

***In vitro* assessment of cell-based drug delivery systems**

Michael Dunne

Assistant Member

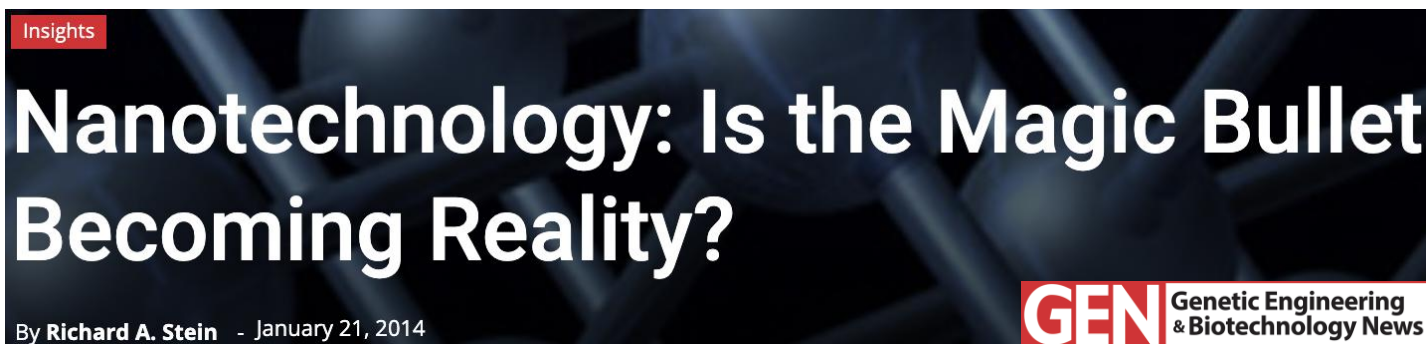
Department of BioEngineering

Moffitt Cancer Center

July 17th, 2025



Issues in Nanomedicine Cancer Drug Development



ACS NANO

What Went Wrong with Anticancer Nanomedicine Design and How to Make It Right

Duxin Sun,* Simon Zhou, and Wei Gao
ACS Nano 2020, 14, 12281–12290

Published: 26 April 2016

Analysis of nanoparticle delivery to tumours

[Stefan Wilhelm](#), [Anthony J. Tavares](#), [Qin Dai](#), [Seiichi Ohta](#), [Julie Audet](#), [Harold F. Dvorak](#) & [Warren C. W. Chan](#) 

[Nature Reviews Materials](#) 1, Article number: 16014 (2016) | [Cite this article](#)

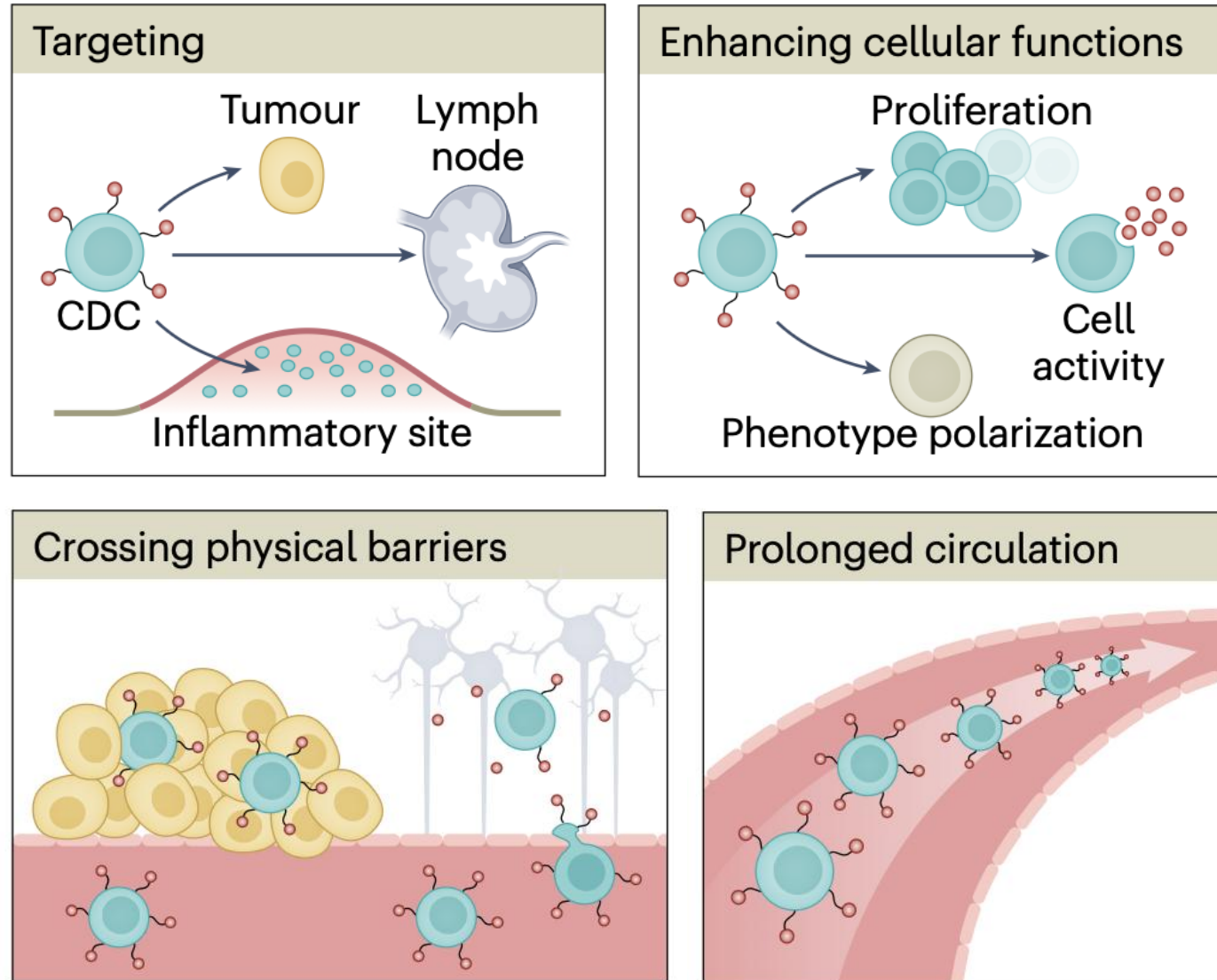
Drug Delivery: Too Much Complexity, Not Enough Reproducibility?

*Jean-Christophe Leroux**

Angewandte
International Edition
Chemie

CERULEAN 
Pharma Inc.
Pioneering the Field of Nanobiology

Cell-based drug delivery





Science

FDA no longer needs to require animal tests before human drug trials

10 JAN 2023 • 5:30 PM ET • BY [MEREDITH WADMAN](#)

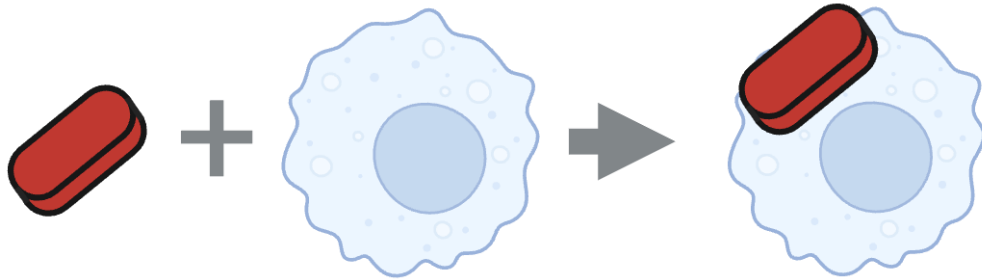
NEWS RELEASE | Jul 8, 2025

In Landmark Shift, NIH Announces
No More Exclusive Funding for
Animal Experiments

Cell-based drug delivery



Cellular Backpacks

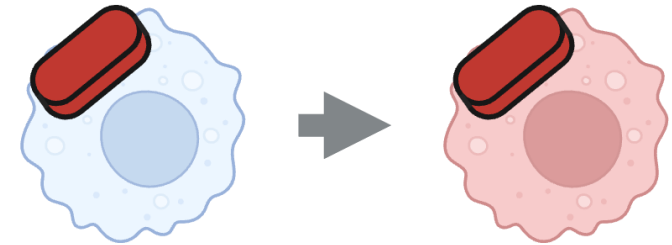


Geometry Prevents
Phagocytosis

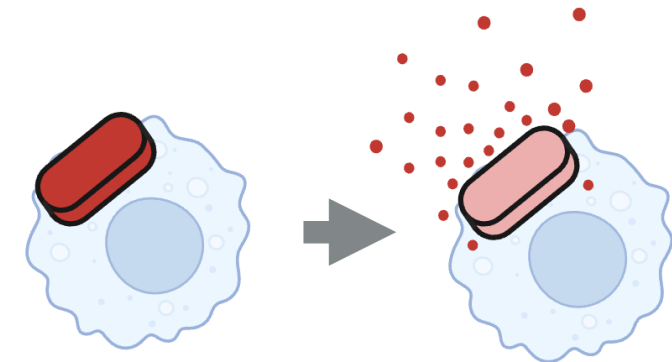
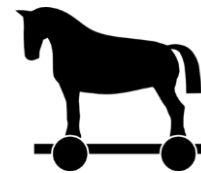


Methods of Employing Backpacks

Control



Delivery

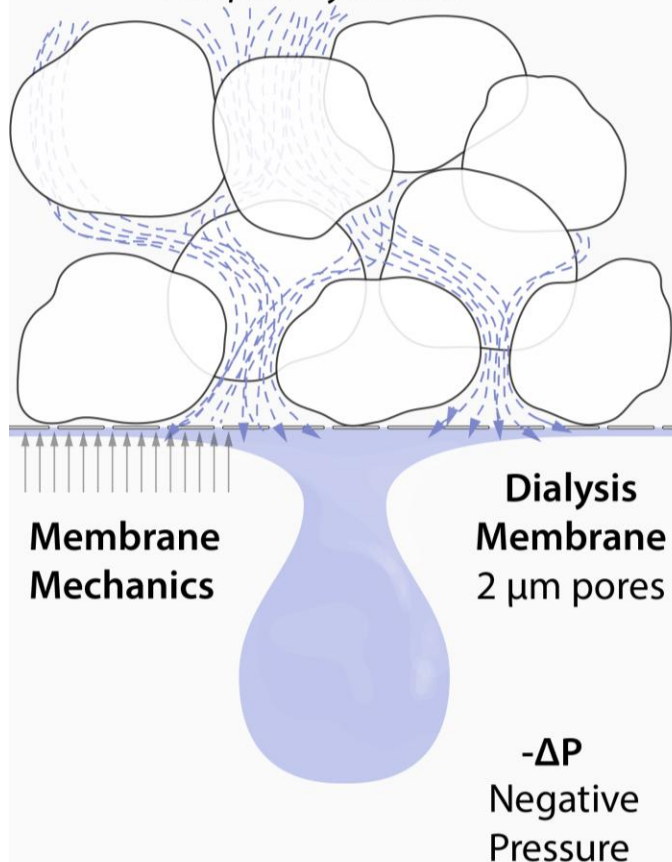


In vitro experimental setup



Perfusion Occurs through the
Interstitial Space in the LLS™

*Tuned to Mimic Capillary Bed
Transport Dynamics*



200 μ l wells for LLS™ (24x)

6 ml of liquid media in each quadrant
12 ml isolated effluent collection quadrants

Liquid Media
(4 quadrants / 24 wells)

