

Poly(β -amino ester) Backpacks for Adoptive Macrophage Transfers in High-Grade Serous Carcinoma

Presenter: Courtney Bailey

Advisors: Drs. Benjamin Bitler and Wyatt Shields
University of Colorado

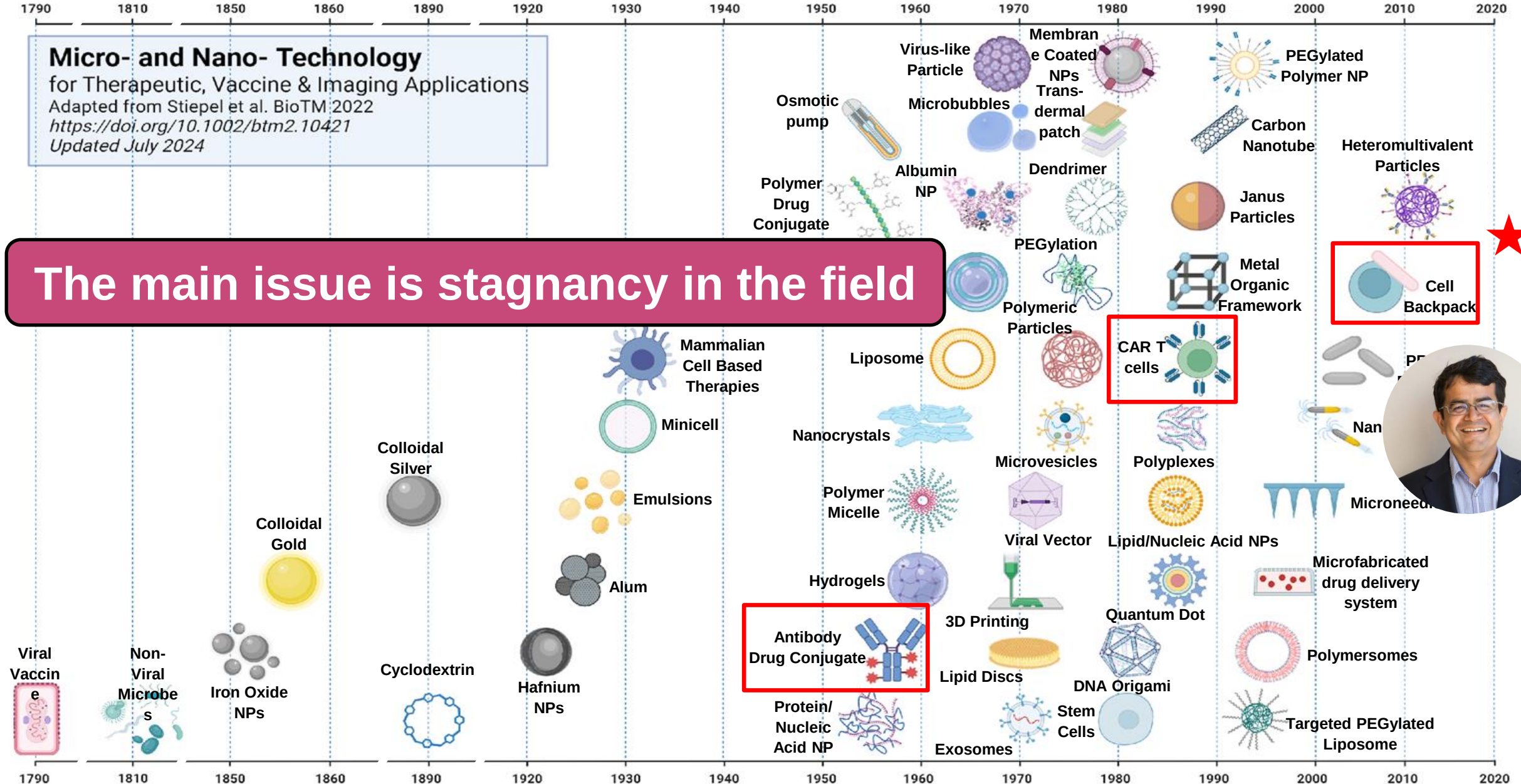


Importance of Studying Women's Health



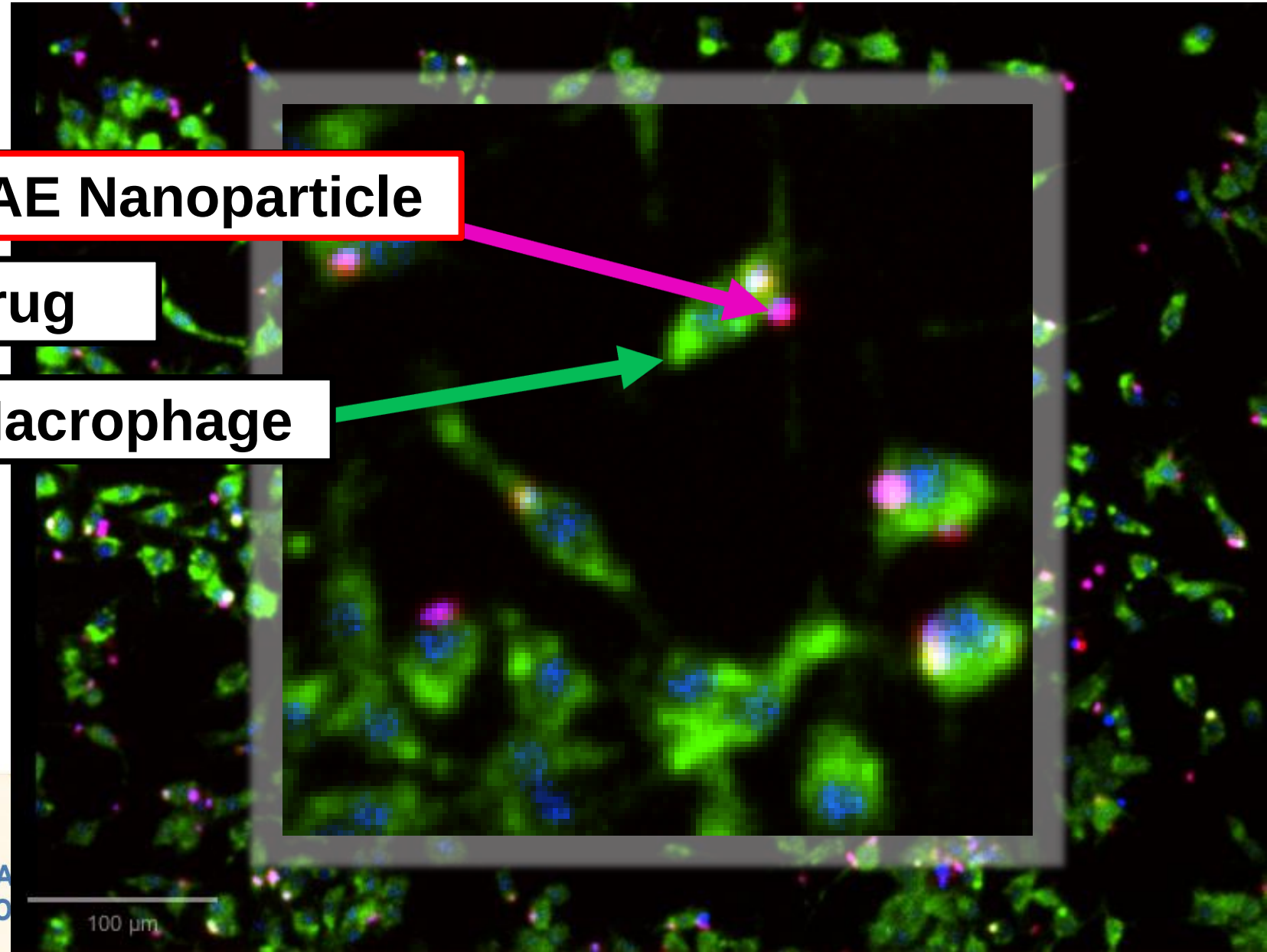
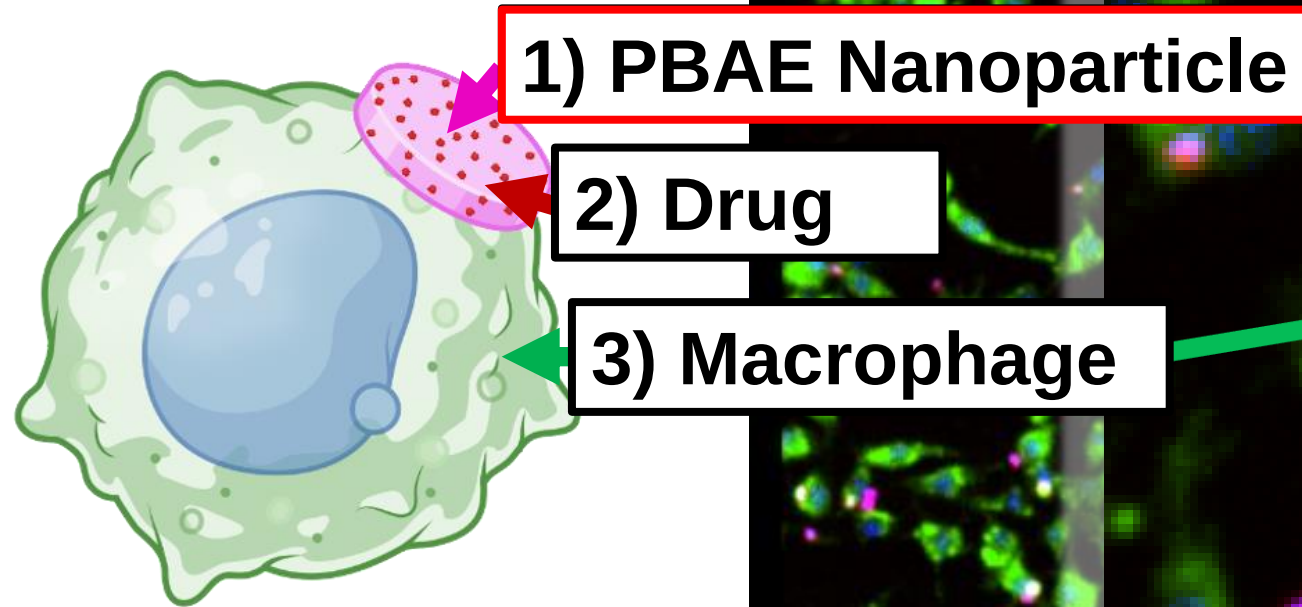
- Ovarian cancer is one of the deadliest gynecologic malignancies
 - High-grade serous carcinoma (HGSC) is the most common subtype with a 5-year survival rate around ~30%
1. Late detection
 2. Limited therapeutic options
 - Platinum
 - PARP inhibitors

Innovation Lags in Ovarian Cancer



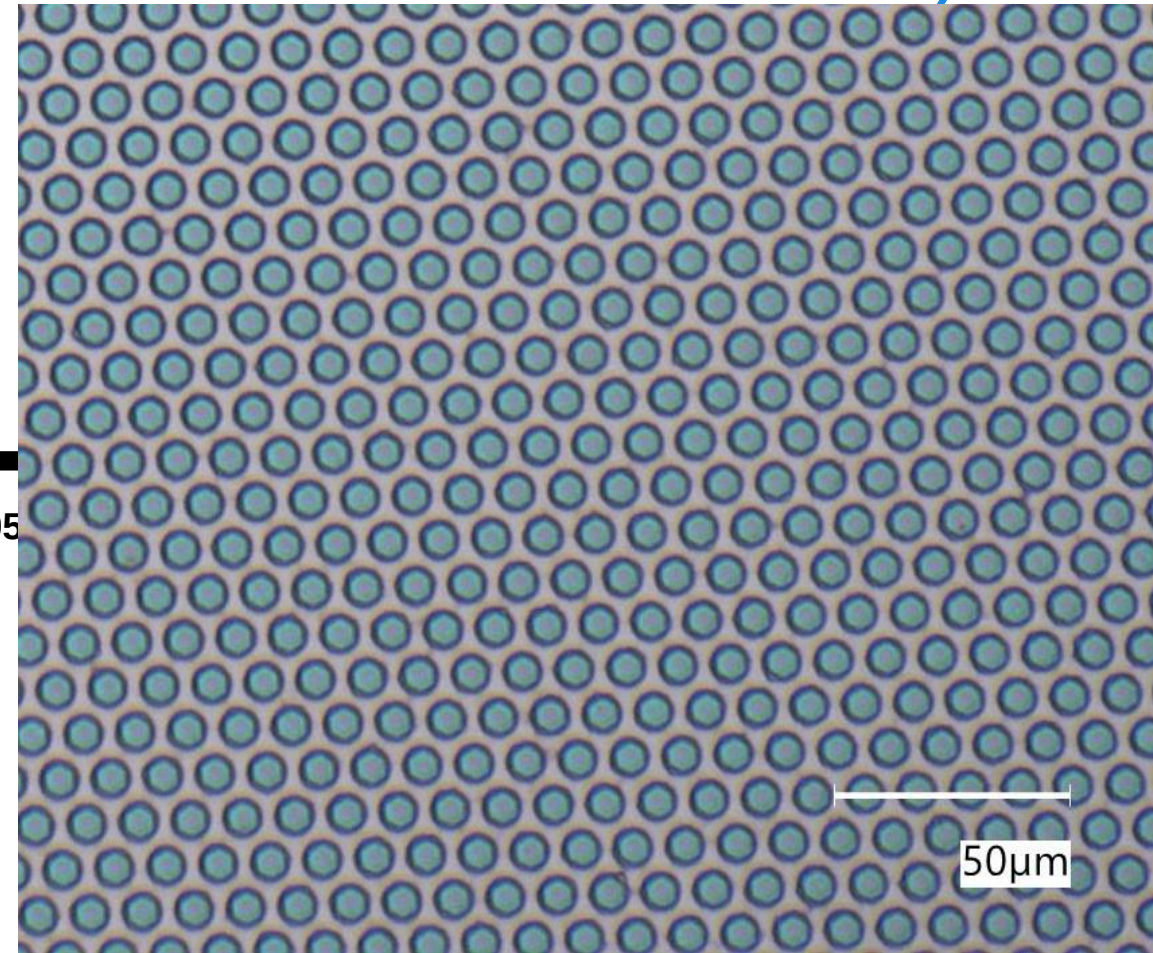
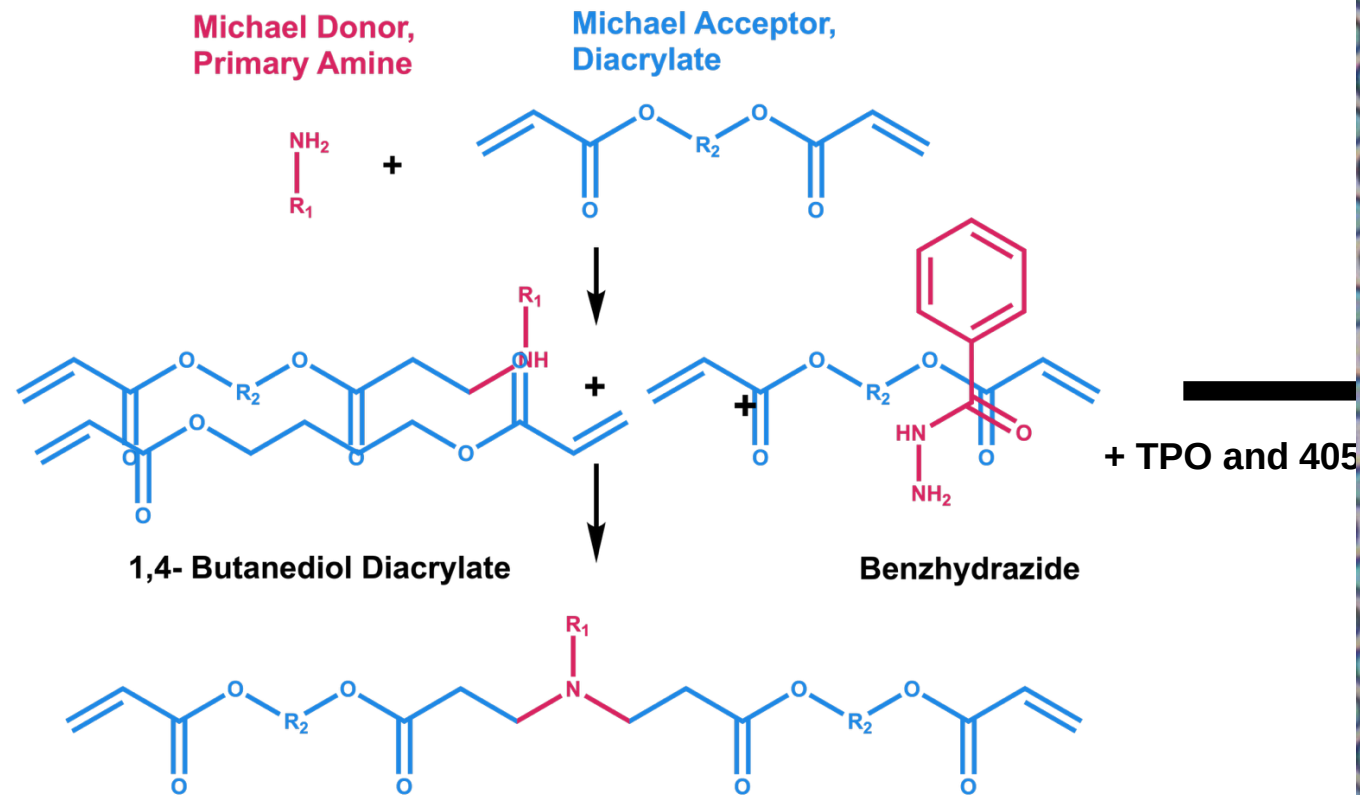


