THE UNIVERSITY OF QUEENSLAND
AUSTRALIA
CREATE CHANGE

Understanding polymeric nanoparticle accumulation in tumours using dynamic microfluidic systems

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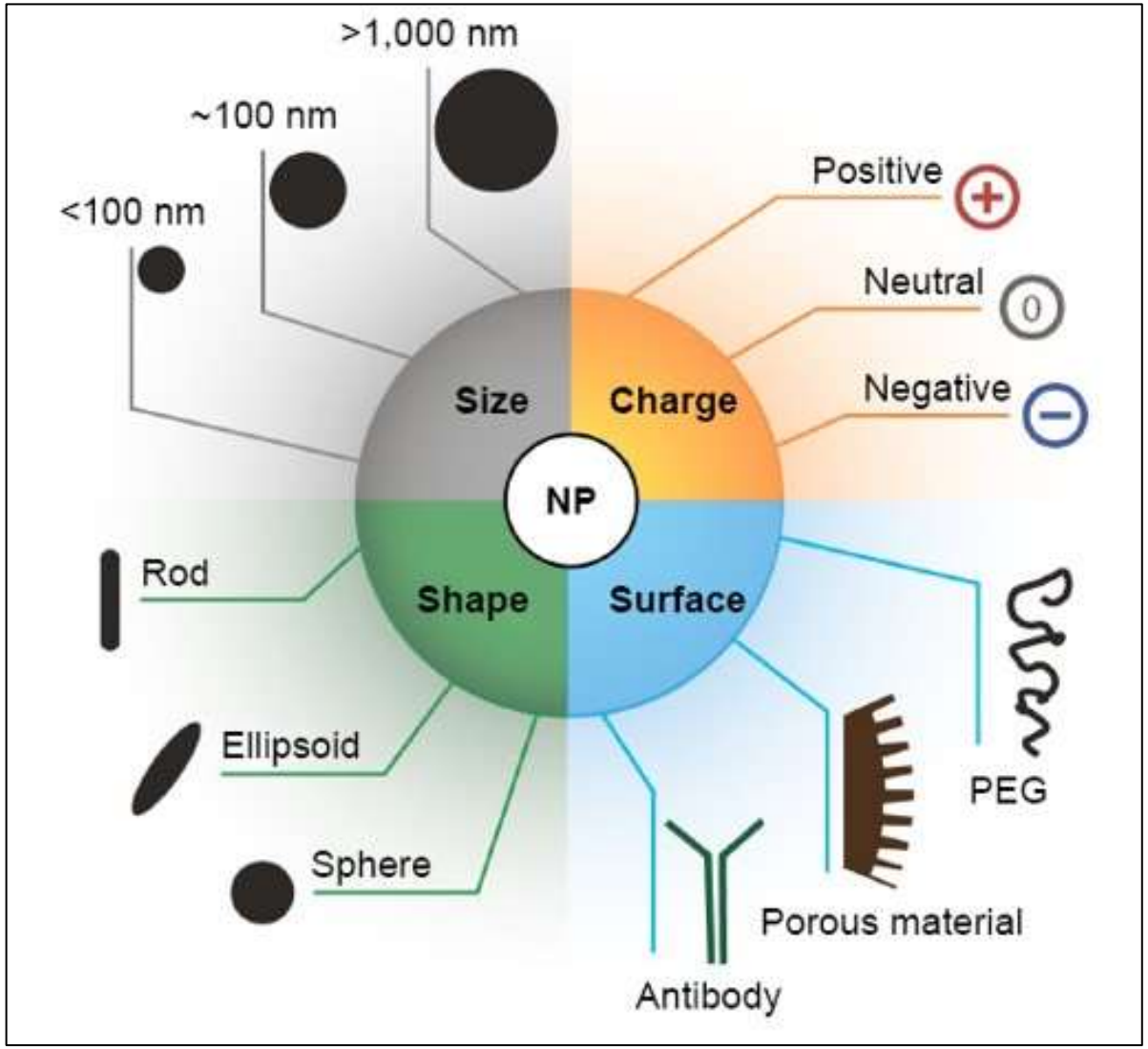
PhD Student
Thurecht Group

Nanomedicine for treating cancer

- Improved efficacy
- Bioavailability
- Targeting efficiency

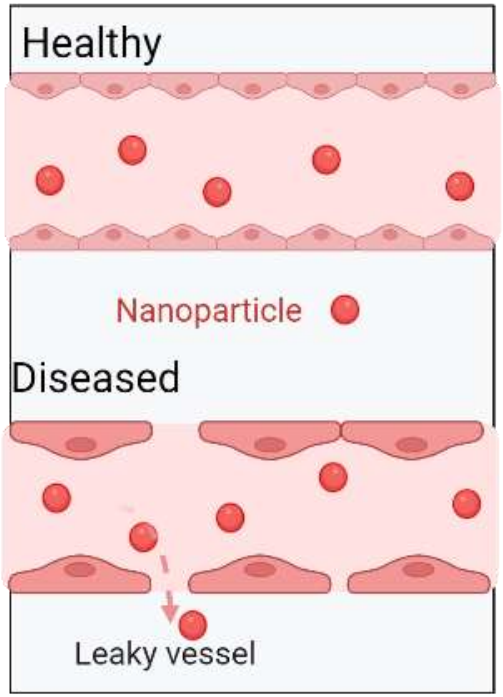


Wicki, A., et al. (2015). "Nanomedicine in cancer therapy: Challenges, opportunities, and clinical applications." Journal of Controlled Release **200: 138-157.**

Biological Barriers that Nanoparticles Encounter

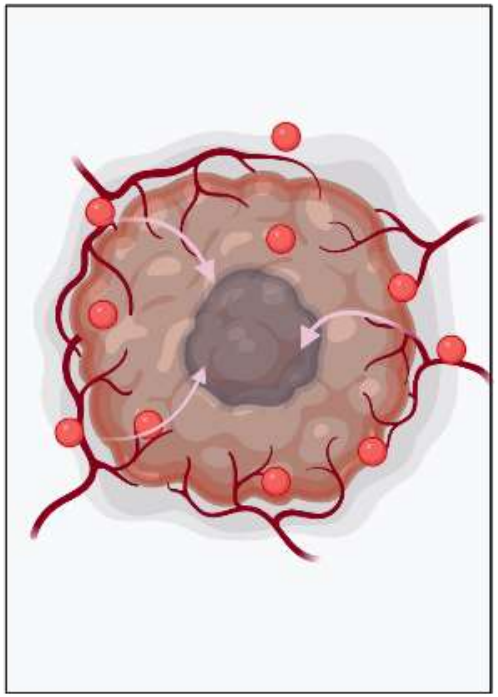
1

Endothelial Barrier



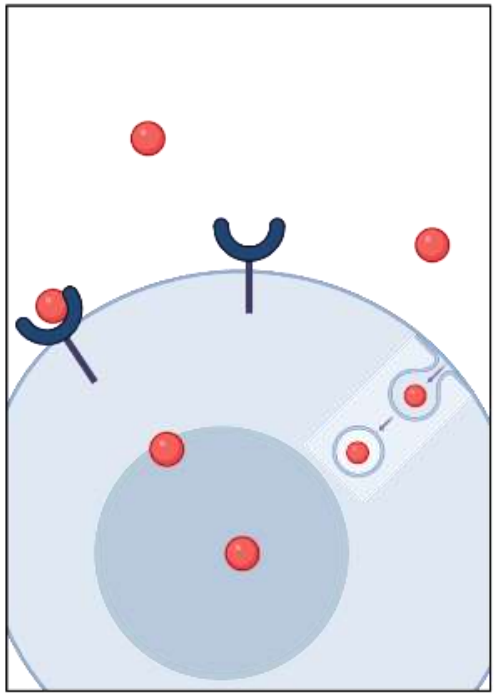
2

Extracellular Matrix (ECM)

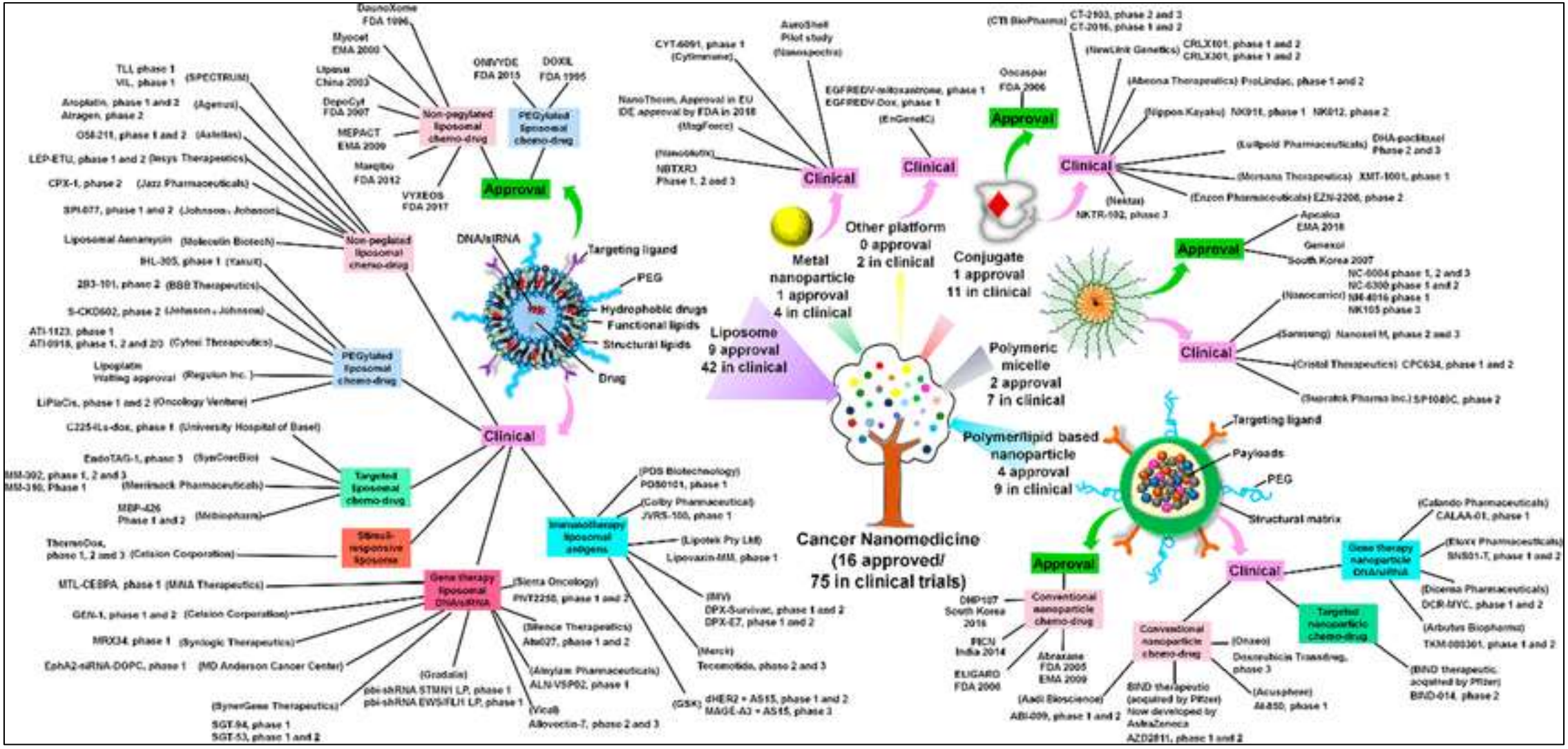


3

Plasma membrane and intracellular localisation



Translating nanomedicine into the clinic



Bobo, D., et al. (2016). "Nanoparticle-Based Medicines: A Review of FDA-Approved Materials and Clinical Trials to Date." Pharmaceutical Research **33(10): 2373-2387.**

