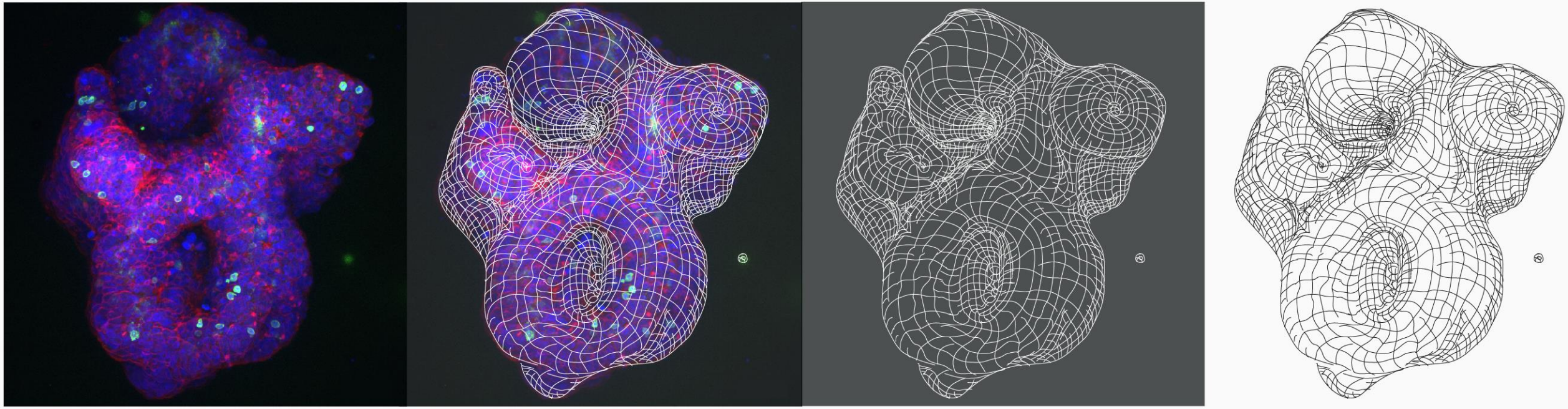
BIOENGINEERING AT MOFFITT

Prof. W. Gregory Sawyer

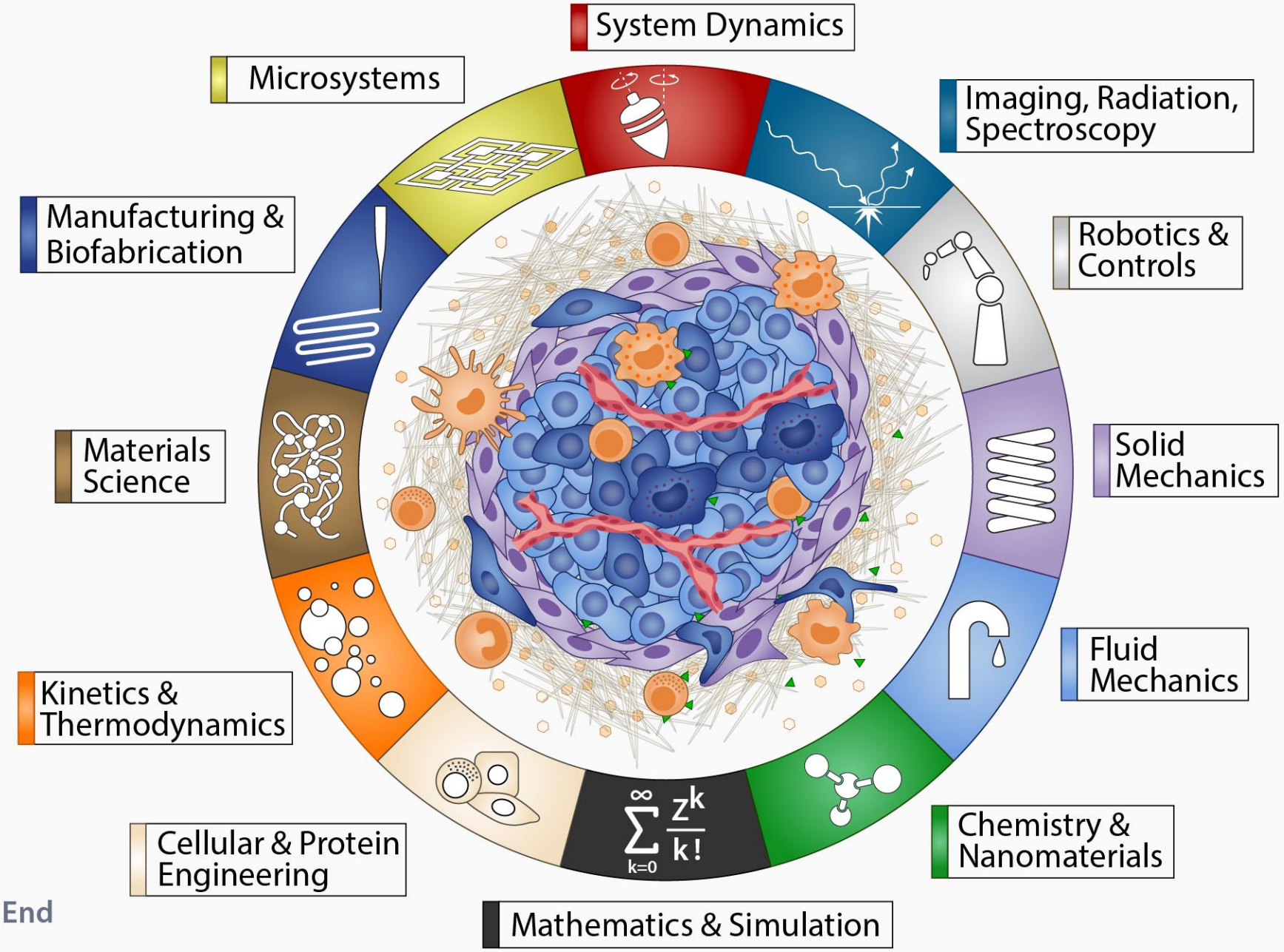
# Engineering Cancer's End

## *Cancer Engineering | Confronting the Complexities of Cancer*



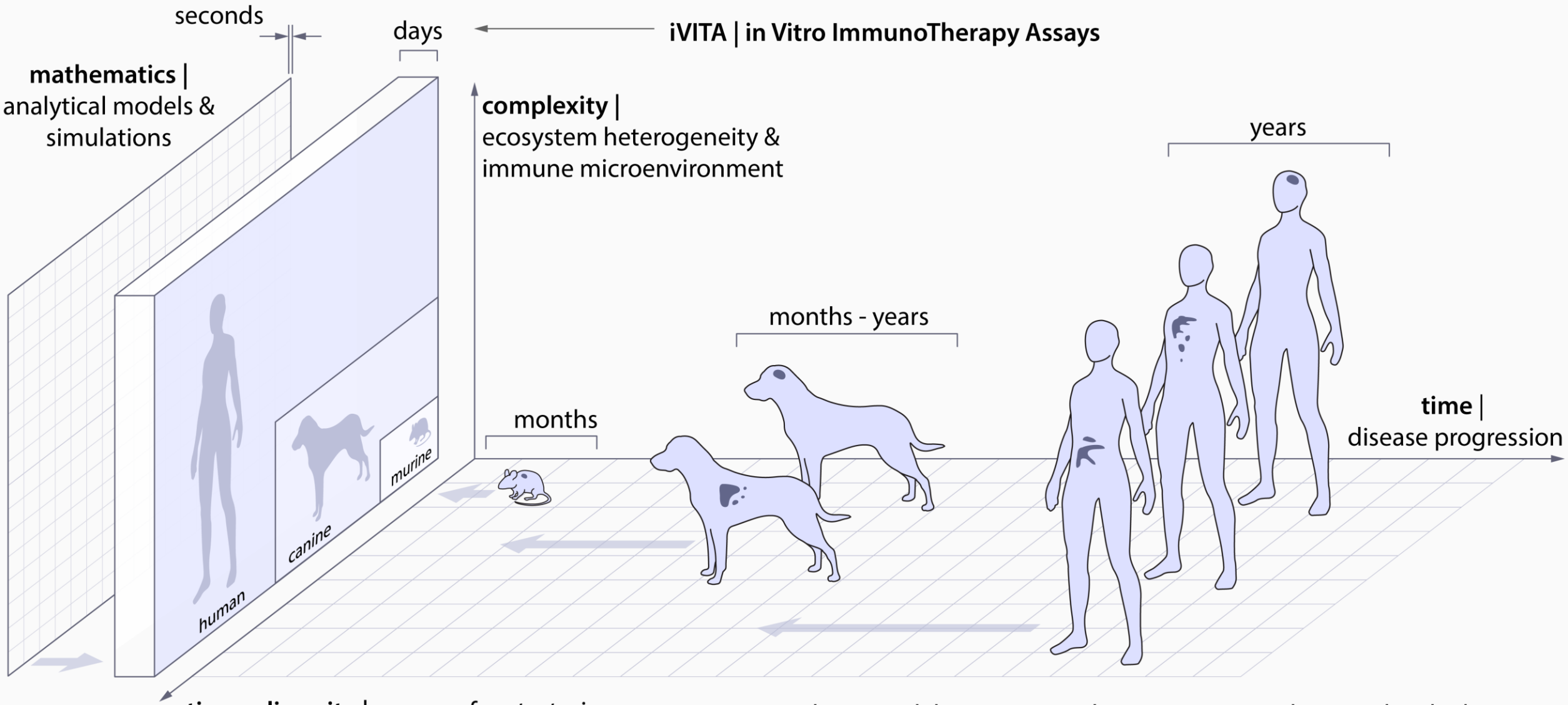
*CRC µTumoroid | MSS POLE Mutation - day 4*