Macrophage Backpack System



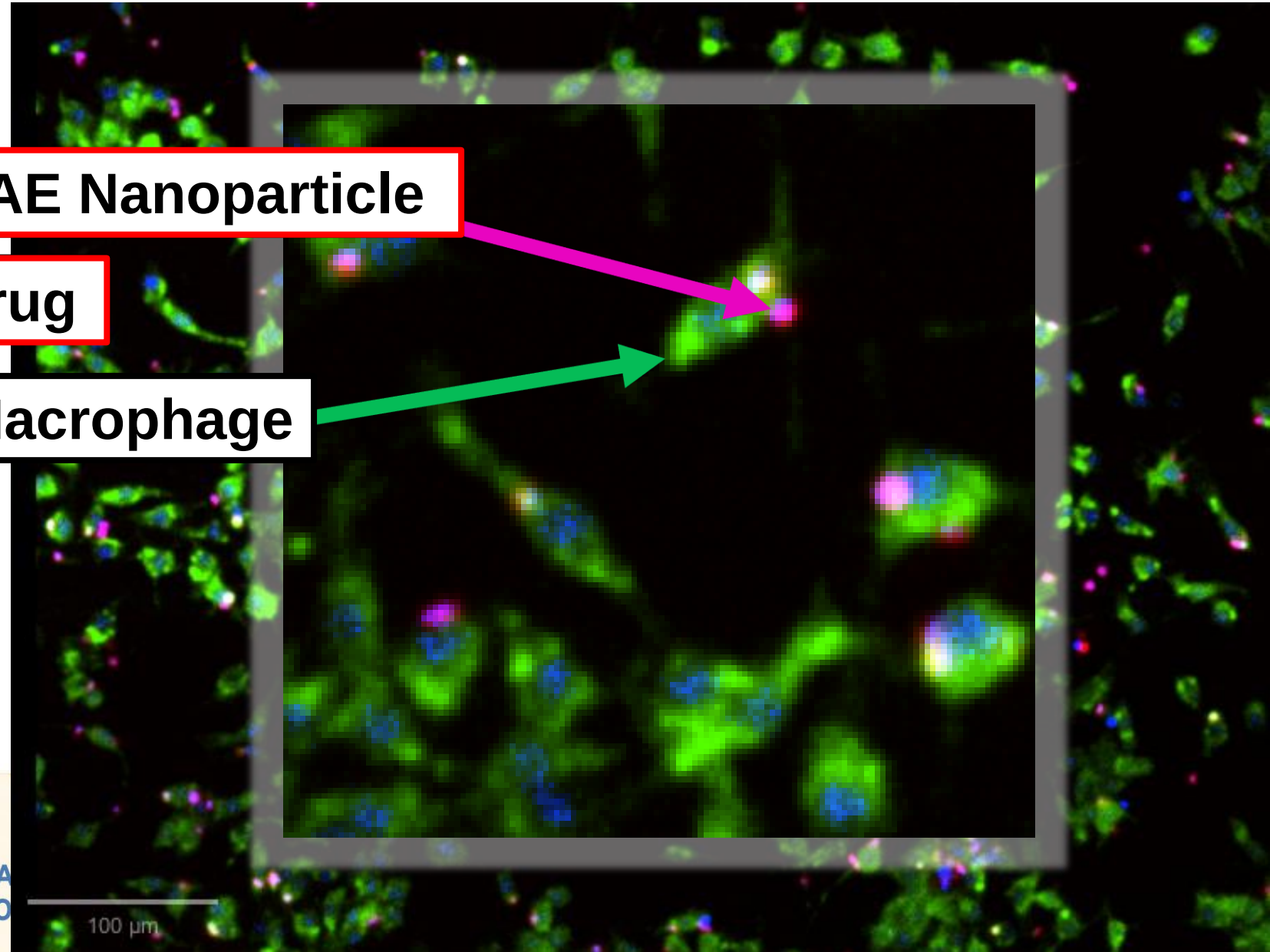
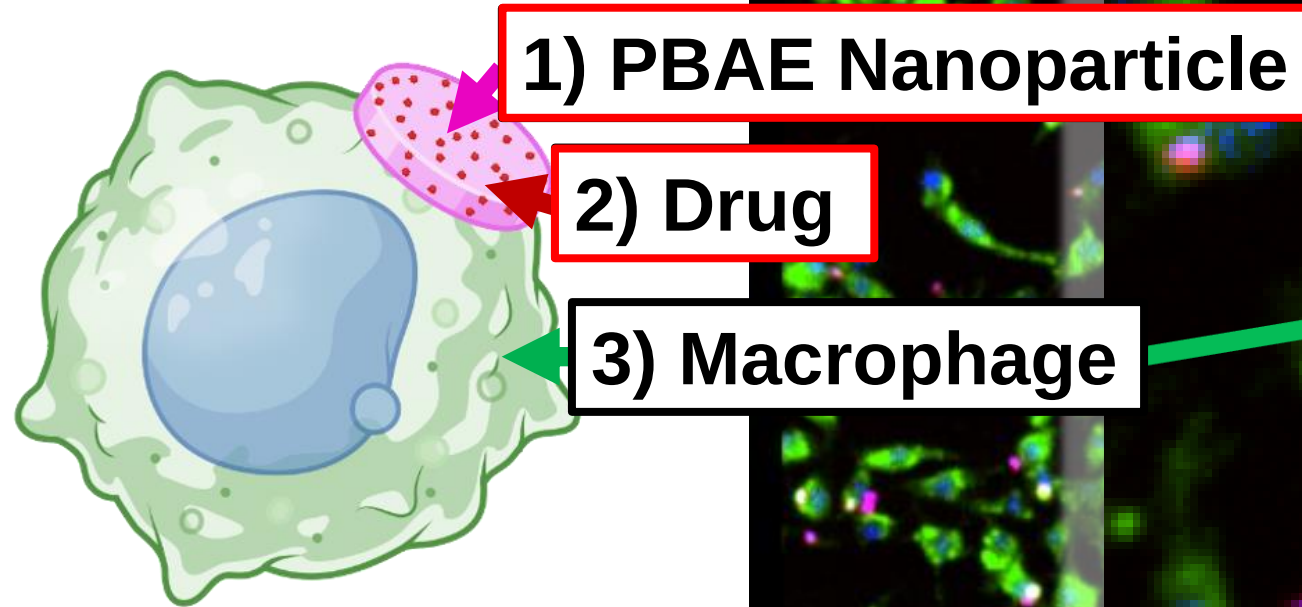


Poly(β -Amino Ester) Macromers



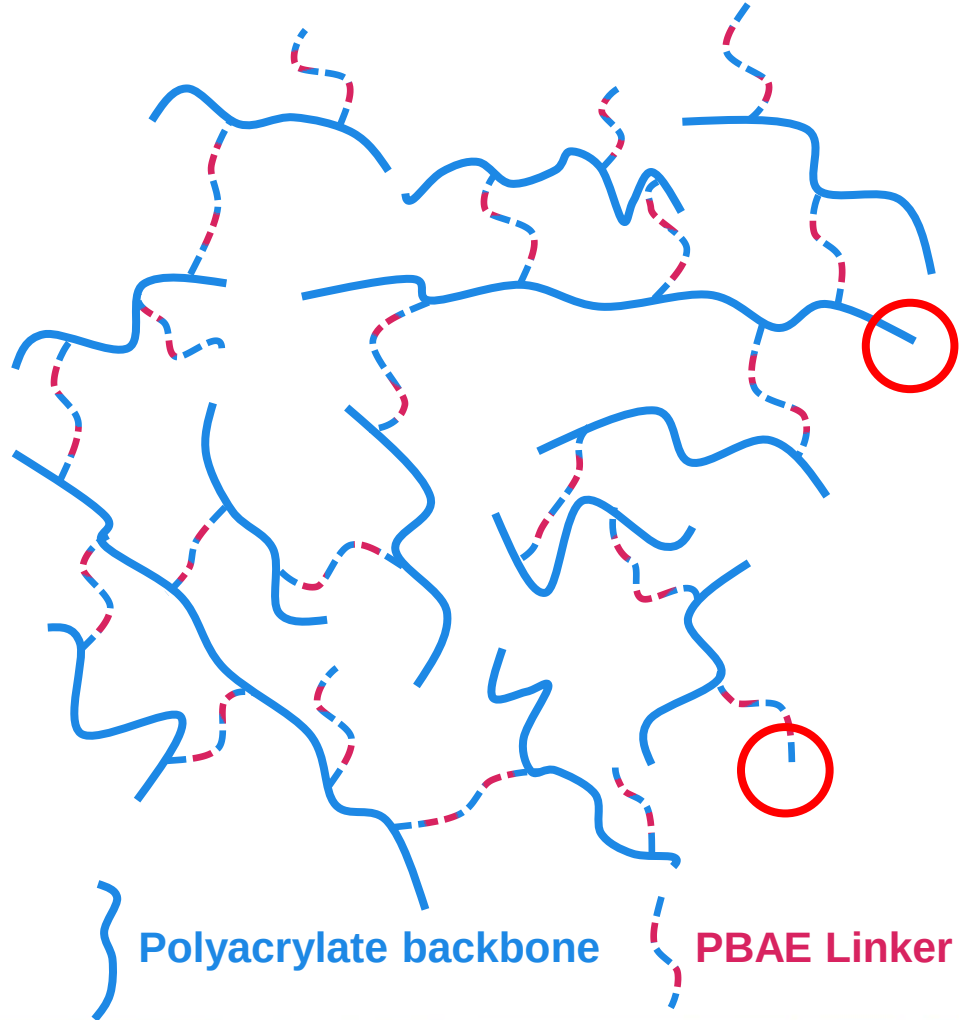


Macrophage Backpack System





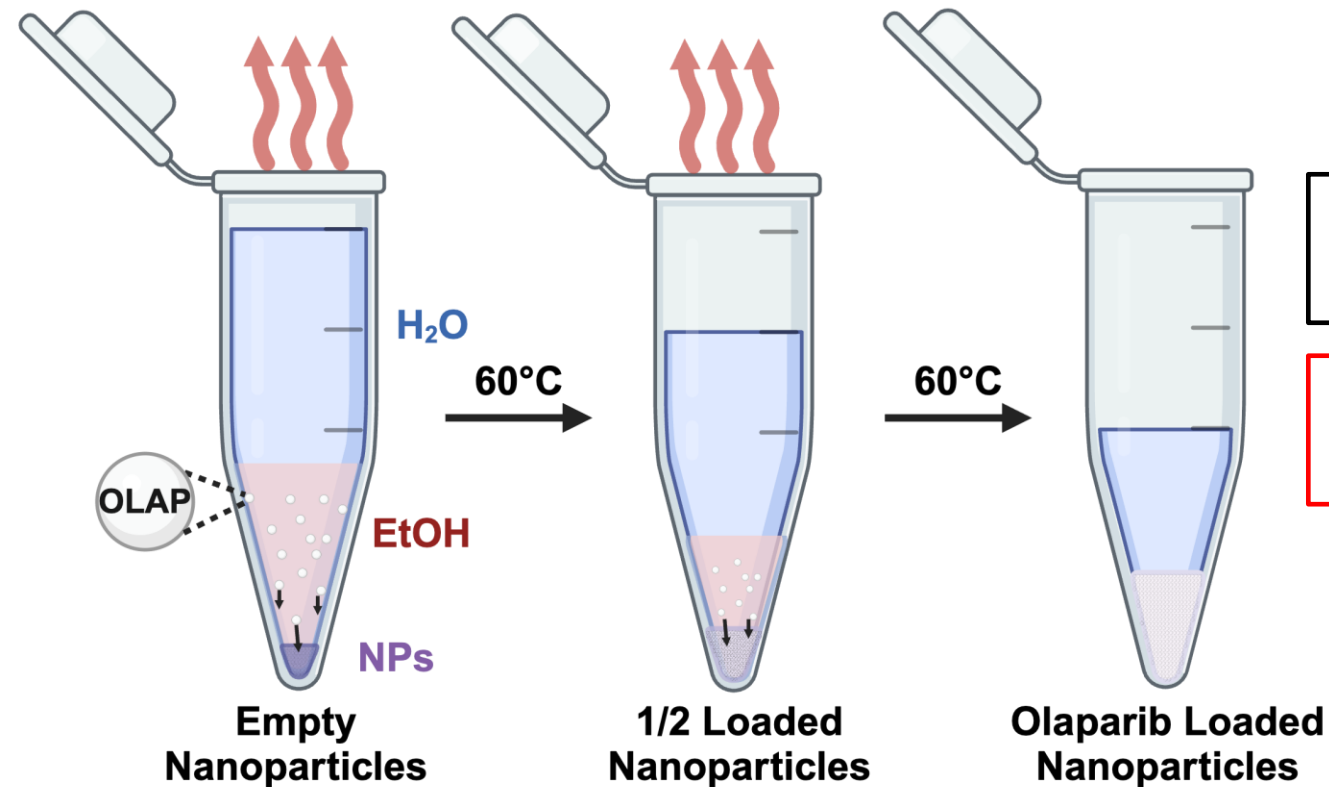
Poly(β -Amino Ester) Macromers



1. Free diacrylates can be functionalized to bind drug into the particle



Poly(β -Amino Ester) Macromers



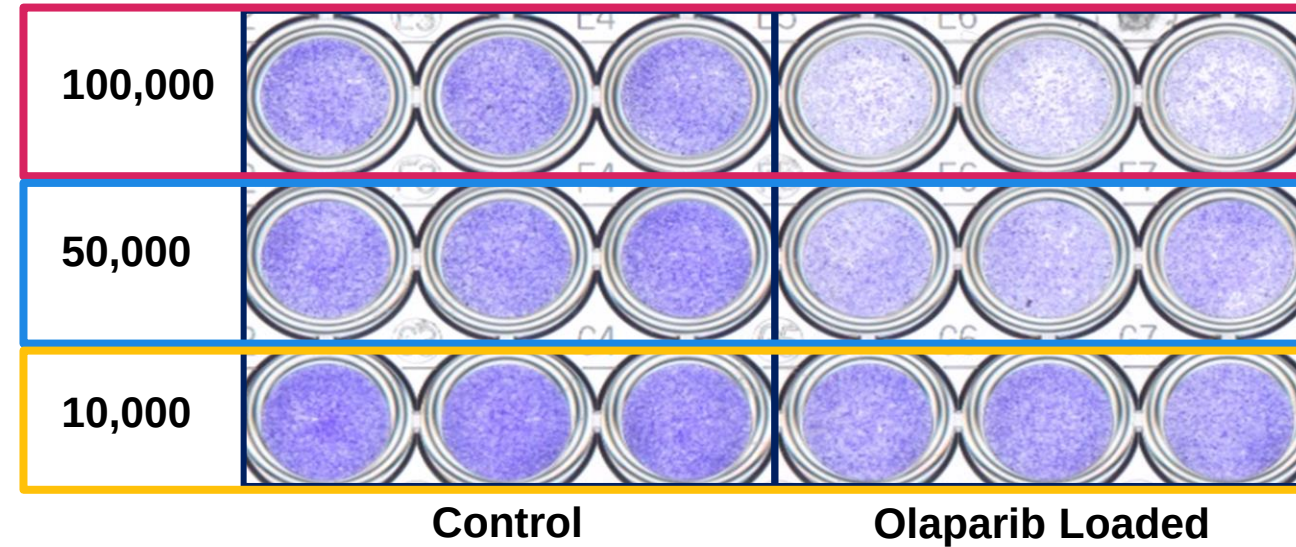
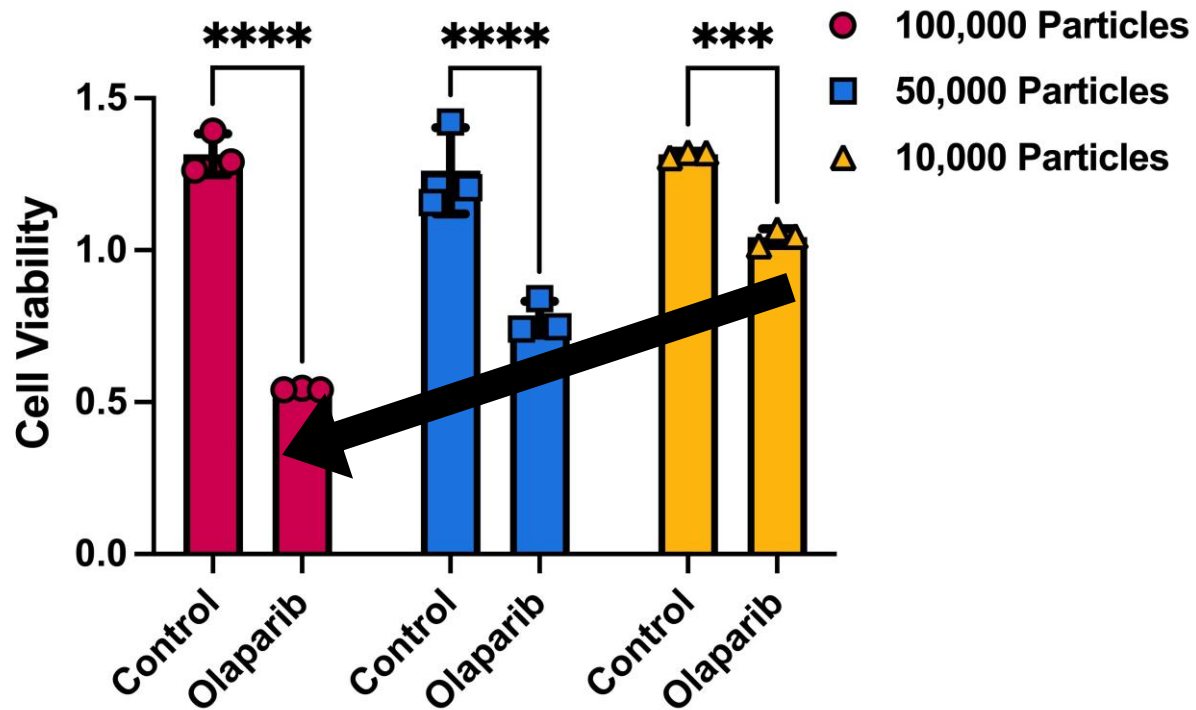
1. Free diacrylates can be functionalized to bind drug into the particle

