 days ectoderm, 5 days Mesoderm and Endoderm), flow cytometry analysis of at least 10,000 events, report percent positive for lineage specific markers (below), raw FCS data to be supplied for troubleshooting/reanalysis.
- Ectoderm – PAX6 and Nestin
- Mesoderm – Brachyury and CXCR4
- Endoderm – SOX17 and FOXA2

## **Karyotype**

- Analysis of at least 20 metaphase spreads by accredited cytogeneticist, comprehensive report outlining findings, resolution, number of cells counted, analyzed and karyogrammed.

## **SNP Array**

- Analysis of sample for any abnormalities not detected by g-banding, interpretation by accredited cytogeneticist, comprehensive report outlining findings, specifications and limitations.

## **Sequencing/ Gene Expression**

- Whole Exome Sequencing or Whole Genome Sequencing. Gene expression determination using the NanoString platform

## **Undifferentiated Marker Expression**

- Flow cytometry analysis of up to 7 markers (e.g. Oct4, Nanog, Sox2, TRA-1-60, TRA-1-81, SSEA3 and SSEA4). At least 10,000 events, report percent positive for each marker, raw FCS data to be supplied for troubleshooting/reanalysis.

# Cellaria's Methods of Engagement with Customers

- Standard commercial transaction for Cellaria's Patient Specific Cell Models, Cell Culture Media and/or any combination of services
- Prospective patient enrollment, using customer defined criteria, for the development of patient cohorts used for in vitro assays
- 2D, 3D and 3D co-culture drug screening
- Off the Shelf Proteomic services
- Genomic and/or Proteomic Dataset generation

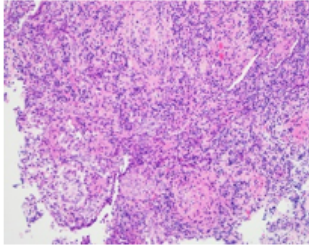
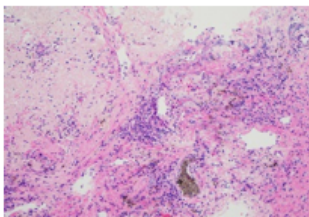
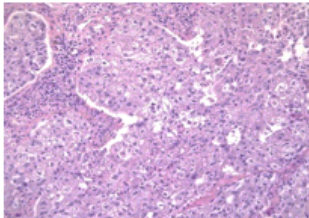
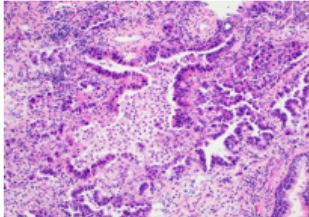
# Cellaria's Disease Models

## Expanding Patient Cohorts for Pancreatic Cancer and Other Disease Categories

Cell Line	Diagnosis	TNM Stage	Stage Group	Clinical Info	Co-Indications
<b>Basket</b>	Invasive, moderately differentiated ductal adenocarcinoma of the pancreatic head.	T3N1Mx	G2	70-75-year-old Caucasian Female	Jaundice, Osteoporosis, Anxiety, Arthritis
<b>Chocolate</b>	Ductal type, poorly differentiated adenocarcinoma of the pancreatic head	T3N0Mx	N/A	50-55-year-old Caucasian Female	Diabetes Mellitus, Jaundice, Biliary stricture
<b>Stew</b>	Invasive moderately differentiated adenocarcinoma of the pancreatic head	T3N1M0	G2	65-70-year-old Caucasian Male	Diabetes Mellitus, Congestive Heart Failure, COPD, Emphysema, Arthritis



# Cellaria's Disease Catalogue (NSCLC)

Model Name	M/F	Age	Mutational Analysis (Whole Genome/Exome)	Clinical Diagnosis	H&E Image	H&E Report (CD: Consistent with Diagnosis? C%: % Tumor, N%: % Necrotic, T%: % TIL)
<b>Bastion</b>	F	70-75	No Mutations	Squamous cell carcinoma		<u>CD:Y</u> , C%:5, N%:0, T%:n
<b>Boulder</b>	M	65-70	63%APC, 62%SMARCA4, 54%ATM(T-A), 43%ATM(Y-H), 37%TP53, 35%PTPN11, 33%CDKN2A(R-Q), 29%CDKN2A(L-S), 16%SMO, 9%TSC1	Squamous cell carcinoma		<u>CD:N</u> , C%:0, T%:NA
<b>Jacket</b>	M	70-75	100%AR, 100%KRAS, 100%TP53, 62%MUTYH, 32%MSH6	Adeno-carcinoma of the lung		
<b>Pincer</b>	F	65-70	75%PBRM1, 70%BMP1A, 47%TP53, 12%SMO, 8%KDR (VEGFR2), 7%RAF1	Adeno-carcinoma, invasive		<u>CD:Y</u> , C%:40, N%:0, T%:<5