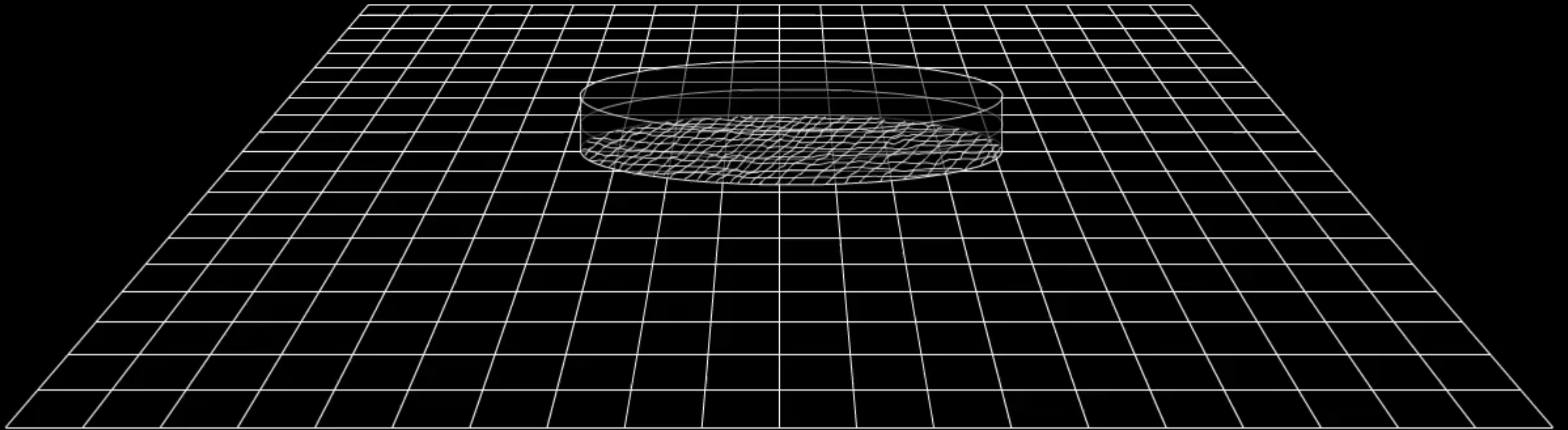


Darcy's Law

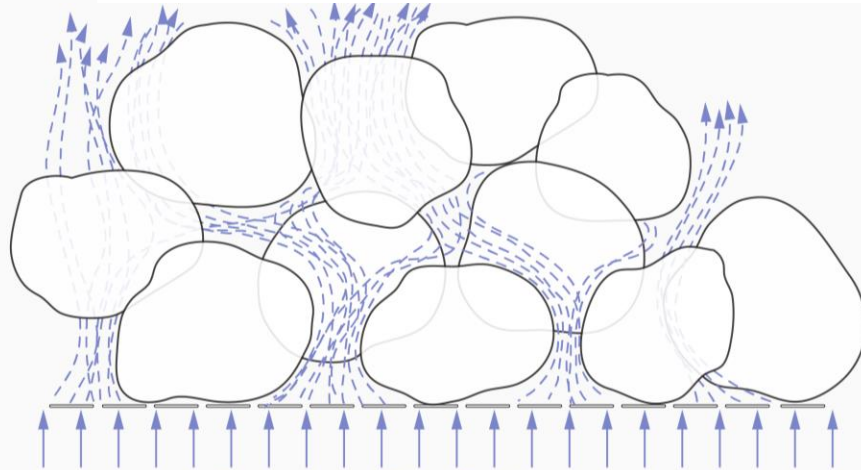
Flowrate is controlled by the Pressure Gradient and Permeability

24 hour timelapse video

Biology Research in Two Dimensions

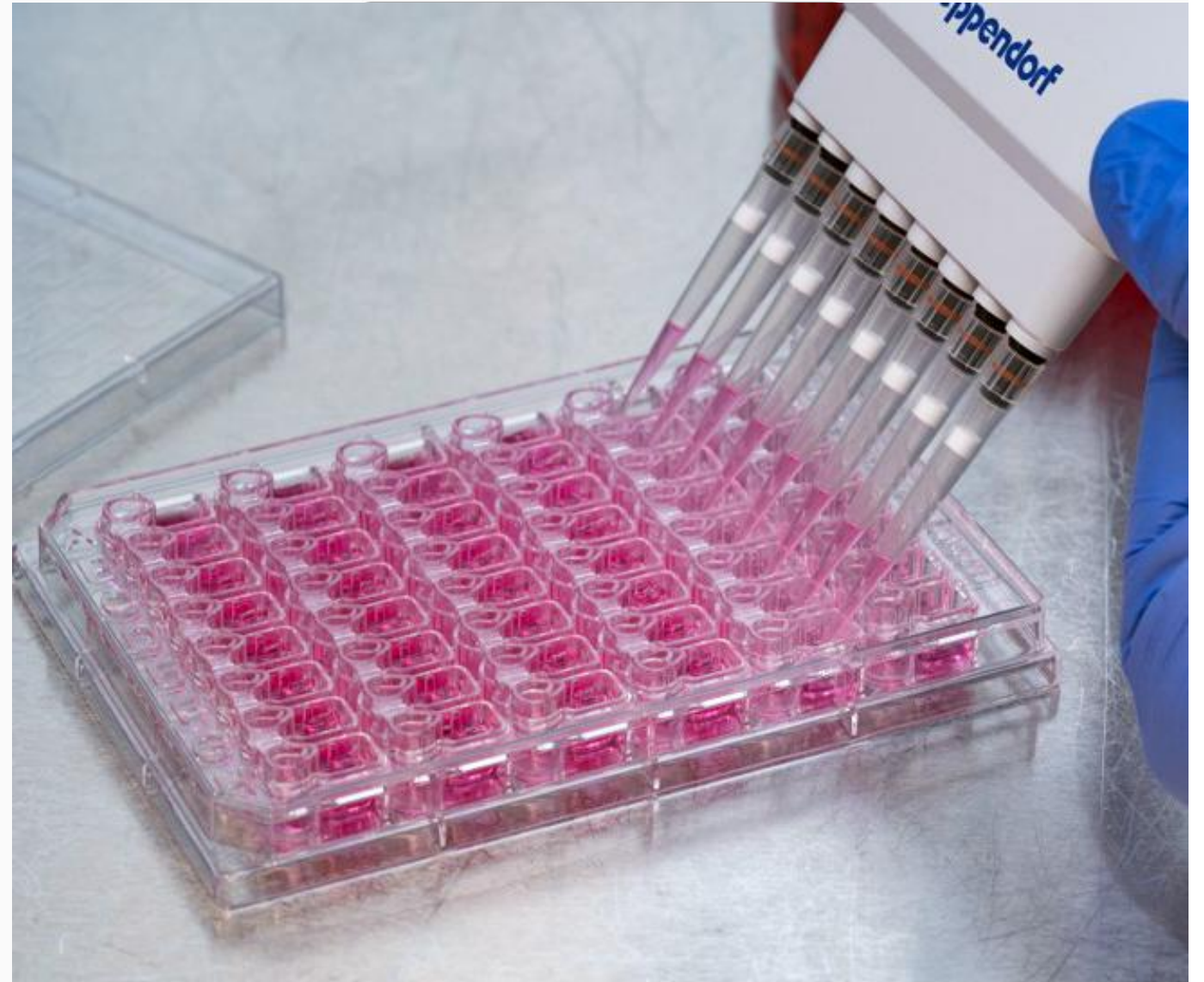
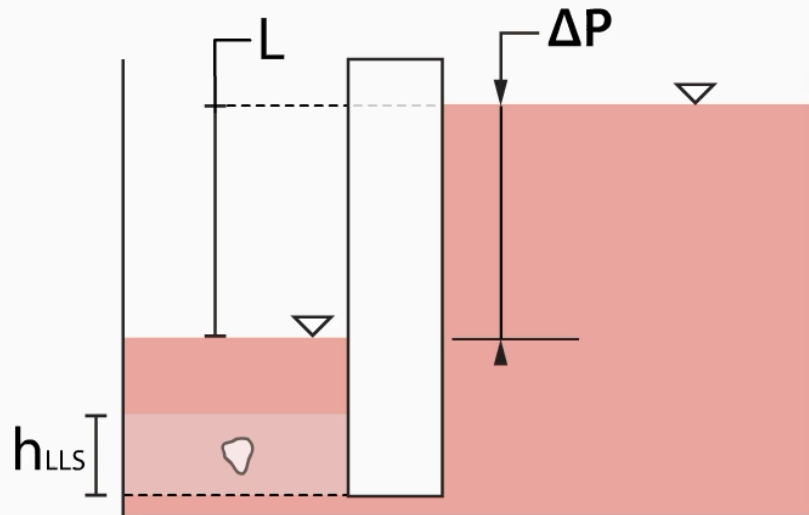


Perfusion plates



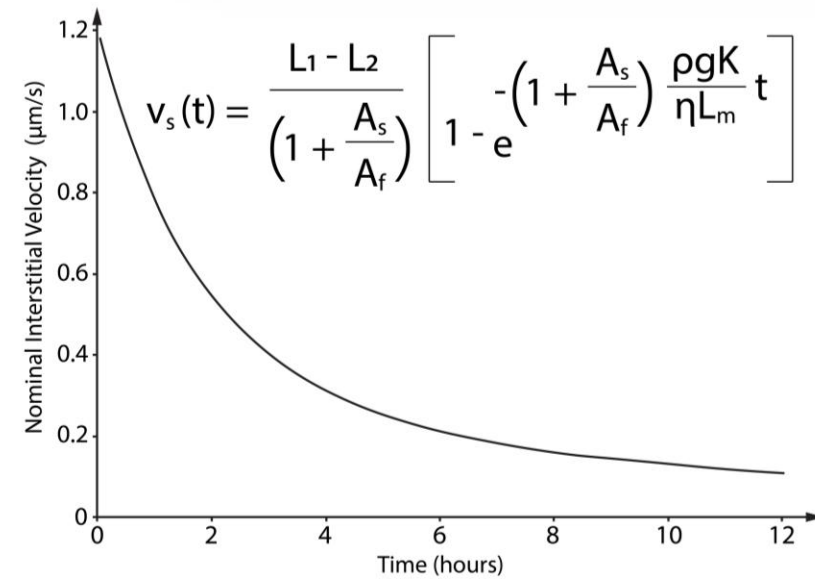
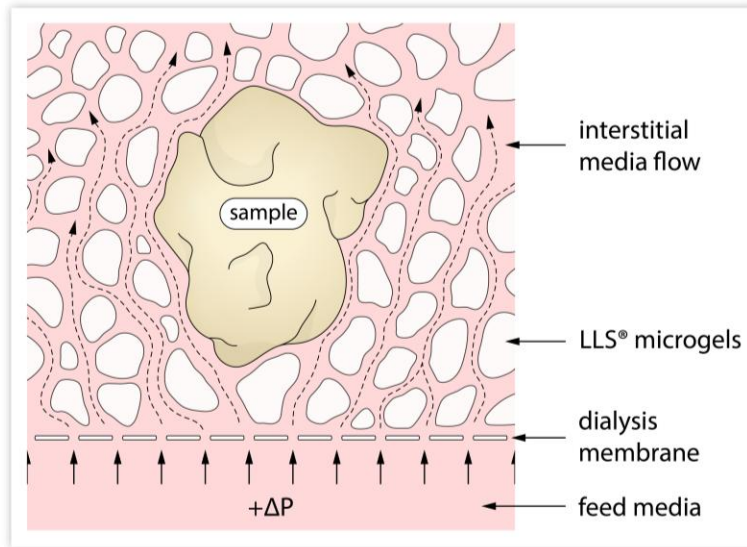
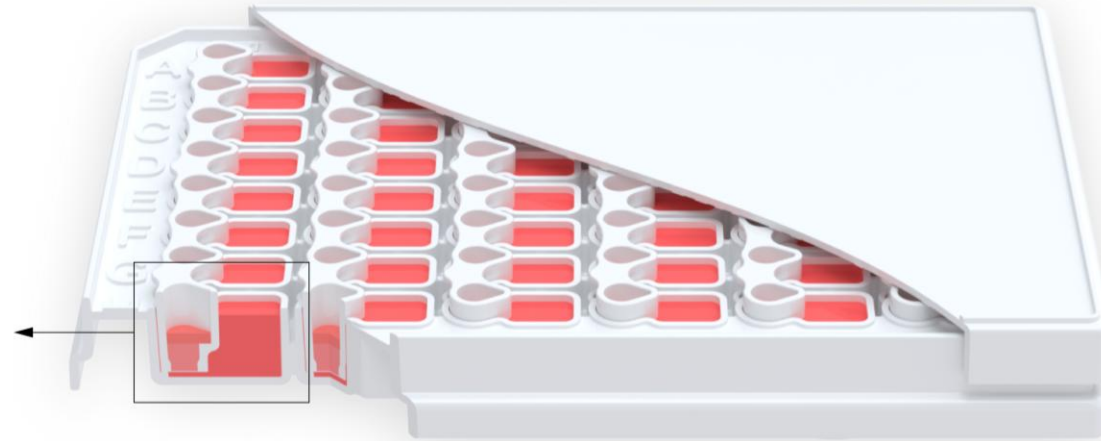
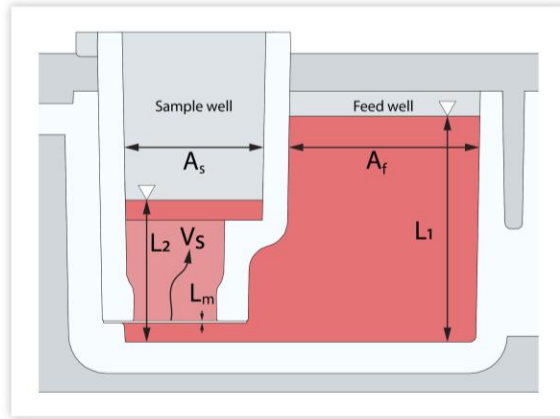
Reverse Perfusion