He, H.; Liu, L.; Morin, E. E.; Liu, M.; Schwendeman, A. Survey of Clinical Translation of Cancer Nanomedicines—Lessons Learned from Successes and Failures. *Accounts of Chemical Research* ***2019, 52 (9), 2445-2461***

Cell studies to animal models

2D Cell Culture:

Bridging

Animal models:

cell coculture

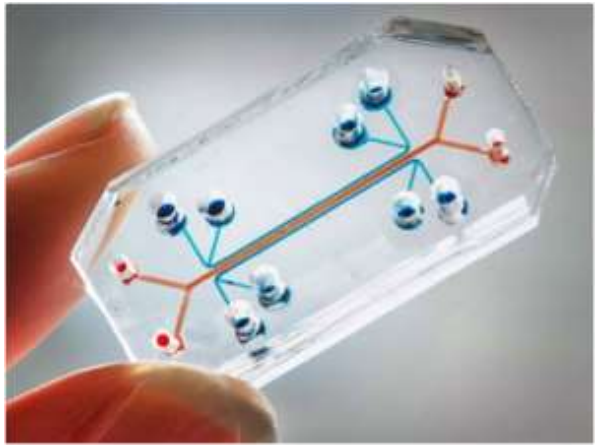
3D cell culture

Bioprinted cell/tissue culture

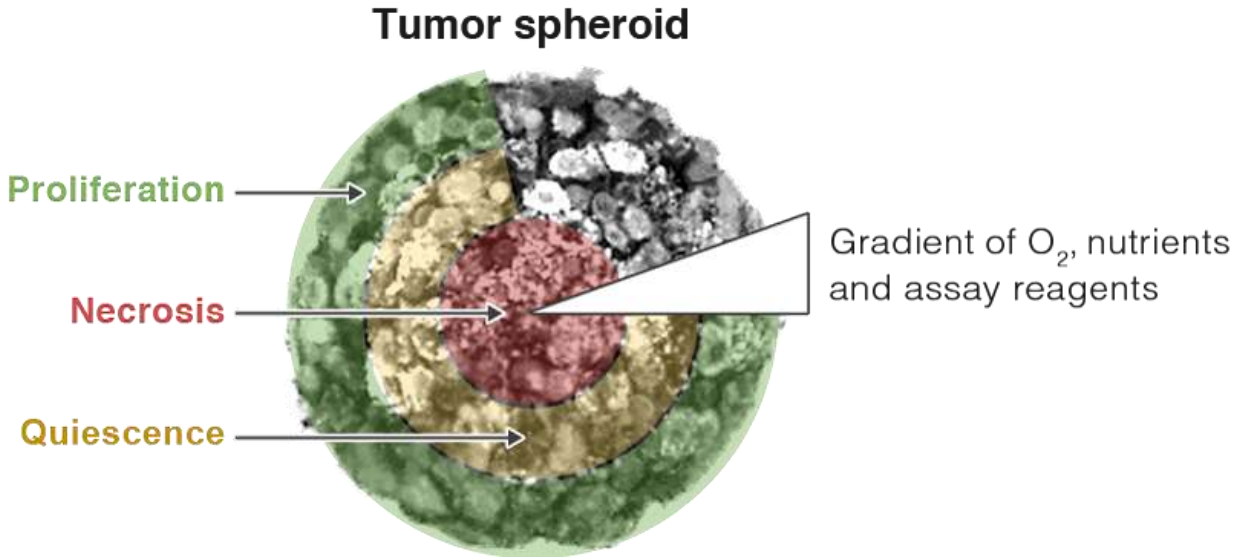
Microfluidics and flow assays

Bjornmalm, M., et al. (2017). "Bridging Bio-Nano Science and Cancer Nanomedicine." ACS Nano **11(10): 9594-9613.**

Microfluidic Devices



Complex cellular models

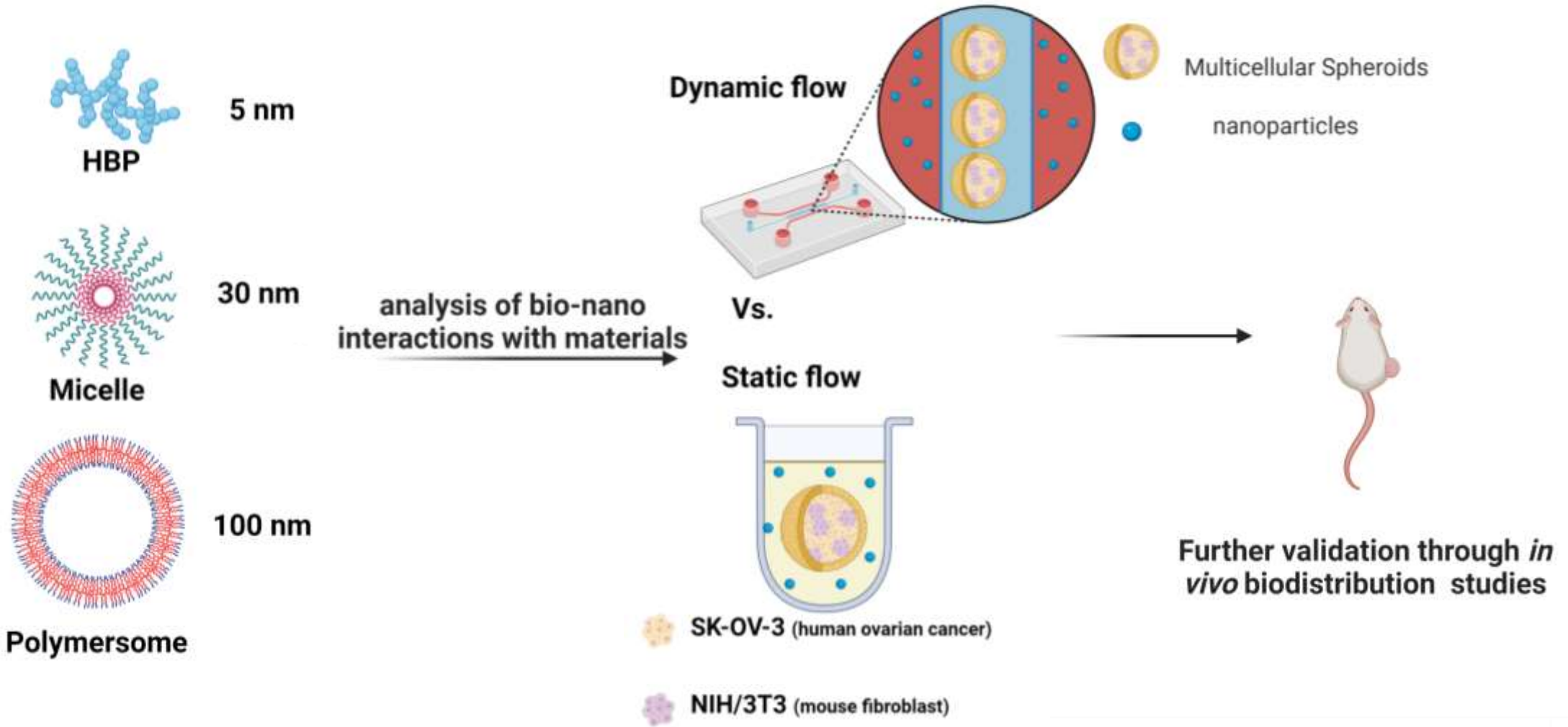


- Inexpensive, high-throughput screening capabilities
- Recapitulate biologic transport as well as microenvironments
- Enables studies of cell behaviour in real time

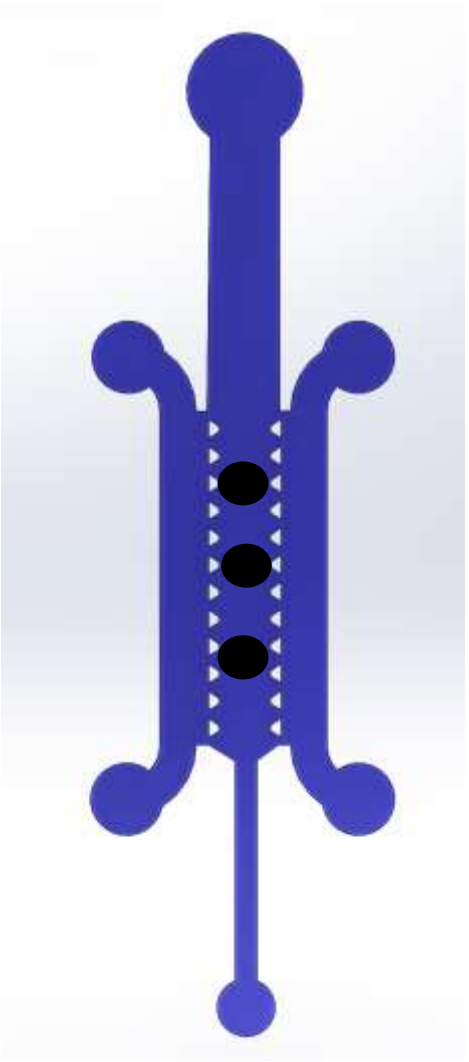
- Can incorporate healthy and diseased cells
- Creates nutrient gradients typical of vascularised tissue
- Nanoparticle uptake and penetration can be visualised