# Cancer Engineering | *An Interdisciplinary Approach*




Engineering Cancer's End
*Cancer Cell (2024)*

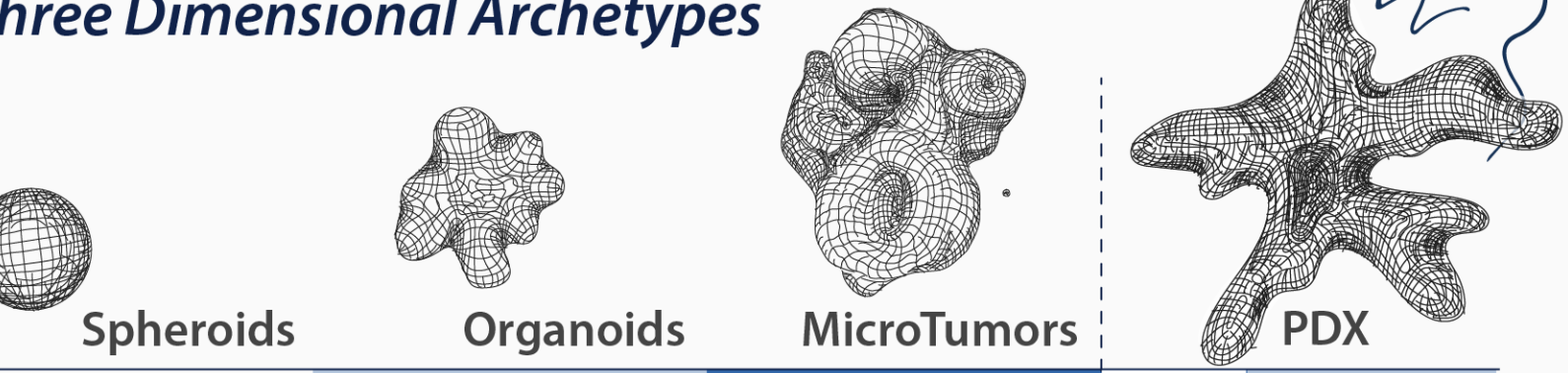
# Chasing Cancer: *Precision Medicine and Preclinical Models*




These models give an insight into cancer etiology, molecular basis, host tumor interaction, the role of microenvironment, and tumor heterogeneity in tumor metastasis.