2. Any drug that is hydrophobic and small molecule and be loaded using cosolvents



Backpacks Alone Improved Pharmacokinetics

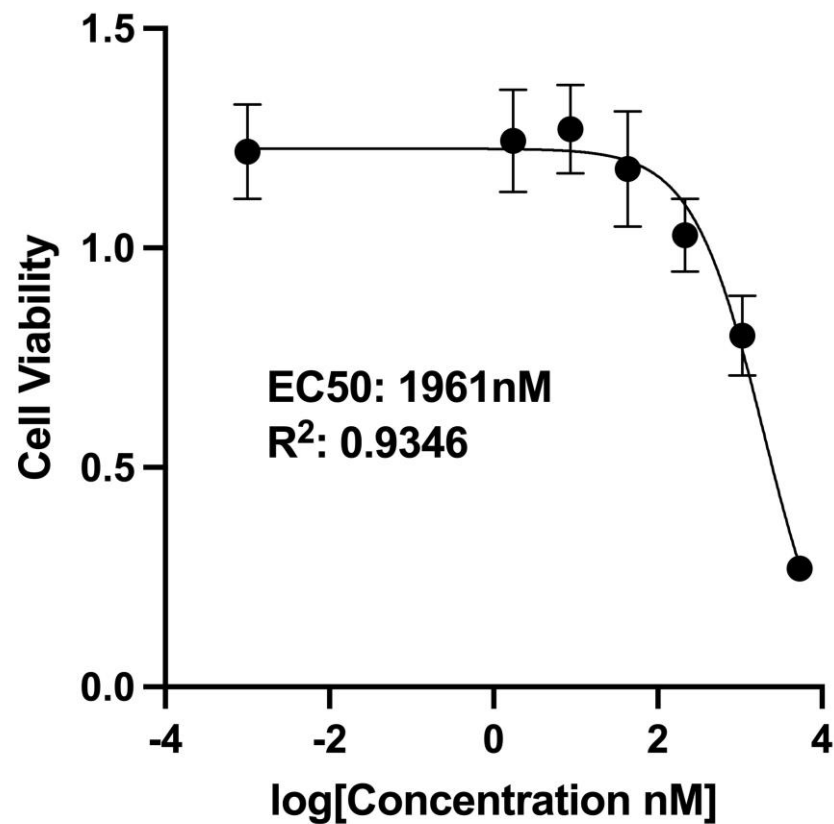
HGSC Cells and BPs



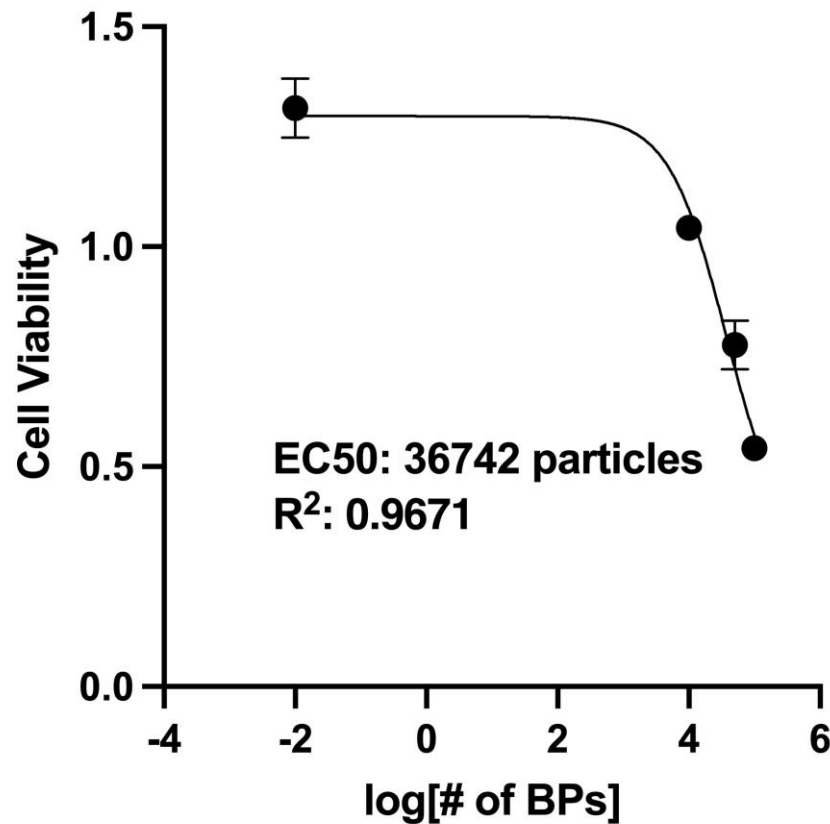
Backpacks Alone Improved Pharmacokinetics



Viability of HGSC Cells Treated With Solubilized OLAP



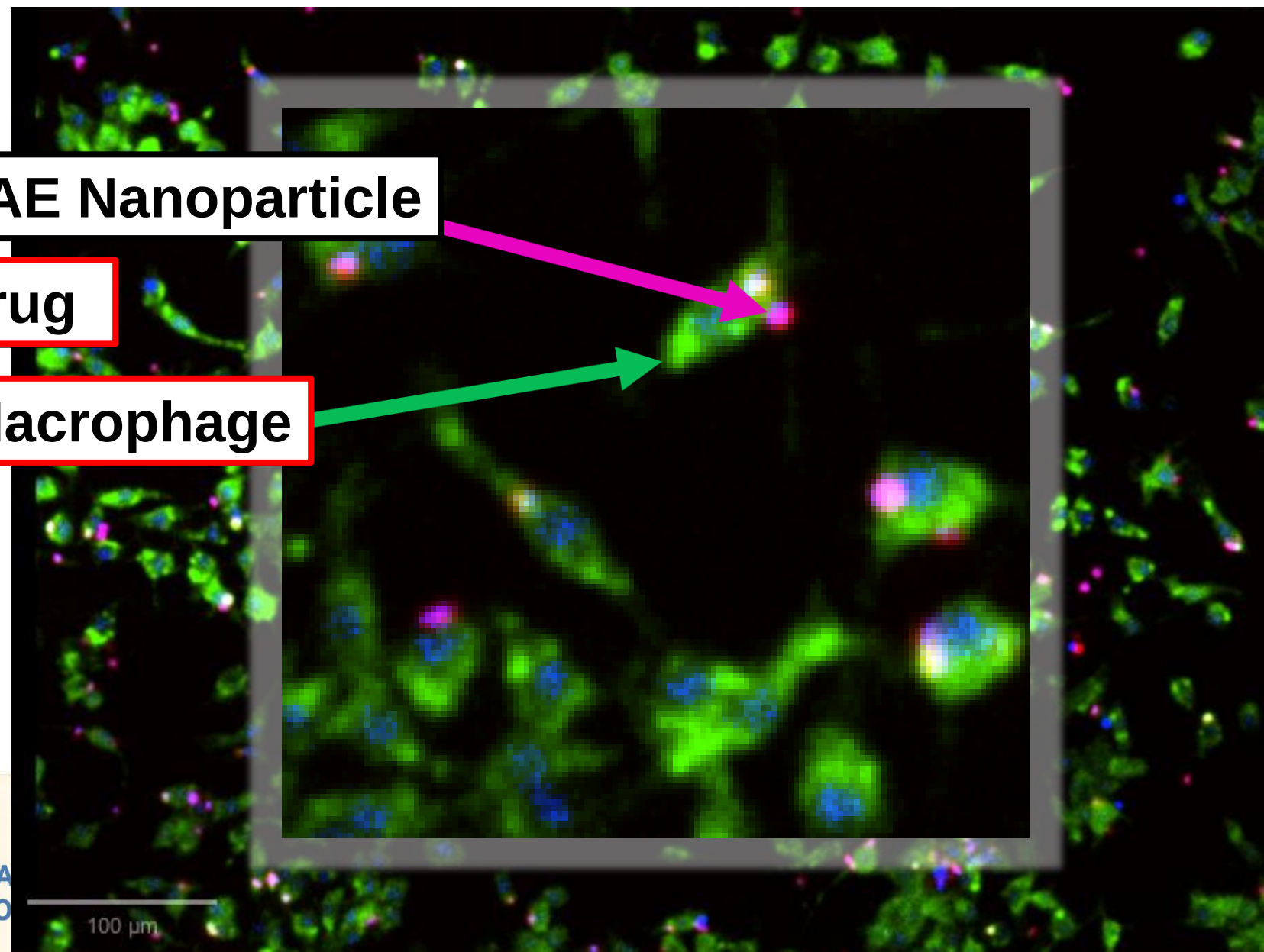
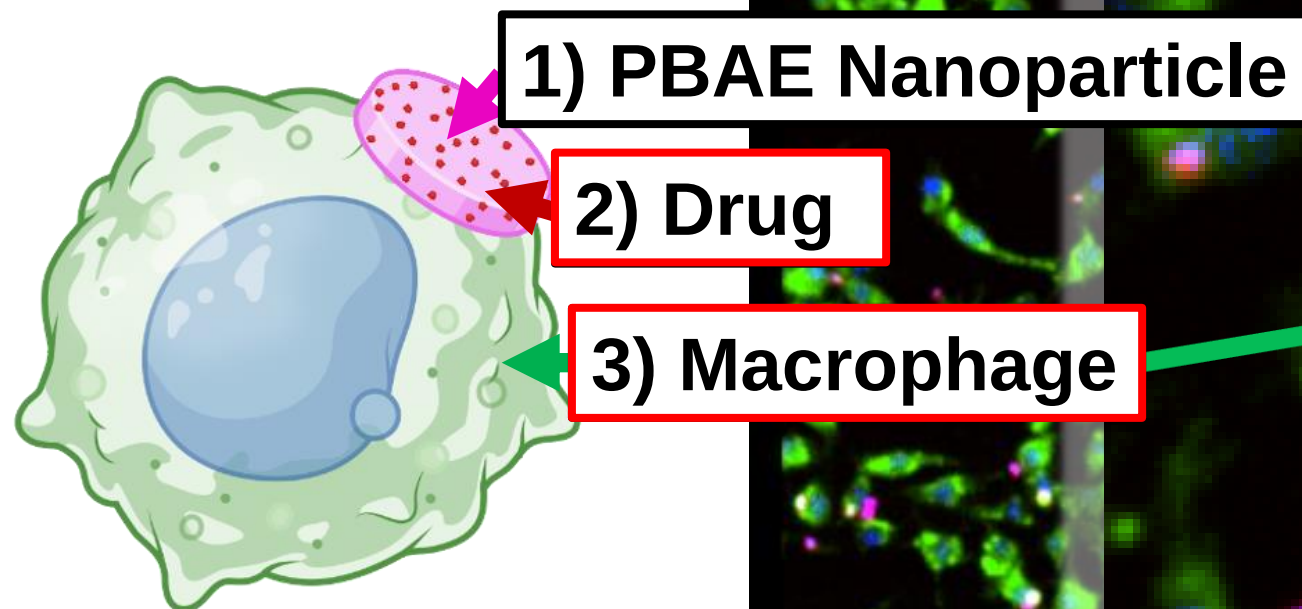
Viability of HGSC Cells Treated With OLAP BPs



EC50 in 36742 particles equivalent to ~960nM of solubilized (non-particle encapsulated) olaparib