viscous forces oppose gravitational
body forces to maintain permeability



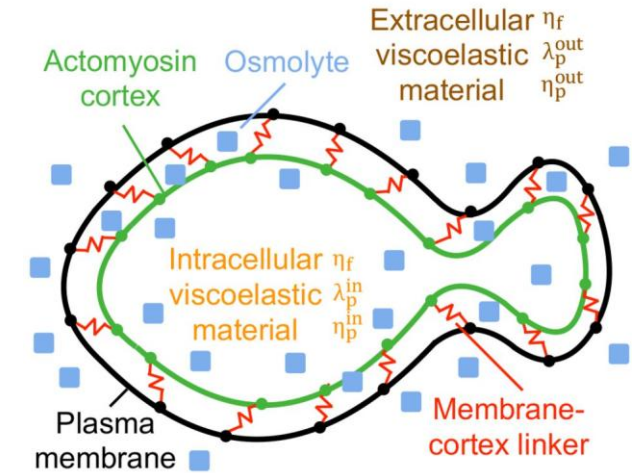
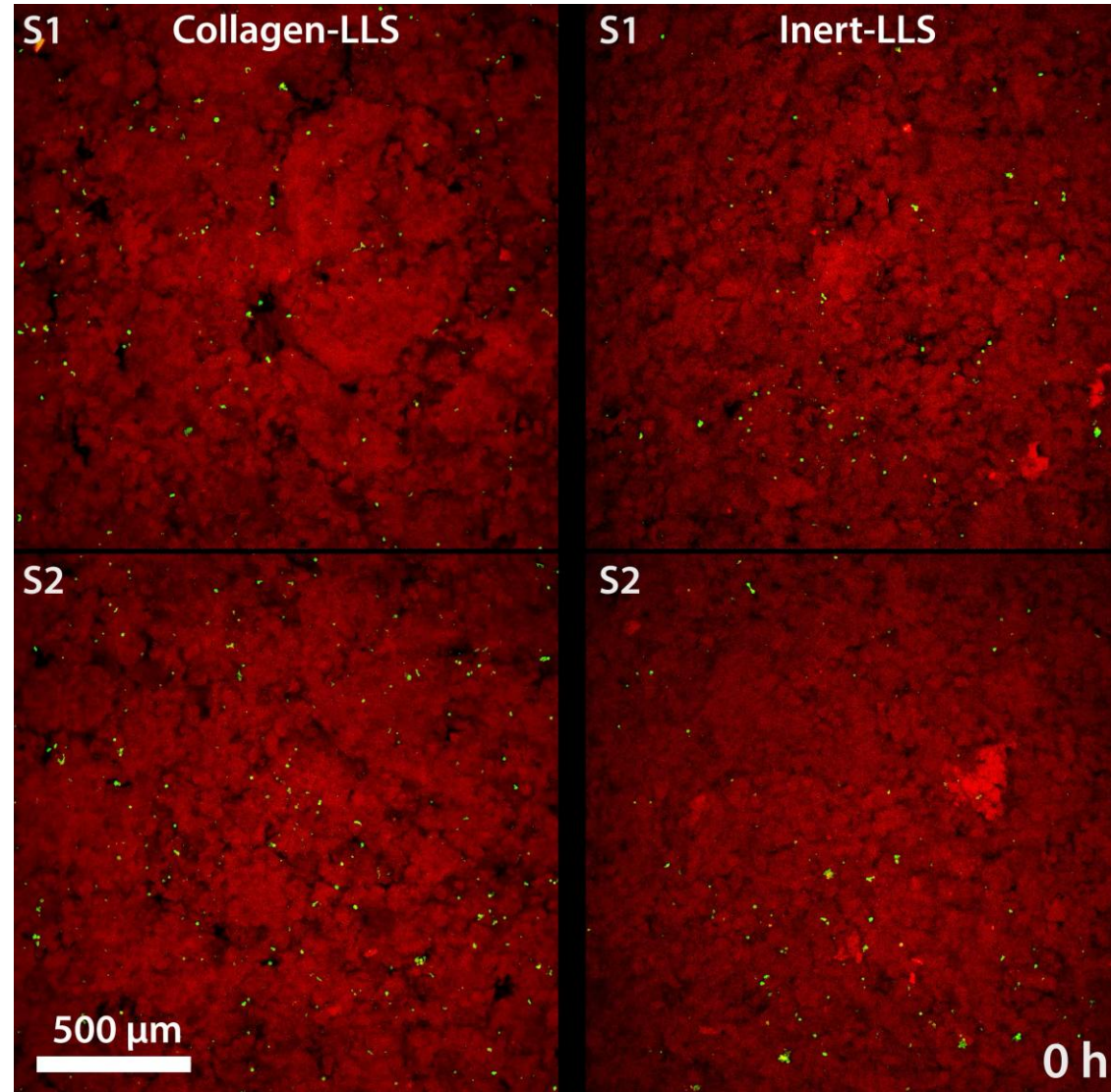
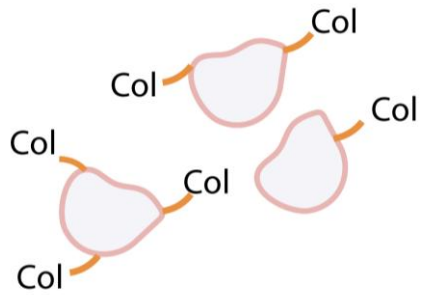
48 paired perfusion wells | *asymptotically approach static culture*

Perfusion plates



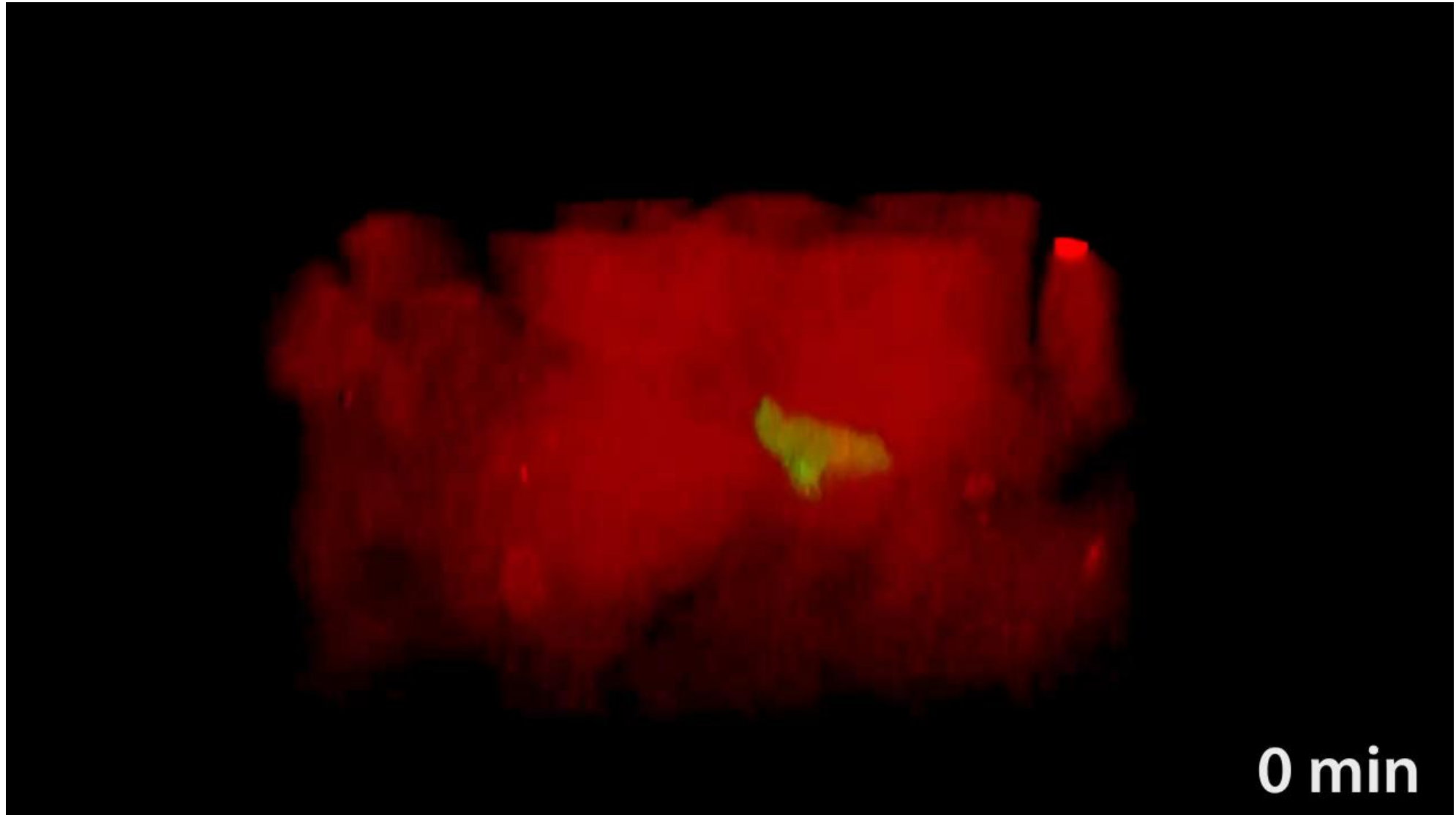
Keeps tissue explants viable for > 2 months