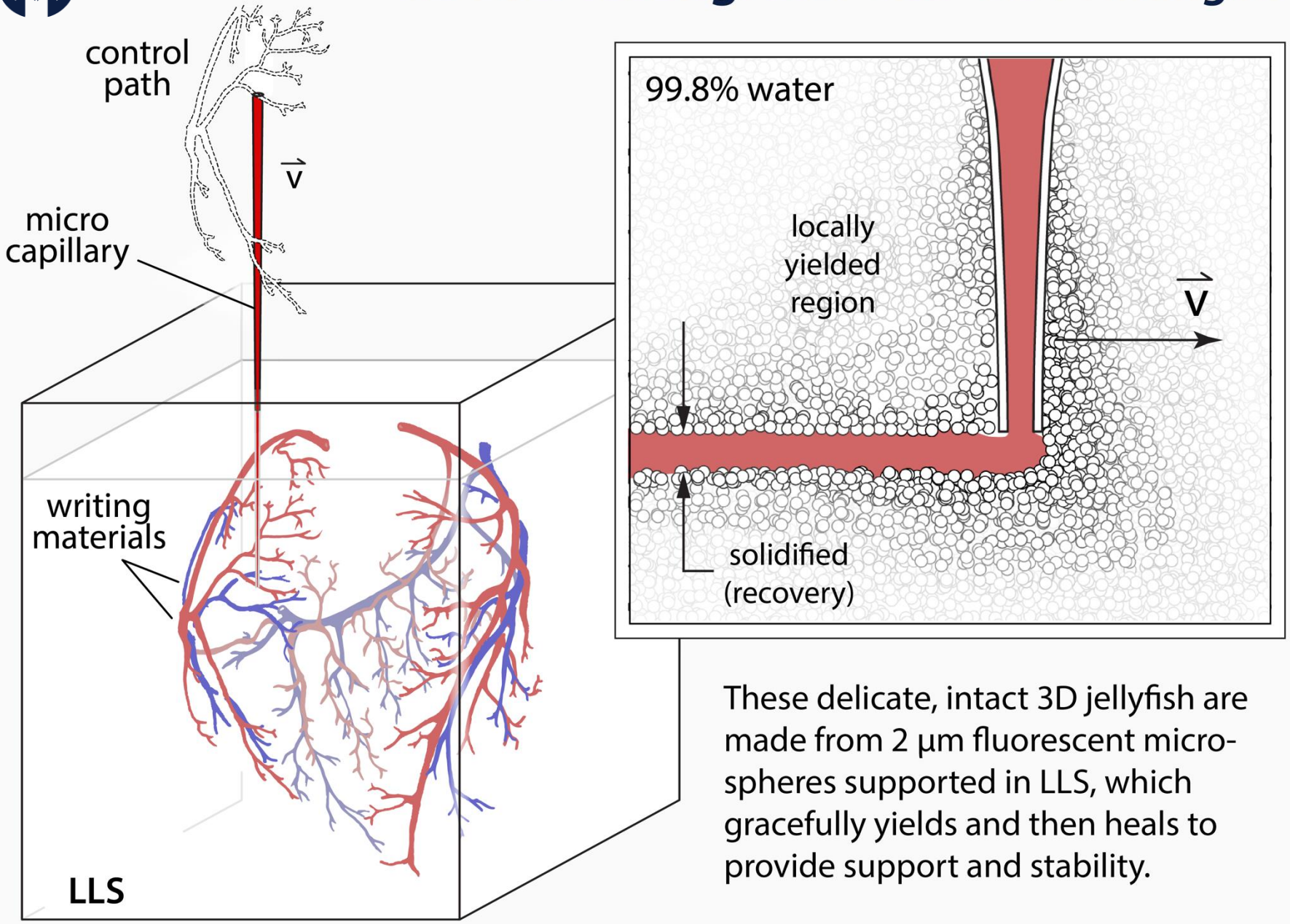
# Accessible In Vitro Models

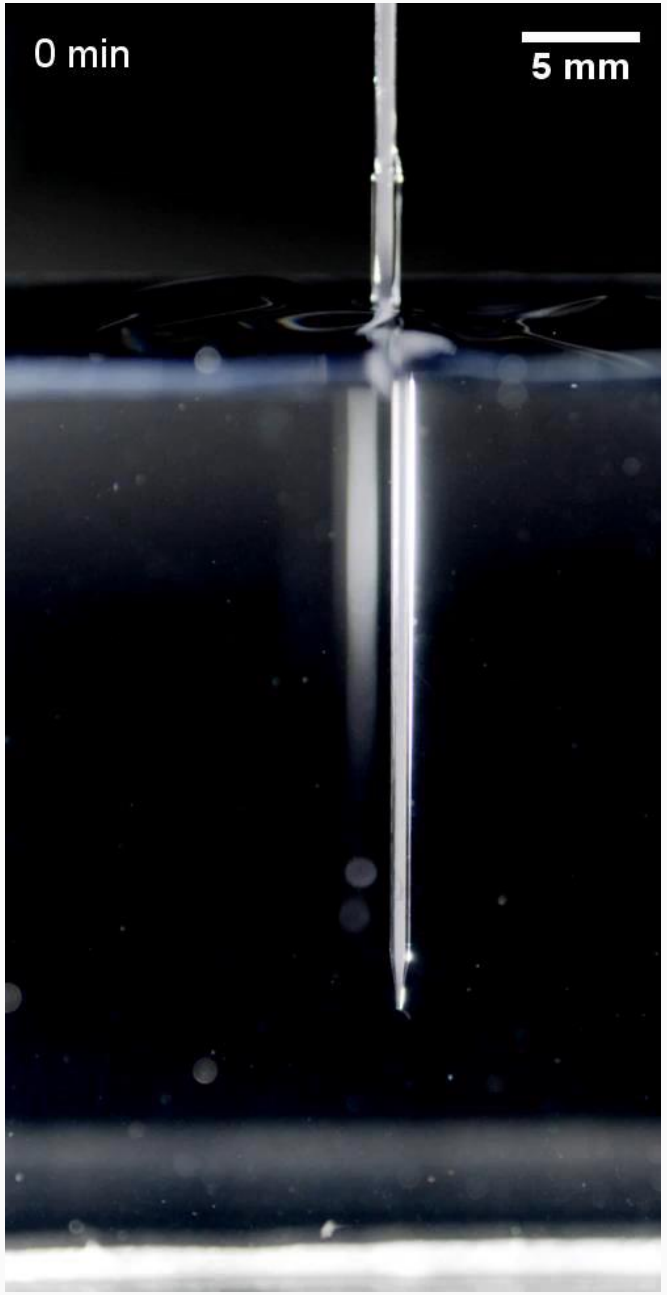
## *Three Dimensional Archetypes*



| | 2D Cell-Lines | Spheroids | Organoids | MicroTumors | PDX |
|---|---|---|---|---|---|
| Cellular Heterogeneity | N/A | N/A | limited | extensive | murine / human: extensive |
| Characteristic Size | monolayer | 50 µm – 100 µm | 80 µm – 250 µm | 100 µm – 1 mm | 300 µm – > 1 mm |
| Cellular Sources | established cell lines | single cell aggregates | stem cells | patient explants → microtissues | patient explants → microtissues |
| Infrastructure Needs | standard | matrigel / 3D matrix | matrigel / 3D matrix | requires perfusion | extensive |
| Imaging | standard | standard/ confocal | confocal | confocal/ multiphoton | intravital/ multiphoton |
| Liquid Media | standard (simple) | standard (simple) | complex | standard / tunable | N/A |
| Extracellular Matrix | surface coating | matrigel / 3D matrix | matrigel / 3D matrix | self-generating | murine / human: mixed ECM |
| Inflitrating Lymphocytes | N/A | N/A | limited | physiological | limited |
| Functional Cellular Interactions | N/A | N/A | limited | physiological | limited |

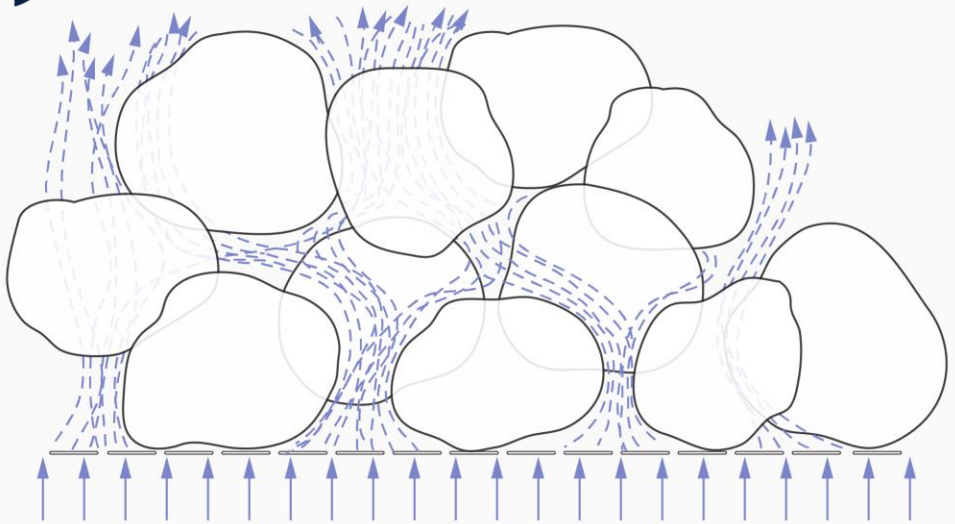
# 3D BioPrinting: BioPelle - *3D Printing in the LLS Medium*