2-fold decrease in amount of drug needed to achieve similar effect

Macrophage Backpack System



Oversimplified Macrophage Polarization



M1- Like

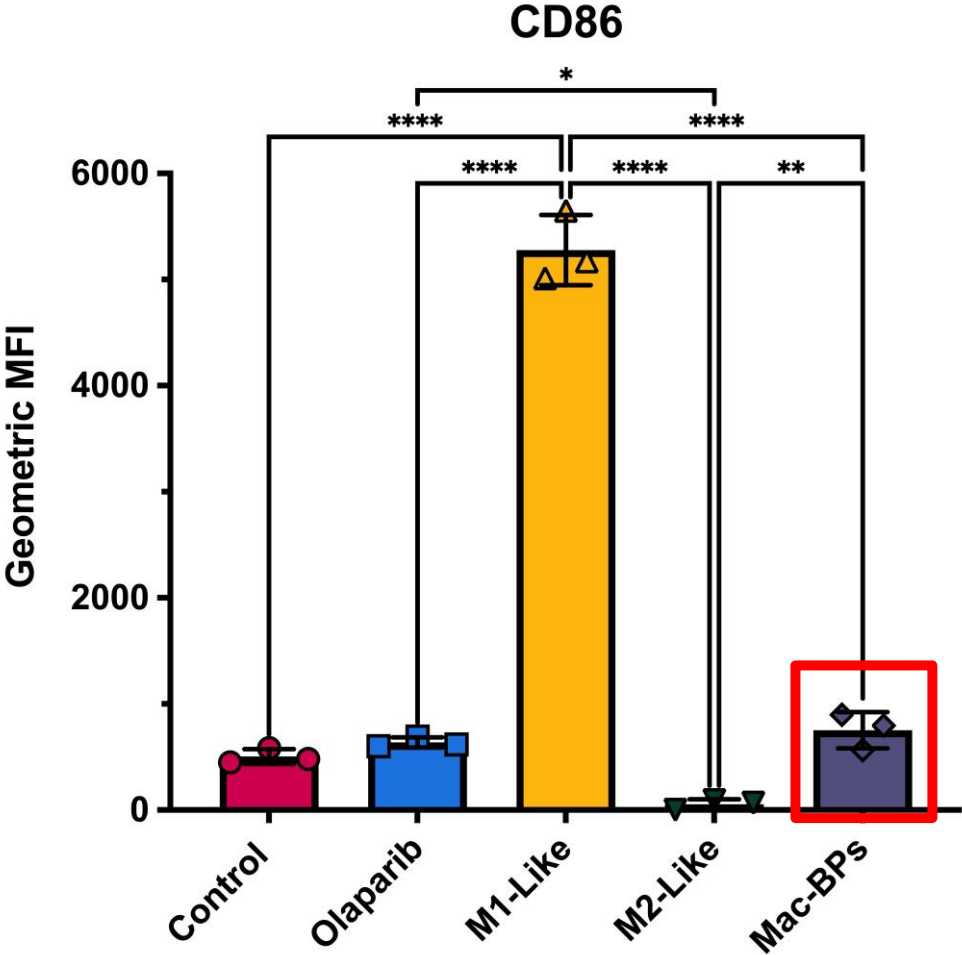
Anti-tumoral and pro-inflammatory

M2- Like

Pro-tumoral and anti-inflammatory



Macrophage Polarization Remains Neutral with BP-Loading

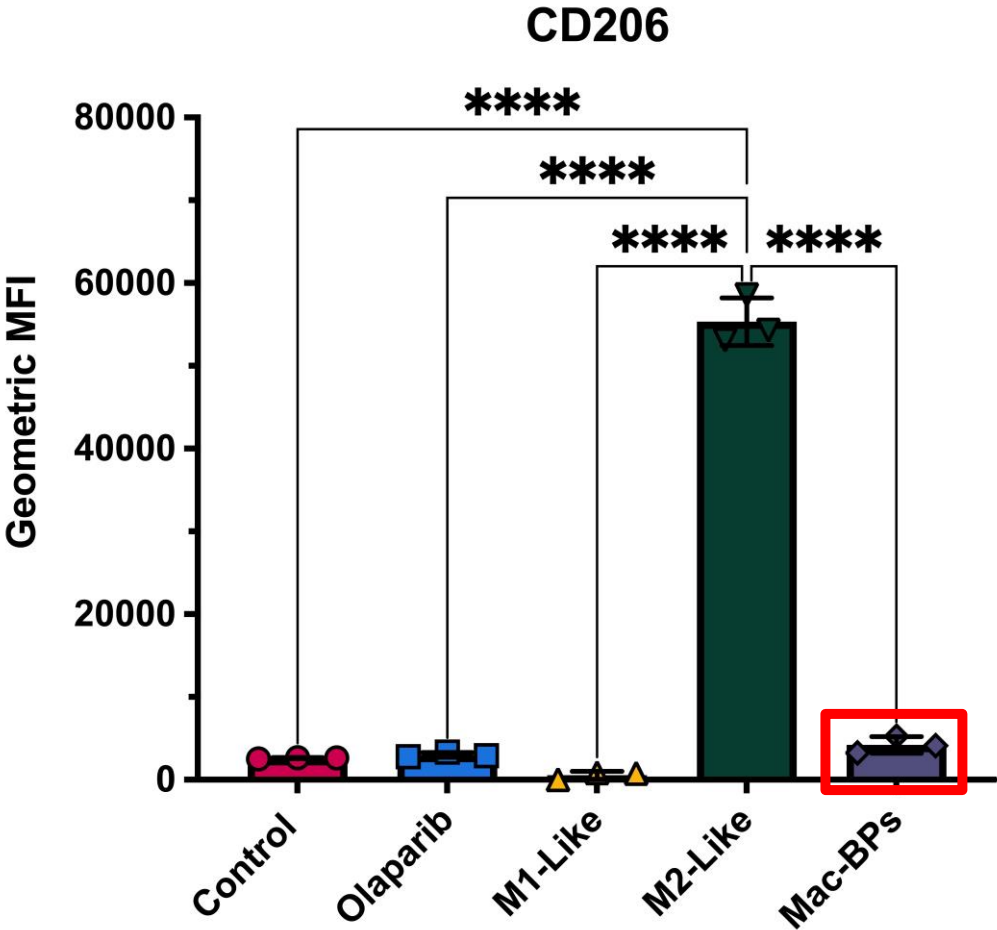


Control	Treatment
Negative Ctrl Macs	No treatment
Olaparib Treated	1961nM for 72 hrs (EC50)
Positive Ctrl M1-like Macs	LPS (100ng/mL 72 hrs)
Positive Ctrl M2-like Macs	IL4 and IL13 (50ng/mL 72 hrs)
Mac-BPs	Macrophages bound to BPs for 72 hrs

CD86 is an M1 (anti-tumoral, pro-inflammatory) marker



Macrophage Polarization Remains Neutral with BP-Loading



Control	Treatment
Negative Ctrl Macs	No treatment
Olaparib Treated	1961nM for 72 hrs (EC50)
Positive Ctrl M1-like Macs	LPS (100ng/mL 72 hrs)
Positive Ctrl M2-like Macs	IL4 and IL13 (50ng/mL 72 hrs)
Mac-BPs	Macrophages bound to BPs for 72 hrs

CD206 is an M2 (pro-tumoral, anti-inflammatory) marker

Biodistribution Study Design



ID8 Injection or
PBS



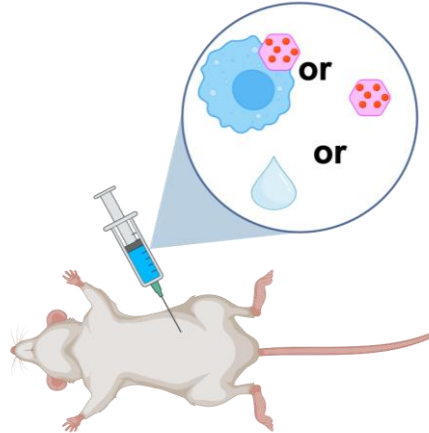
Day 0

Group 1: No ID8 cells,
vehicle injected IP

Group 2: 5 million ID8
tumor cells injected IP

Group 3: 5 million ID8
tumor cells injected IP

Injection

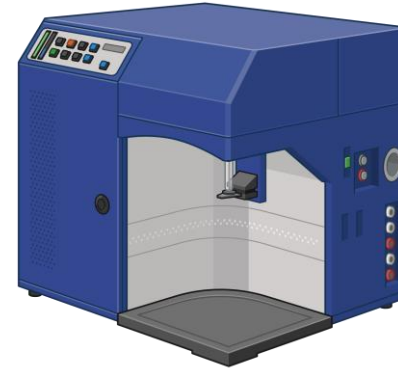


Day 7

Group 1: Mac-BPs
injected IP

Group 2: Mac-BPs
injected IP

Group 3: BPs only
injected IP



Day 8

Sacrifice 12 hours after
injection

Tissues were weighed
then dissociated into
single cell suspensions
for flow cytometry

3 mice per group, 15 total

Tissues and specimens
collected:

Tumor/Omentum

Uterus

Liver

Lung

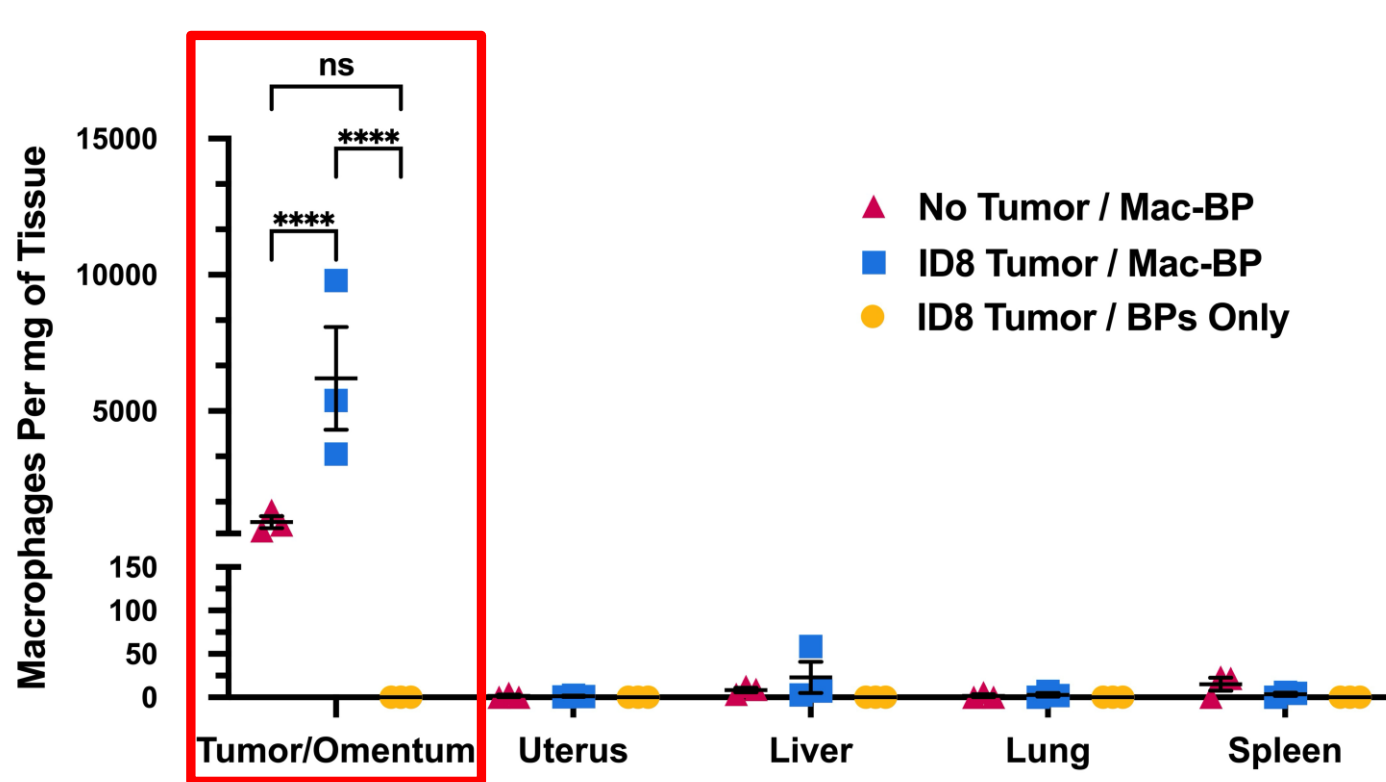
Spleen

Bone Marrow (BM)

Blood

Peritoneal Wash (Wash)

Biodistribution Study in Female C57/Blk6 Mice



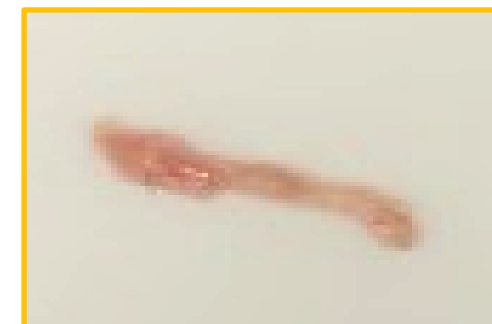
6.72-fold increase in number of Mac-BPs found in the omentum when tumor is present



No Tumor / Mac-BP



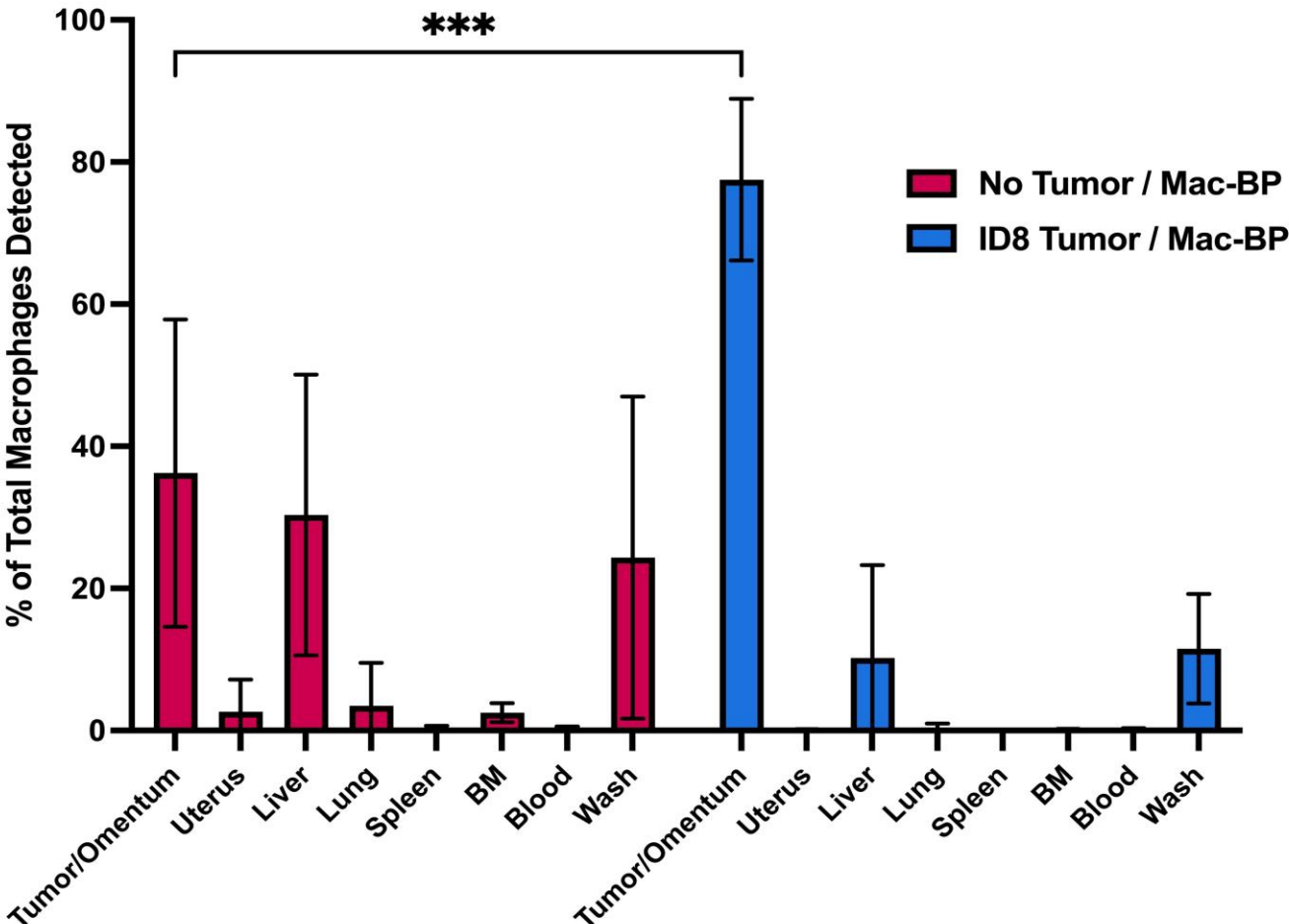
ID8 Tumor / Mac-BP



ID8 Tumor / BPs only



Greater Variability in Biodistribution With No Tumor Present

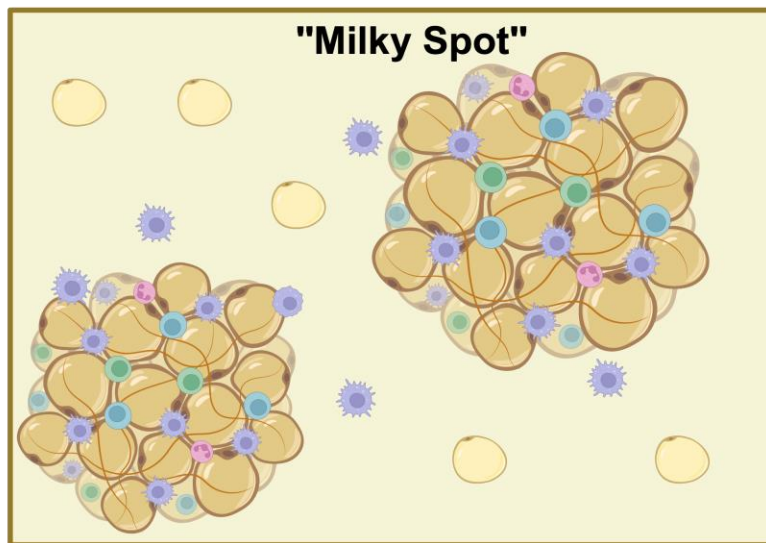


No Tumor / Mac-BP

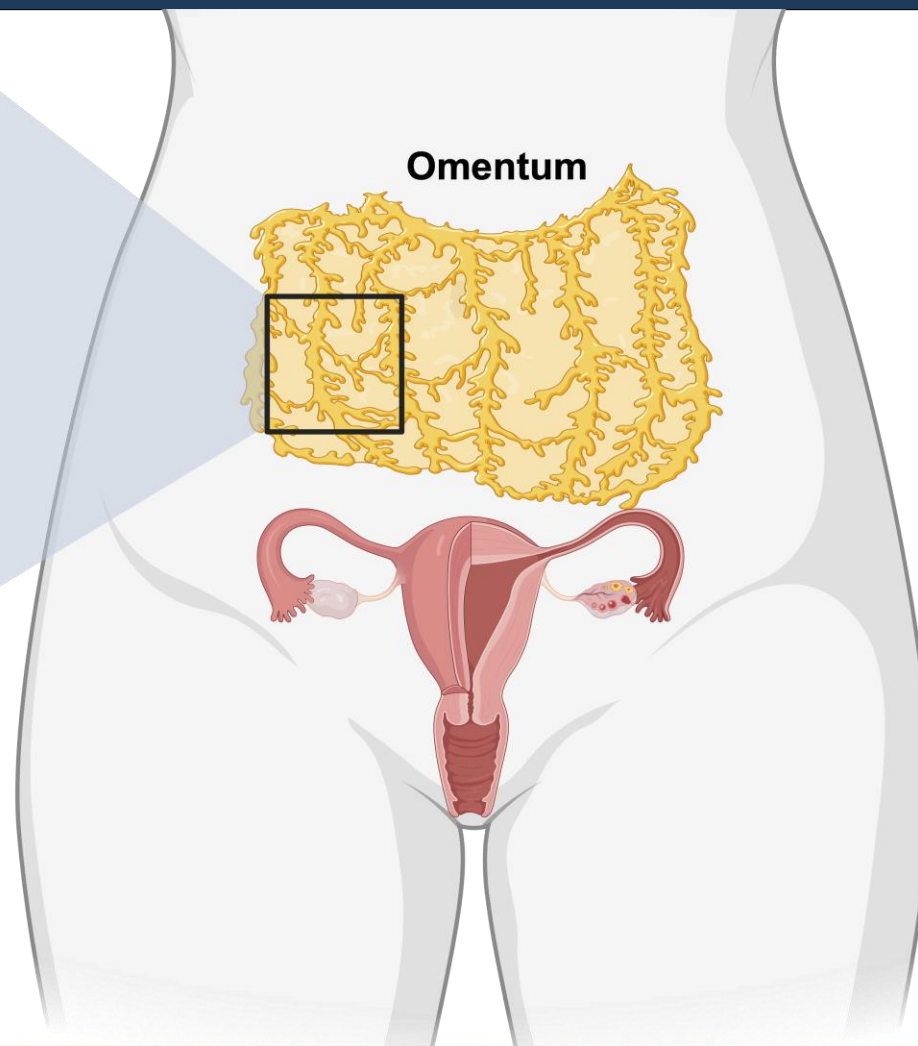


ID8 Tumor / Mac-BP

“Milky Spots” in Omentum May Encourage Macrophage Trafficking



-  Adipocyte
-  Macrophage
-  Neutrophil
-  B-Cell
-  T-Cell



Increased macrophage density has been shown to increase disease score in omenta from ovarian cancer patients