T cell migration in liquid-like solid

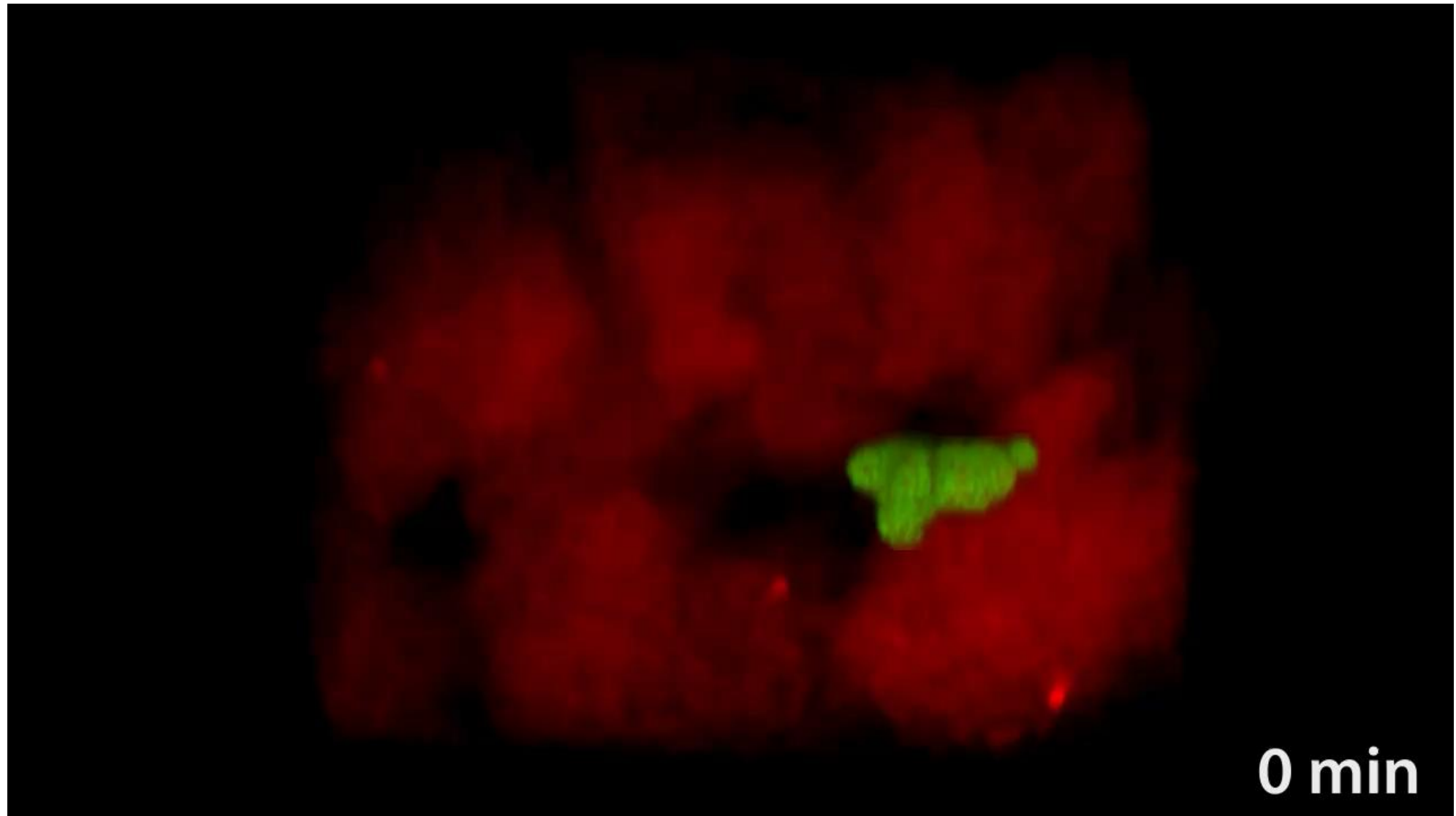


Human CD8+ T cells
CD3 + CD28 activation

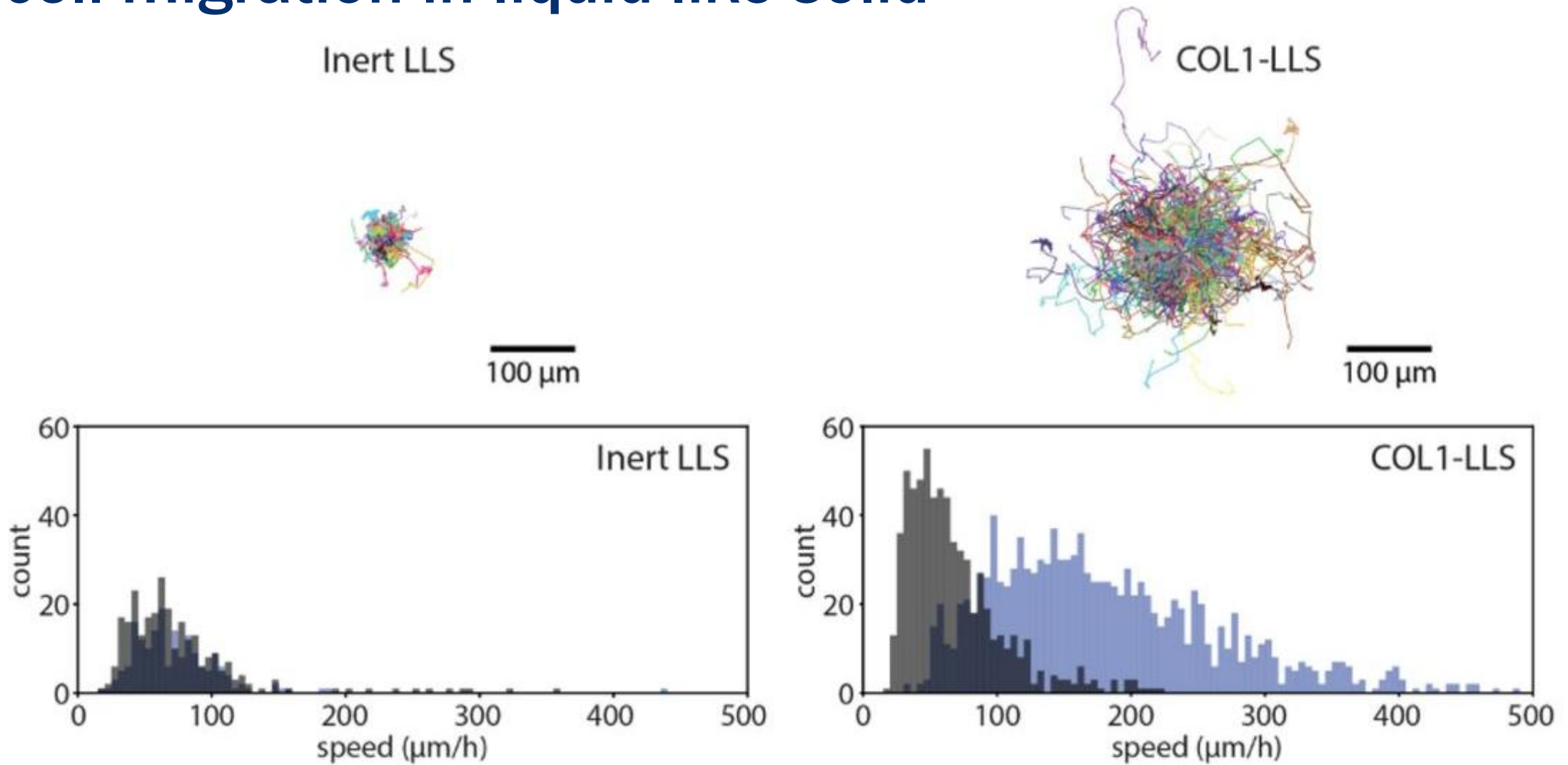
T cell migration in liquid-like solid



T cell migration in liquid-like solid

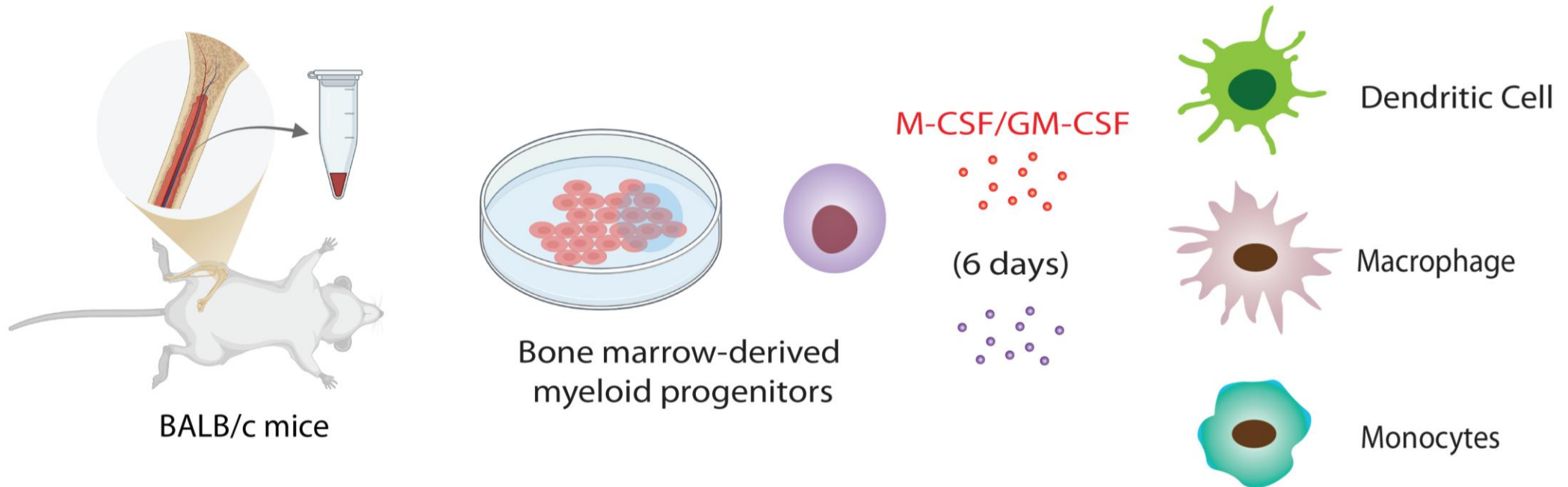


T cell migration in liquid-like solid



T cells migrate faster and farther in collagen coated LLS

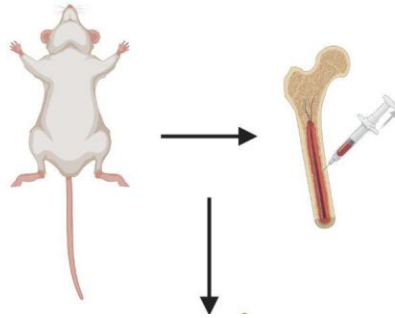
Myeloid Cell Differentiation



Myeloid cell characterization



Bone marrow extraction

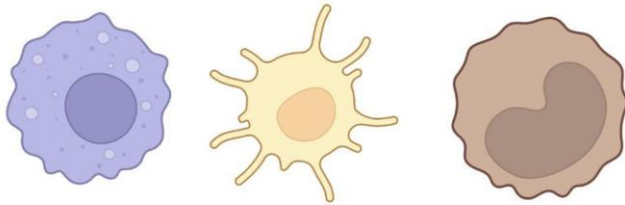


Cell differentiation

Dendritic Cells

Macrophages

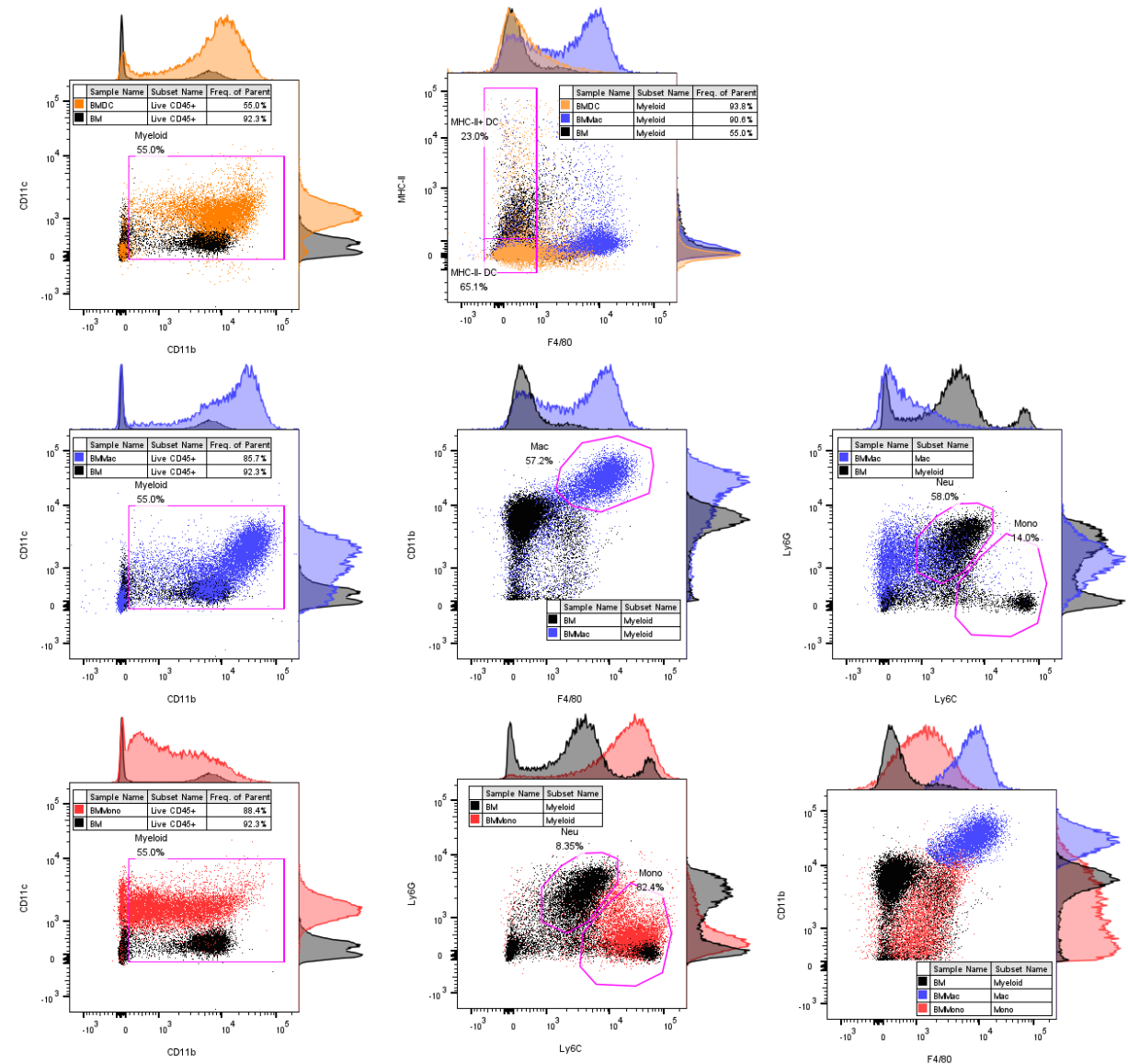
Monocytes



Dendritic Cells

Macrophages

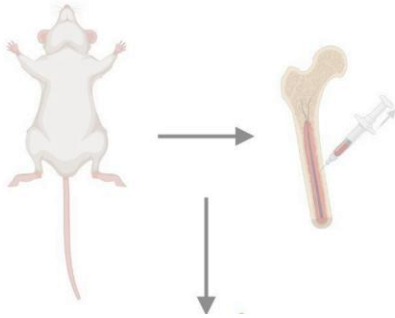
Monocytes



In vitro myeloid cell migration



Bone marrow extraction

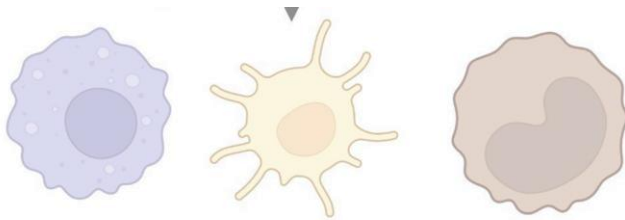