# Cellaria's Patient Enrollment Priorities (Example)

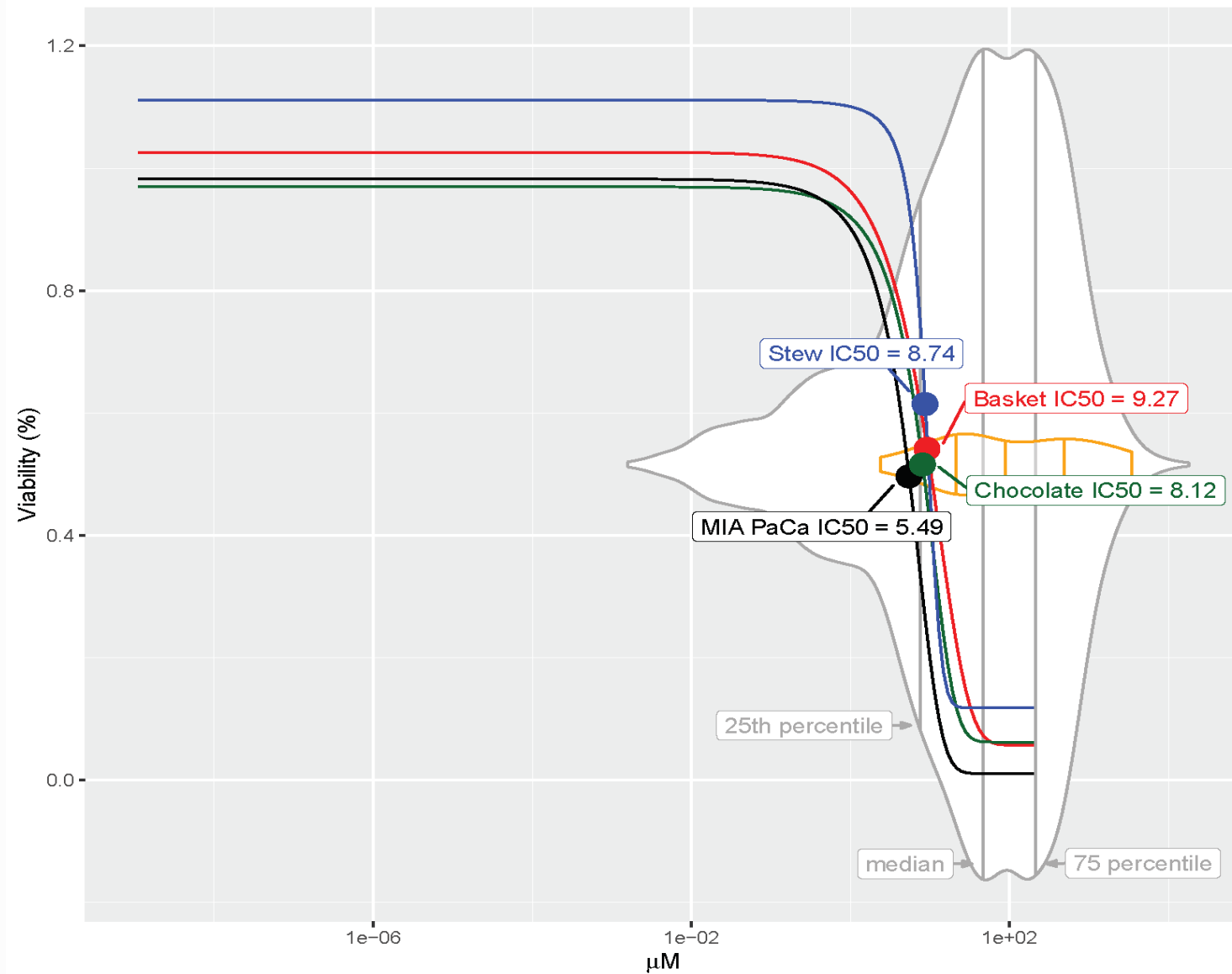
## Enrolling – Breast Cancer

Cell Code	Diagnosis	ER/PR	Her2	Other Drugs
	Her2+ Recurrent, post-treatment		pos	Tam
	Her2- Recurrent, post-treatment		neg	Olaparib
	ER+/PR+/Her2- Low Ki67	pos/pos		
	ER+/PR+/Her2- High Ki67	pos/pos	pos	
	ER-/PR-/Her2-	neg/neg	neg	

## Enrolling – Ovarian Cancer

Cell Code	Diagnosis	Condition	Her2	Other Drugs
	Her2+ High Grade Serous	Initial Diagnosis	pos	
	High Grade Serous	Adjuvant Chemo		

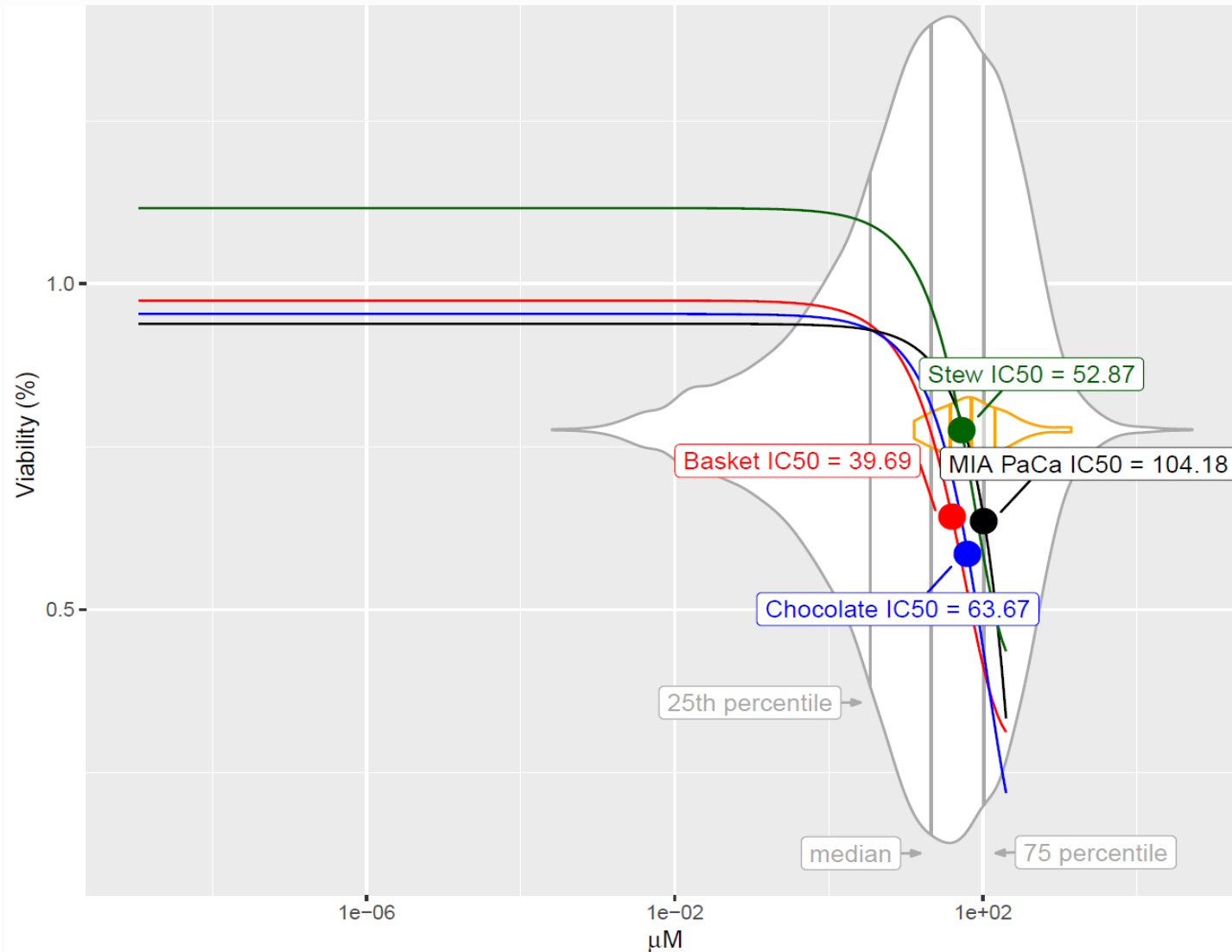
# Drug Response: Cisplatin with PanCa 2D