Pearce et al., 2018



17

JULY

TECH SESSION V: GENE
DELIVERY AND GENE
EDITING III



11:38 AM - 11:49 AM

Microrobot-Assisted Delivery of Circular RNA-Lipid Nanoparticles to Treat Lung-Associated Diseases

Bianca Santana

Poster:
Immuno
Delivery
(Focus Group
- ID)



POSTER # 244

Particle shape modulates macrophage phenotype: Insights for cell-mediated drug delivery systems

Matt Kwan

17

JULY

TECH SESSION V:
NANOMEDICINE AND
NANOSCALE DELIVERY
(FOCUS: NANO)



11:38 AM - 11:49 AM

Poly (β -amino ester) particles with programmable shape, stiffness, and degradation for drug release

Katie Trese

THANK YOU



Bitler Lab

Ben Bitler, PhD
Zachary Watson, PhD
Nicole Marjon, MD, PhD
Kian Behbakht, MD
Lindsay Brubaker, MD
Bradley Corr, MD
Natalie Davidson, PhD
Tomomi Yamamoto, PhD
Elizabeth Woodruff,

PhD

Ritsuko Iwanaga, PhD
Alan Elder, PhD
Scott Lin
Francis To
Maia Zoller
Freda Ireigbe
Valerie Arce

Shields Lab

Wyatt Shields, PhD
Ankit Gangrade, PhD
Jin Lee, PhD
Xingrui Zhu, PhD
Taylor Ausec
Bianca de Melo Santana
Abigail Harrell
Collin Kemper
Kendra Kreienbrink
Matthew Kwan

Ritu Raj
Katie Trese
Cara Colwell
Samuel Law



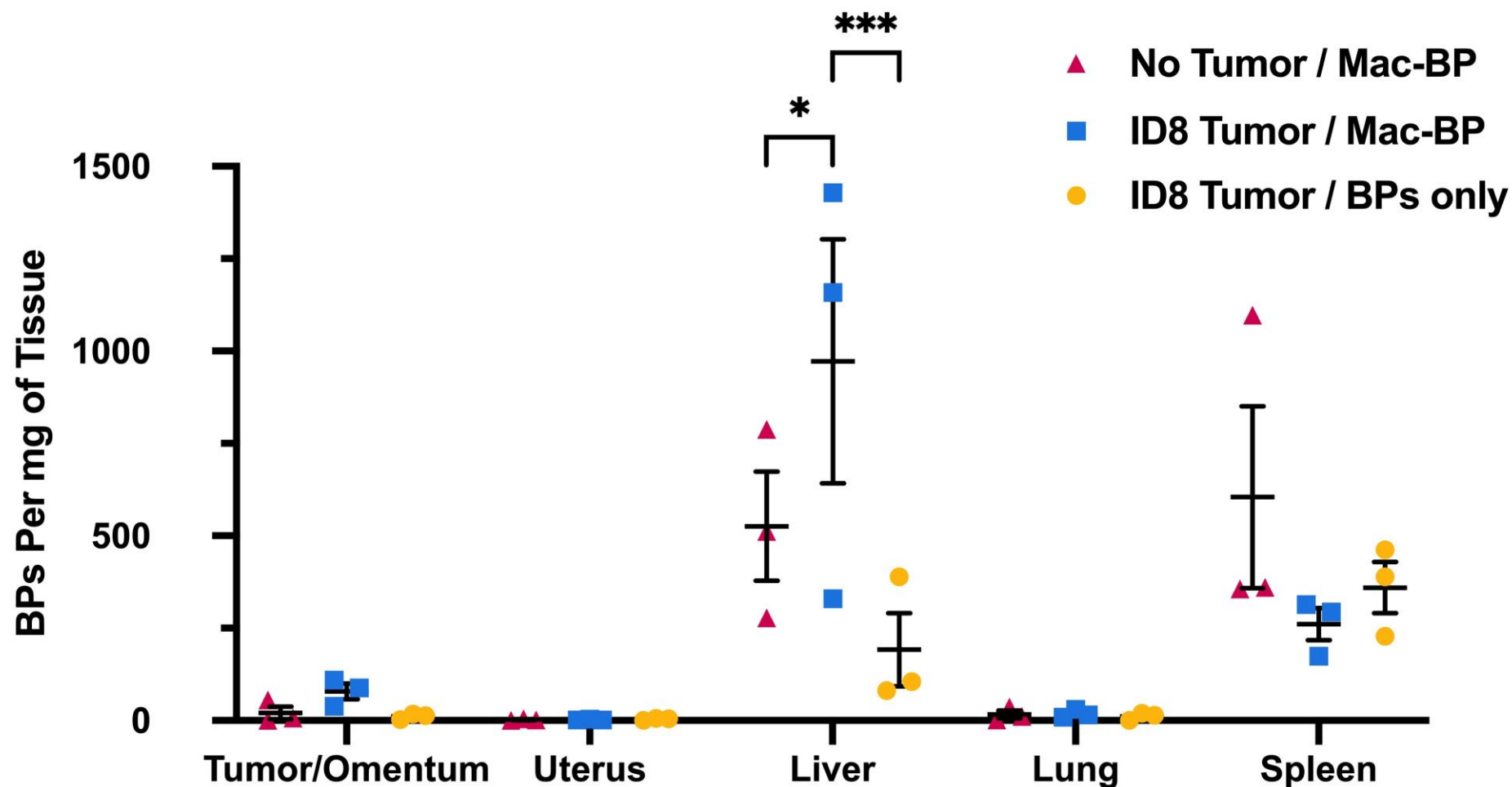
Scan QR code for contact info:
courtney.bailey@colorado.edu



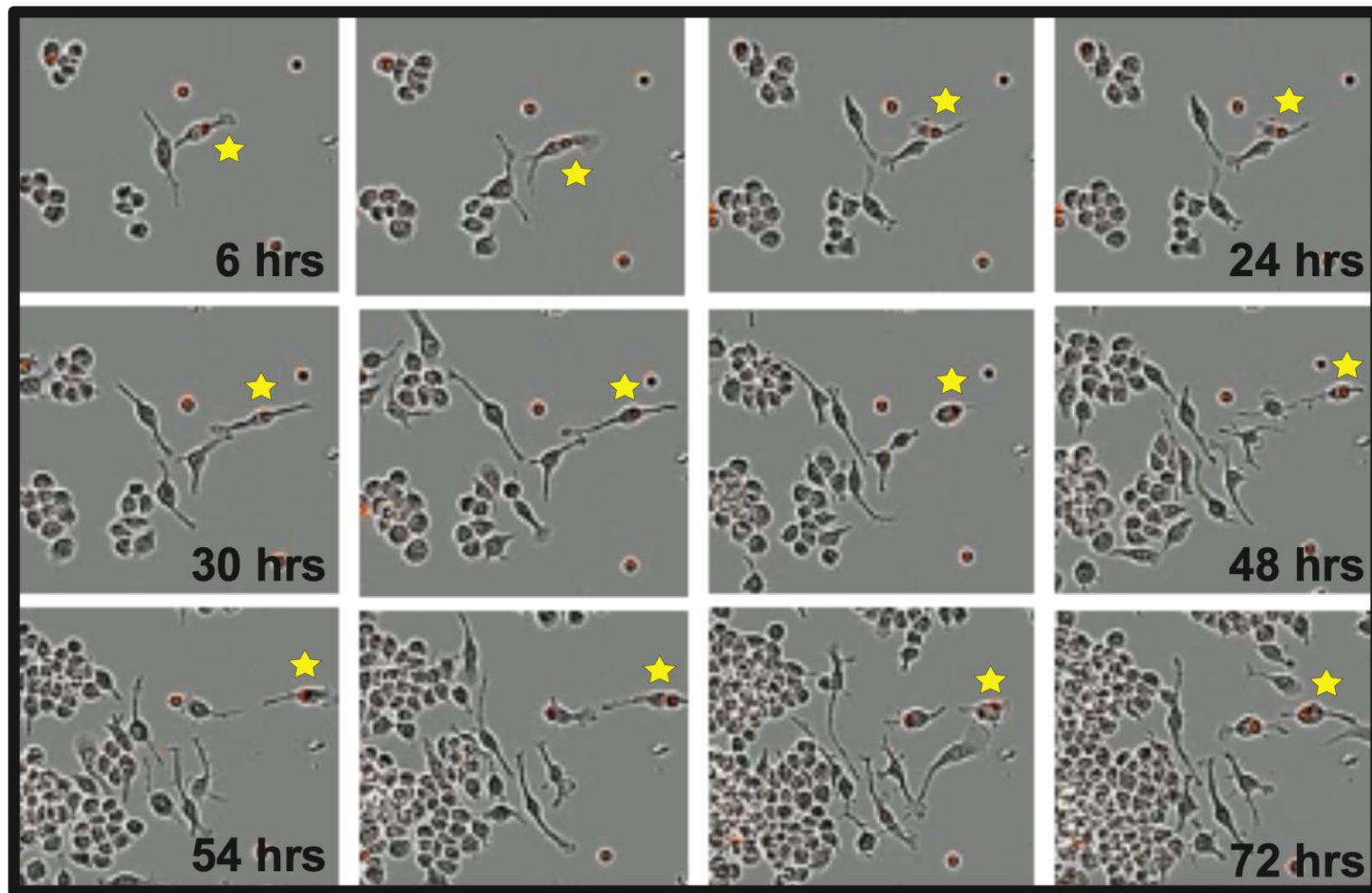
PHILADELPHIA, PA
JULY 13-18, 2025



Biodistribution Study Flow Gating Example

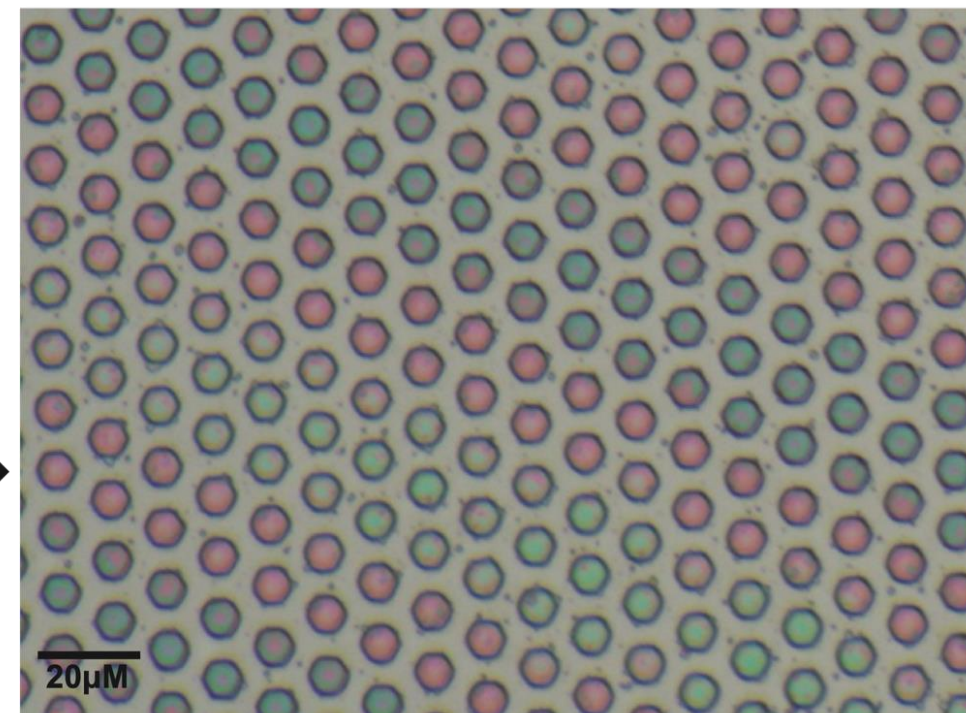
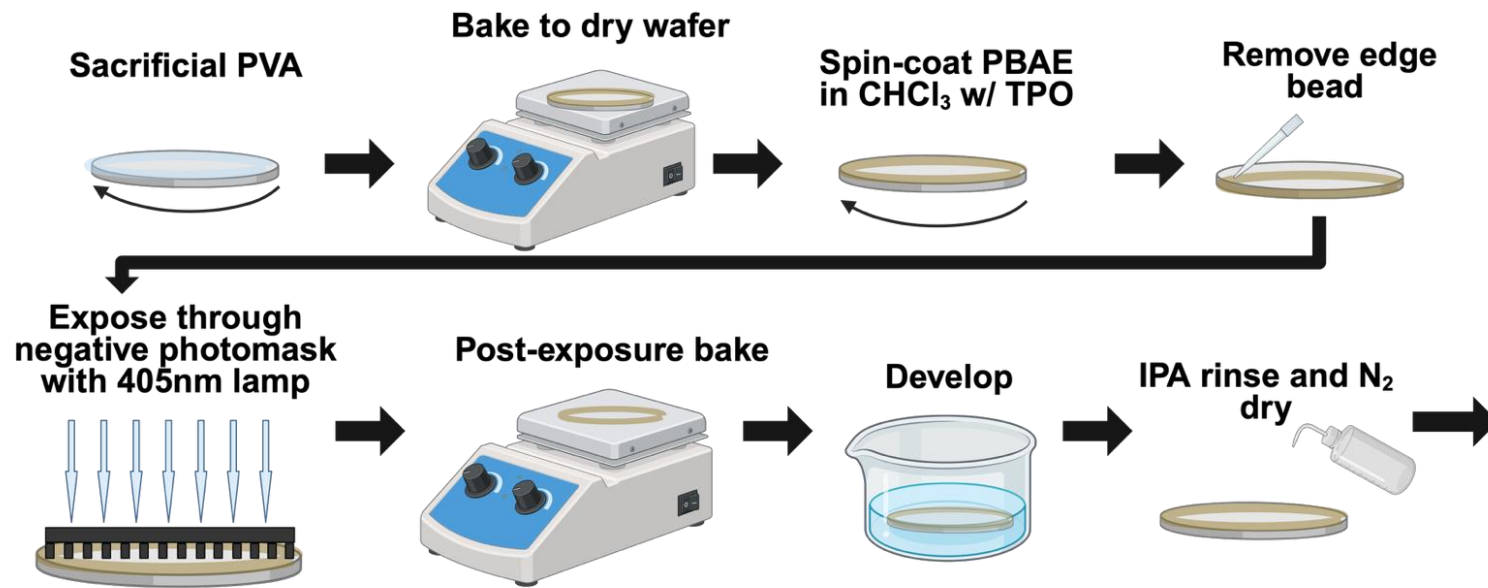