Cell differentiation

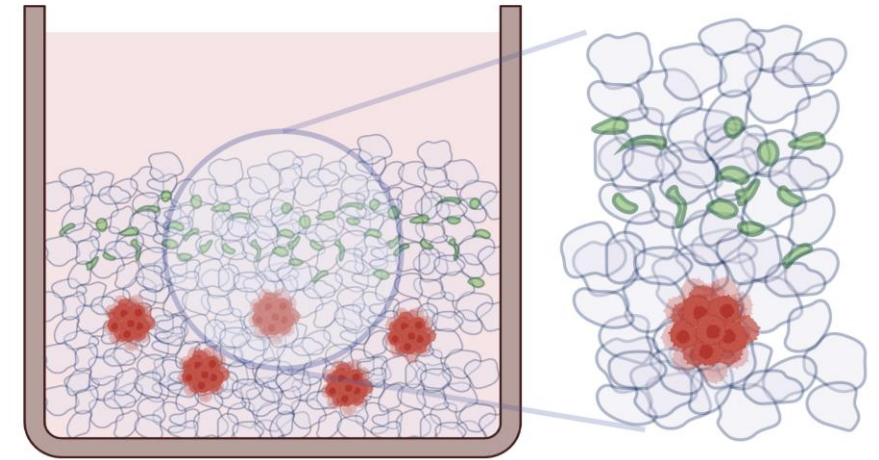
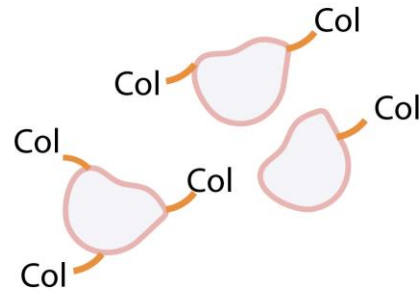
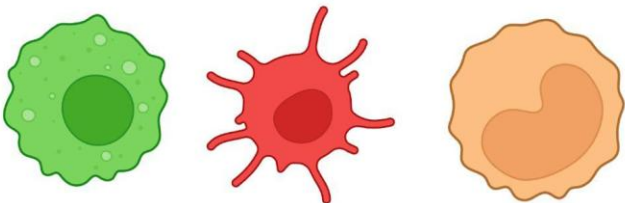
Dendritic Cells

Macrophages

Monocytes



Cell labelling (fluorescent dye)



Immune cell
cocktail

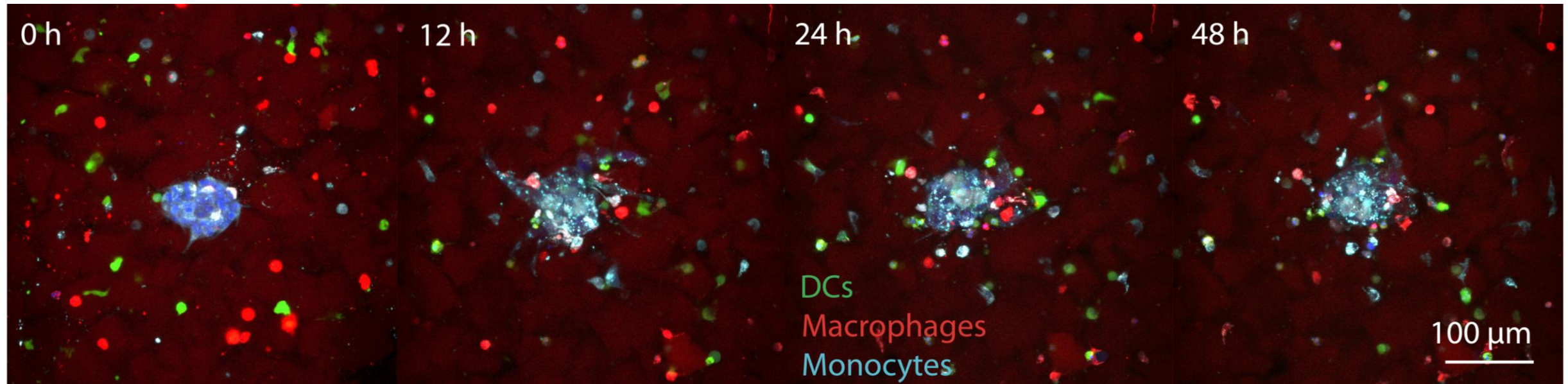
Tumor

Col-LLS

Tumor adhesion on Collagen-LLS

4T1 mammary carcinoma explants

In vitro myeloid cell migration

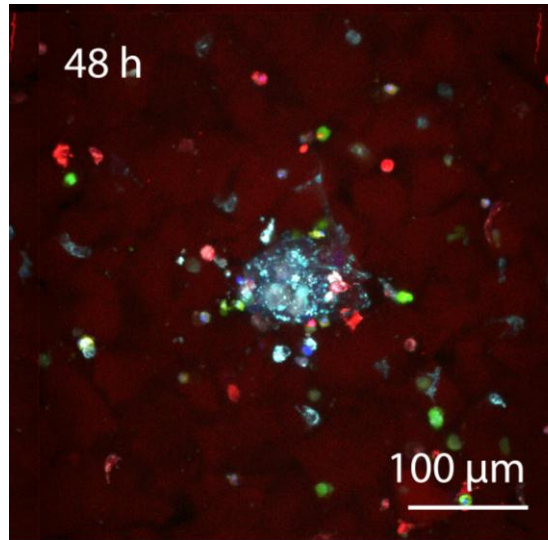
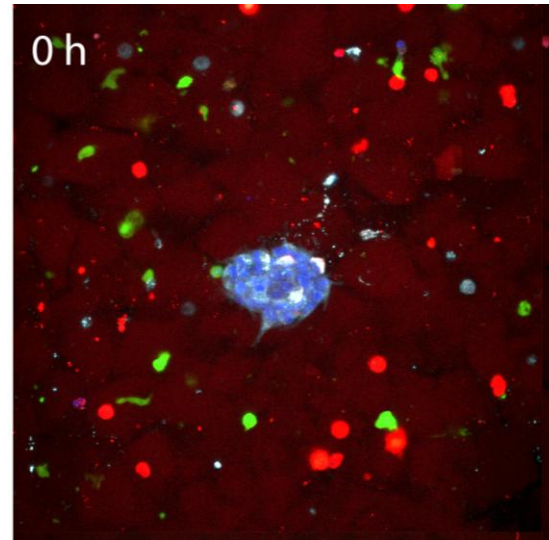


4T1 mammary carcinoma explants

In vitro myeloid cell migration

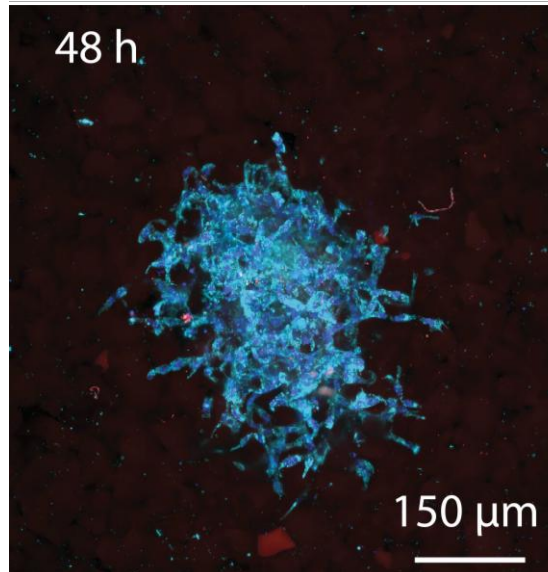
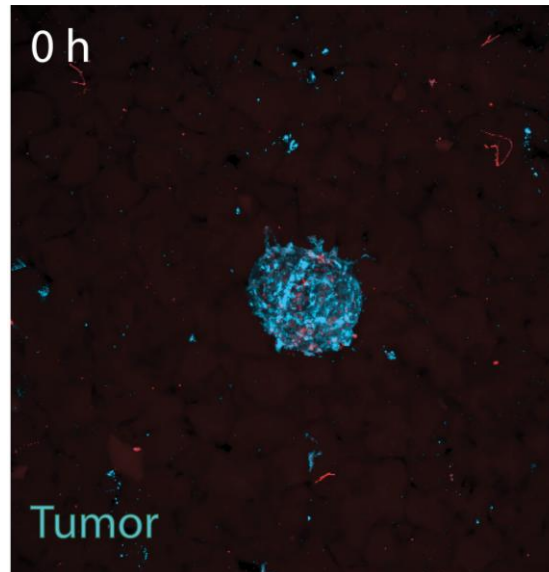


Immune cells →



Dendritic Cells
Macrophages
Monocytes

No immune cells →



4T1 mammary
carcinoma explants

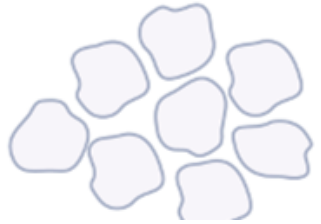
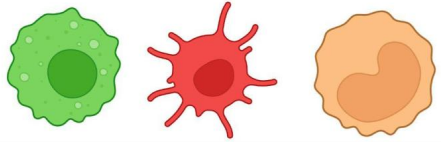
In vitro myeloid cell migration