## Data.Source

- a Basket
- a Chocolate
- a GDSC IC50 data (all drugs)
- a GDSC IC50 data (Cisplatin)
- a MIA PaCa
- a Stew

# Drug Response: Olaparib with PanCa 2D

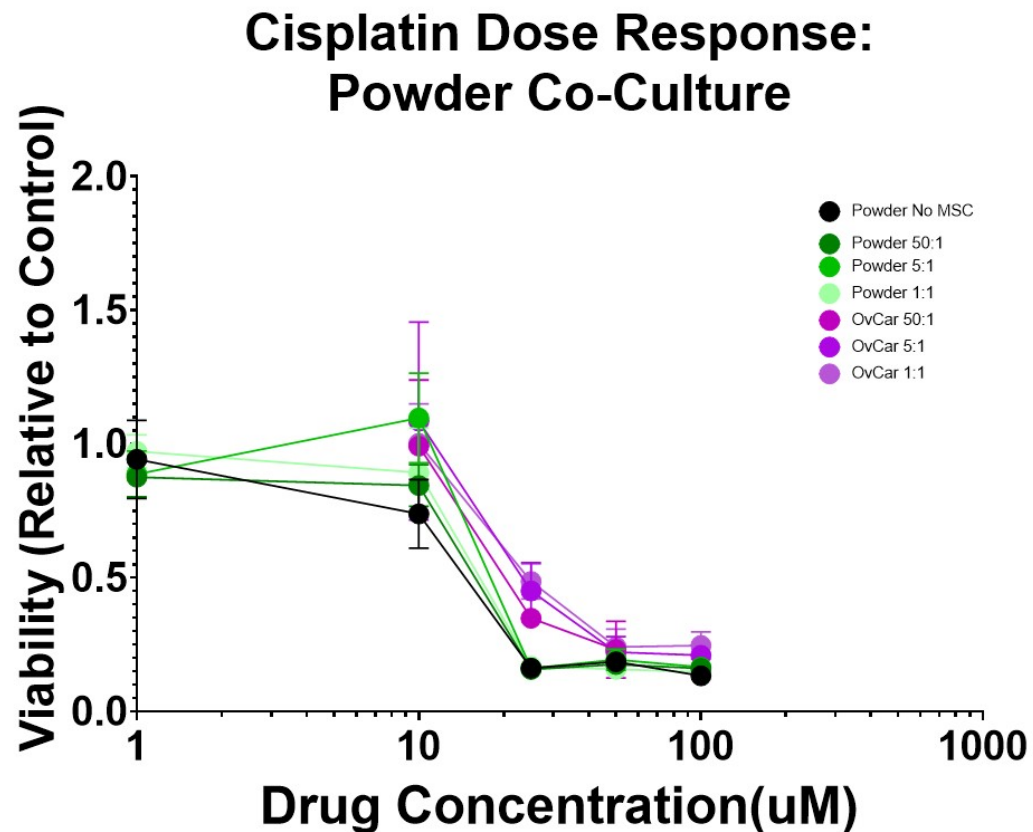


Data.Source

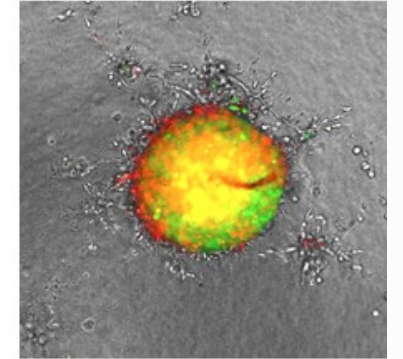
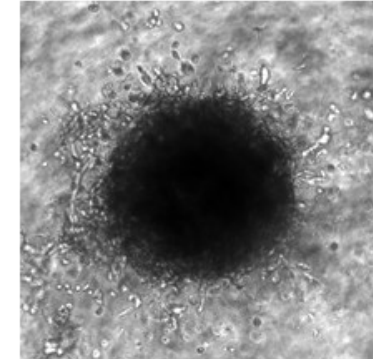
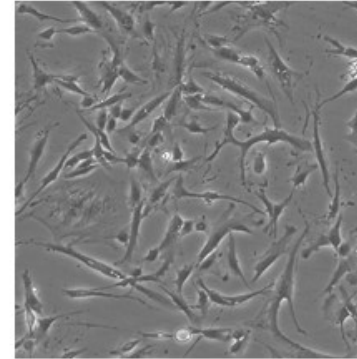
- a Basket
- a Chocolate
- a GDSC pancreas data (all drugs)
- a GDSC pancreas data (Olaparib)
- a MIA PaCa
- a Stew

14,252 GDSC cell-lines of same tumor type  
84 GDSC cell-lines of same type type and drug