Backpacks Remain Attached for 66 Hours



Macrophage divides twice even with BP on board. Yellow star marks one macrophage

Particle Synthesis Allows for Large Yields



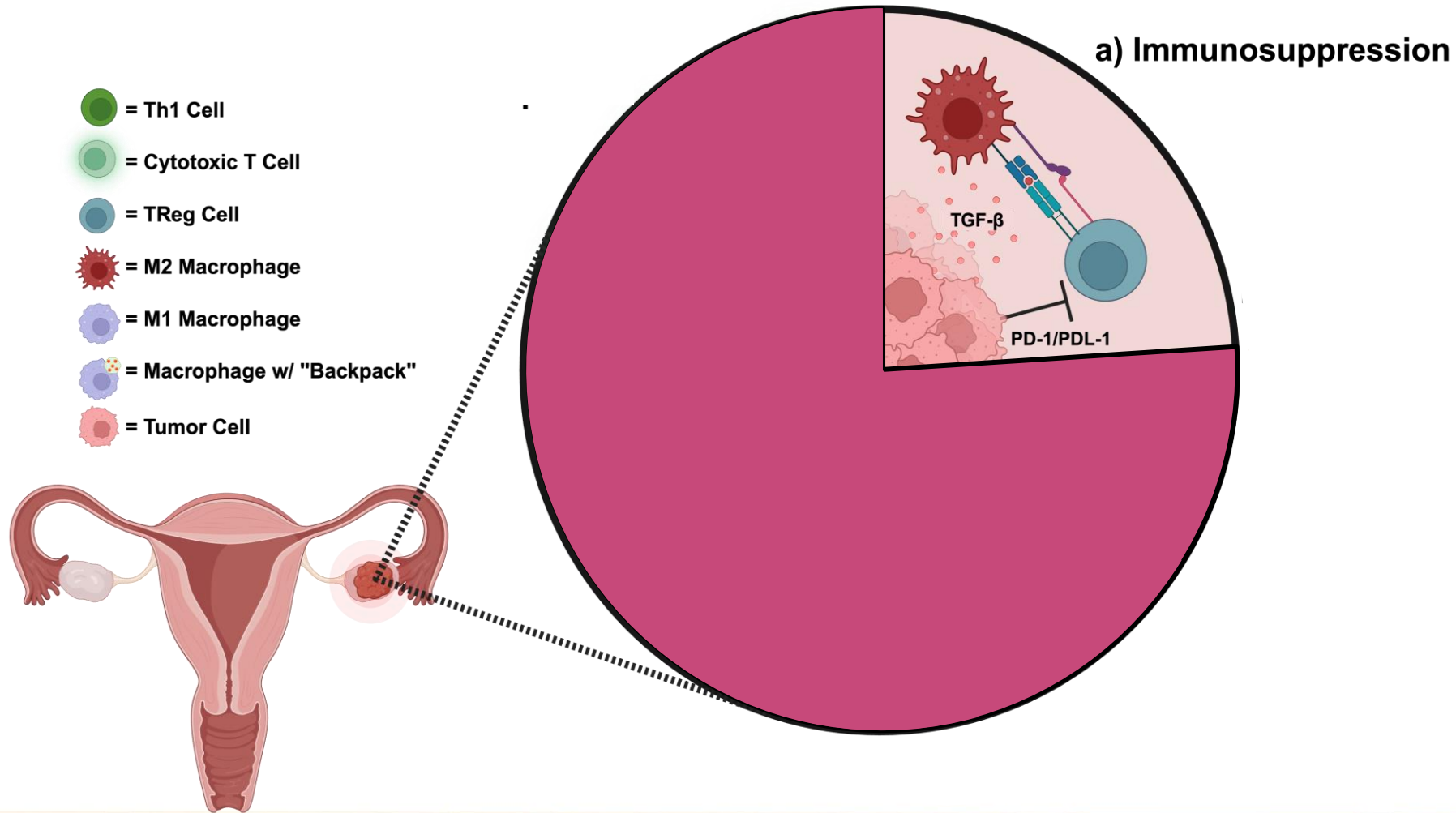
Backpacks

Photolithography allows for scalable production

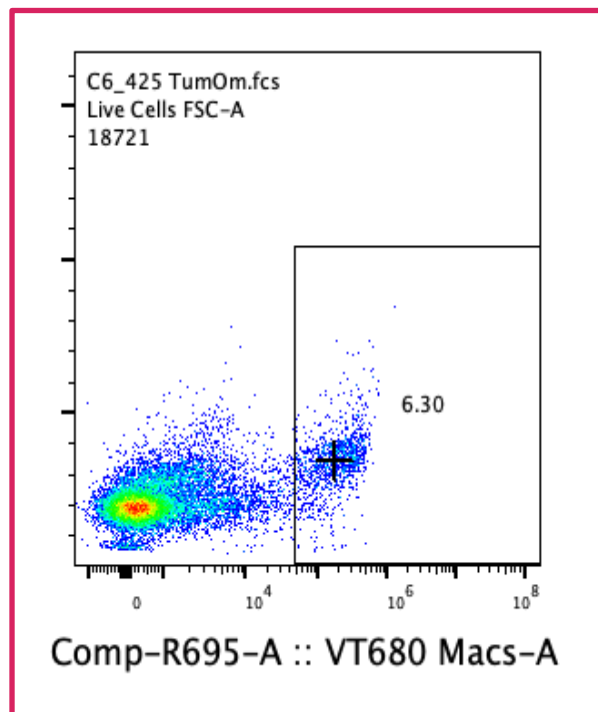
30mL of 5wt% PBAE resin 48-hour synthesis
 15 wafers per vial of resin
 1 wafer ~17 million backpacks or "BPs" in 5min

$\sim 2.55 \times 10^8$ BPs in 3 days

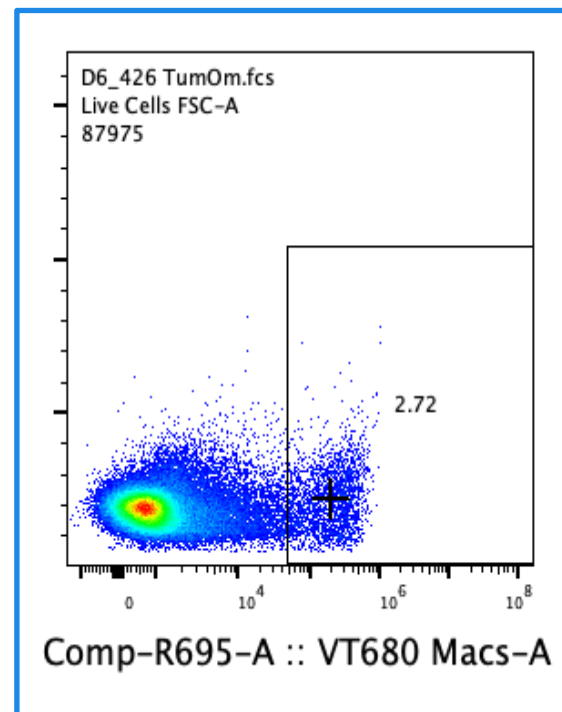
Intended Therapeutic Impacts of Macrophage “Backpacks”



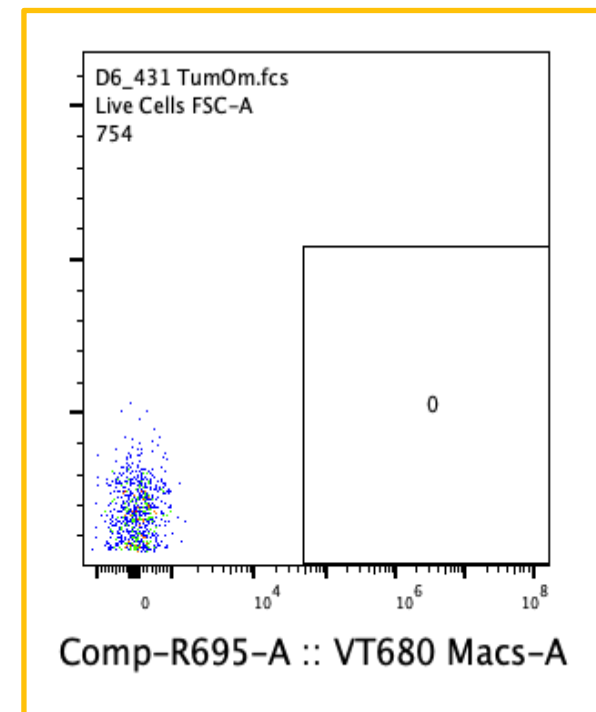
Biodistribution Study Flow Gating Example



No Tumor/ Mac-BP



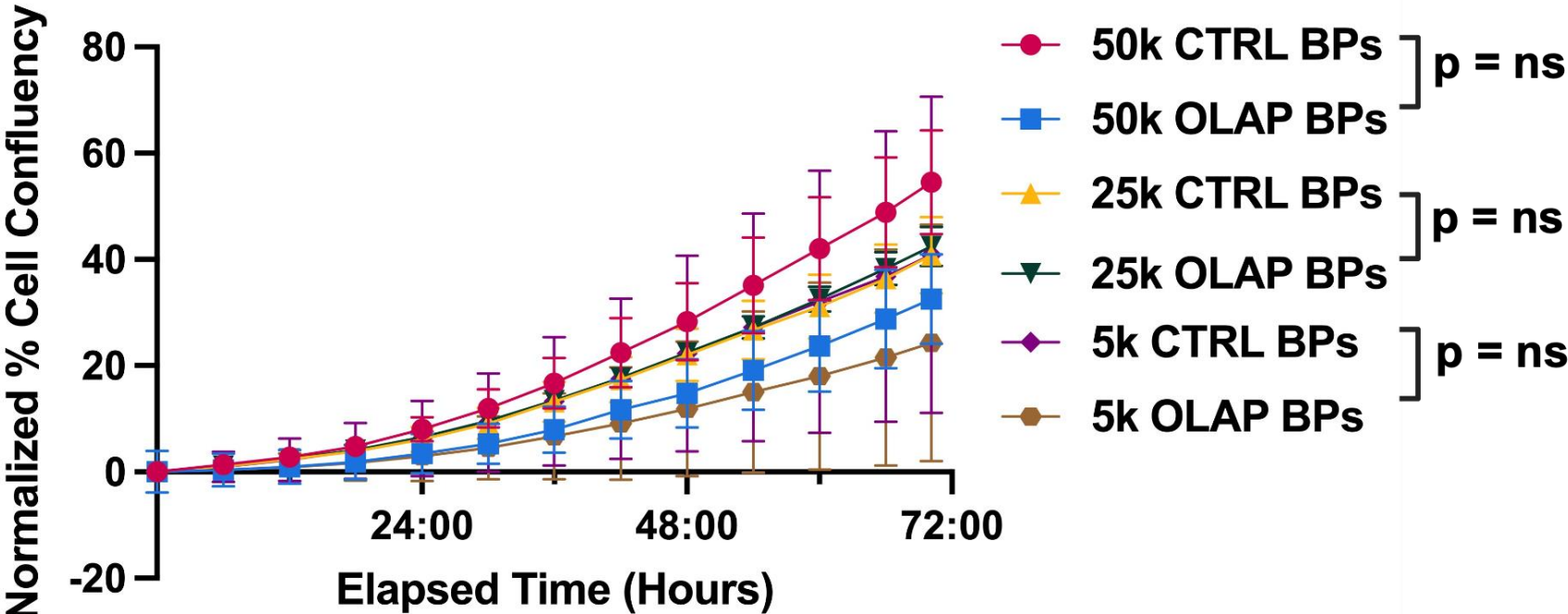
ID8 Tumor/ Mac-BP



ID8 Tumor/ BPs only

Particles on RAW 264.7 Macrophages

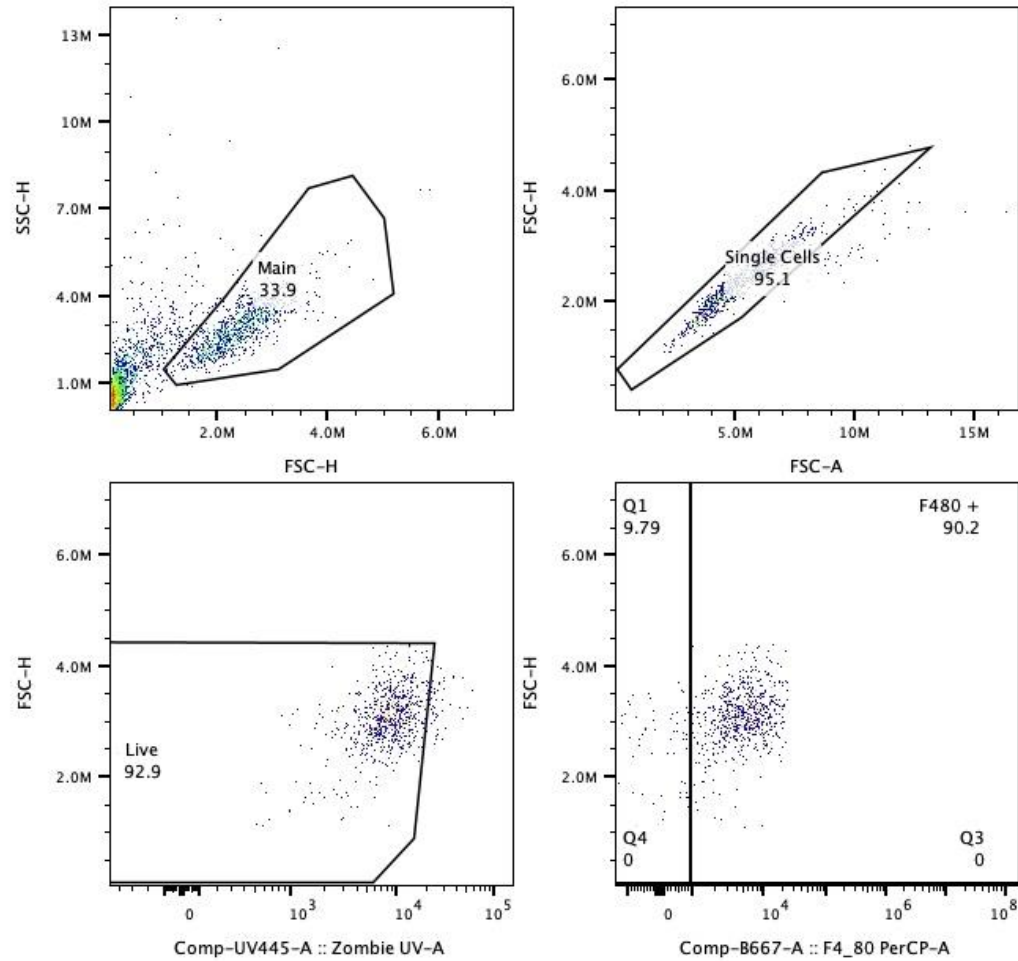
Proliferation of Macrophages Carrying BPs



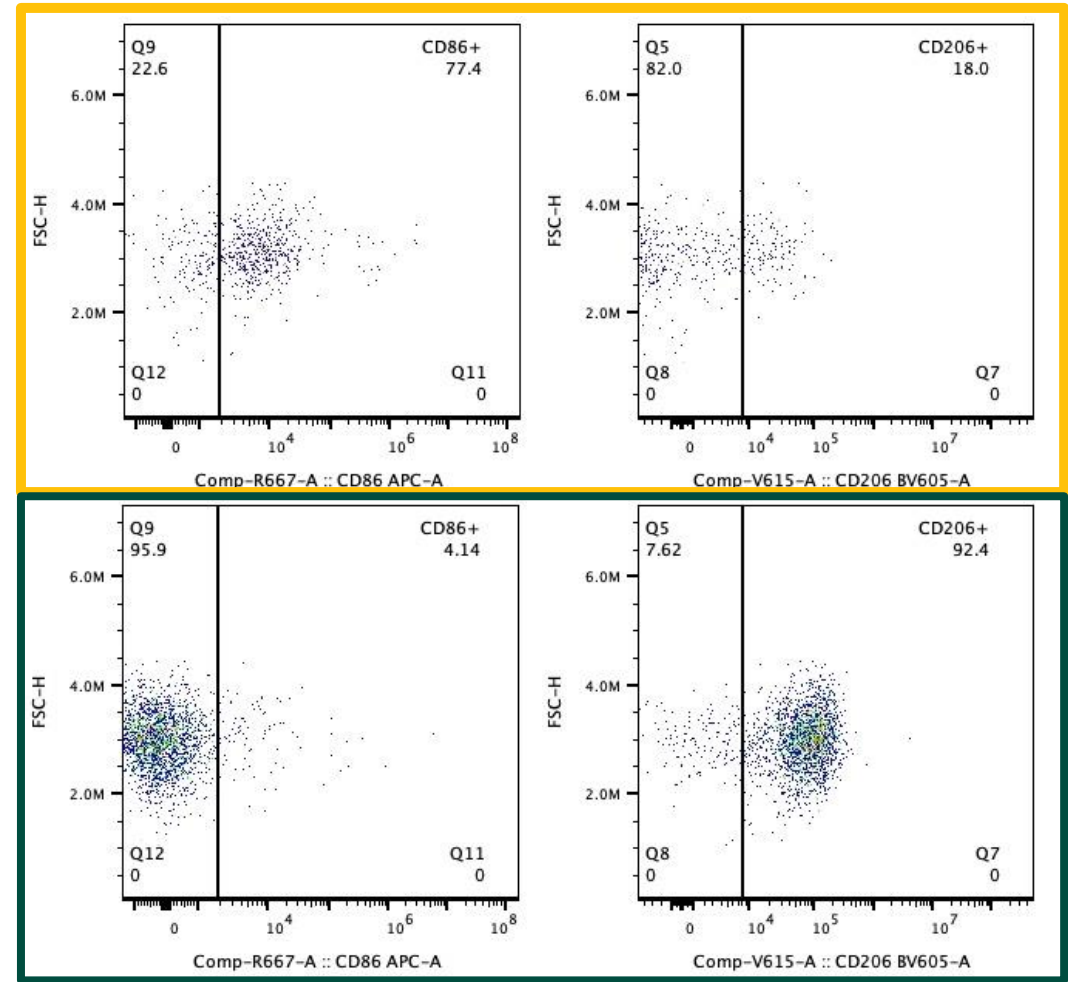
Error bars are SD and p-values determined using 2-way ANOVA, 0.1234 (ns), 0.0332 (*), 0.0021 (**), 0.0002 (***), <0.0001 (****).