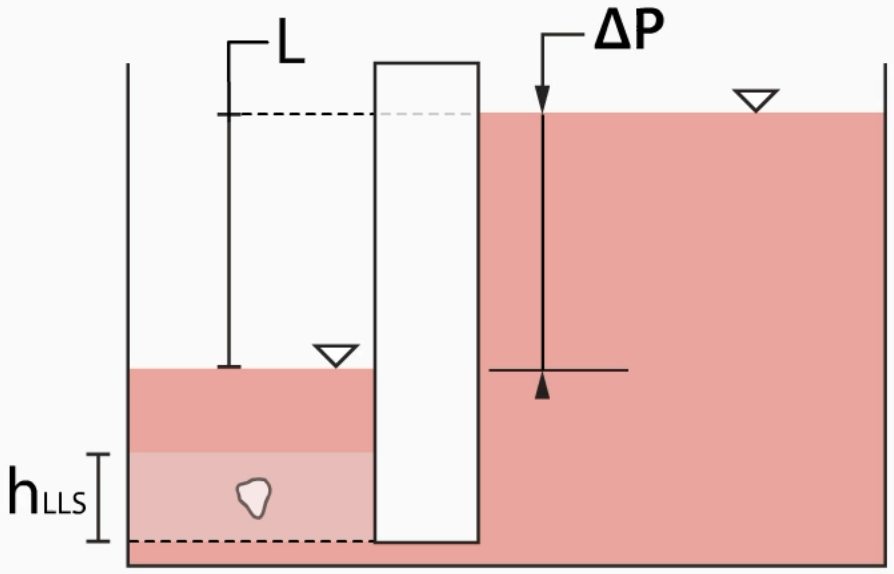



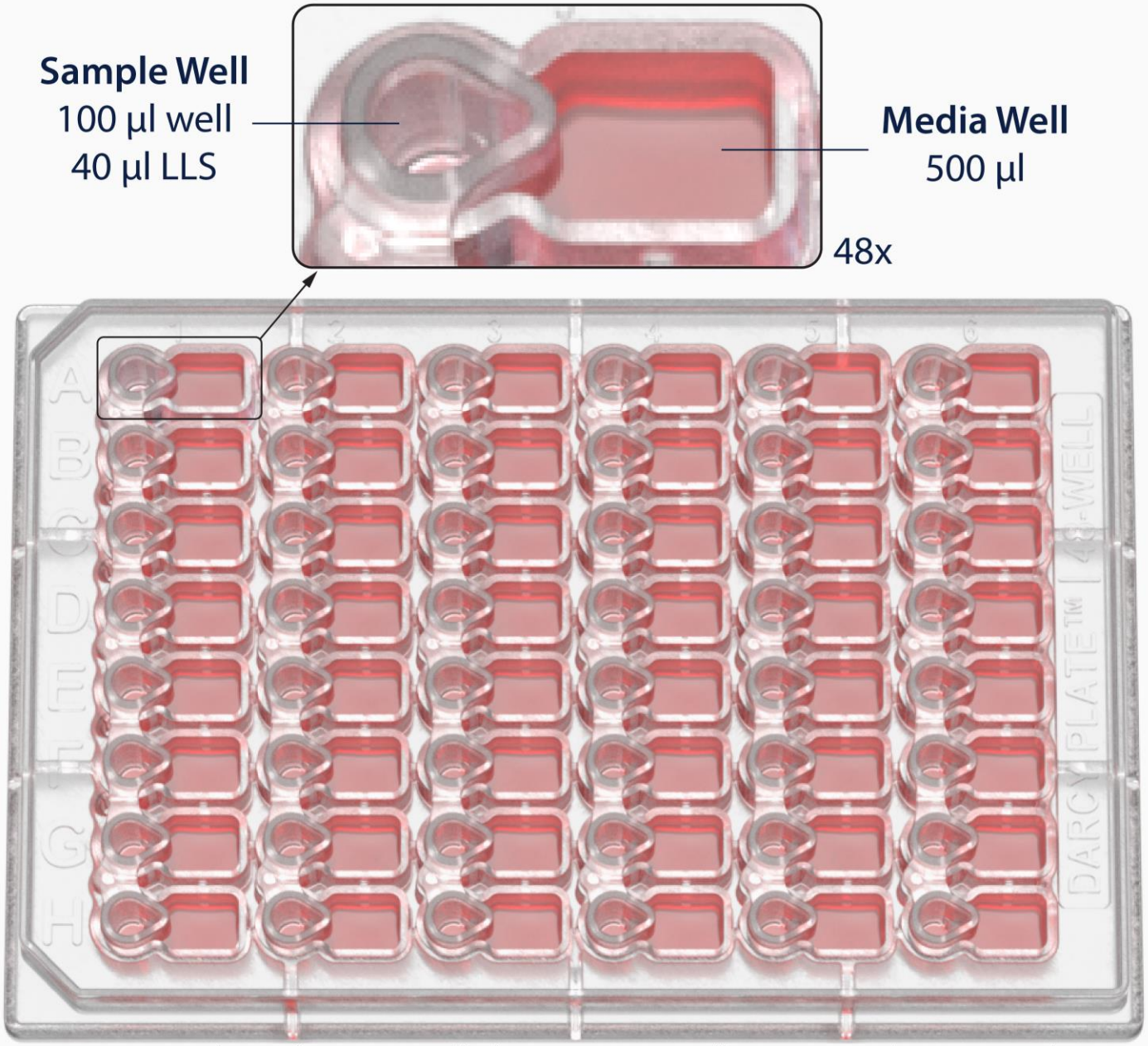

These delicate, intact 3D jellyfish are made from 2 µm fluorescent micro-spheres supported in LLS, which gracefully yields and then heals to provide support and stability.