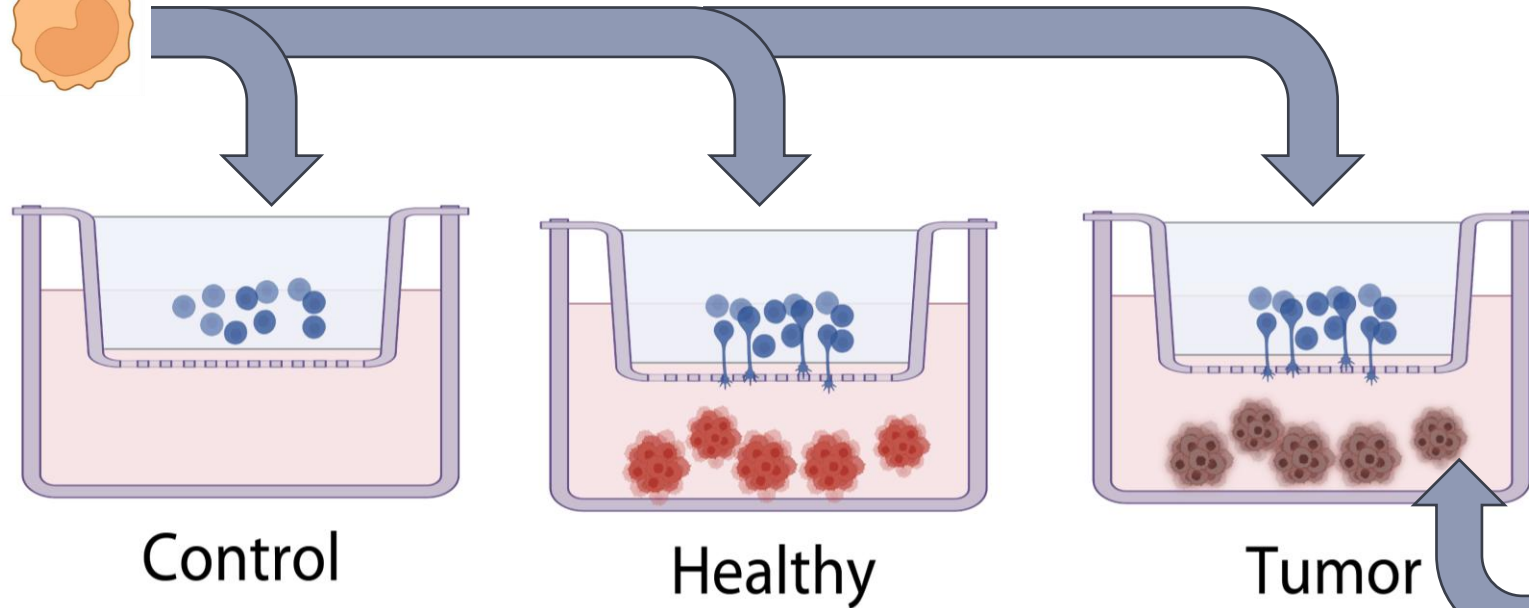
Dendritic Cells

Macrophages

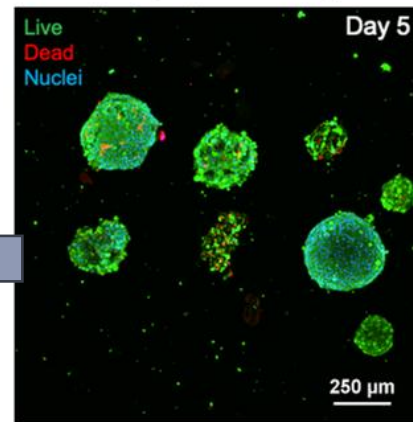
Monocytes



Collagen-conjugated
liquid like solid gels
in lower chamber



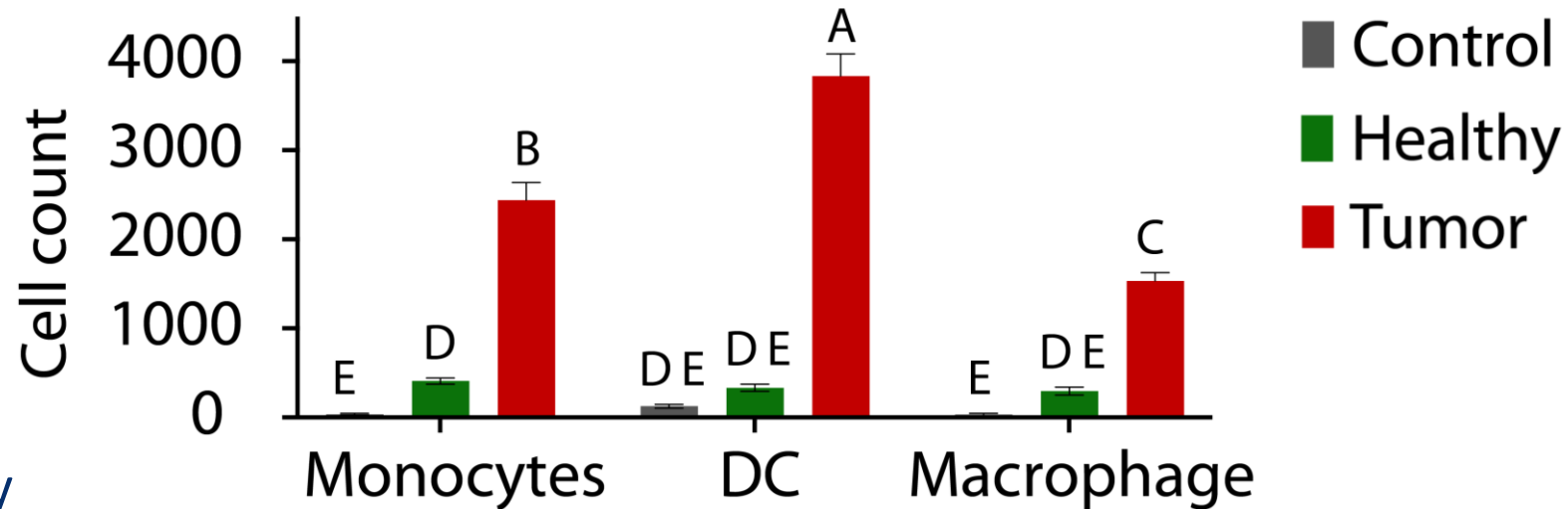
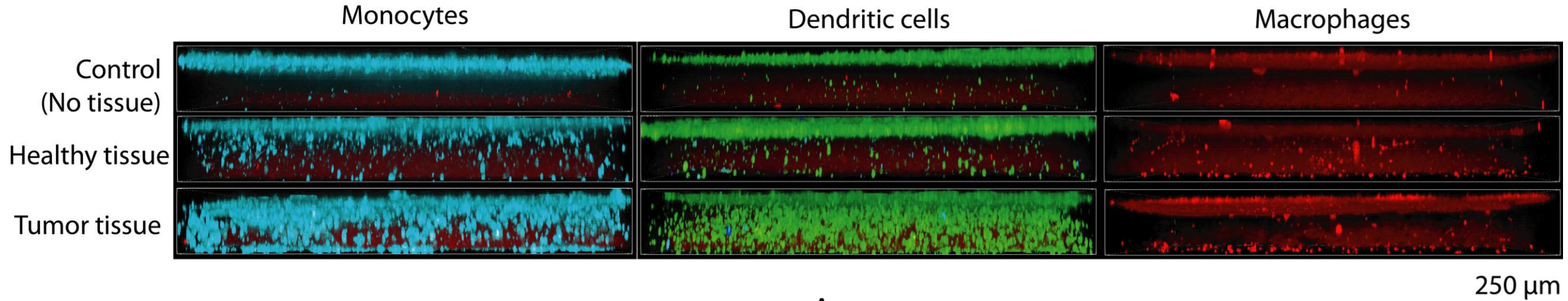
Live/dead staining



24 h migration assay

4T1 mammary carcinoma explants

In vitro myeloid cell migration



24 h migration assay

Groups that share a letter don't show significant difference ($P < 0.05$)

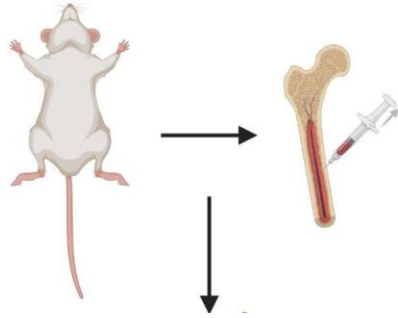
4T1 explants

Dendritic cells > Monocytes > Macrophages in terms of migration towards tumor

In vivo myeloid cell migration



Bone marrow extraction

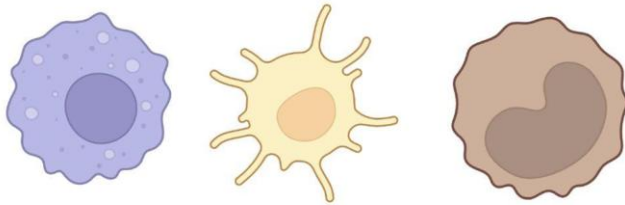


Cell differentiation

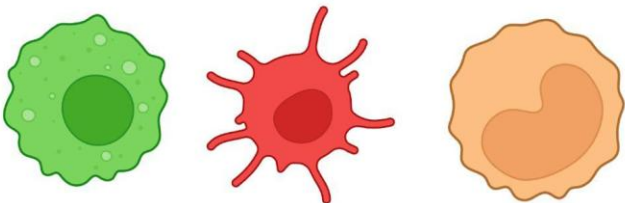
Dendritic Cells

Macrophages

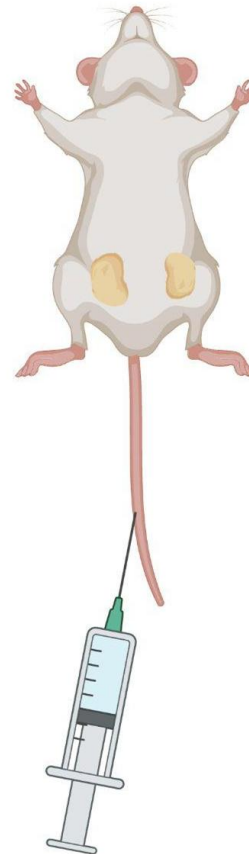
Monocytes



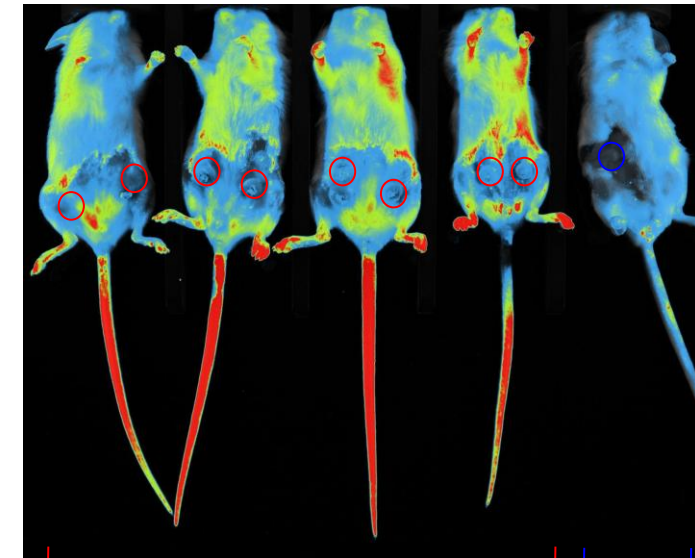
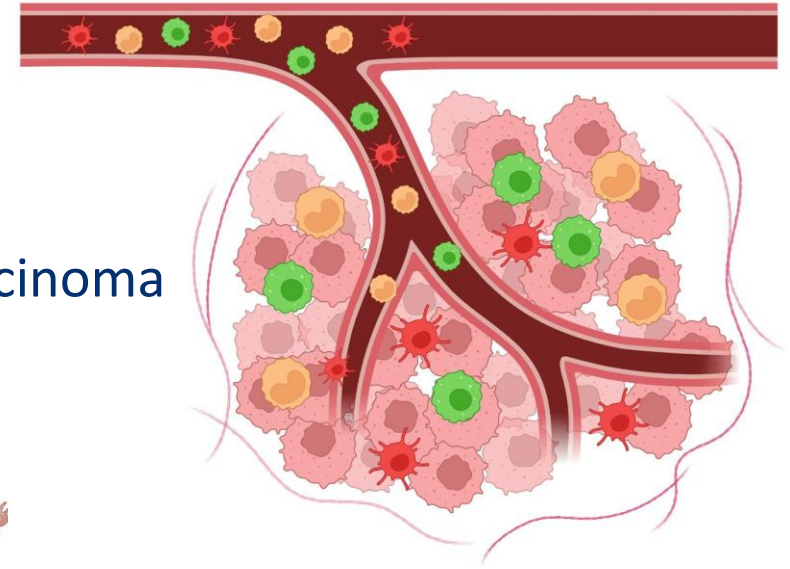
Cell labelling (fluorescent dye)