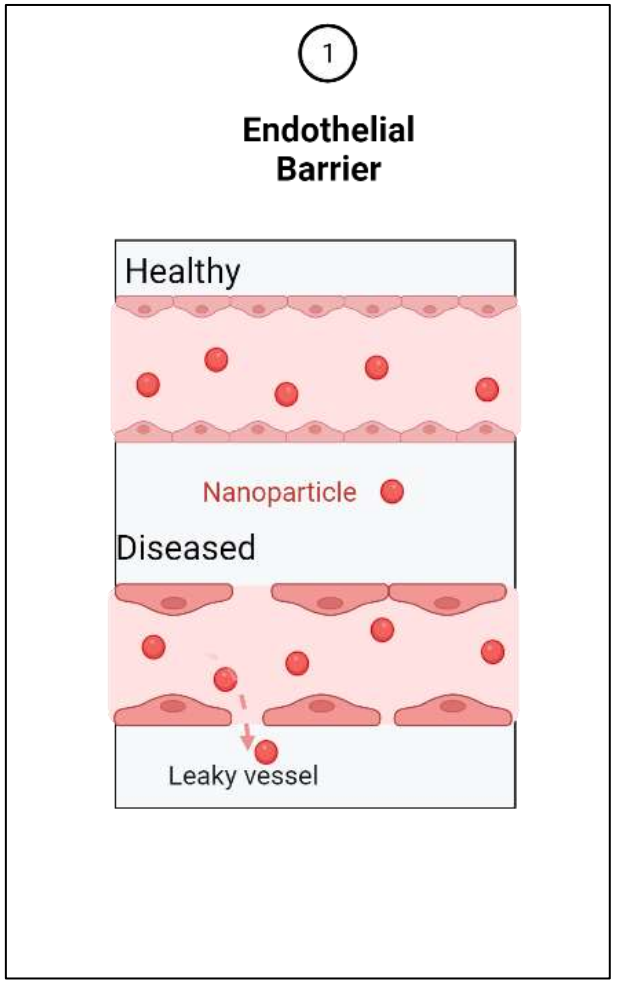
Bhise, N. S., et al. (2014). "Organ-on-a-chip platforms for studying drug delivery systems." J Control Release **190: 82-93.**
Albanese, A., et al. (2013). "Tumour-on-a-chip provides an optical window into nanoparticle tissue transport." Nature Communications **4(1): 2718.**
Sontheimer-Phelps, A., et al. (2019). "Modelling cancer in microfluidic human organs-on-chips." Nature Reviews Cancer **19(2): 65-81.**