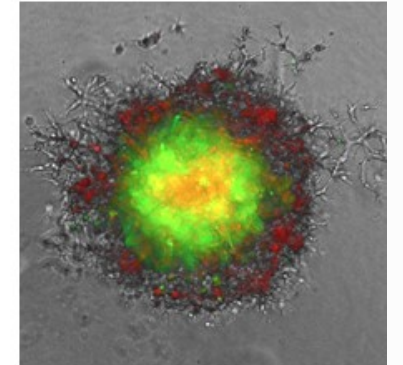
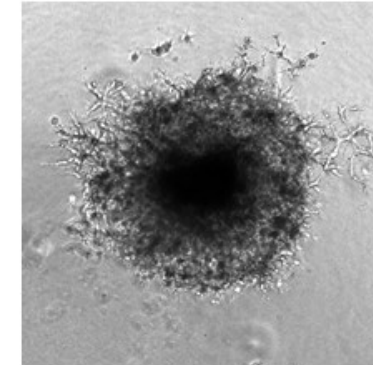
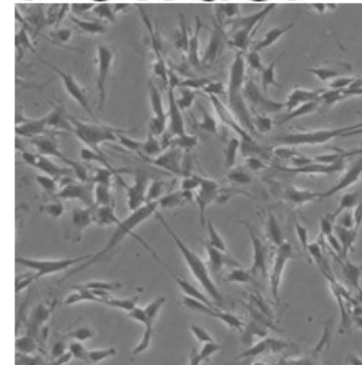
# Carousel and Powder Ovarian Cancer tumor metastatic model with MSCs co-culture



Carousel



Powder



2D

3D Co-culture

3D Co-culture

Red -MSCs Green-Cancer cells



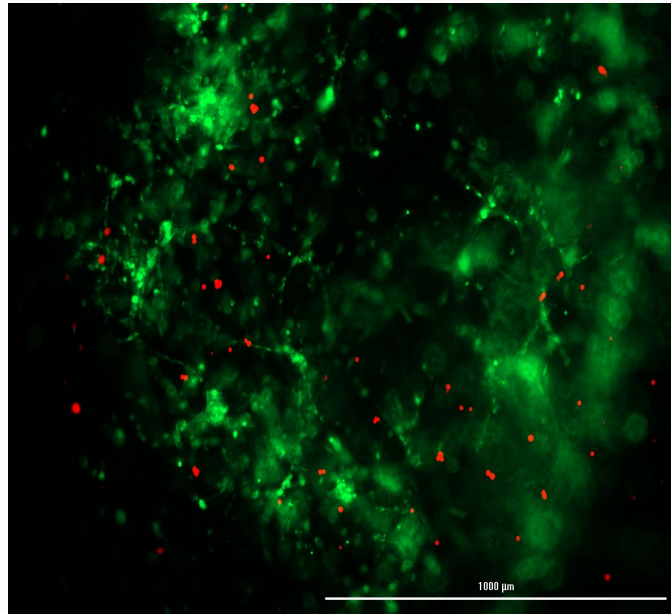
# Cellaria's MINT™ Assay

(Model of the Immune Niche of Tumors ):  
3D Co-Culture to Model TME in the presence of T cells

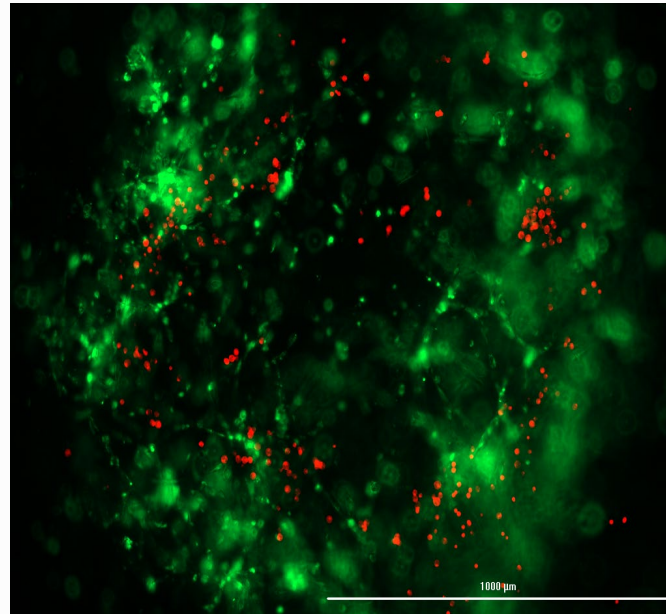
- Utilize repeatable workflow of 3D Co-Culture format to profile T-cell clones within the microenvironment
- Compare performance of patient-matched T-cells to unrelated T-cell donor
- Optimize and standardize flow cytometric characterization of T-cell populations in patient samples and co-culture models
- Evaluate/optimize model performance for the PD-1 pathway and targeting efficacy of CAR-T therapies

# Cellaria's 3D Co-Culture Assay

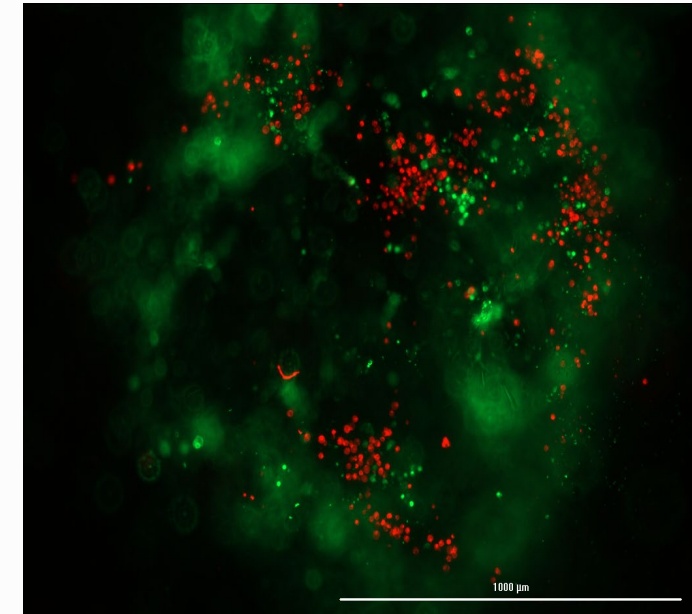
(Basket\_PanCa 3D with Activated T cells)



Time 0 (11:30 AM 9/2/21)



Time 2 hrs (1:30 AM 9/2/21)

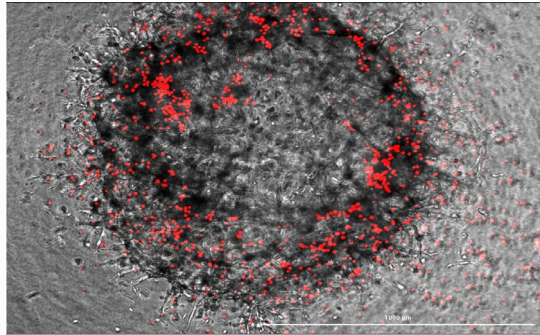


Time 19 hrs (8:30 AM 9/3/21)