IV injection



4T1 mammary carcinoma
BALB/c mice



Myeloid Cell Injection

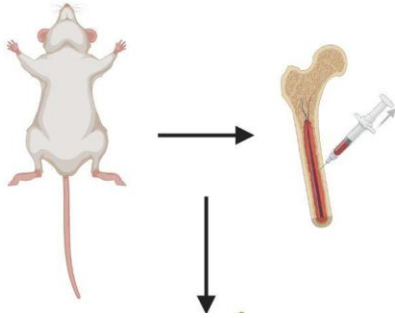
No cells



In vivo myeloid cell migration



Bone marrow extraction



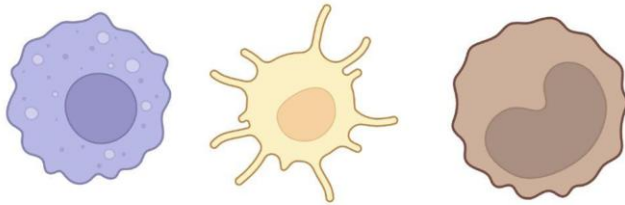
4T1 mammary carcinoma
BALB/c mice

Cell differentiation

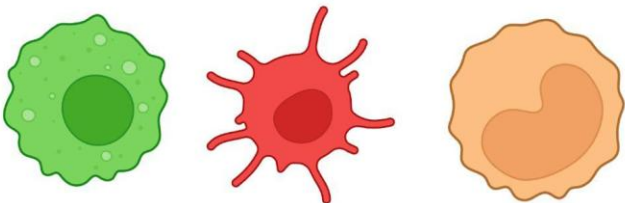
Dendritic Cells

Macrophages

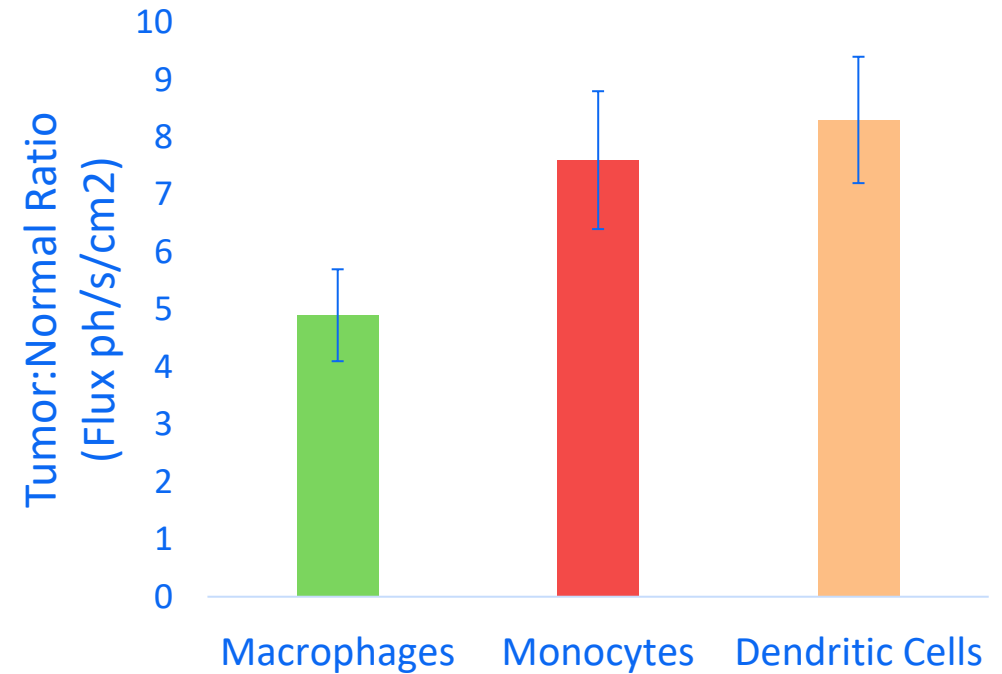
Monocytes



Cell labelling (fluorescent dye)



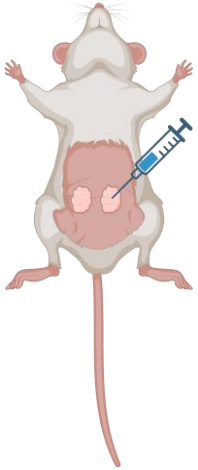
IV injection



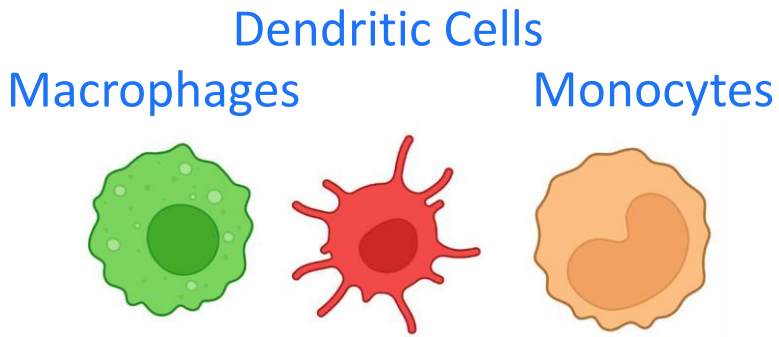
In vivo myeloid cell migration



Day 0

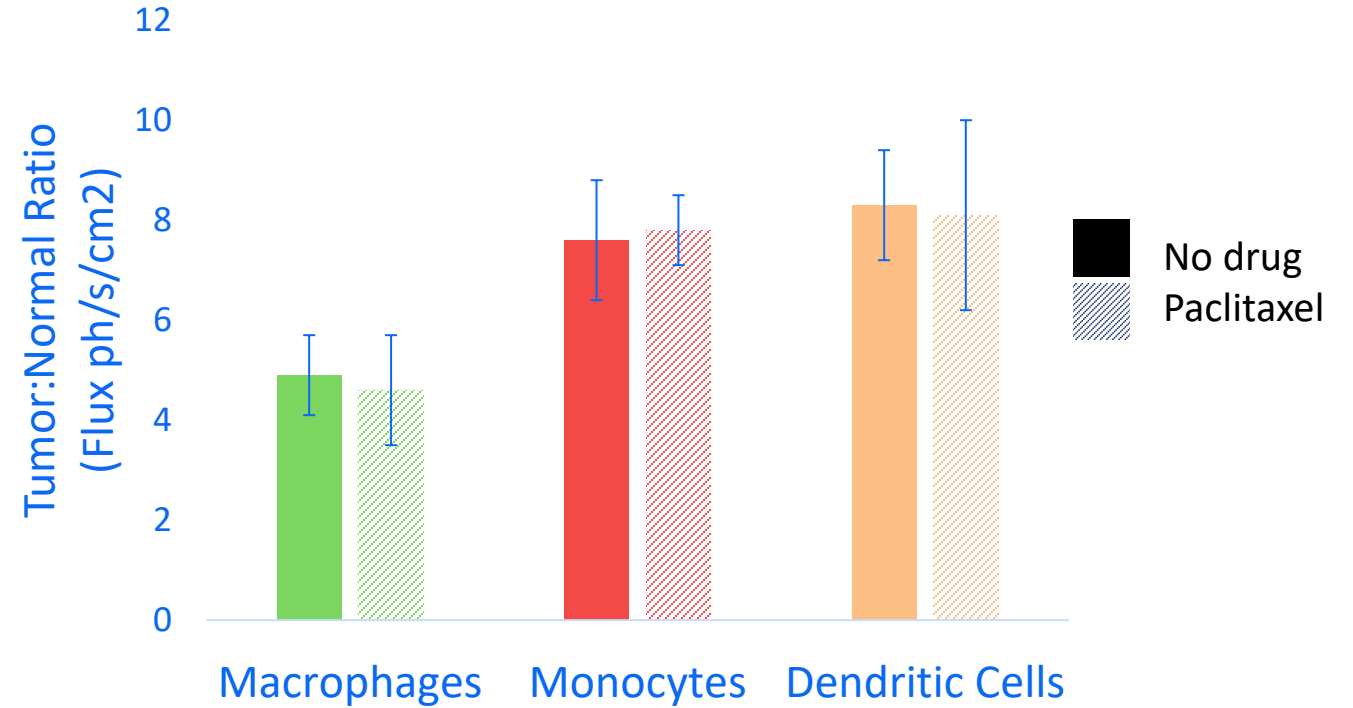


Day 2



Day 4

Sacrifice, resect, image



4T1 mammary carcinoma
BALB/c mice

Acknowledgements



Dunne Lab

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Elsa Flores

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David Odde

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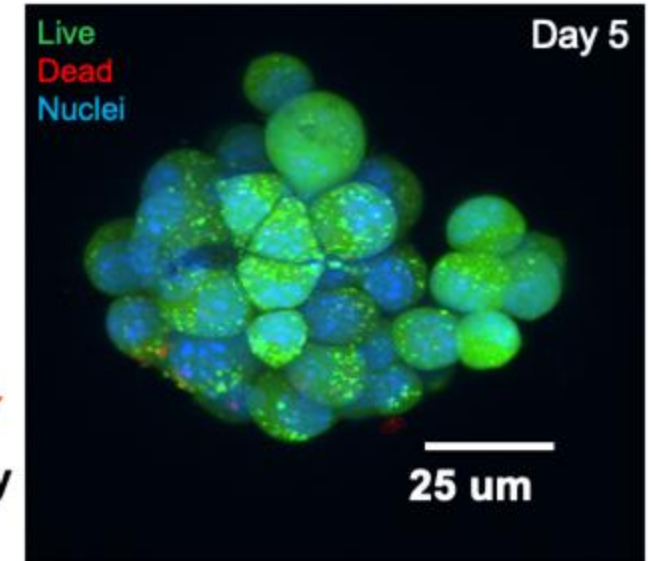
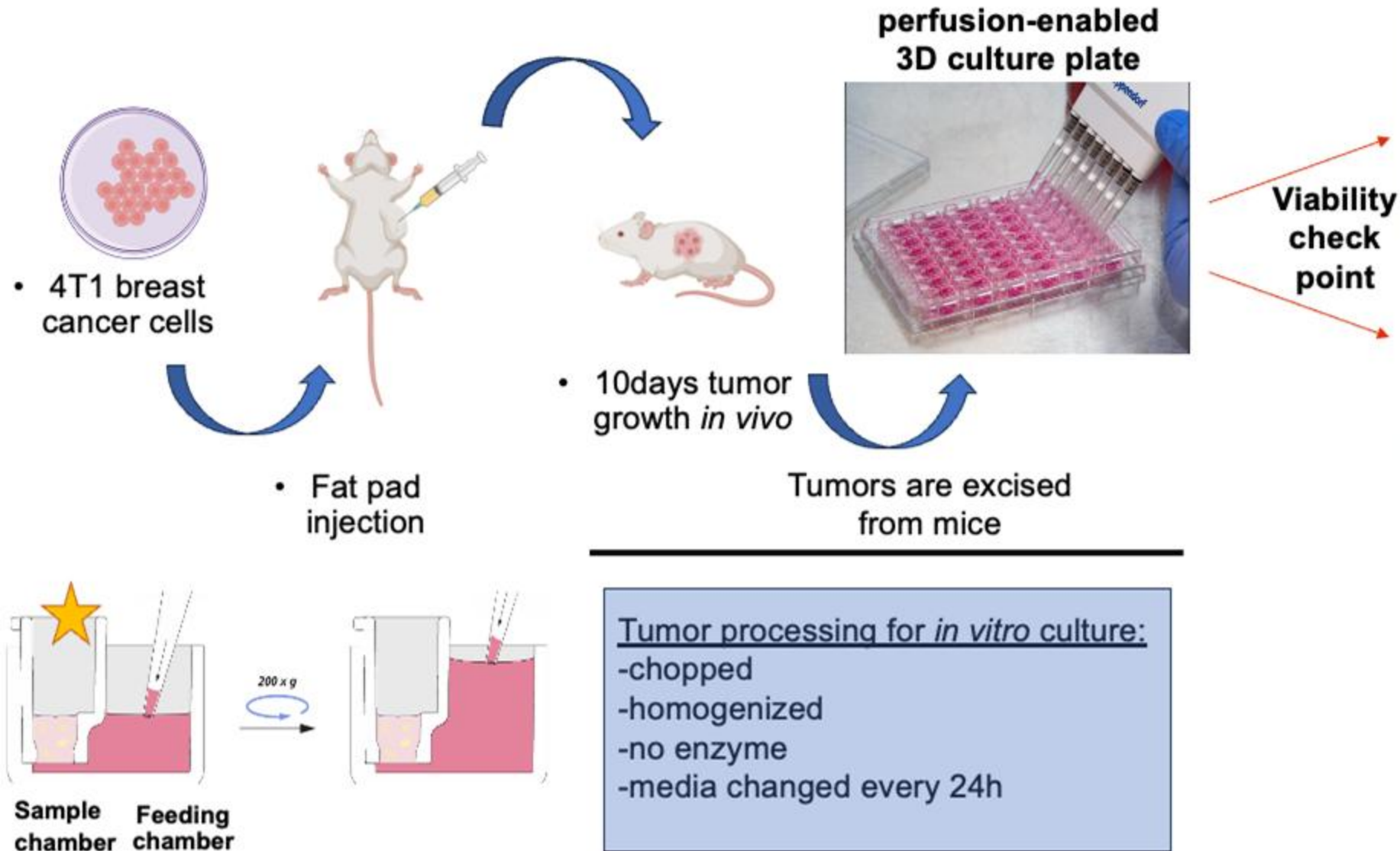
Neda Latifi