Project Overview



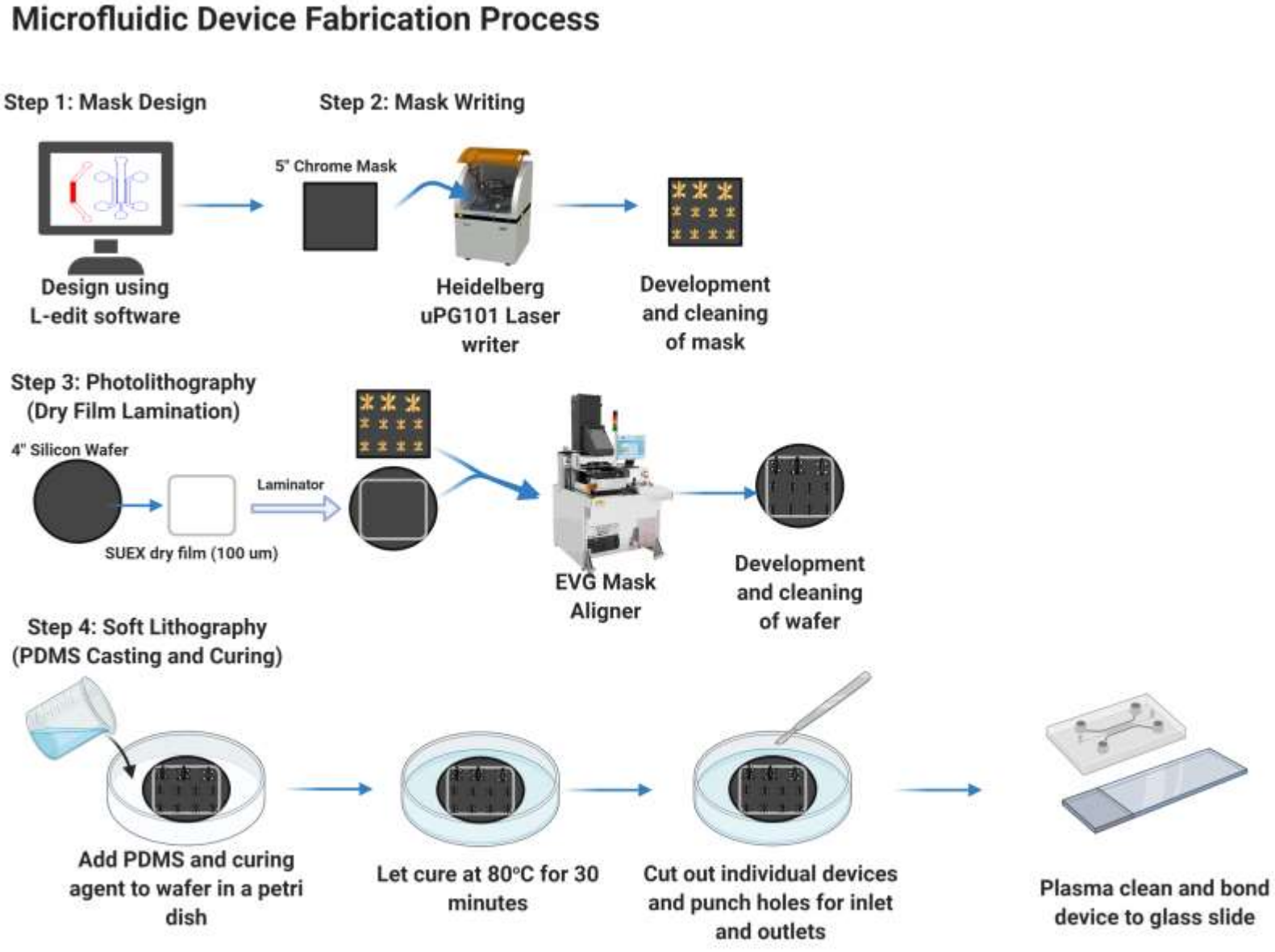
Microfluidic device Rationale

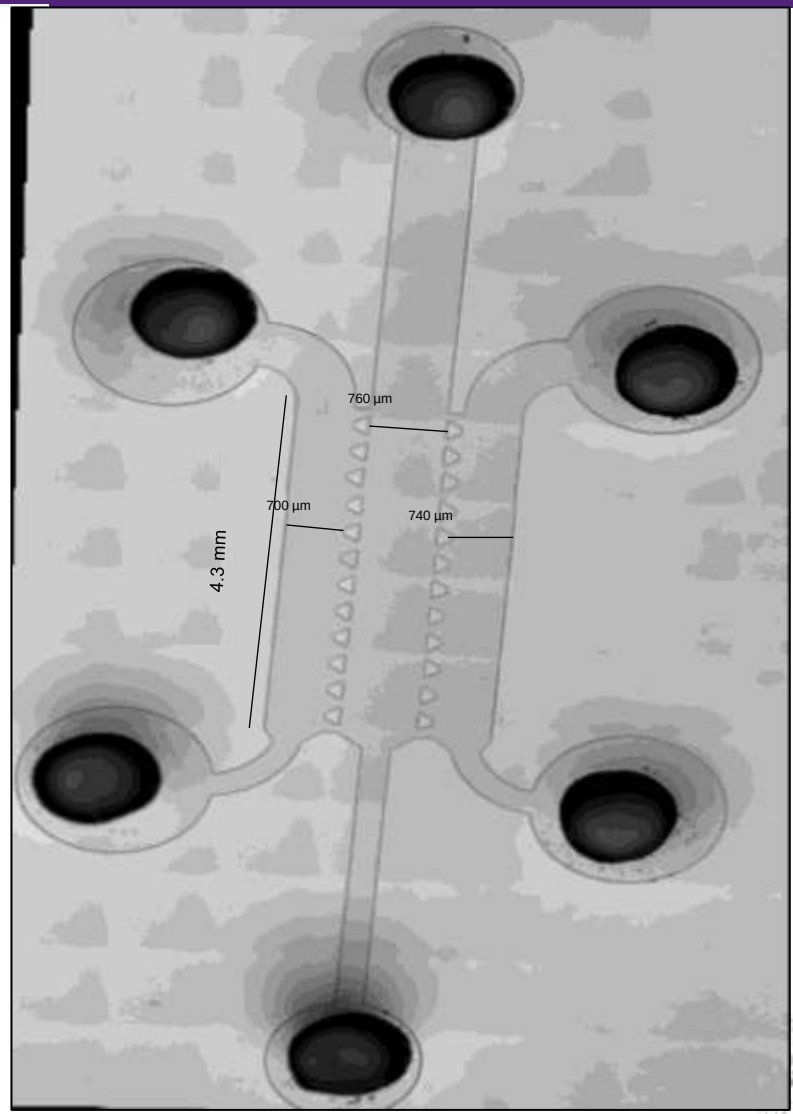




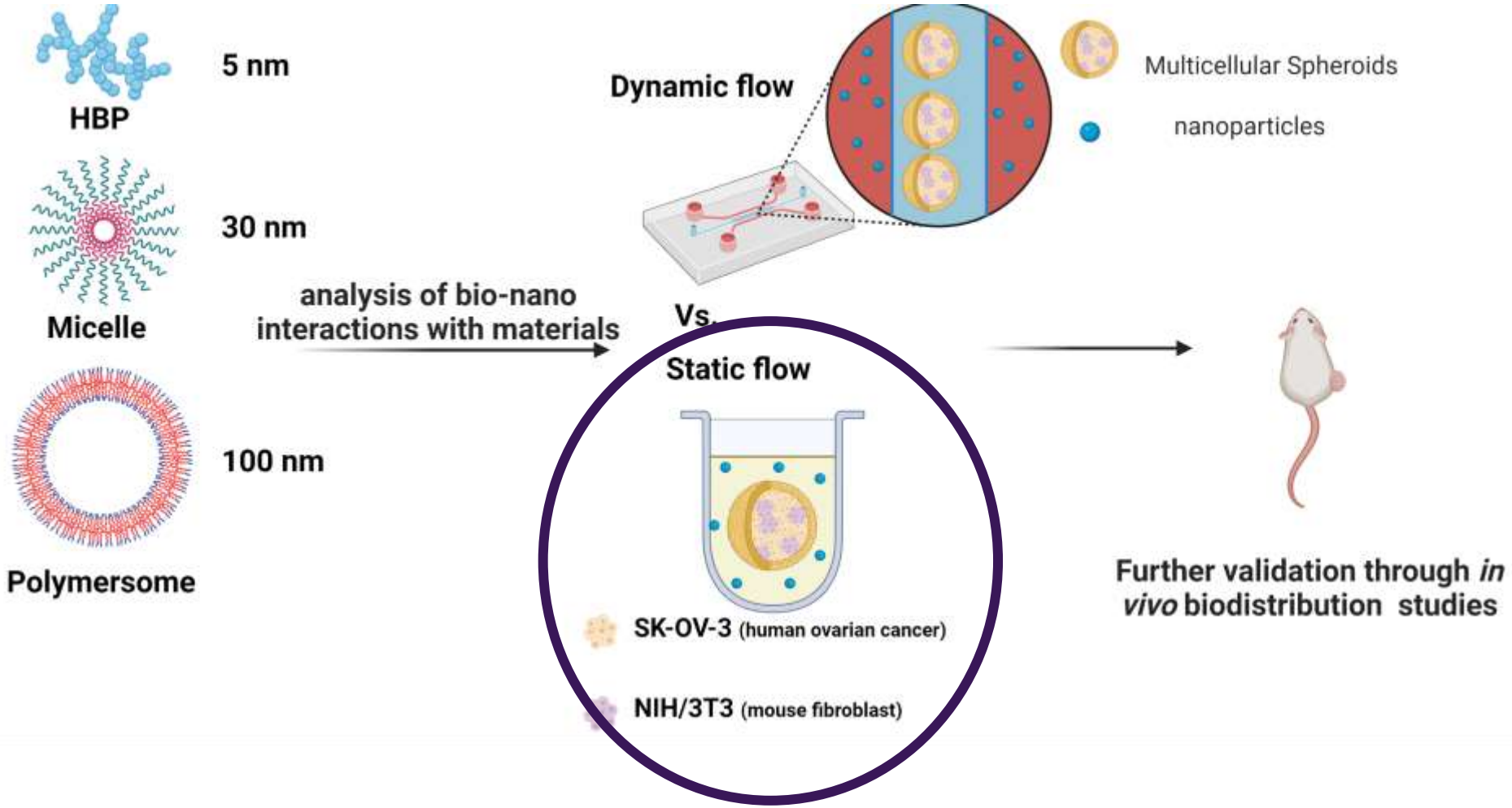
Wang, H.-F., et al. (2018). "Tumor-Vasculature-on-a-Chip for Investigating Nanoparticle Extravasation and Tumor Accumulation." ACS Nano **12**(11): 11600-11609.

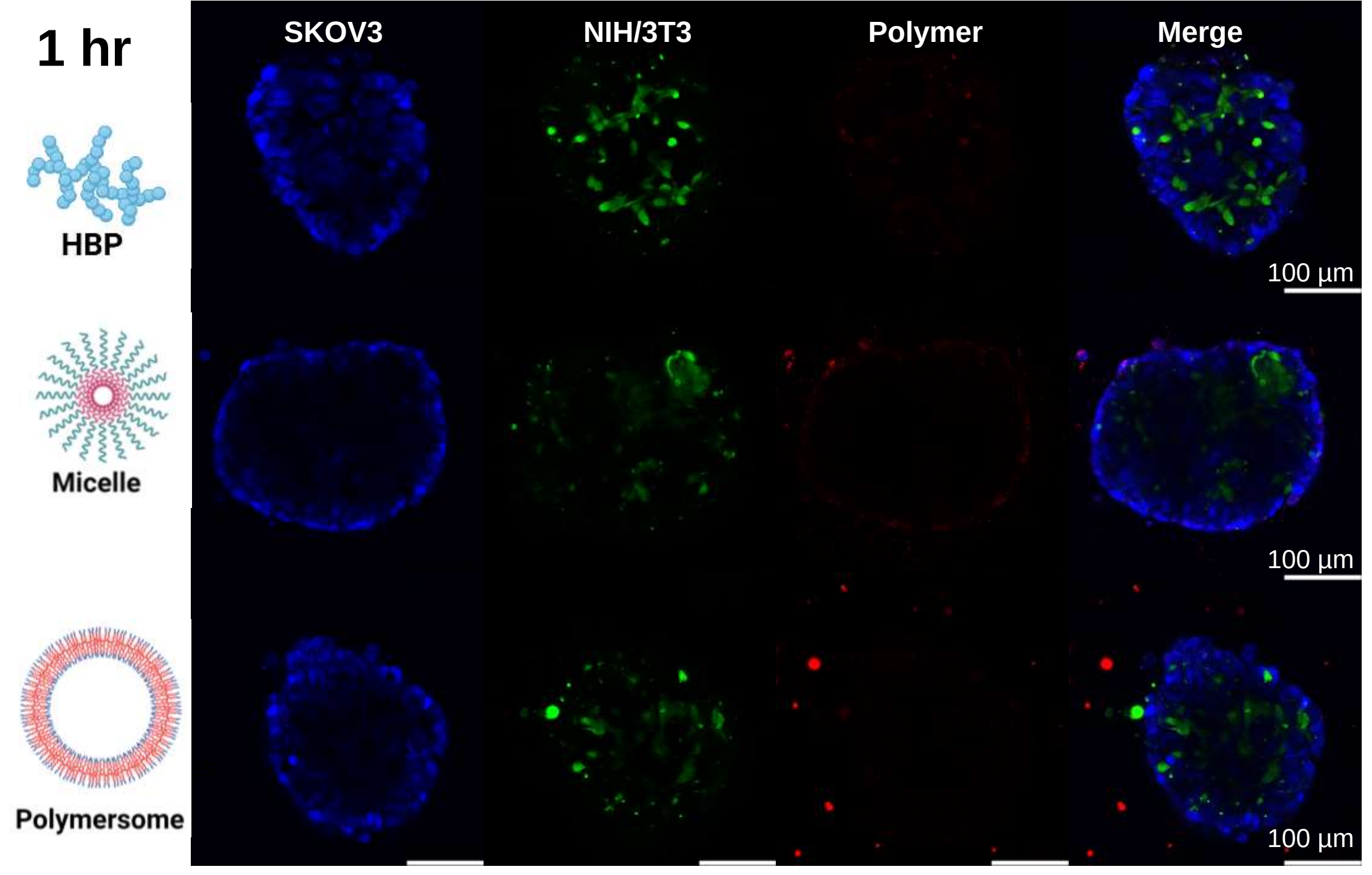
Microfluidic device fabrication





NP accumulation in static spheroids over time

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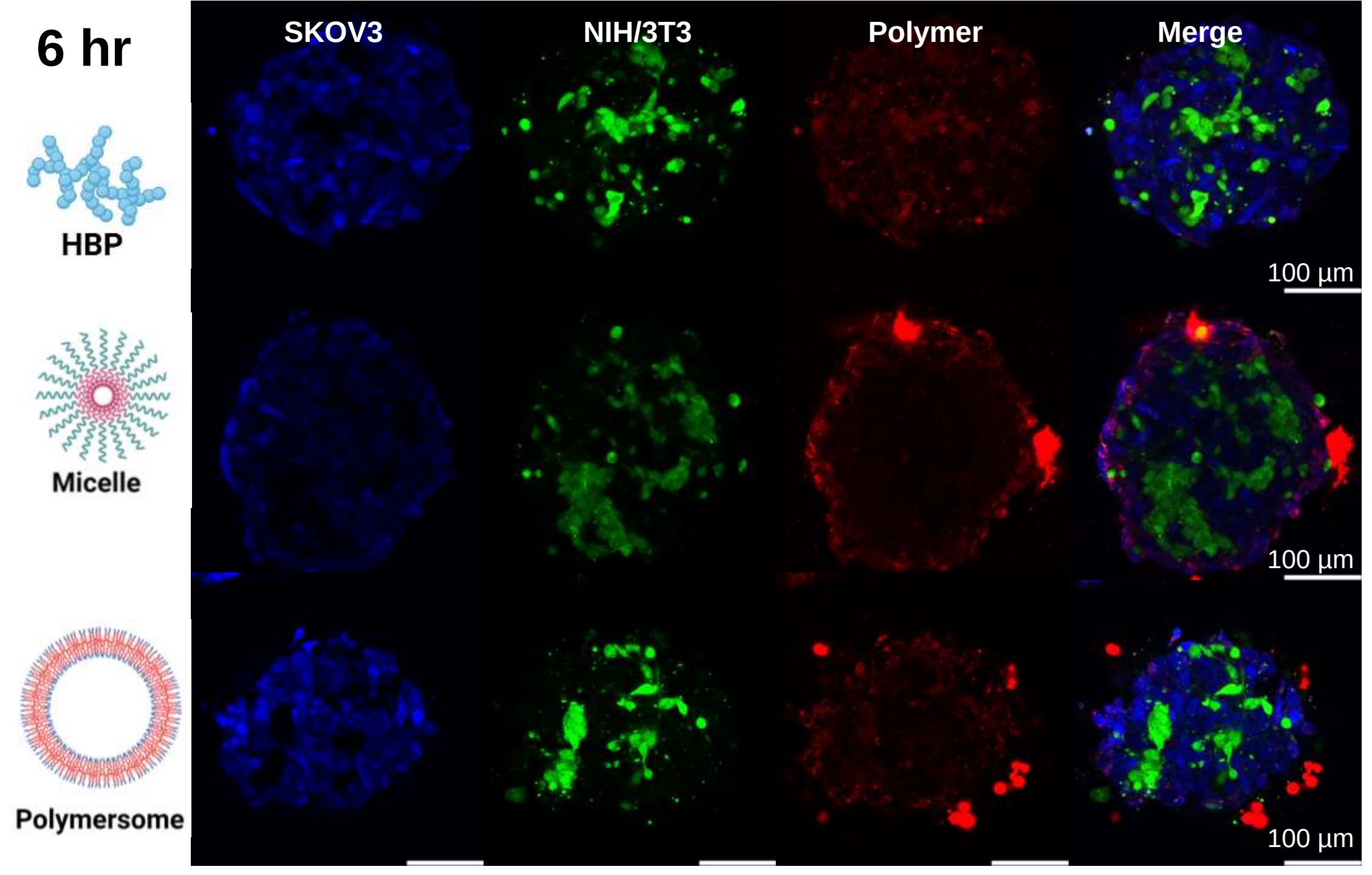
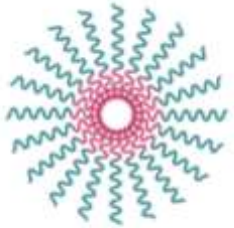
SKOV3
NIH/3T3
Polymer
Merge
HBP
Micelle
Polymersome
100 µm
100 µm
100 µm