P-values in chart are at final timepoint, but no timepoints showed any significant differences in proliferation rates.

BMDM Polarization



M1-Like



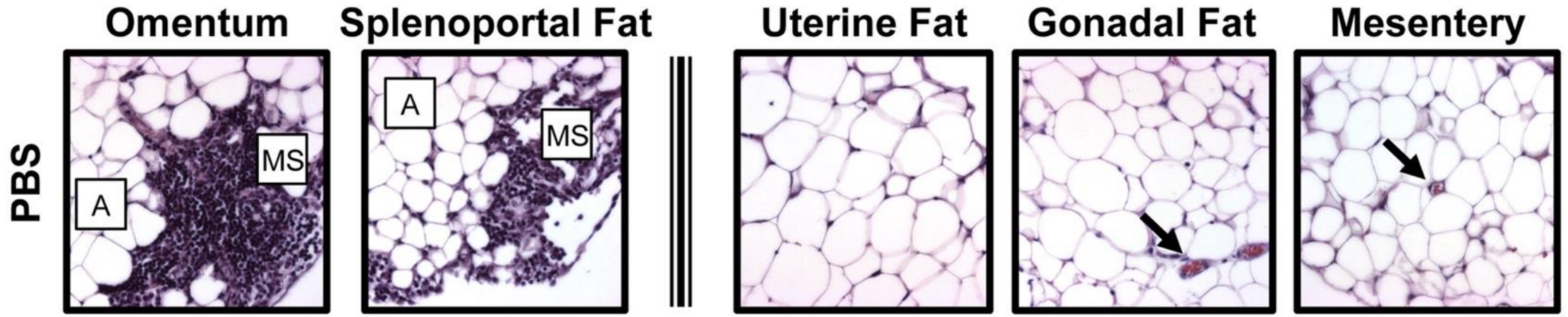
M2-Like

Importance of Studying Women's Health

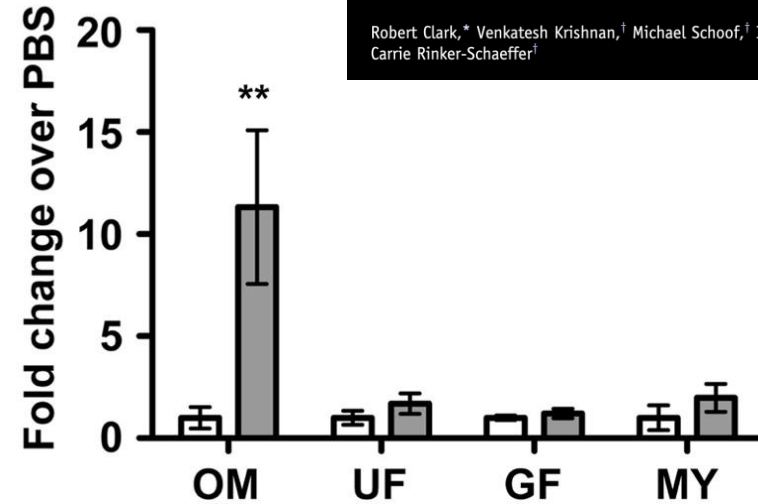
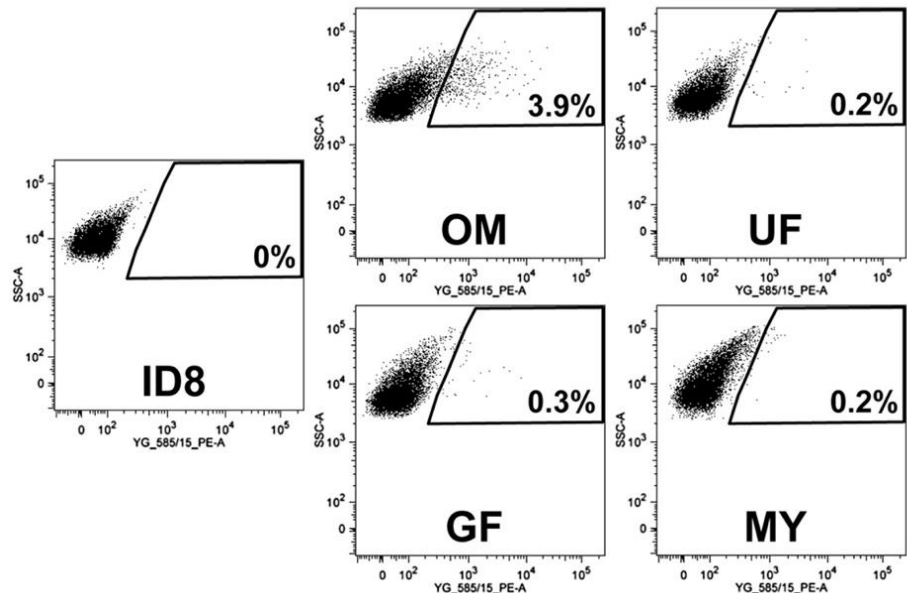
Which of the following are symptoms of Ovarian Cancer?

- a. Bloating, pelvic or abdominal pain, feeling full quickly, difficulty eating, need to urinate urgently or frequently, back pain, bowel habit changes, pain with intercourse
 - b. Need to urinate frequently, burning sensation, cloudy urine, back pain
 - c. Bloating, pelvic or abdominal pain, changes in bowel habits, nausea, back pain, increased hunger
 - d. Bloating, pelvic or abdominal pain, changes in bowel habits, nausea, back pain, difficulty eating, frequent urination, fatigue, abnormal bleeding
 - e. Pelvic or abdominal pain, painful intercourse, abnormal bleeding, fatigue, changes in bowel habits, painful urination
- a. **Ovarian Cancer**
 - b. UTI
 - c. Period or PMS
 - d. Pregnancy
 - e. Endometriosis

A



D

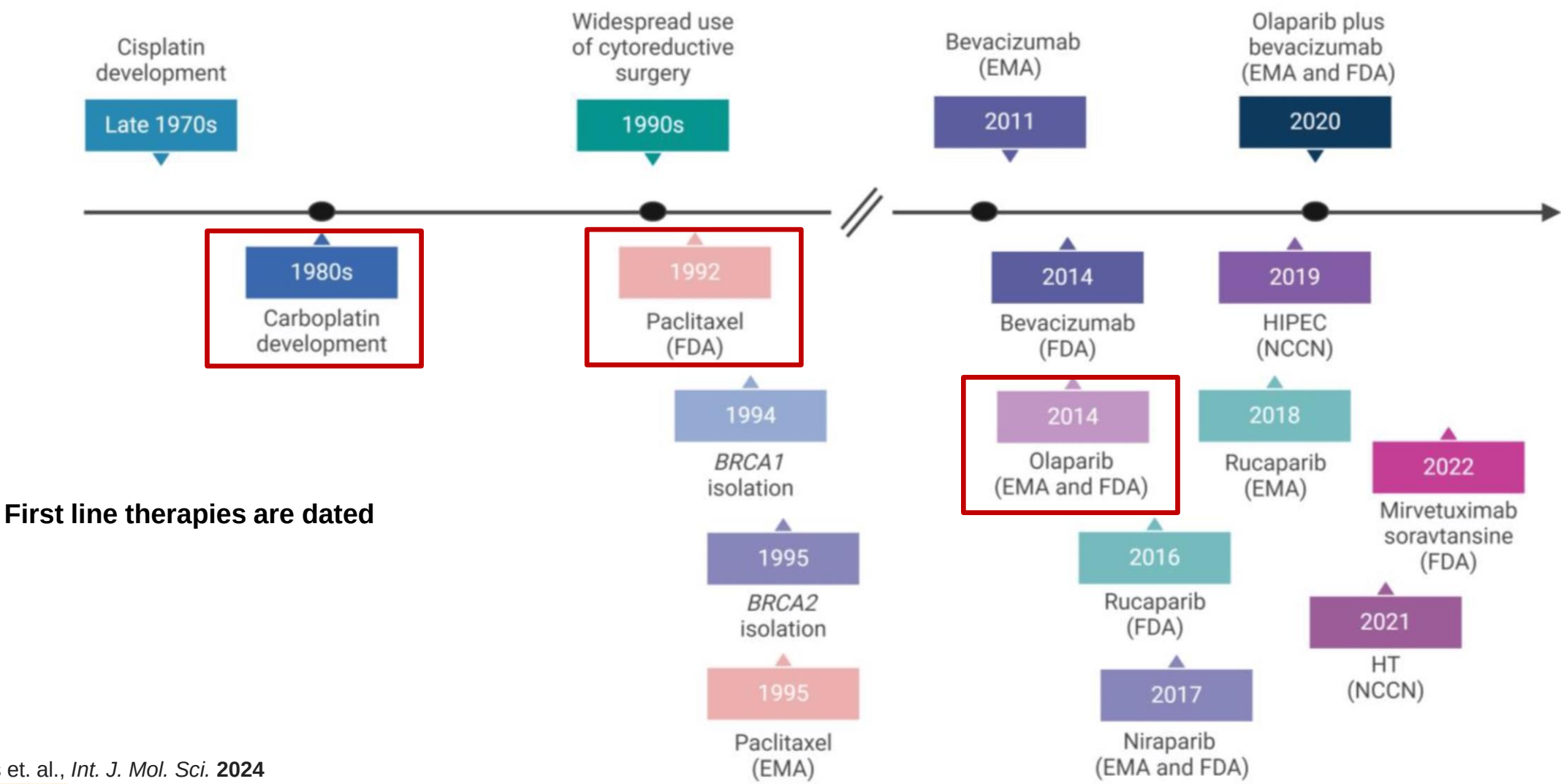


Milky Spots Promote Ovarian Cancer Metastatic Colonization of Peritoneal Adipose in Experimental Models

Robert Clark,^{*} Venkatesh Krishnan,[†] Michael Schoof,[‡] Irving Rodriguez,[†] Betty Theriault,[‡] Marina Chekmareva,[§] and Carrie Rinker-Schaeffer[†]

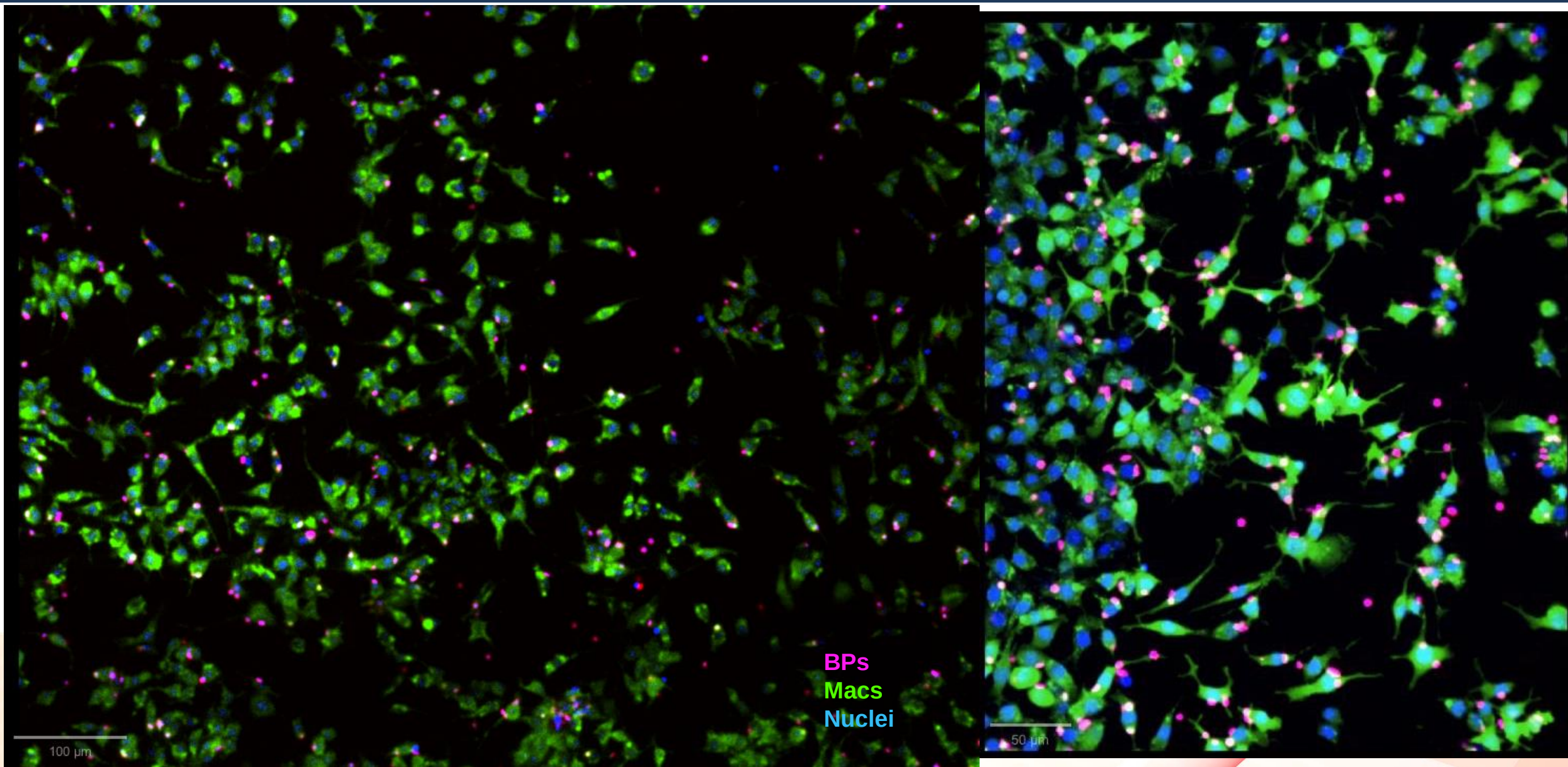
INNOVATION

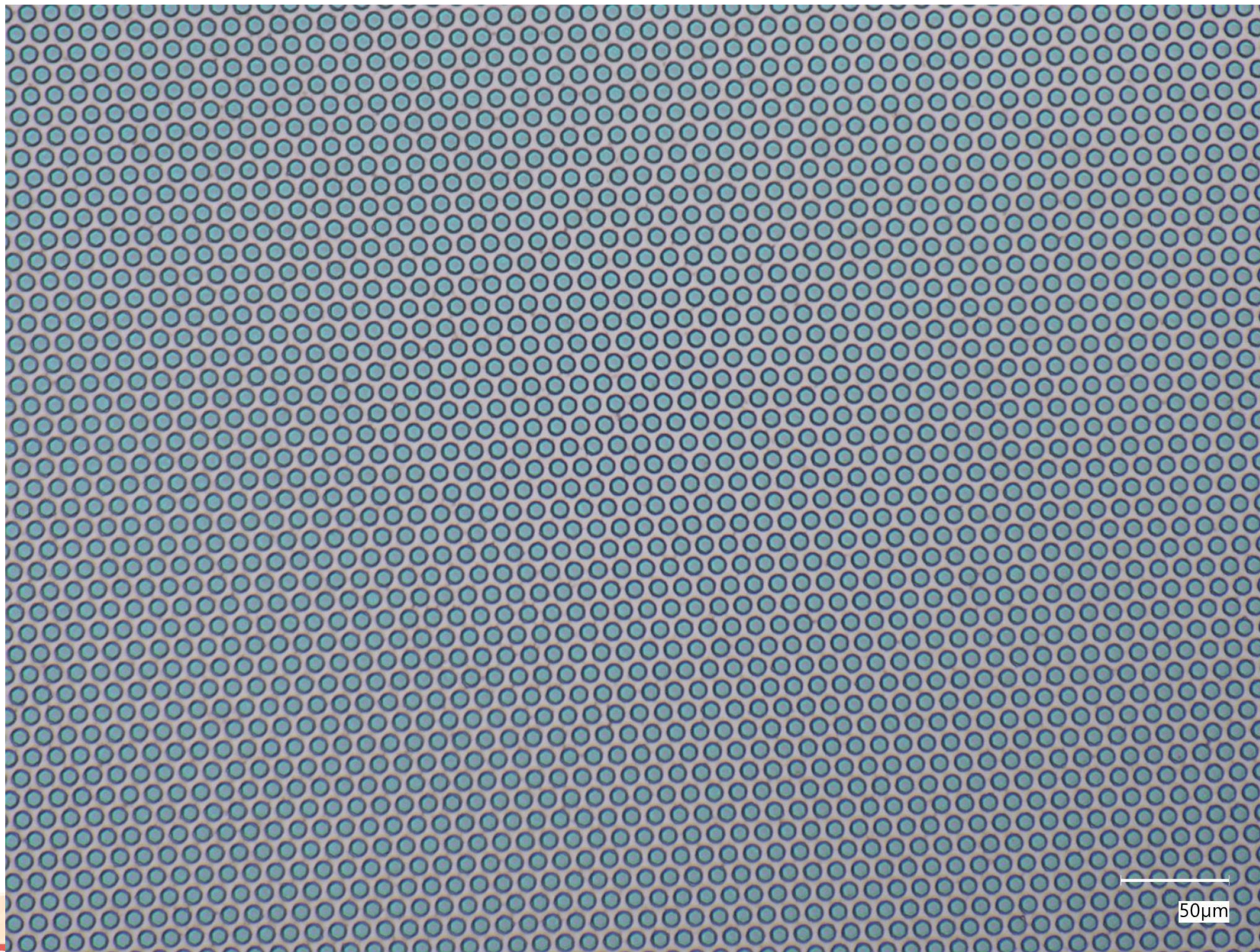
Advances in treatment of ovarian cancer: Leagues Behind