# Multiwell Plate Perfusion | Darcy Plates *Henry Darcy (1803-1858)*



**Reverse Perfusion**
viscous forces oppose gravitational
body forces to maintain permeability




48 paired perfusion wells | *asymptotically approach static culture*

# A Path Towards Personalized Assays: *Drug Screening in Three Dimensions*

**Biopsy**
***(0.1 - 1 gram)***

~ 1 million cells / µl
~ 1 million cells / mg

**1**

**2**

**Mechanical Disaggregation**
***(~1 µl tissues)***

**3**

**BioPelle**
collection of µTissues

**4** **Collection of Immune Cells from a Blood Draw**

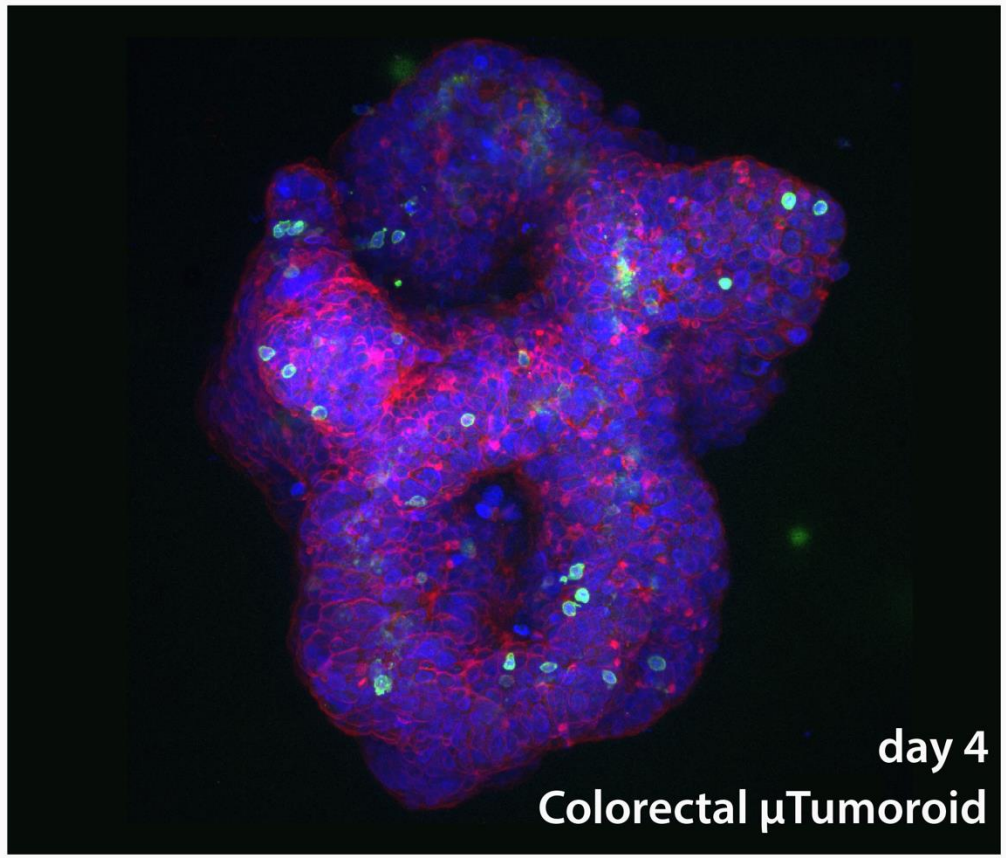
~ 1-2 million cells / ml

**5** immune cells in LLS

**Drug Testing**

**BioPelle**

**6**

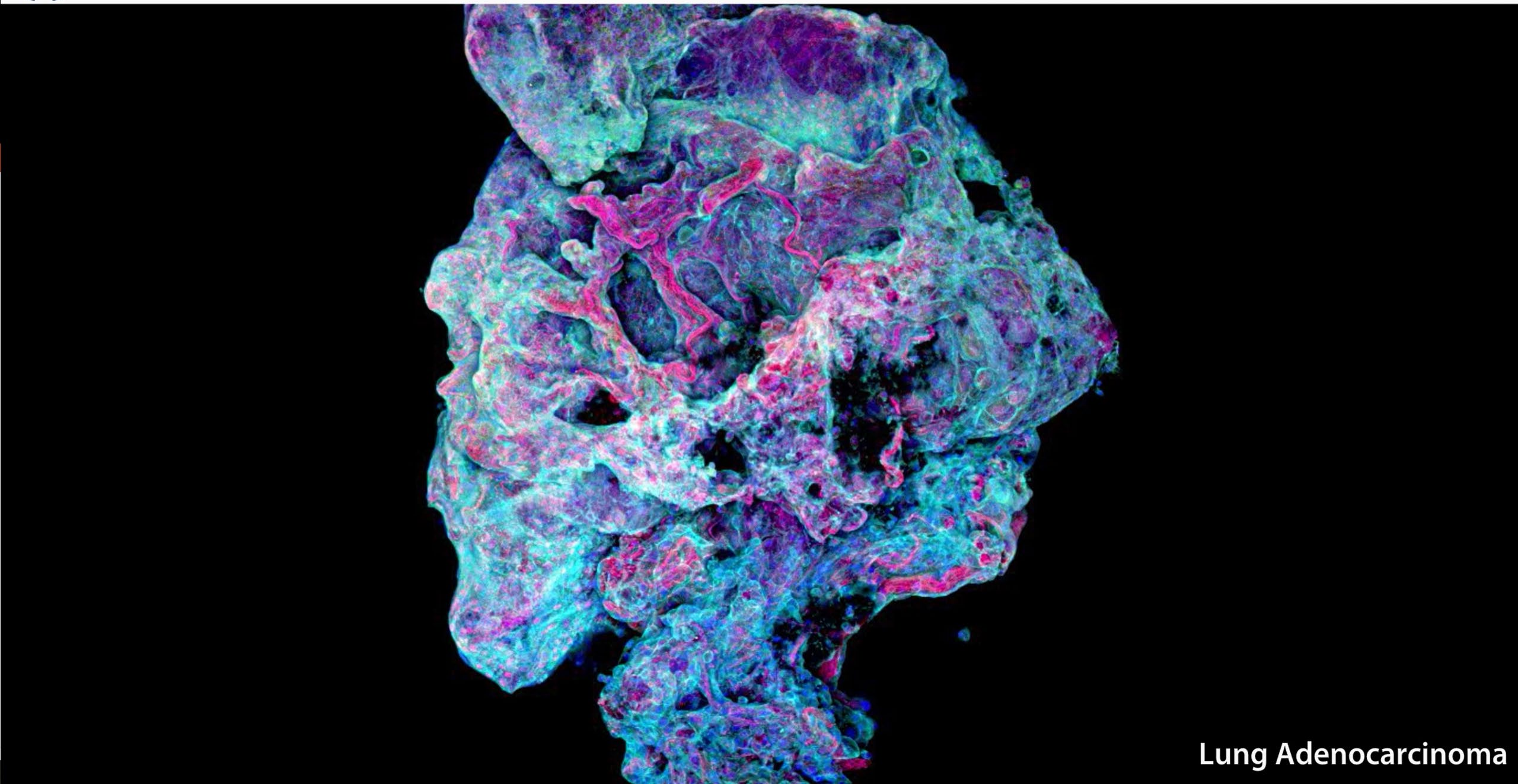



**3D Precision Assays in LLS**

# Patient Avatars - µTumors | *Intratumoral Heterogeneity*

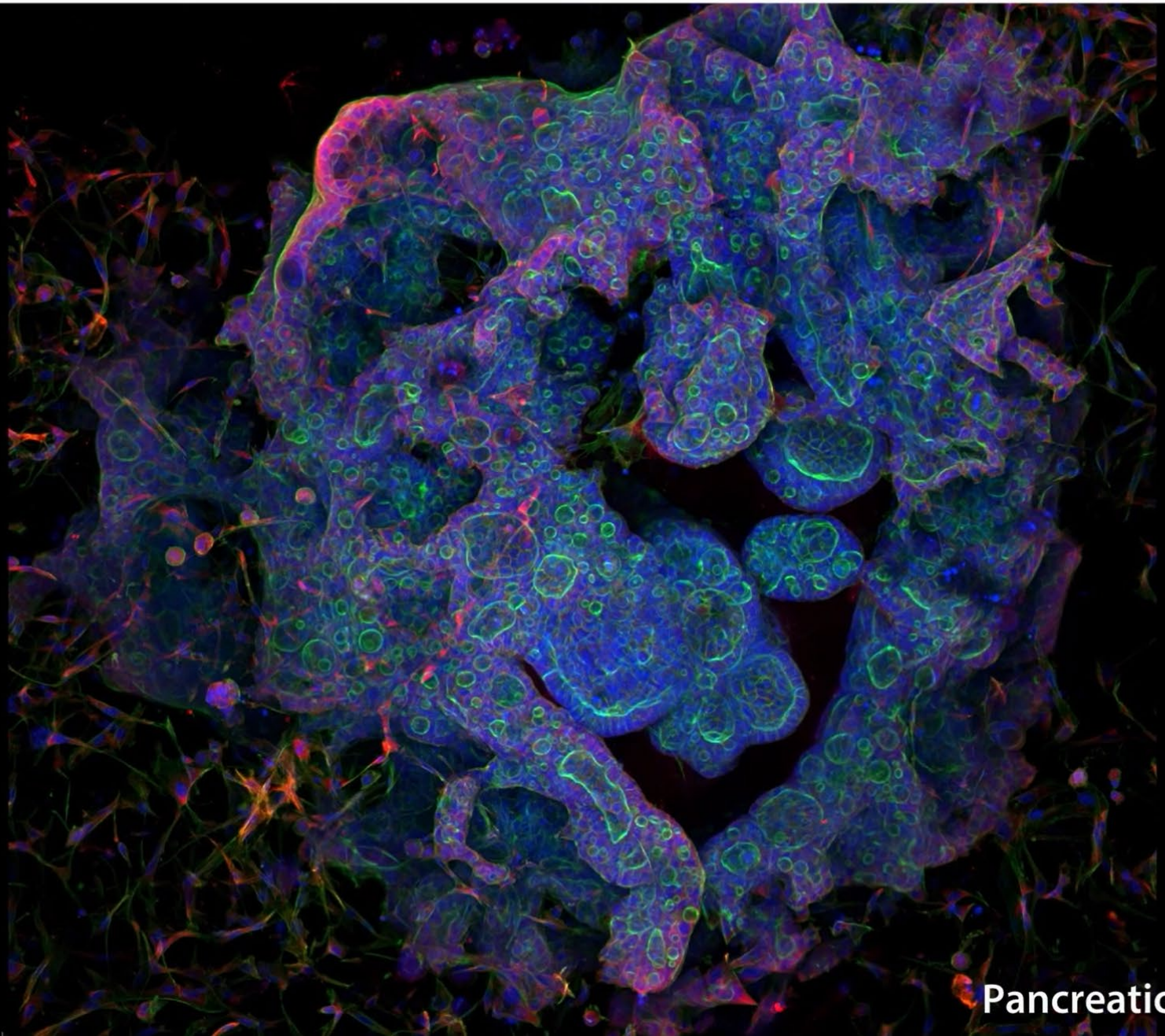
Colorectal MSS POLE Mutation