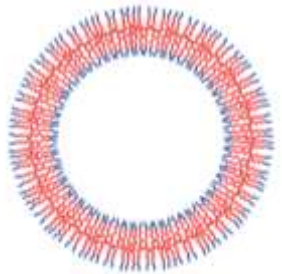

6 hr
SKOV3
NIH/3T3
Polymer
Merge
HBP
Micelle
Polymersome
100 µm
100 µm
100 µm

16 hr

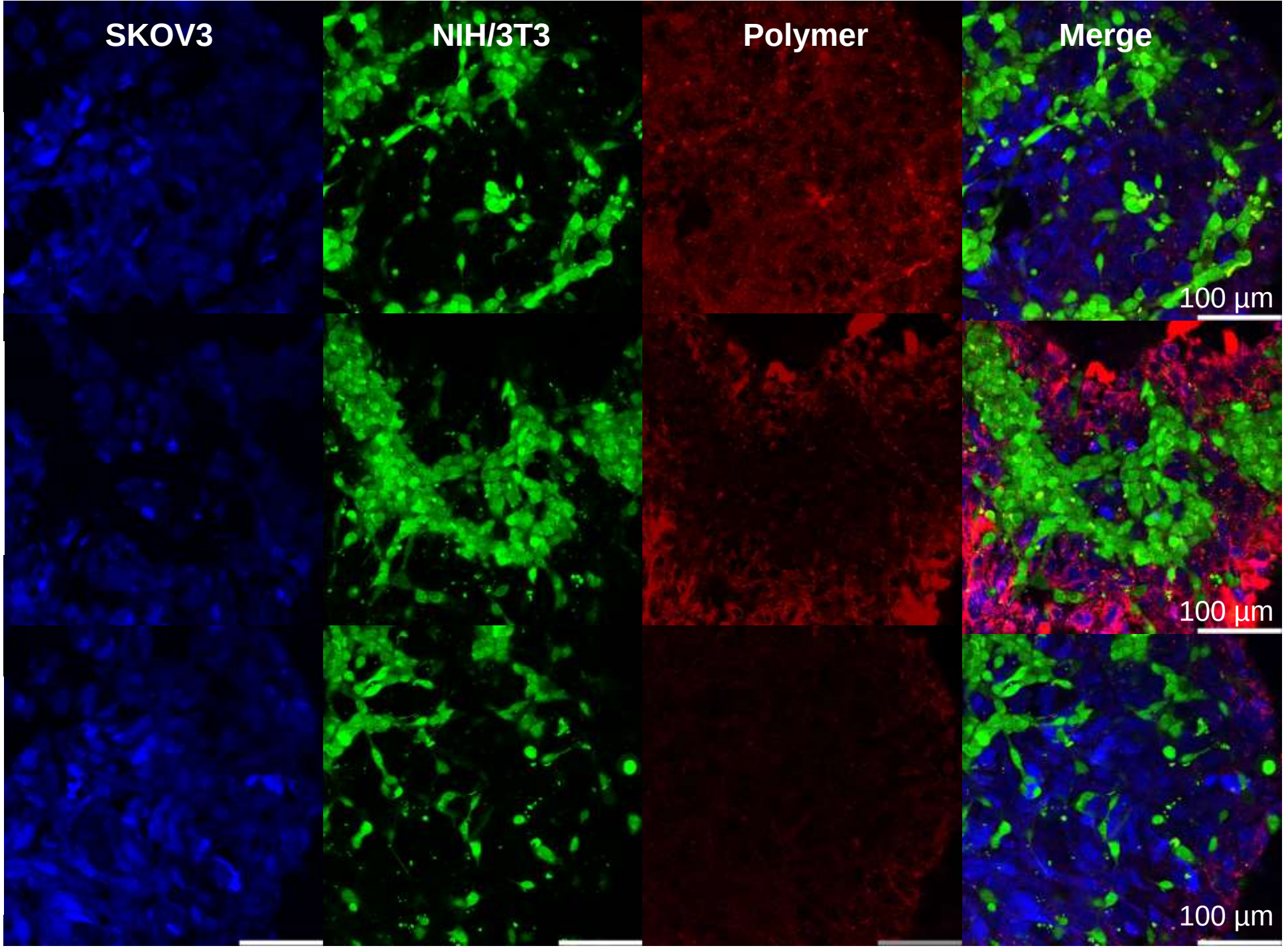
HBP



Micelle



Polymersome



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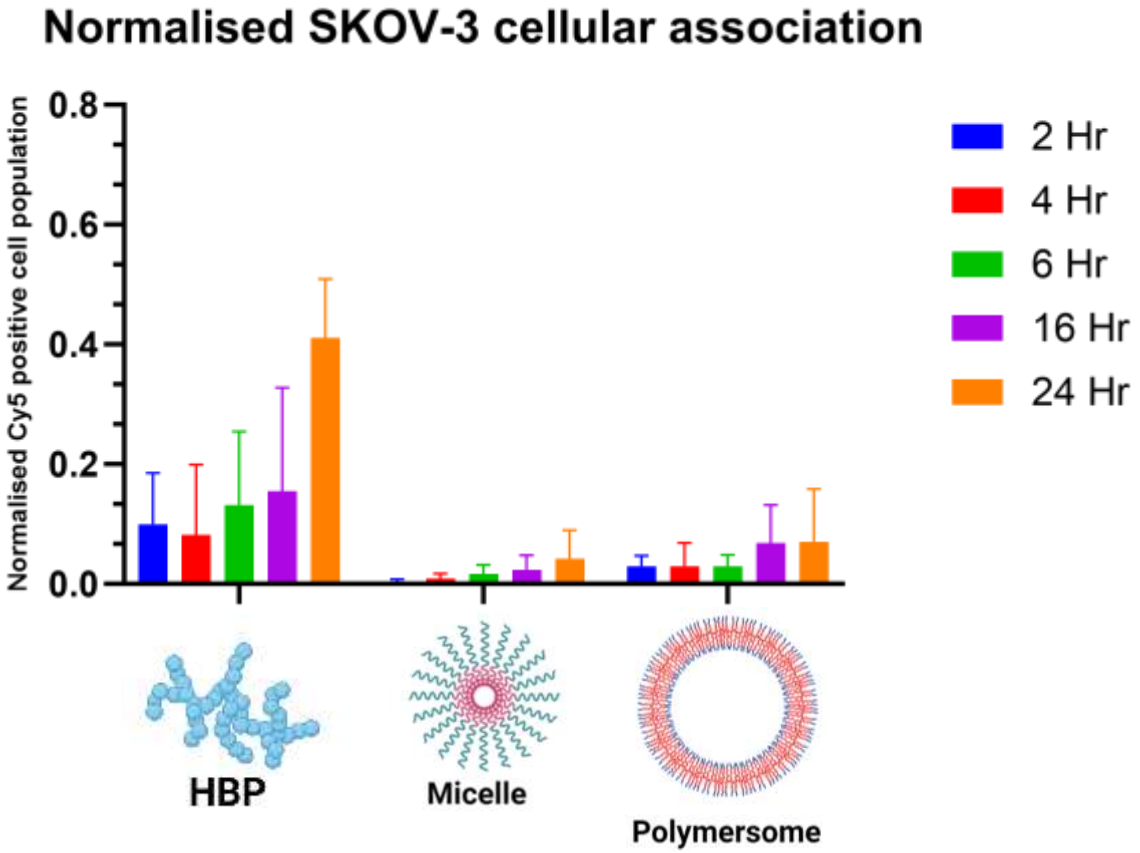
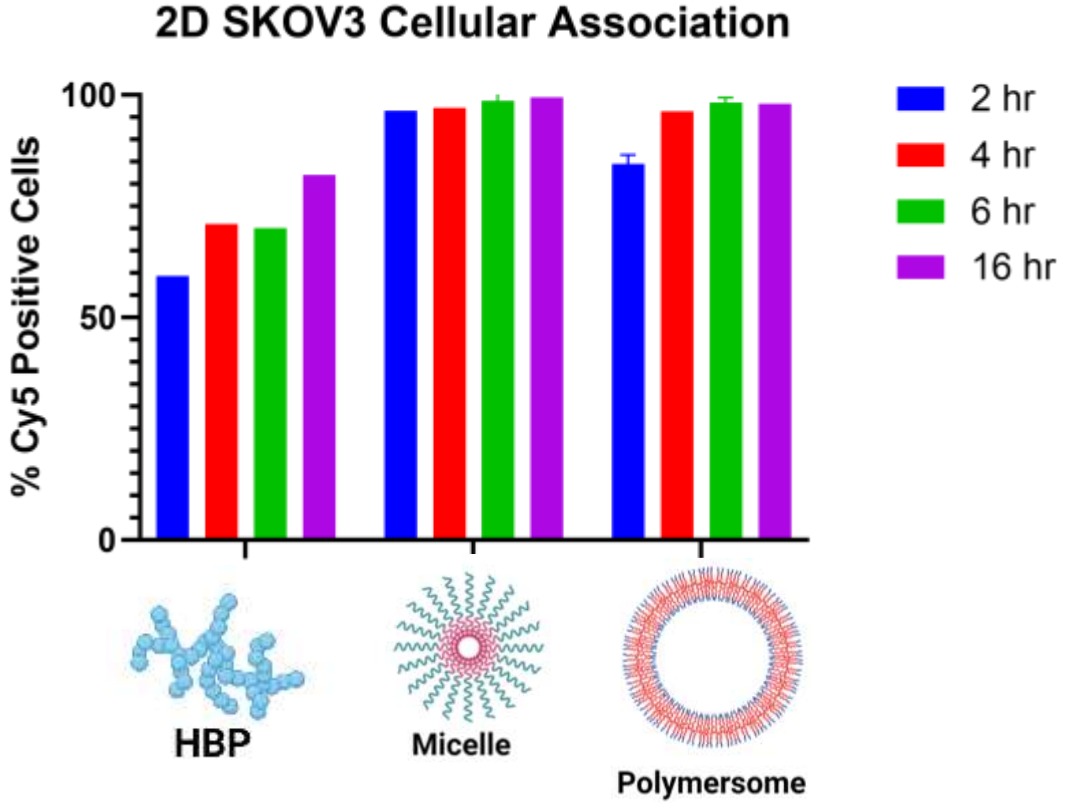
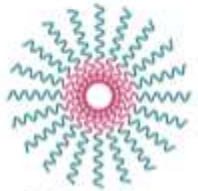
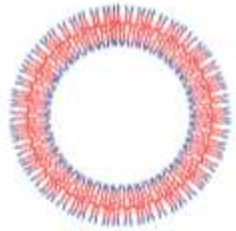
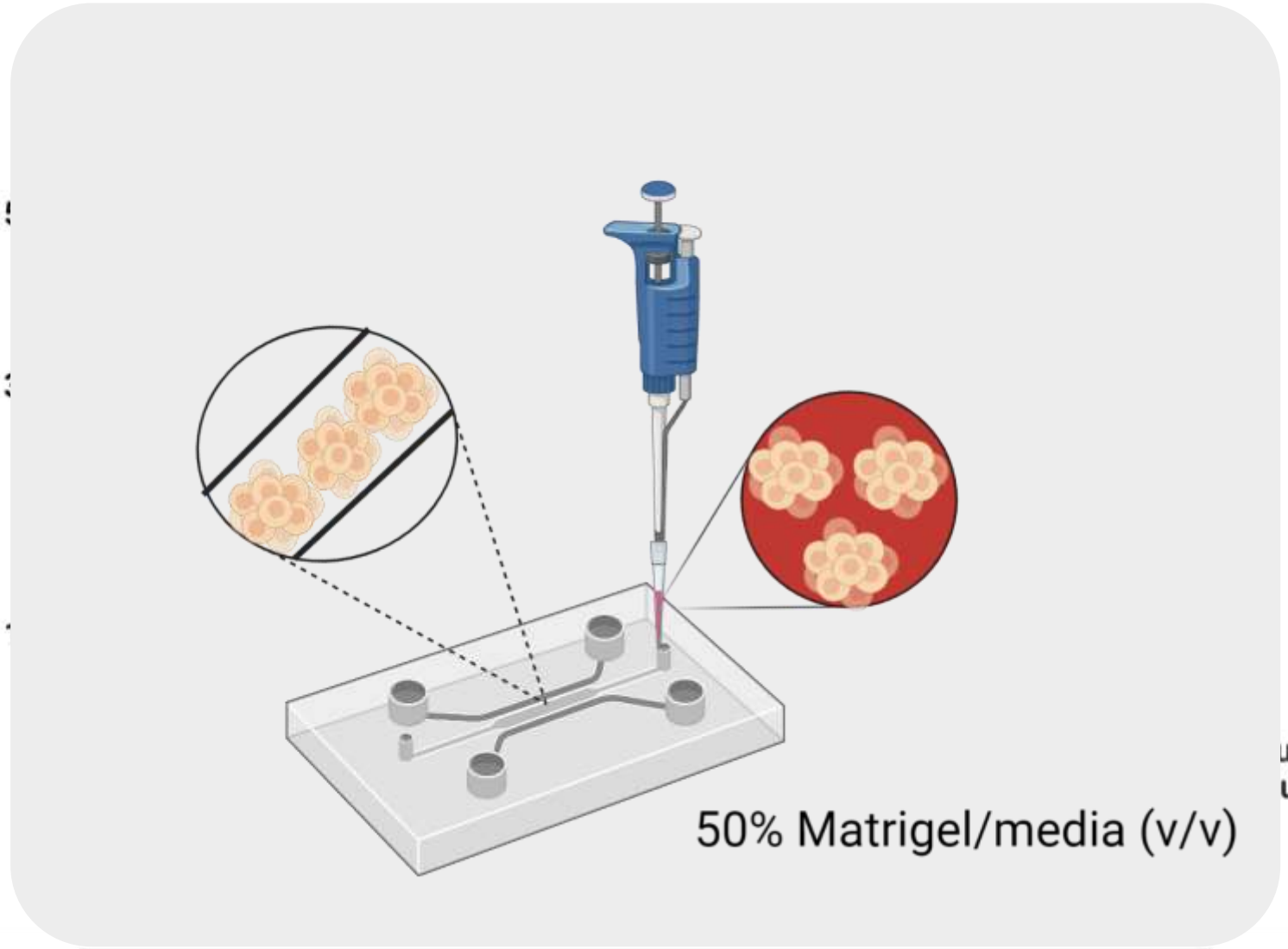