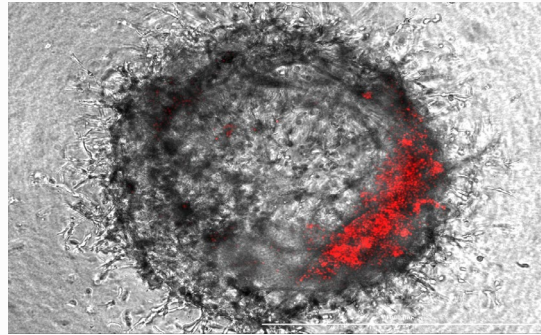
- Activated T-cells quickly migrate toward tumor spheroids

Red – T Cells  
Green – Tumor Cells

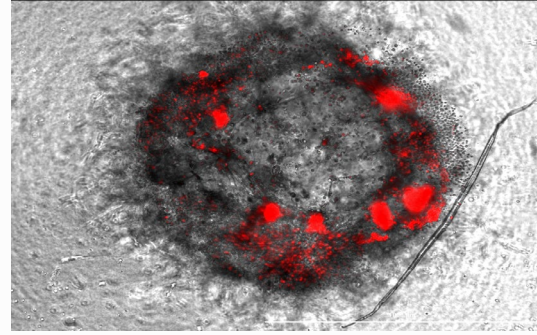
# Cellaria's 3D Co-Culture Assay (Basket\_PanCa 3D with Activated T cells)