# Patient Avatars - µTumors | *Intratumoral Heterogeneity*



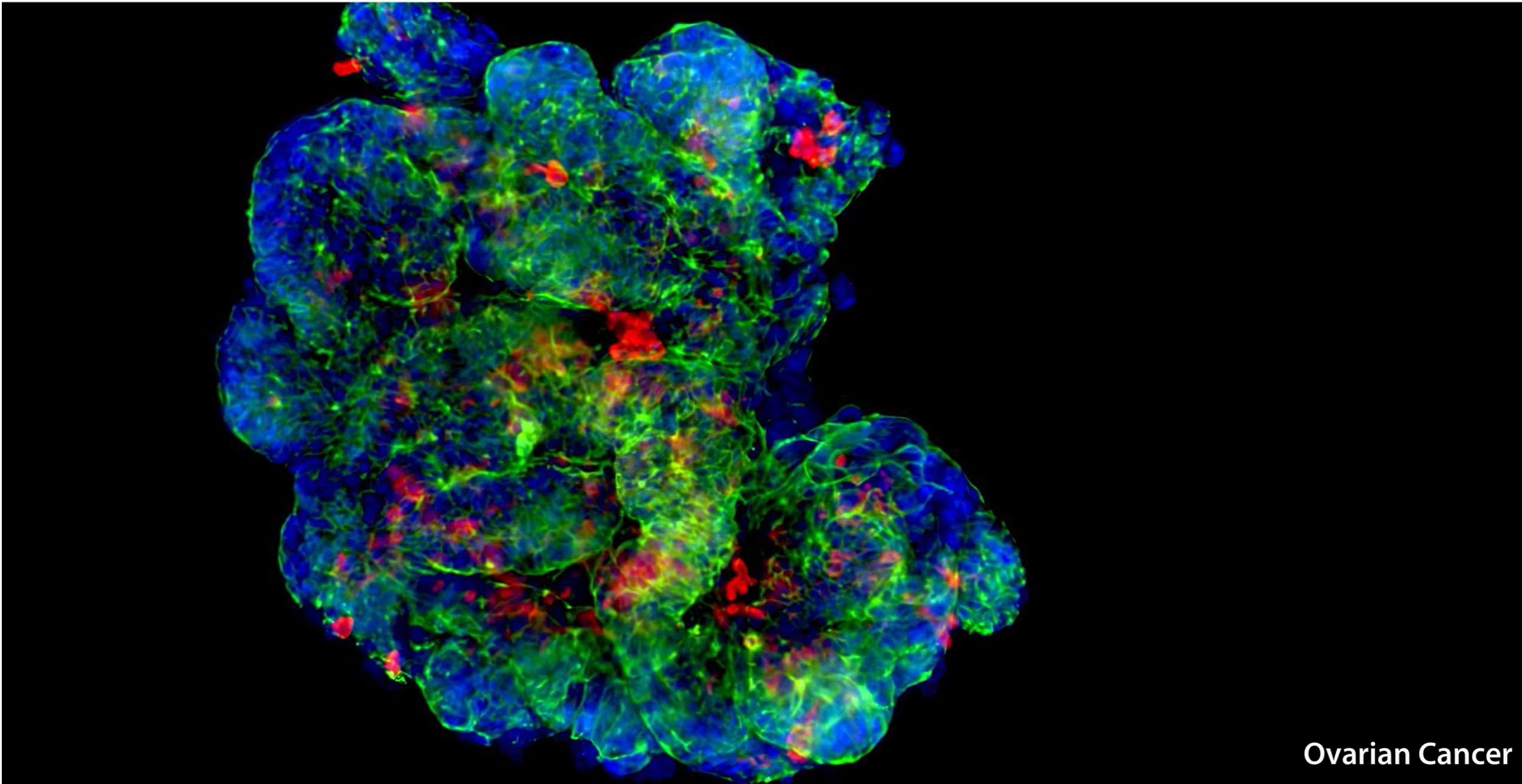
Lung Adenocarcinoma

# Patient Avatars - µTumors | *Intratumoral Heterogeneity*

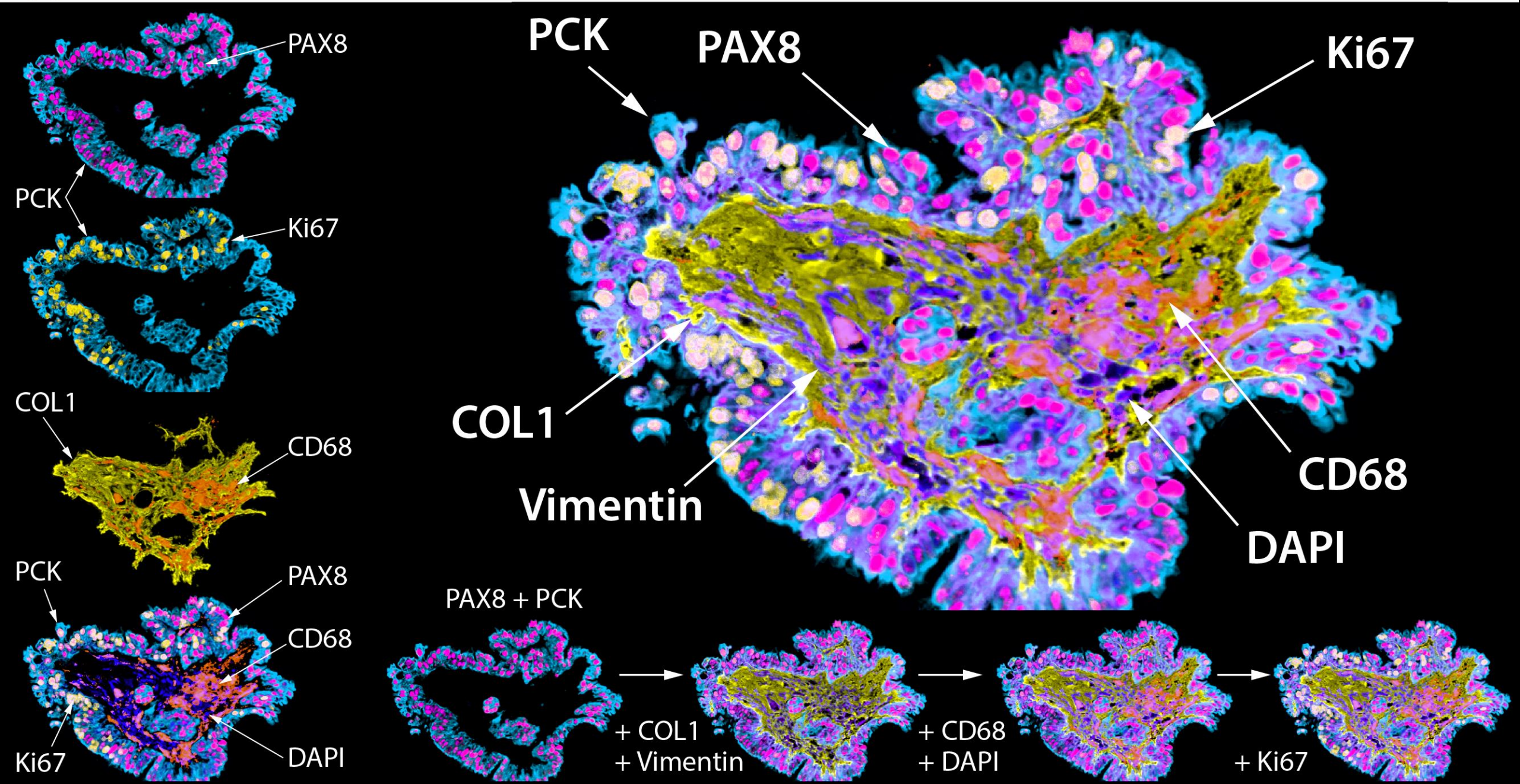


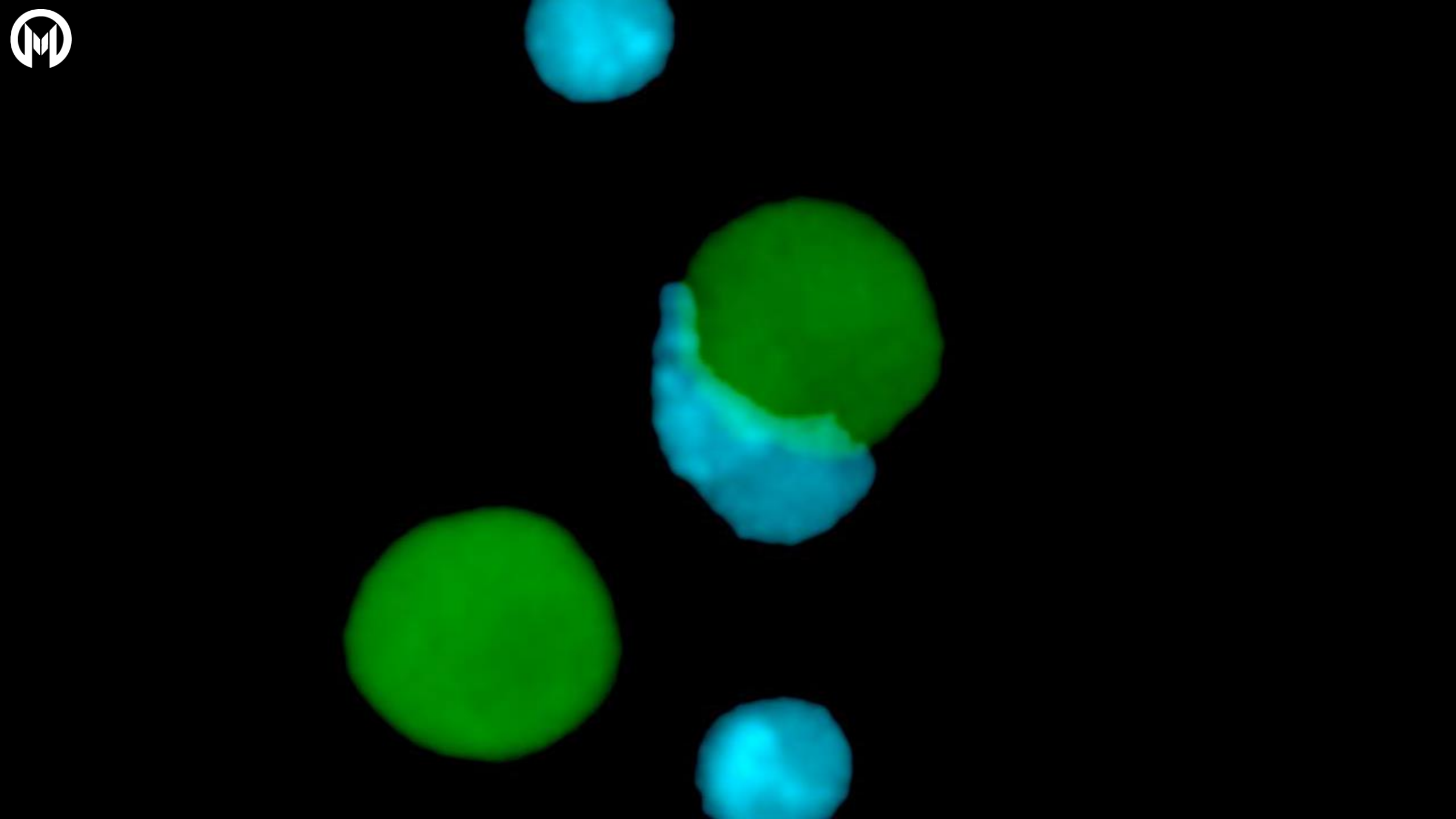
Pancreatic Ductal Adenocarcinoma

# Patient Avatars - µTumors | *Intratumoral Heterogeneity*

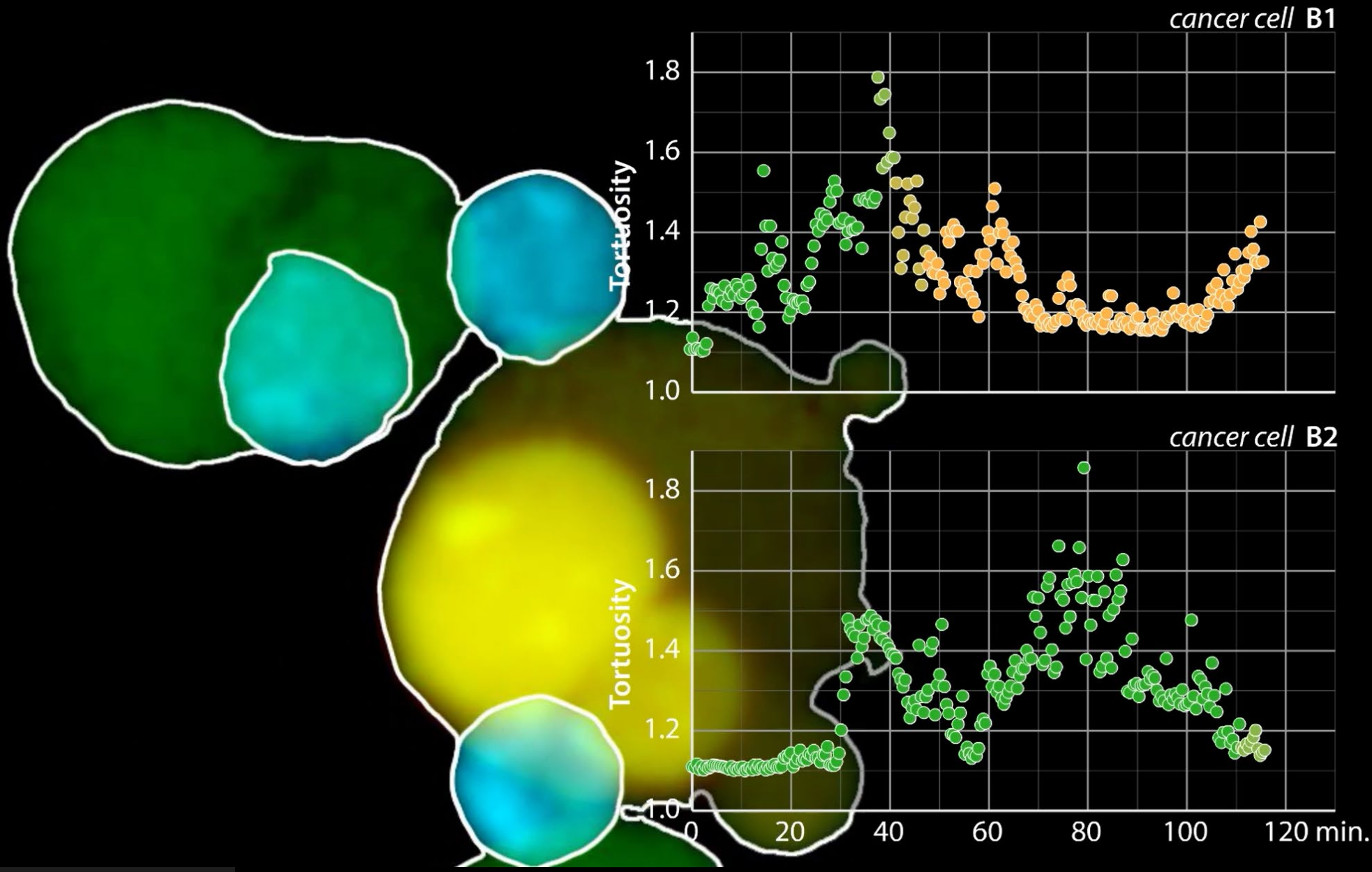


# Patient Avatars, Ovarian Cancer µTumors | *Intratumoral Heterogeneity*

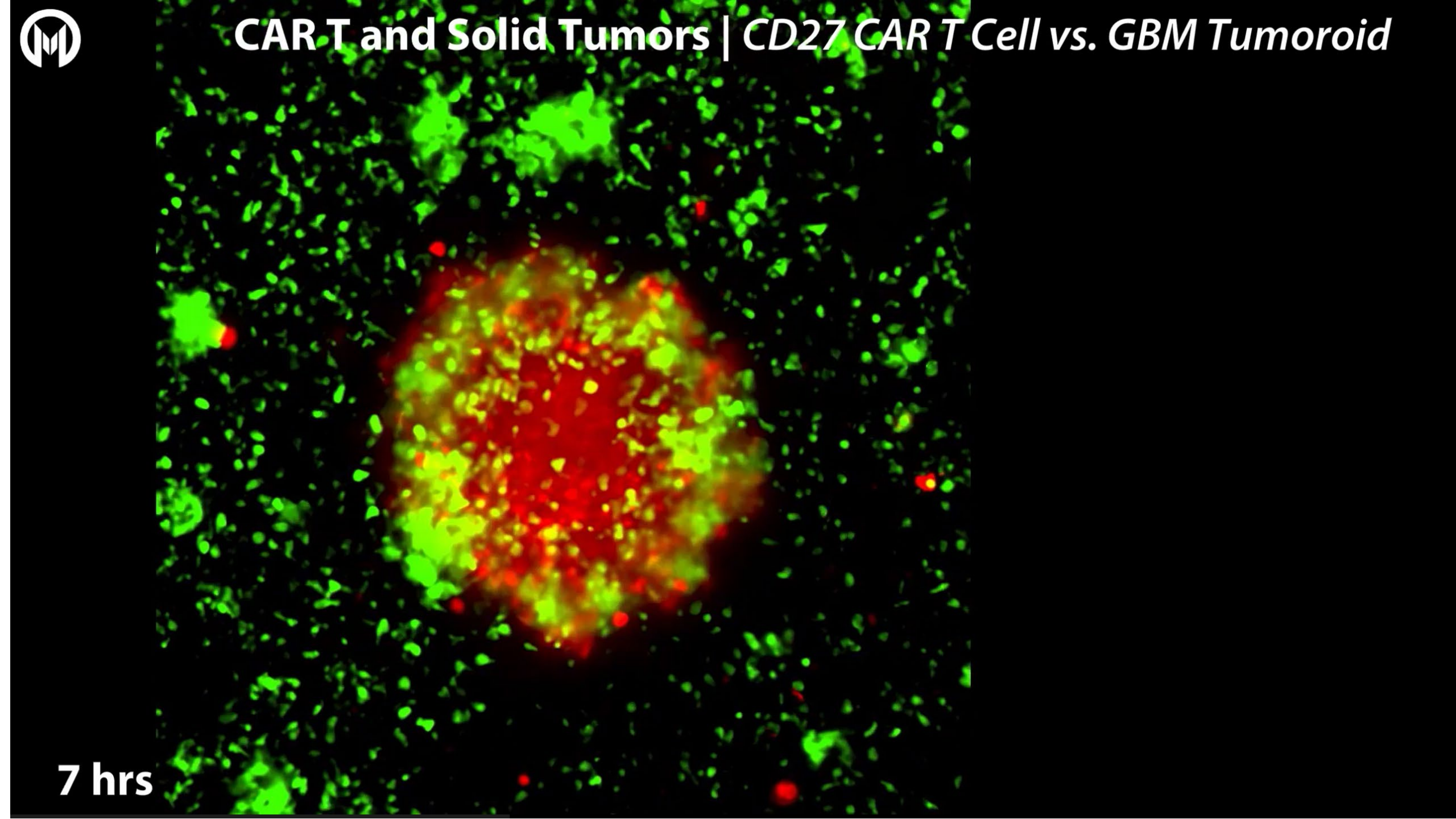