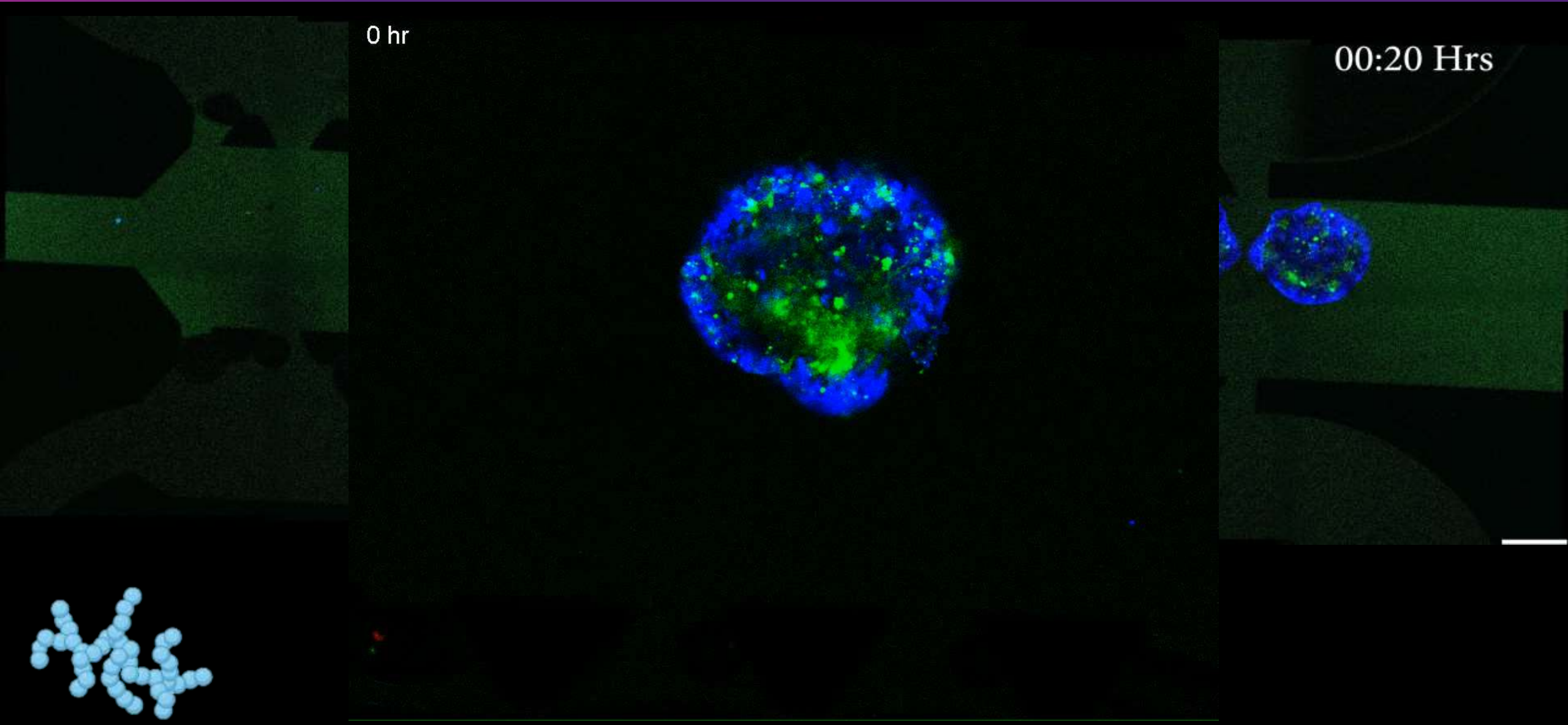
NP accumulation in microfluidic device over time







NP accumulation in microfluidic device over time



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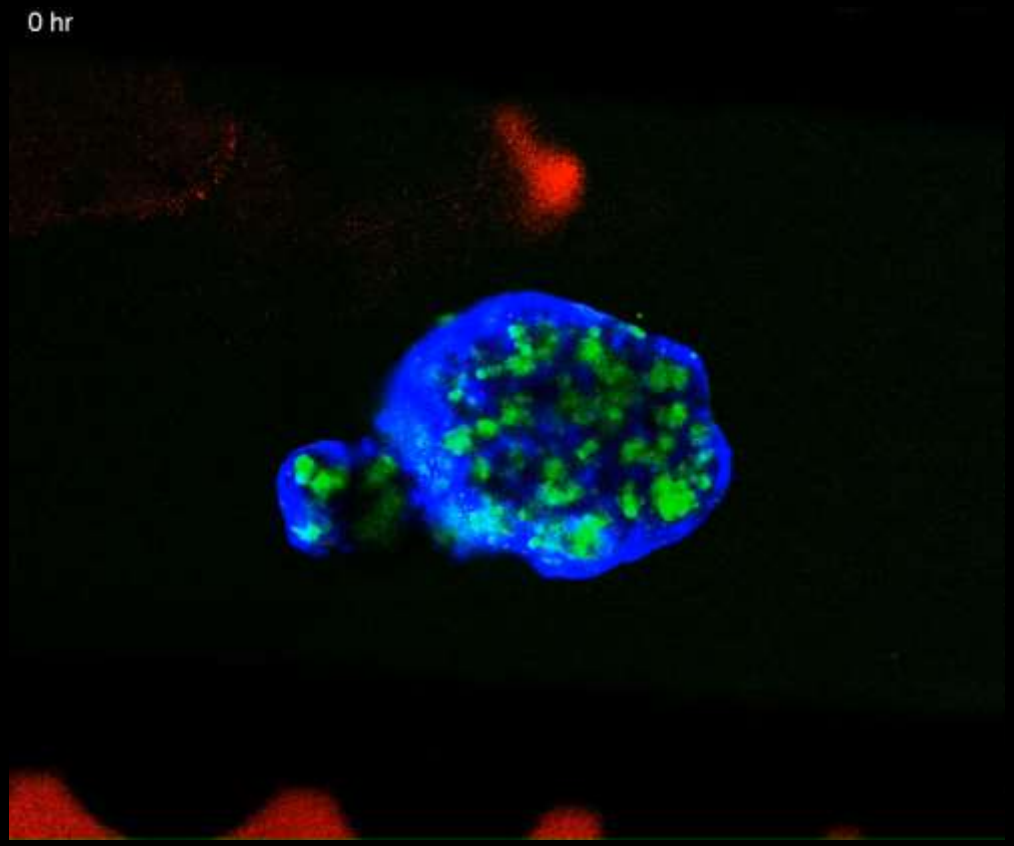