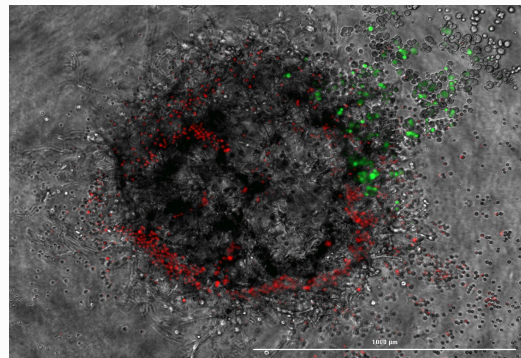
Time 0 hours 9-24 3PM



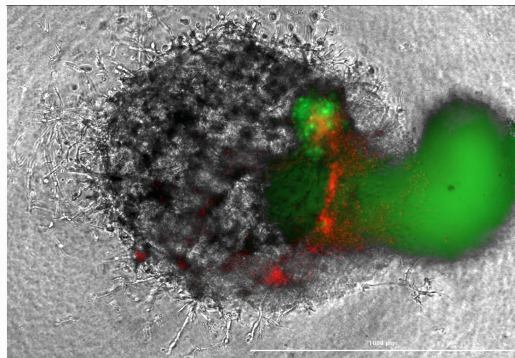
Time 21 hours 9-25  
10AM



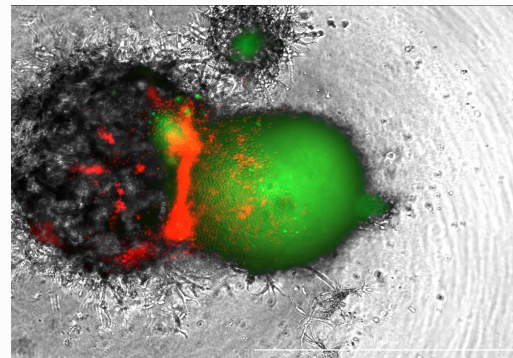
Time 44 hours 9-26  
9AM



Time 0 hours 9-24  
3PM



Time 21 hours 9-25  
10AM



Time 44 hours 9-26  
9AM

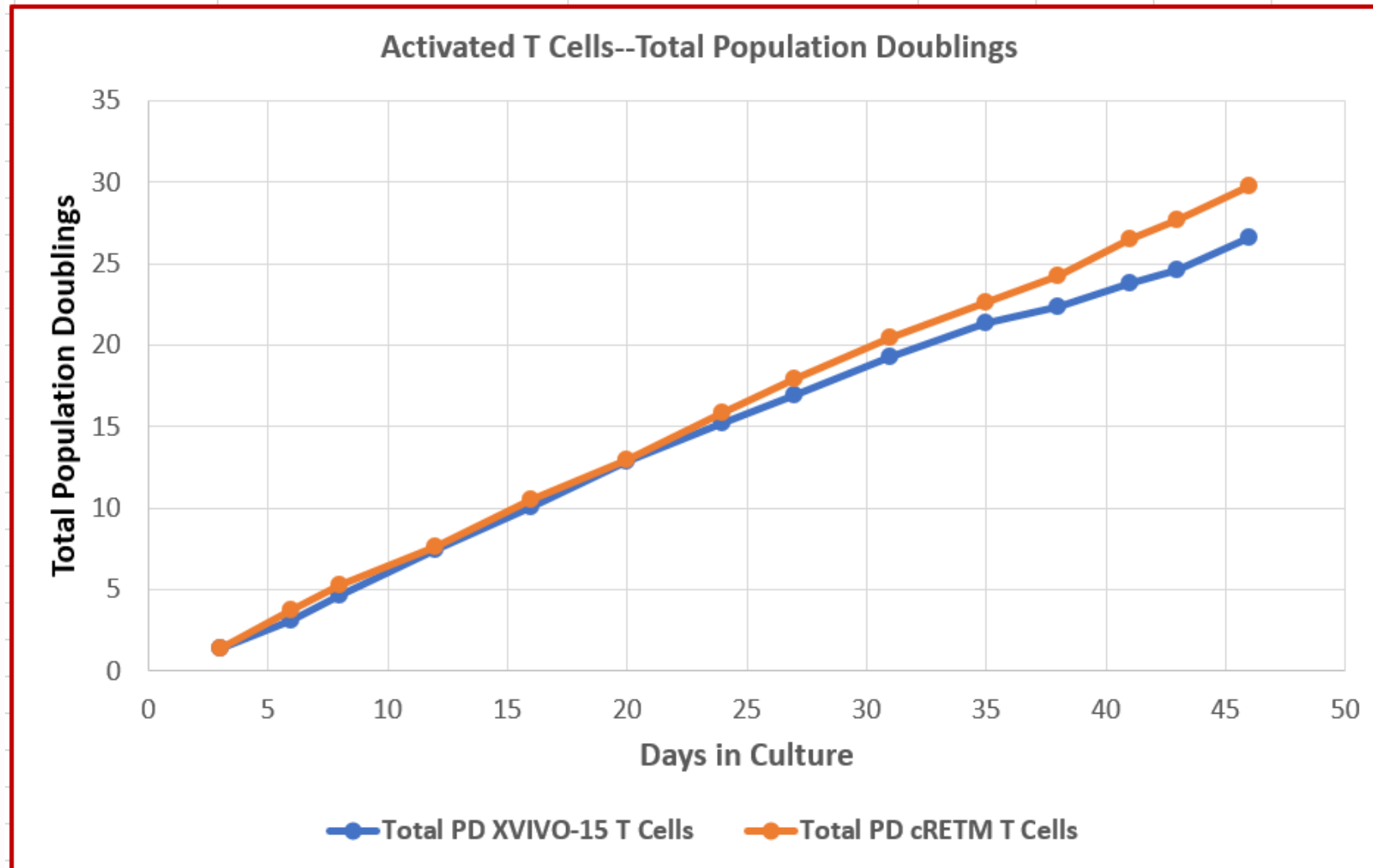
Red – T Cells  
Green – MSCs

- Activated T-cells infiltrate the pancreatic spheroid and migrate within the spheroid
- The addition of mesenchymal stem cells (MSC) at the same time as activated T-cells highlights effects of T-cell migration within pancreatic cancer spheroids