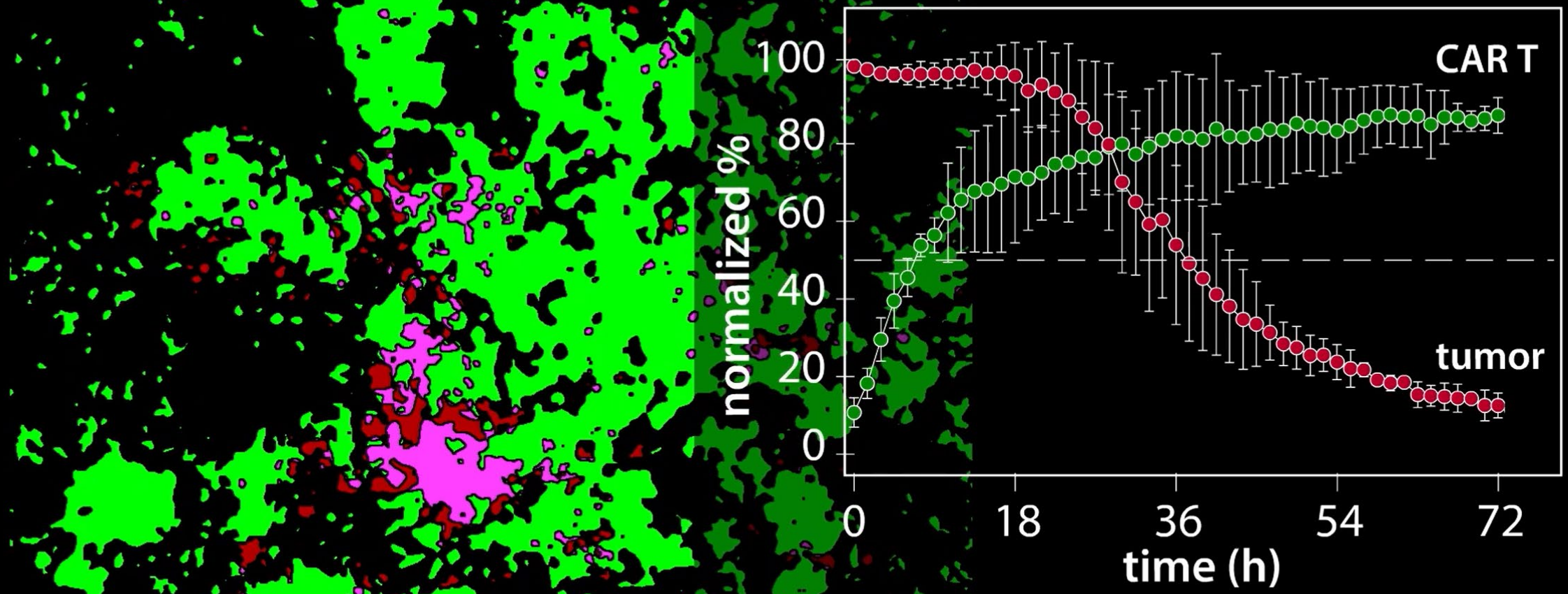
# Cell Therapy | *CAR T aCD19.28z v. Burkitt Lymphoma*




112 min

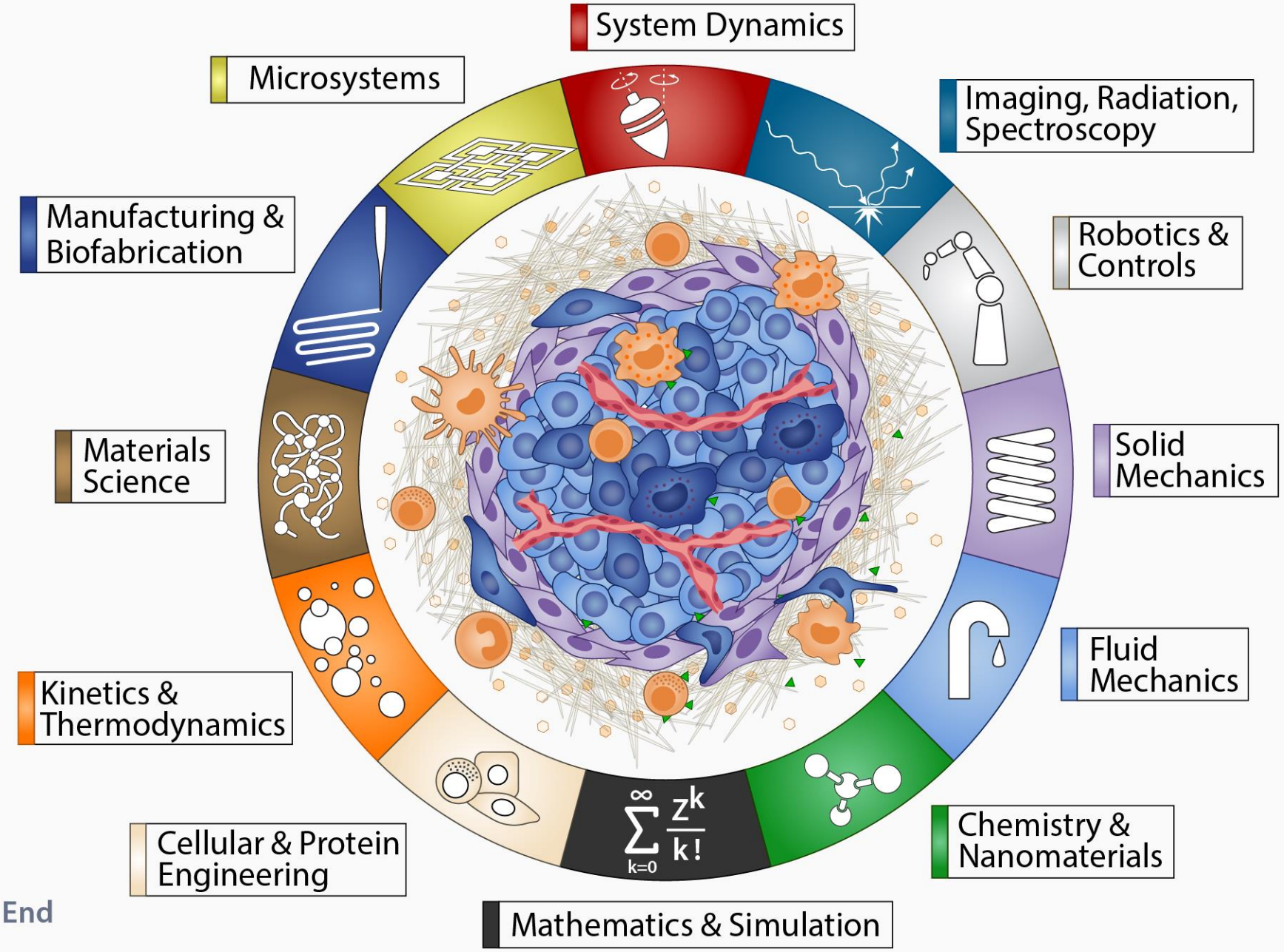

CAR T and Solid Tumors | CD27 CAR T Cell vs. GBM Tumoroid
7 hrs

# CAR T and Solid Tumors | *CD27 CAR T Cell vs. GBM Tumoroid*




19 hrs

# Cancer Engineering | *An Interdisciplinary Approach*

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