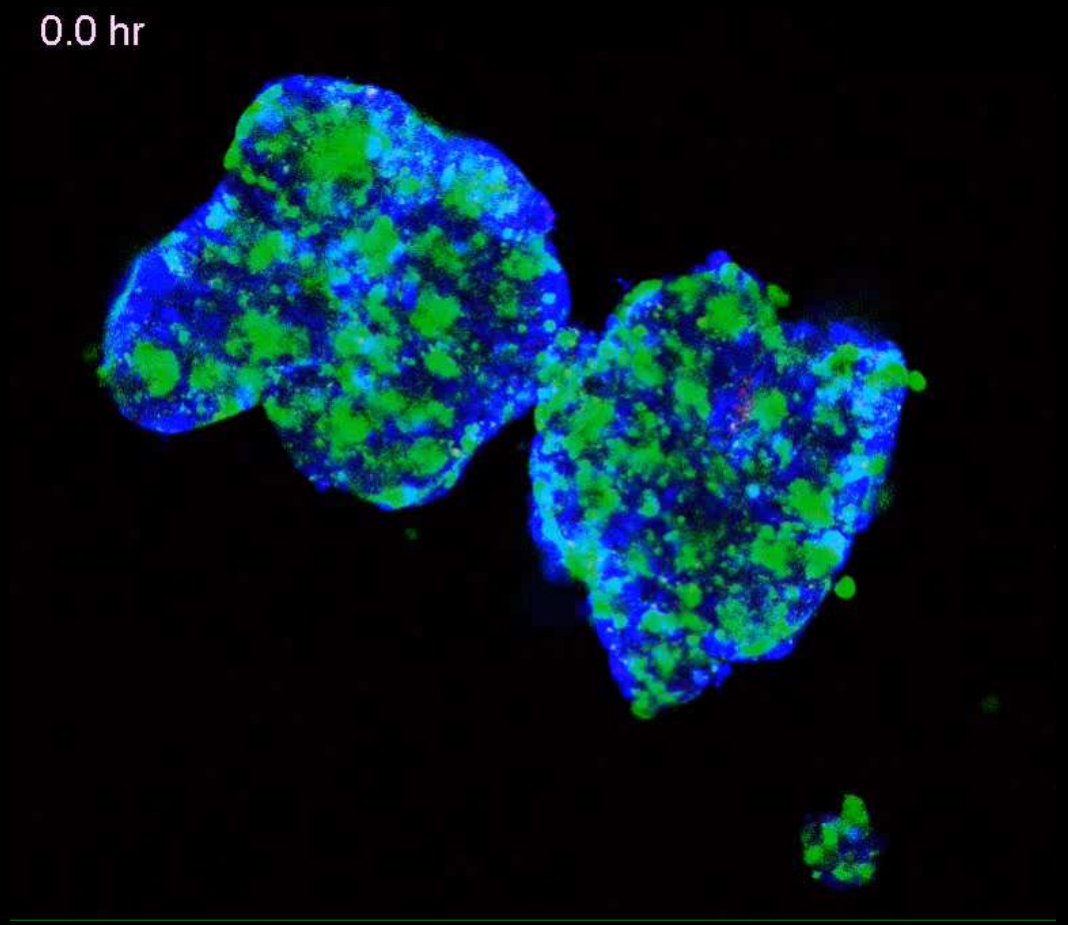

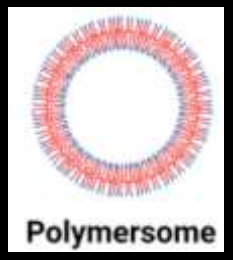

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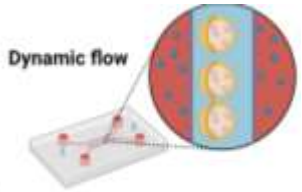
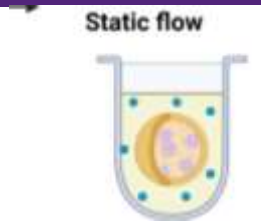
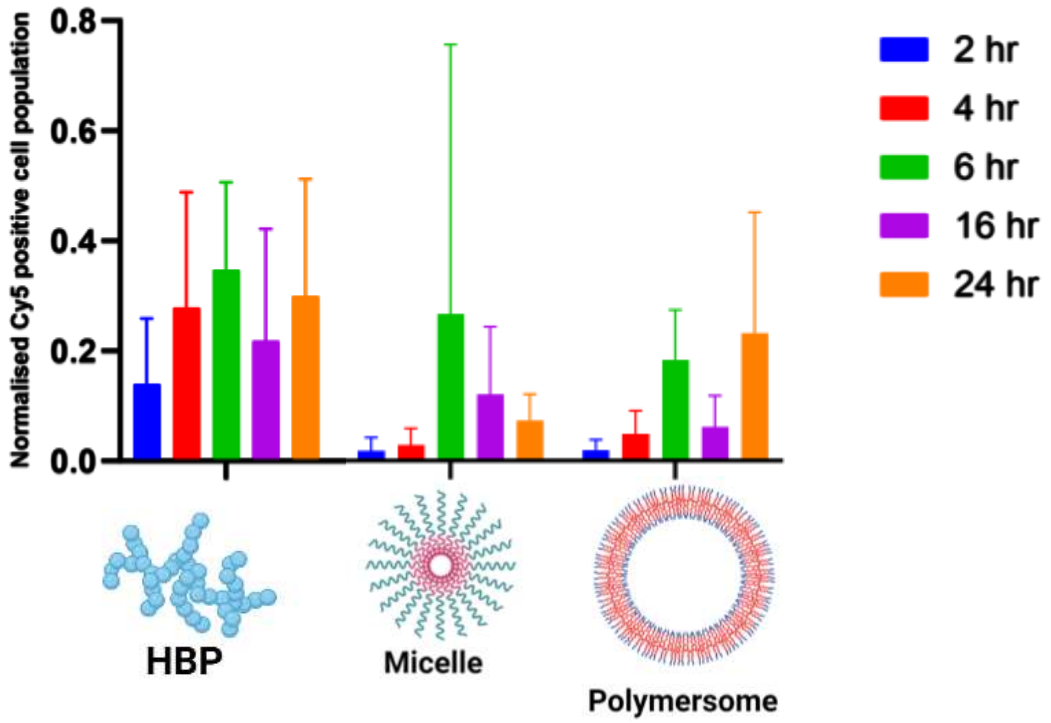
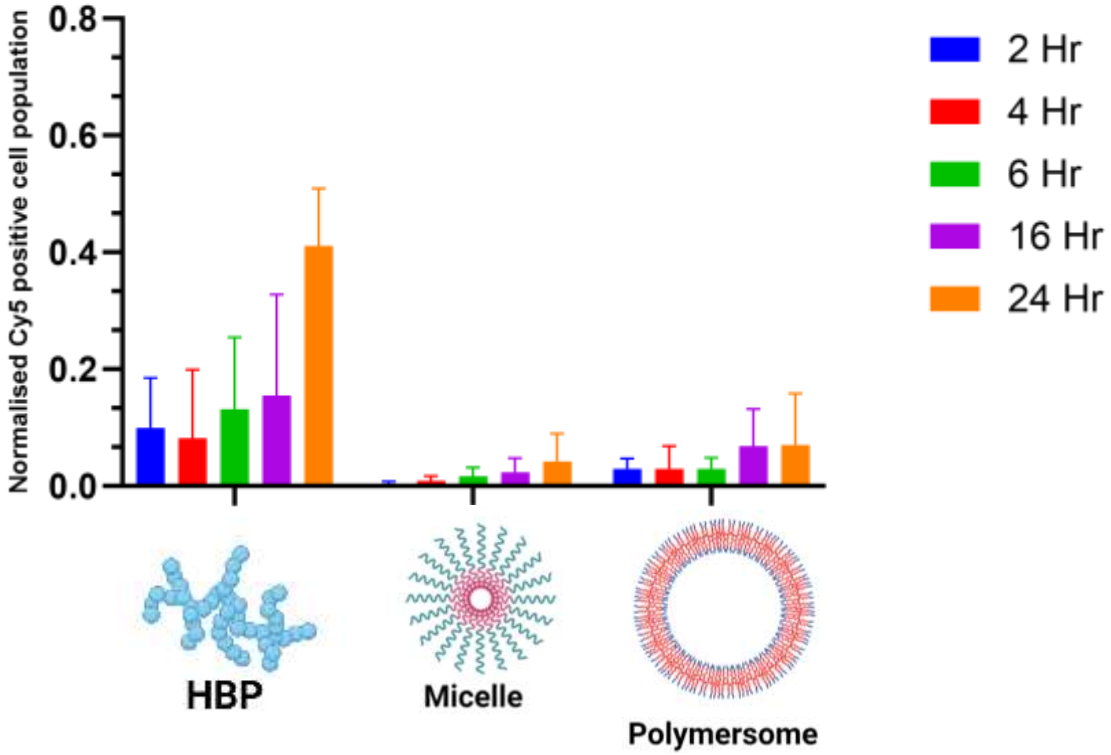