# T-Cell Growth Curve

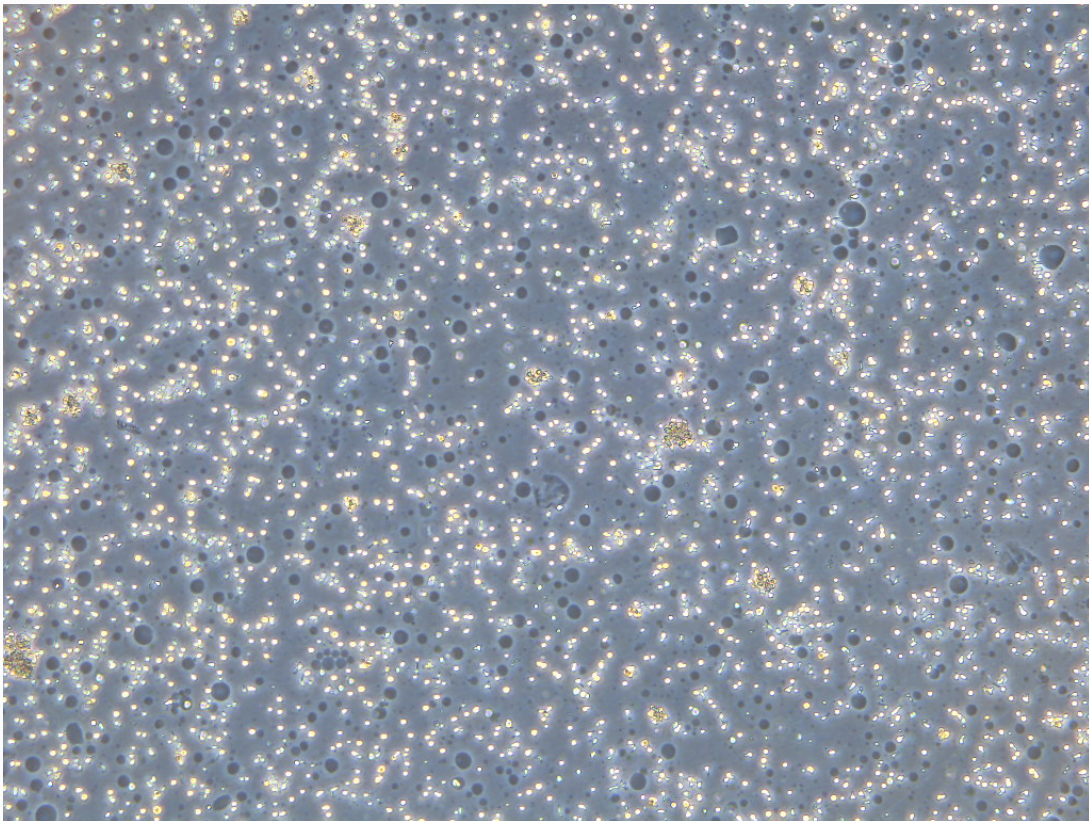
46 Days, 16 Passages



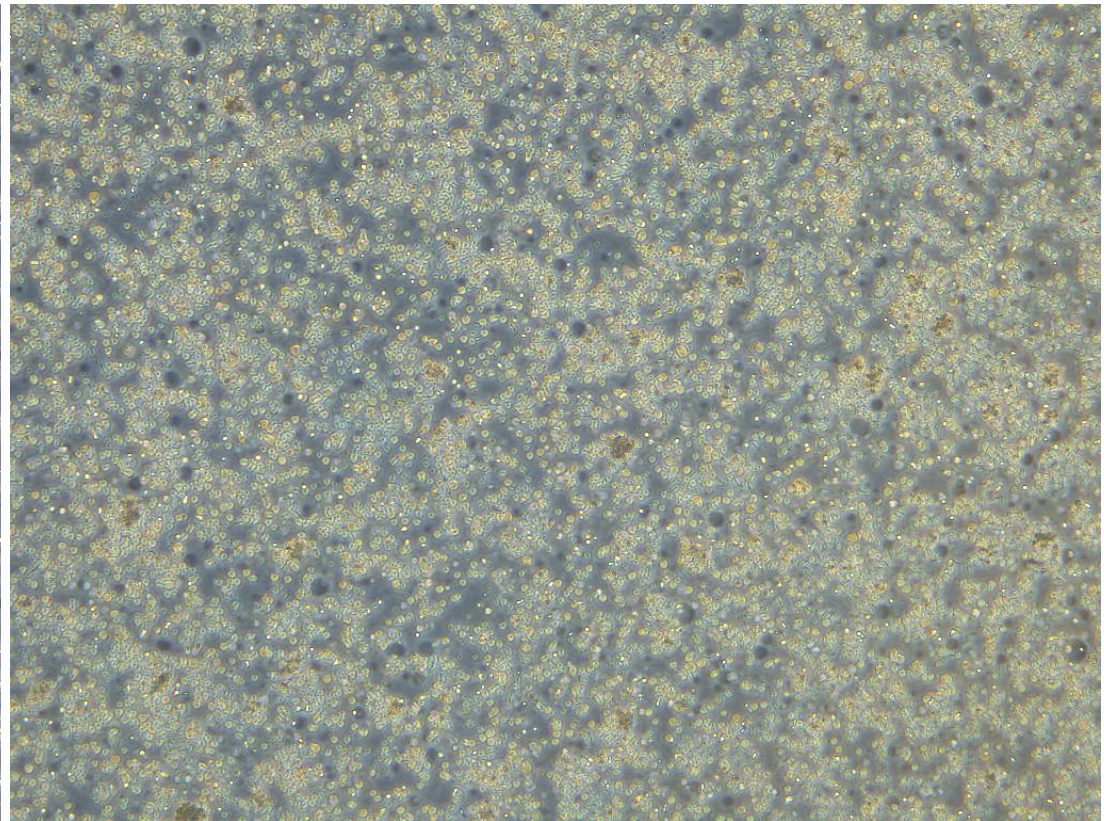
# T Cell Activation **In-Vitro**

**Renaissance Media (5x images): Doubling Time 37 hours**

**20Sep: 1Million Cells Seeded**

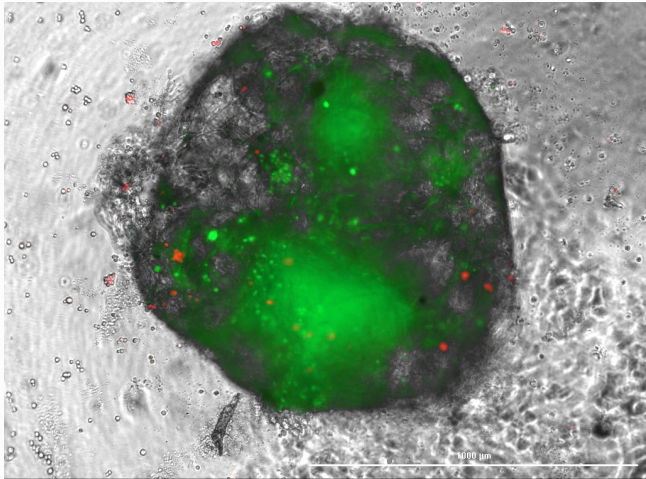


**24Sep: 5.9Million Cells Harvested**

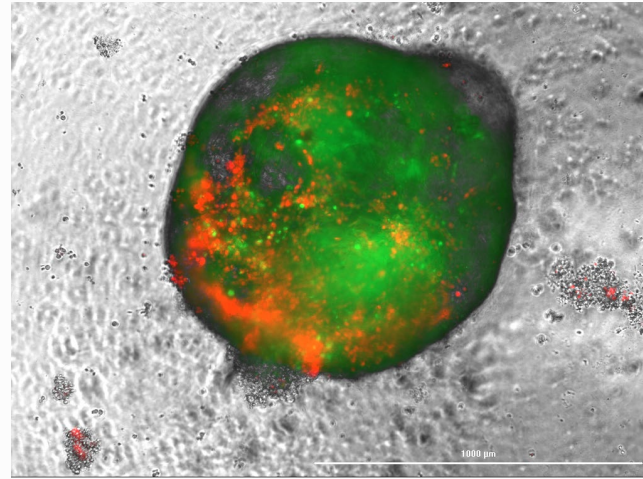


# Cellaria's 3D Co-Culture Assay (Chocolate\_PanCa 3D with Activated T cells)

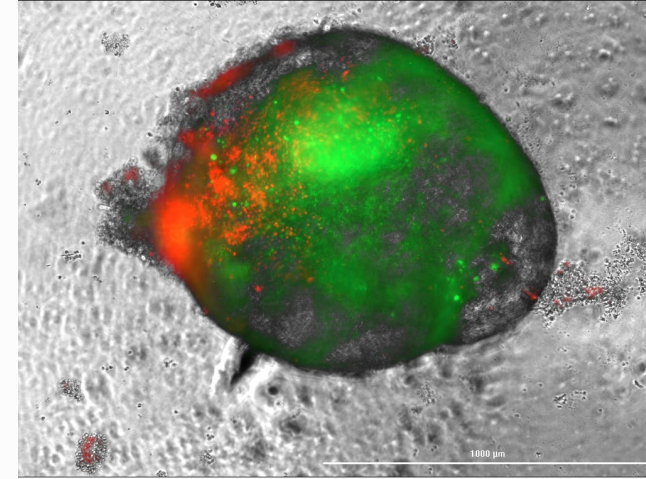