Mark Jaroszewski

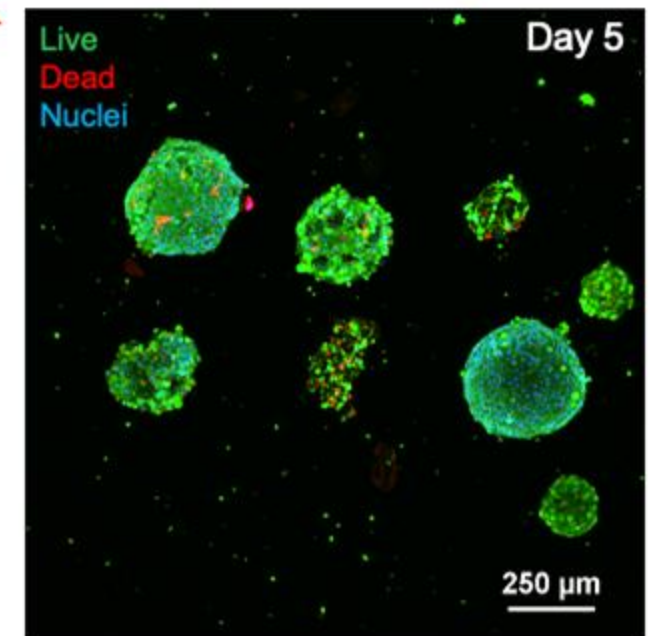




Myeloid Cell Trafficking – *In Vitro*



Live/dead staining

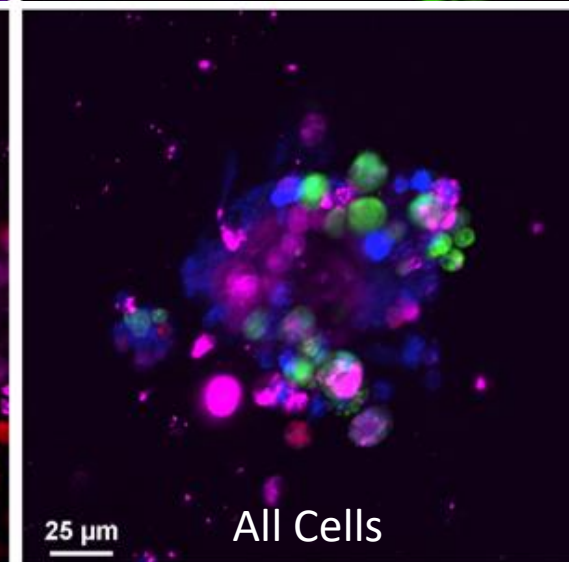
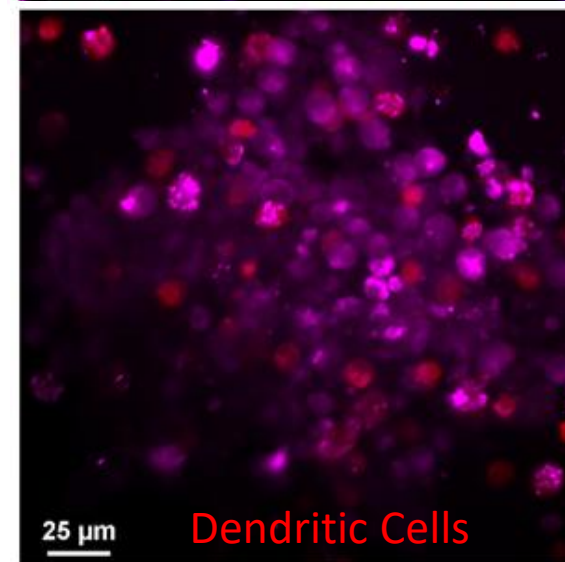
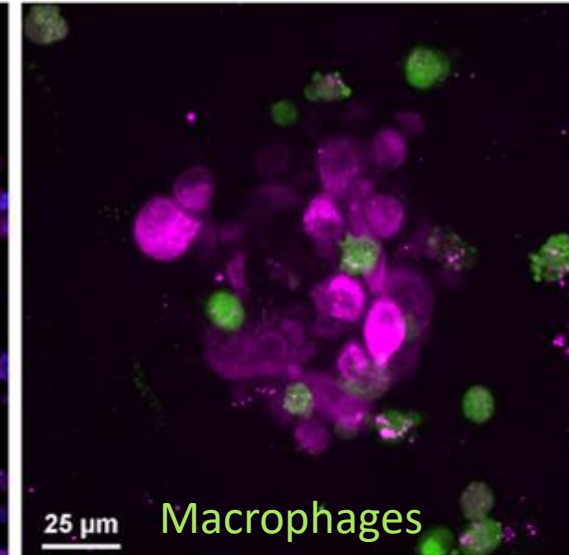
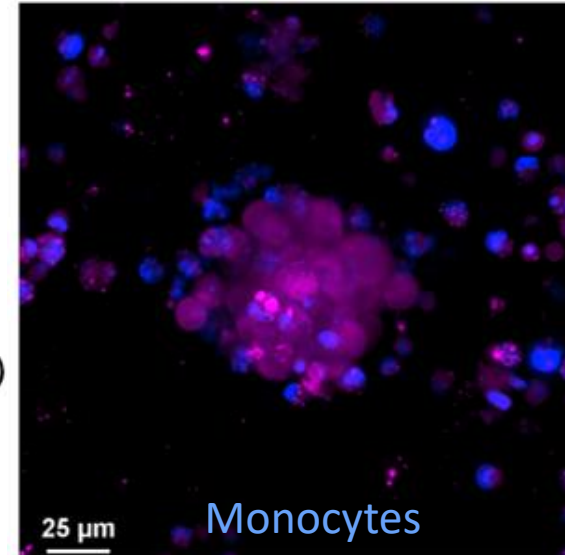
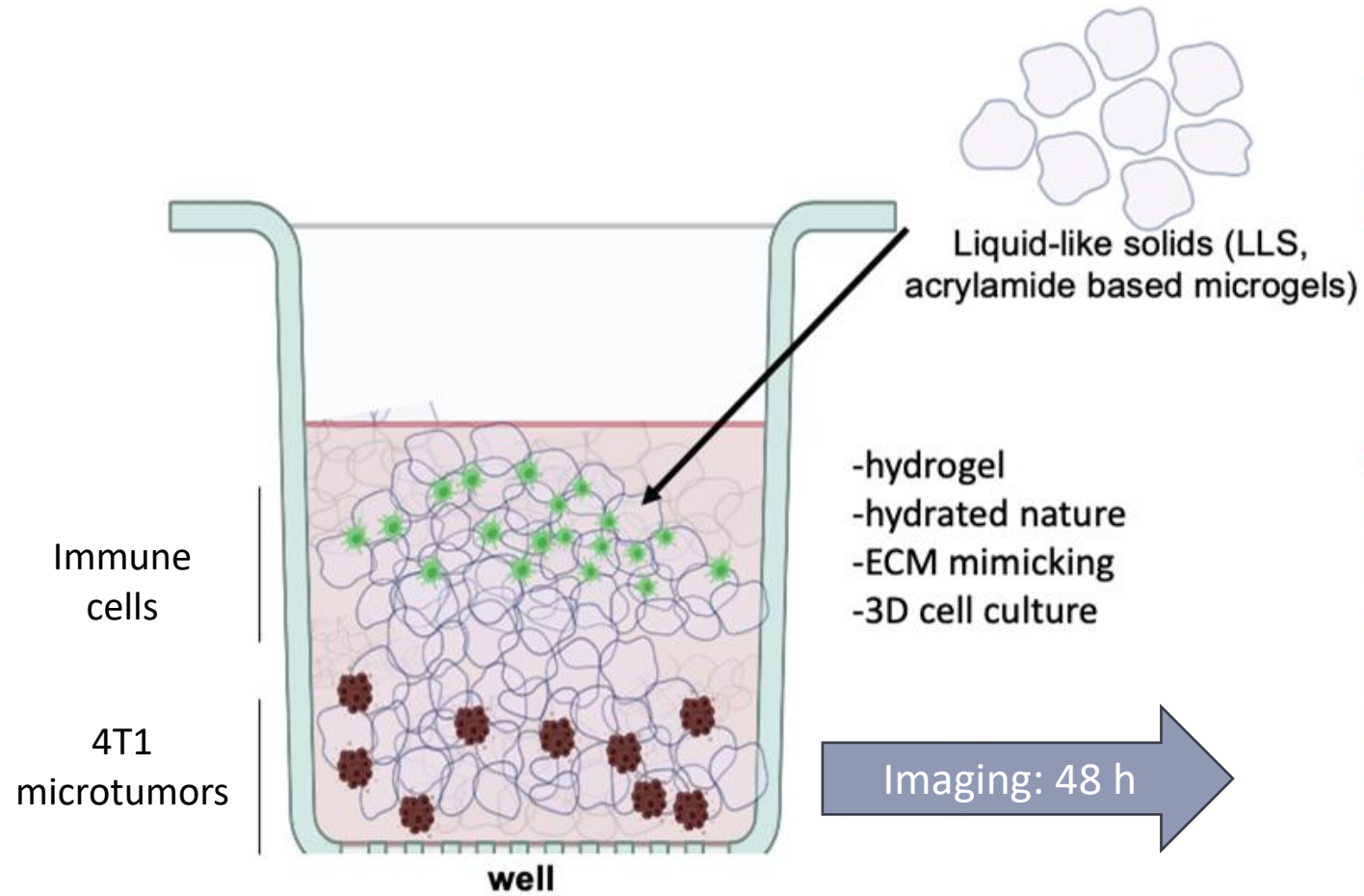


Myeloid Cell Trafficking – *In Vitro*



Immune Cell Infiltration into Melanoma Spheroids: Co-Culture Assessment

■ Tumor tissue (Cy5)



Myeloid Cell Trafficking – *In Vitro*



4T1 tumor tissue-48h

Healthy tissue-48h

deep red: tumor
red: macrophages
green: DCs
Blue: monocytes

100 μm

100 μm