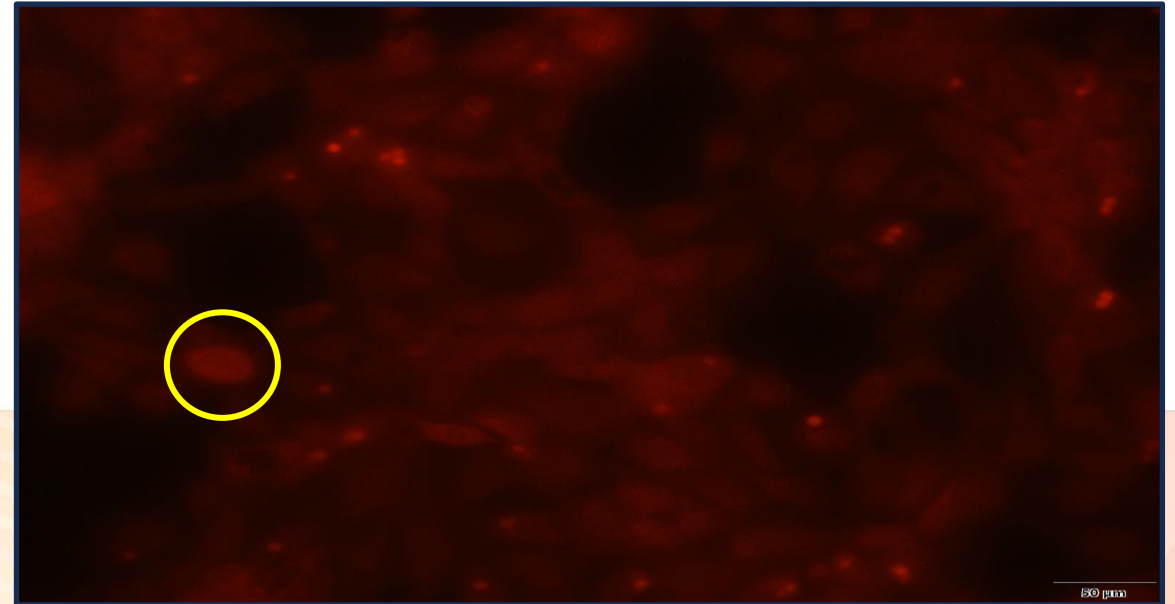
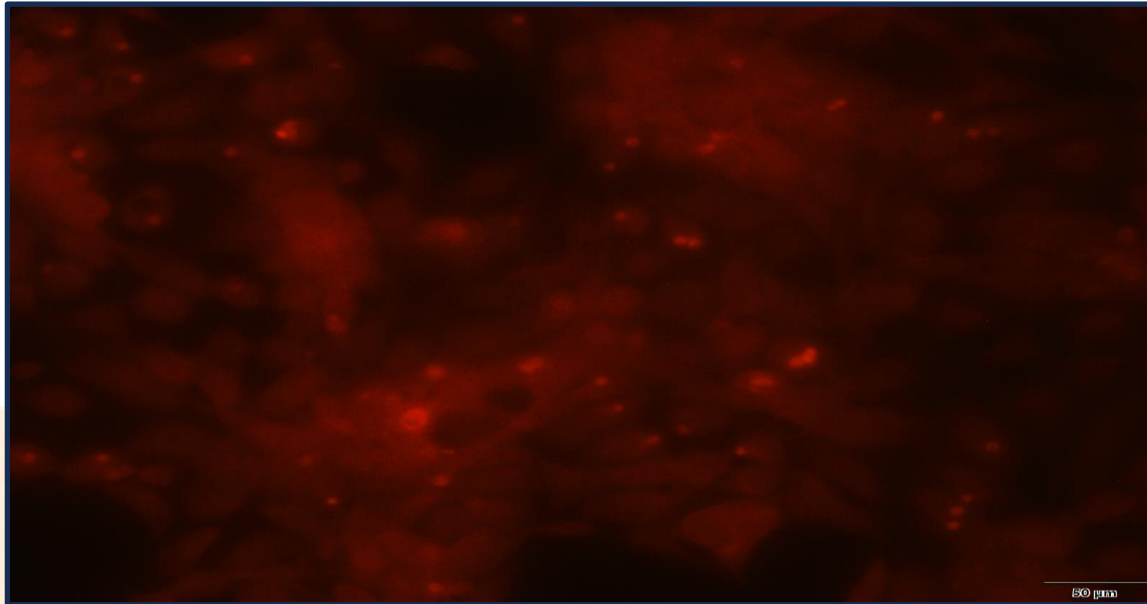
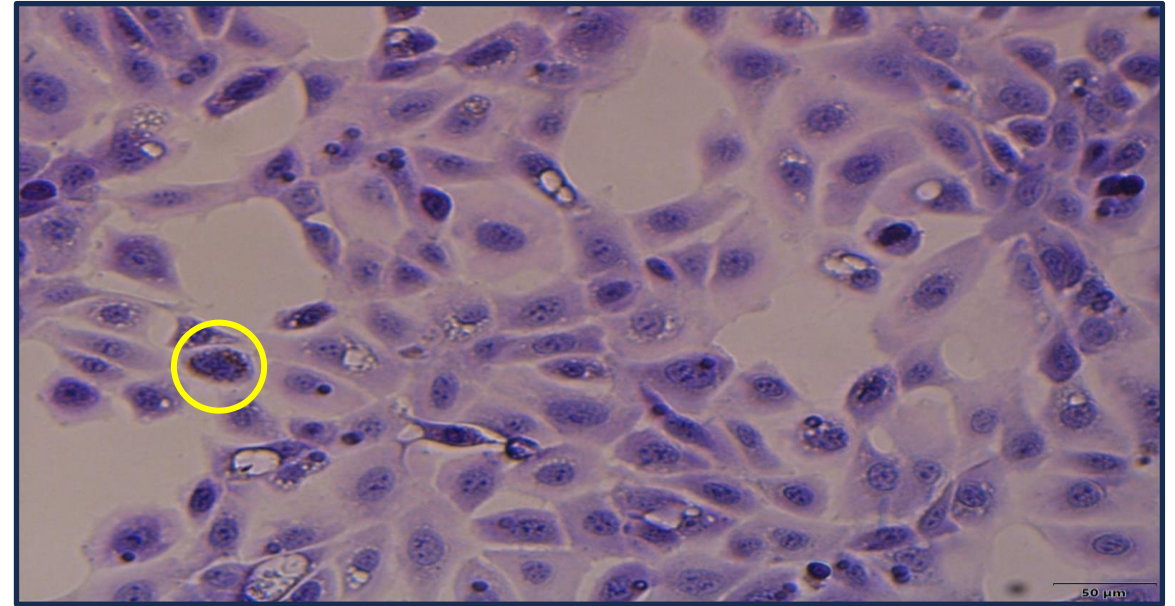
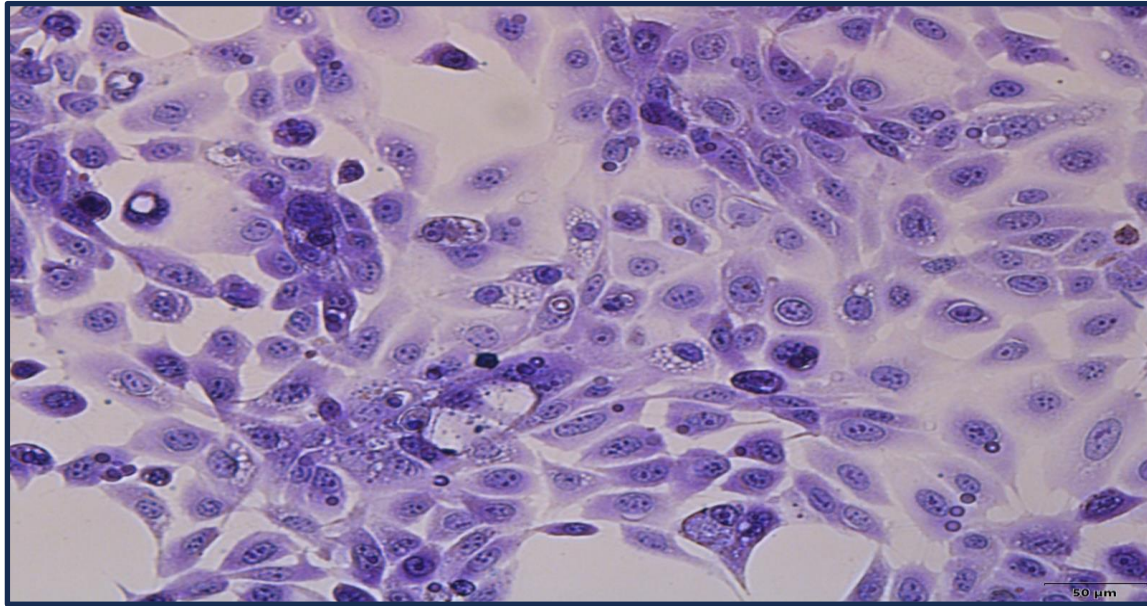
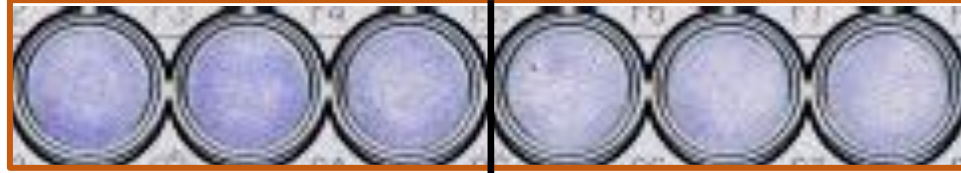
First line therapies are dated

1:1 Nanoparticles to RAW Macrophages 20x Objective

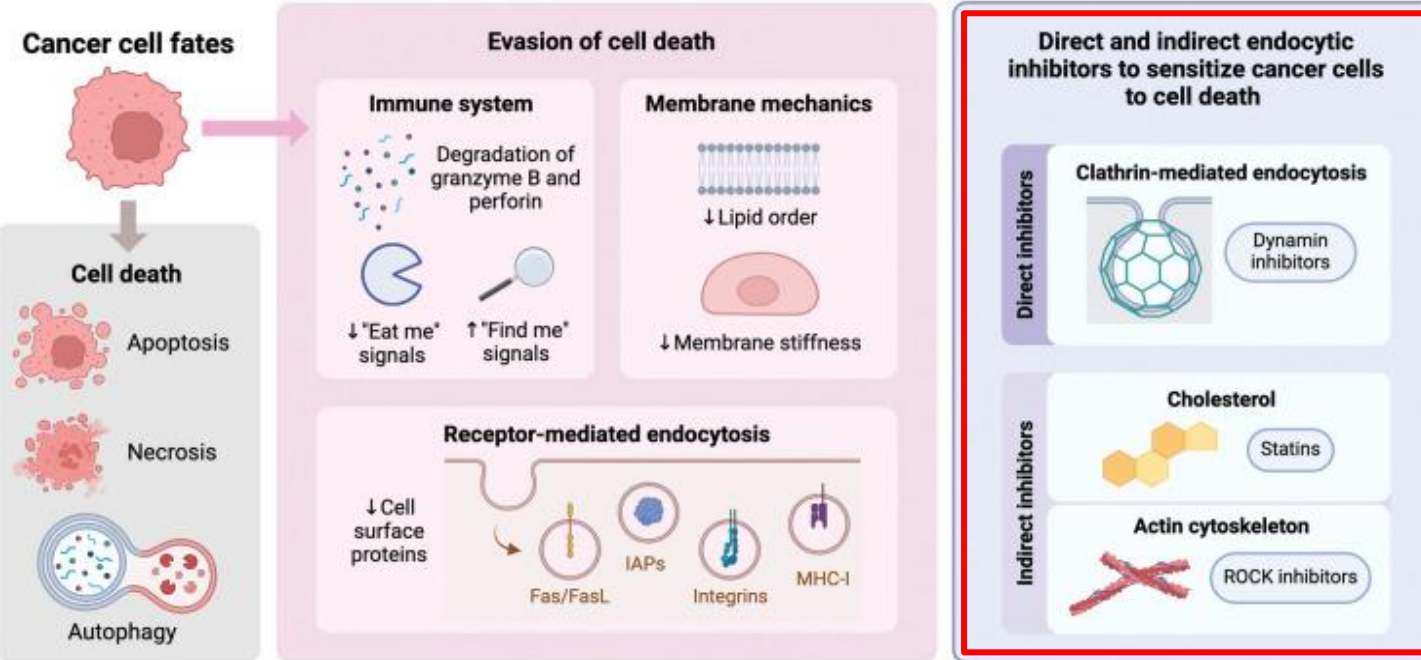
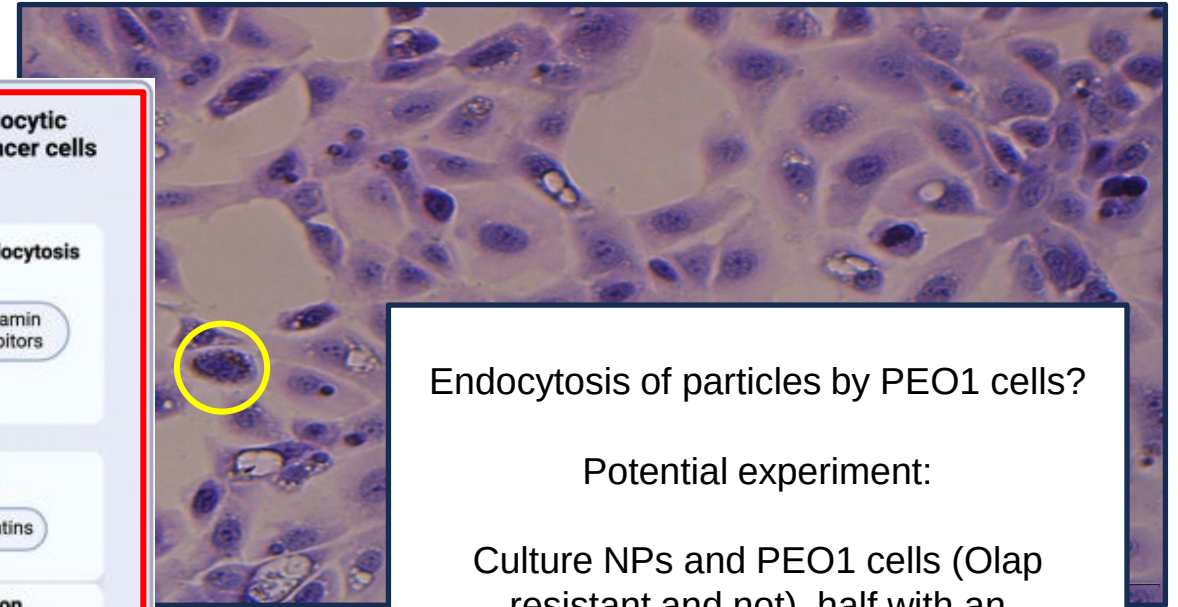
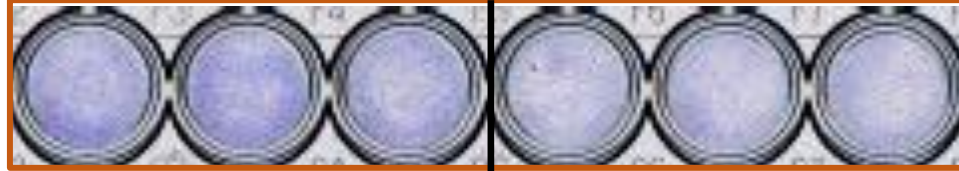




10,000 PETMP NPs (Ctrl/OLAP)



10,000 PETMP NPs (Ctrl/OLAP)



Endocytosis of particles by PEO1 cells?

Potential experiment:

Culture NPs and PEO1 cells (Olap resistant and not), half with an endocytosis inhibitor (drug or 40 degrees) half normal to observe if particle uptake changes. Particles to cells 2:1 ratio.

Targeting endocytosis to sensitize cancer cells to programmed cell death

Emily T Chan¹, Cömert Kural^{1,2,8}