Red – T Cells  
Green – MSCs



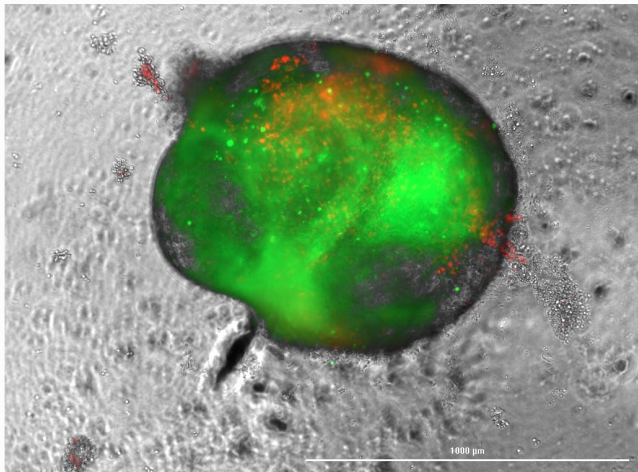
Day 0



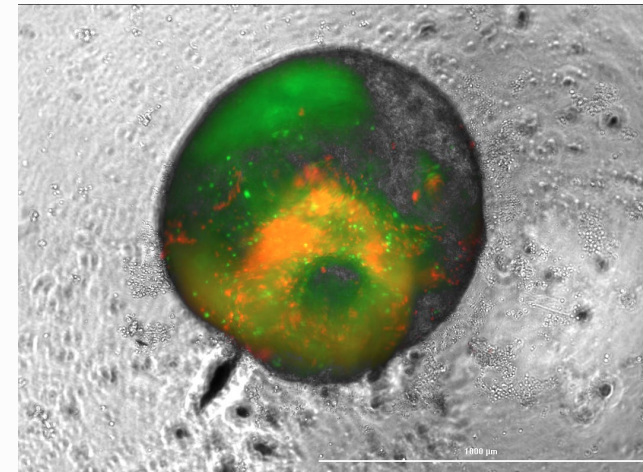
Day 2



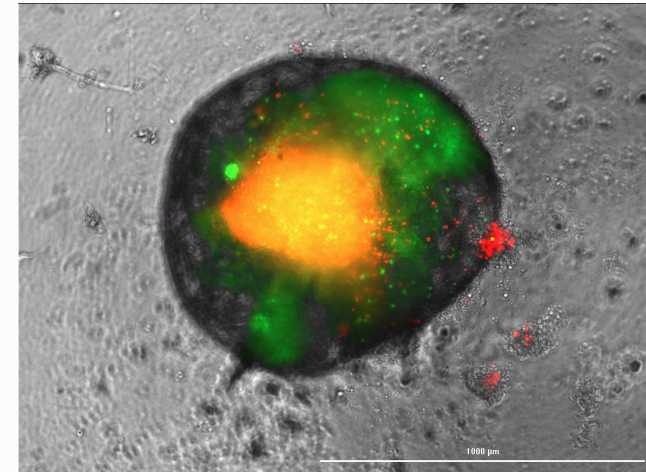
Day 3



Day 5

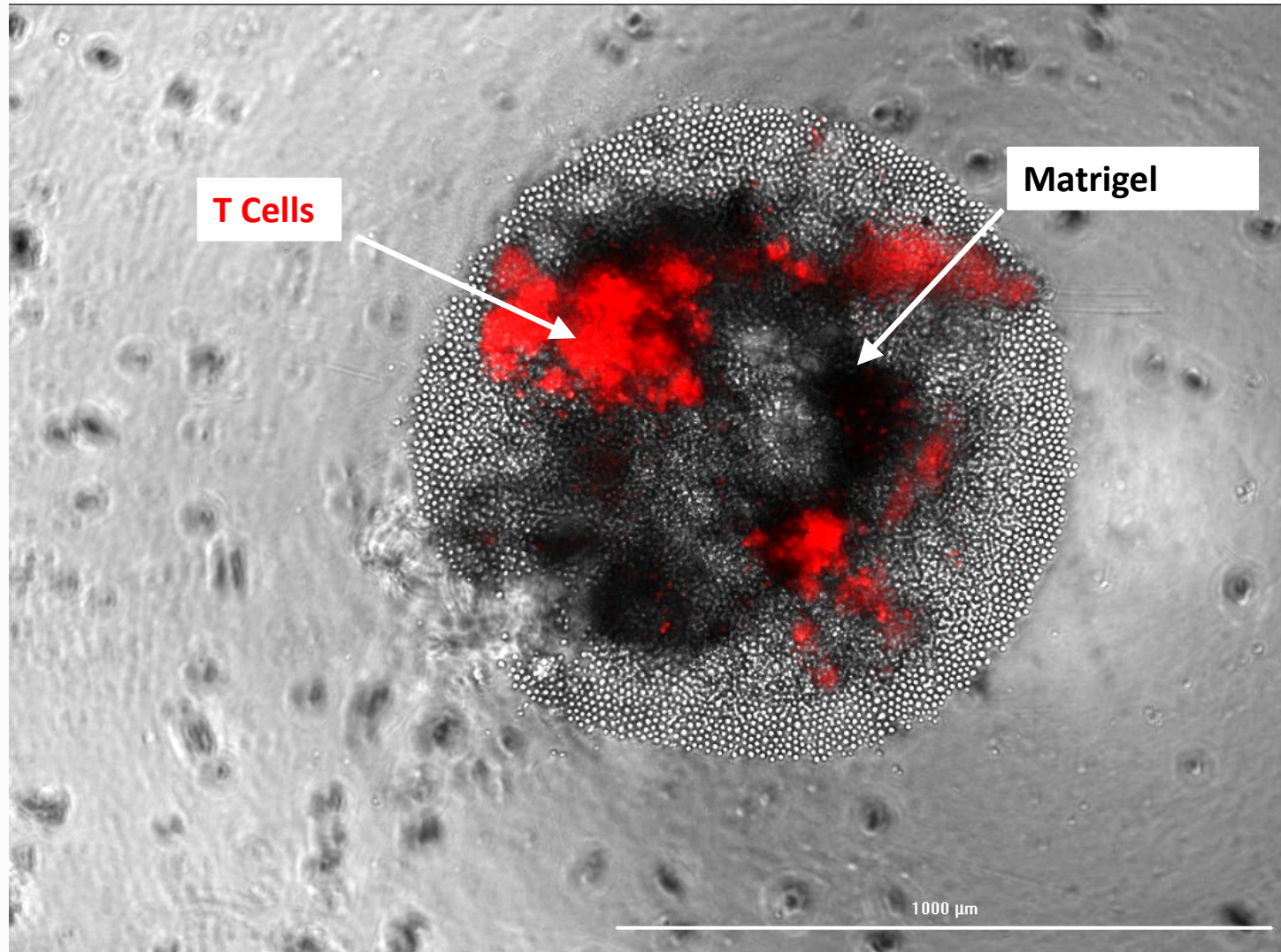


Day 7



Day 13

# Cellaria's 3D Co-Culture Assay (Chocolate\_PanCa 3D with Activated T cells)





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Smarter Search