NP SKOV-3 cell association on tumour-on-a-chip

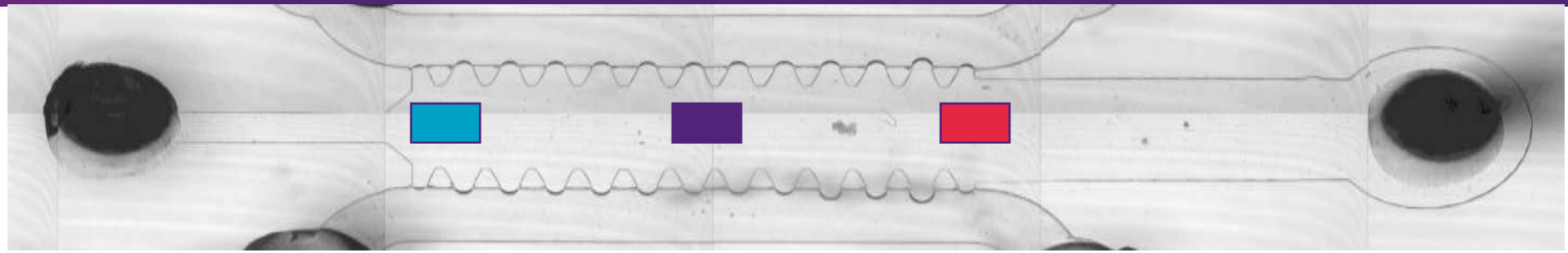


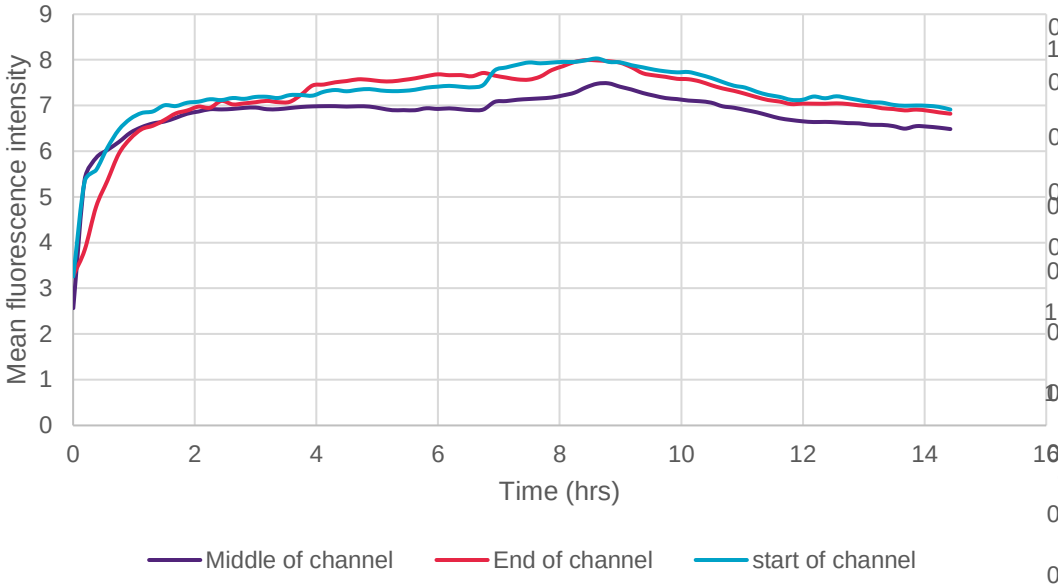
Normalised SKOV-3 cellular association

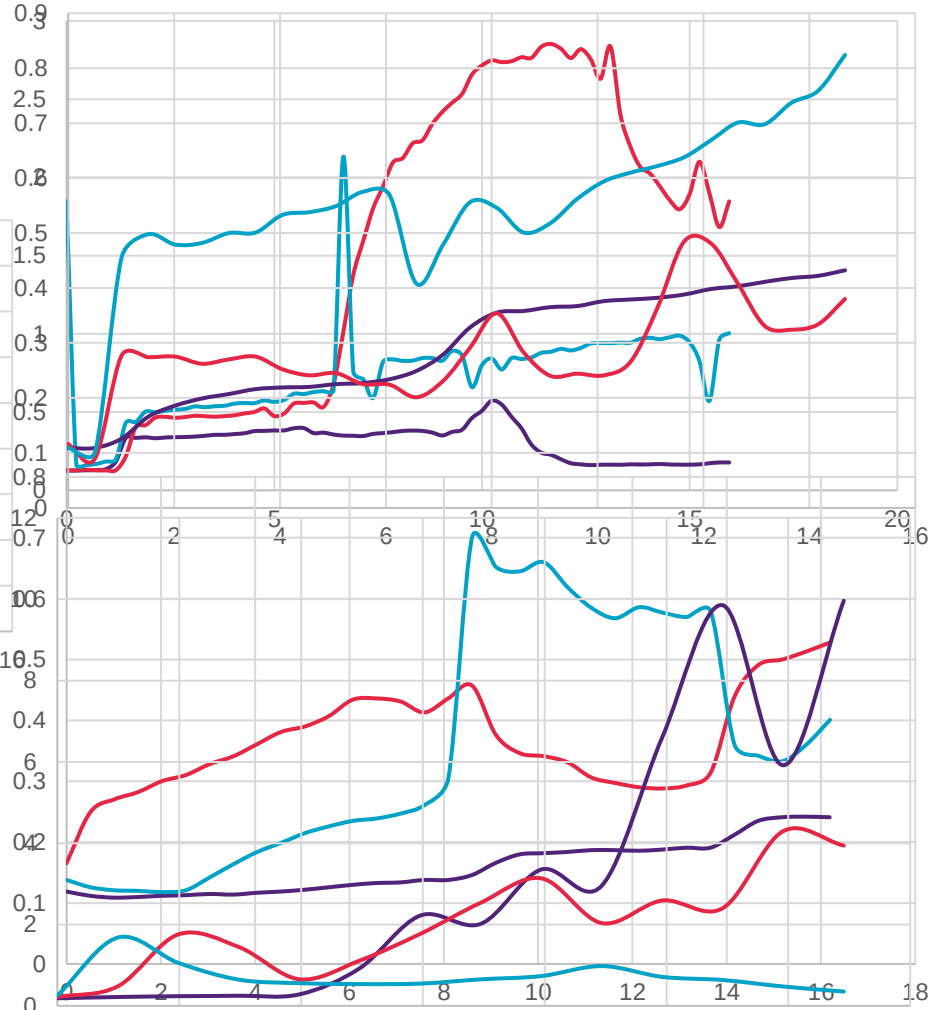


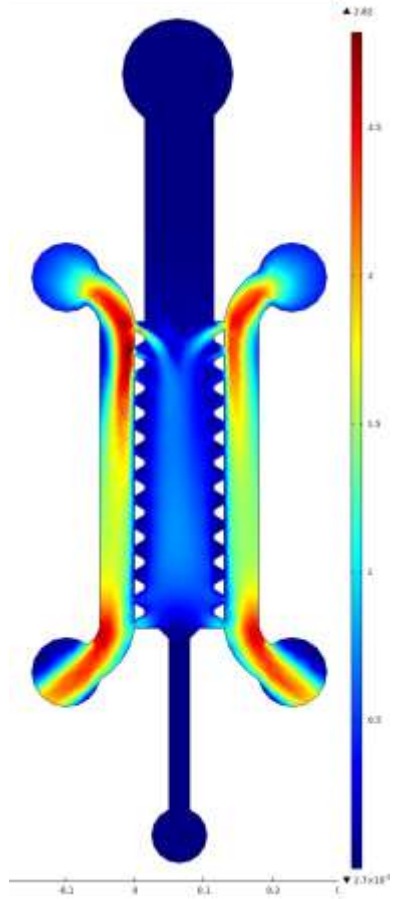
- Large variation in on-chip studies
  - Spheroid's position
  - Inconsistent perfusion of materials

Discrepancies in perfusion

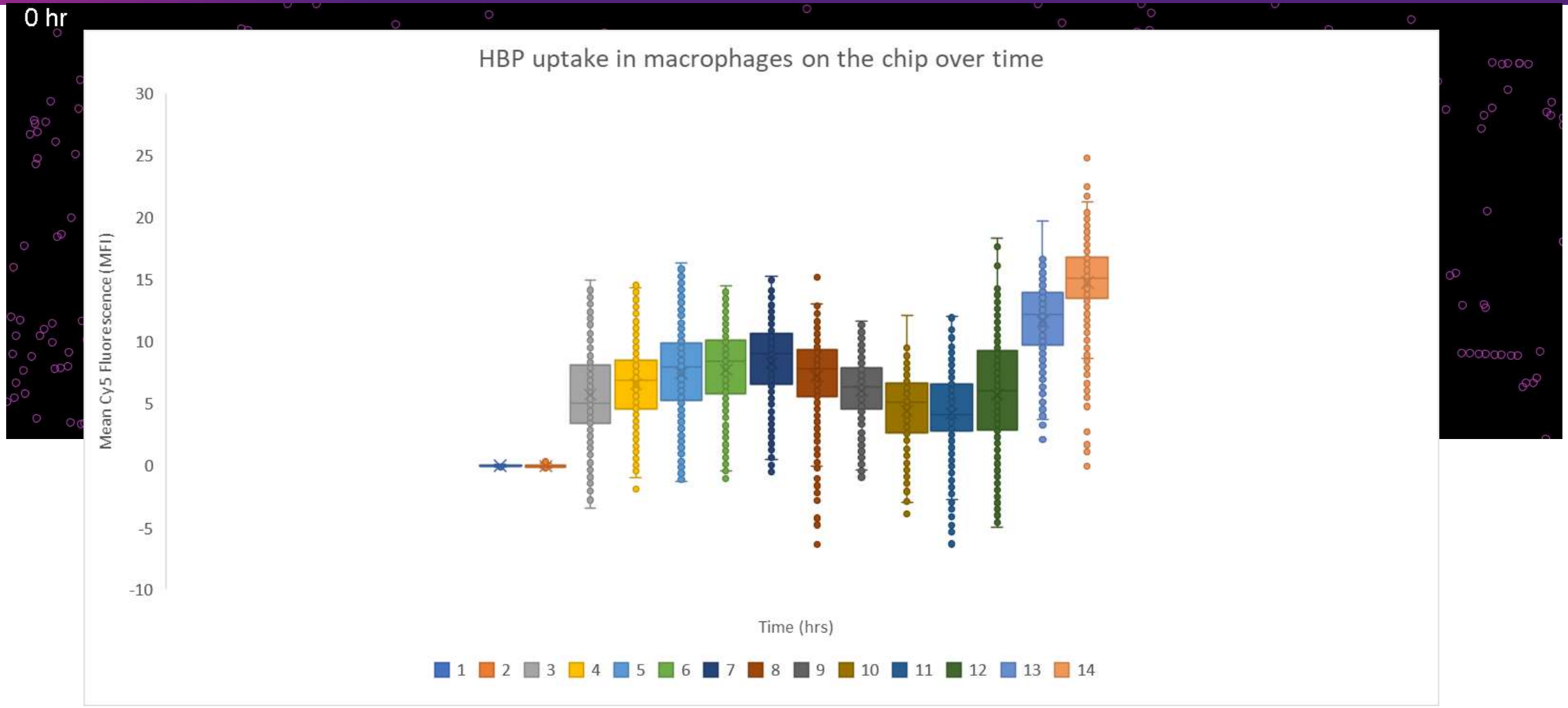








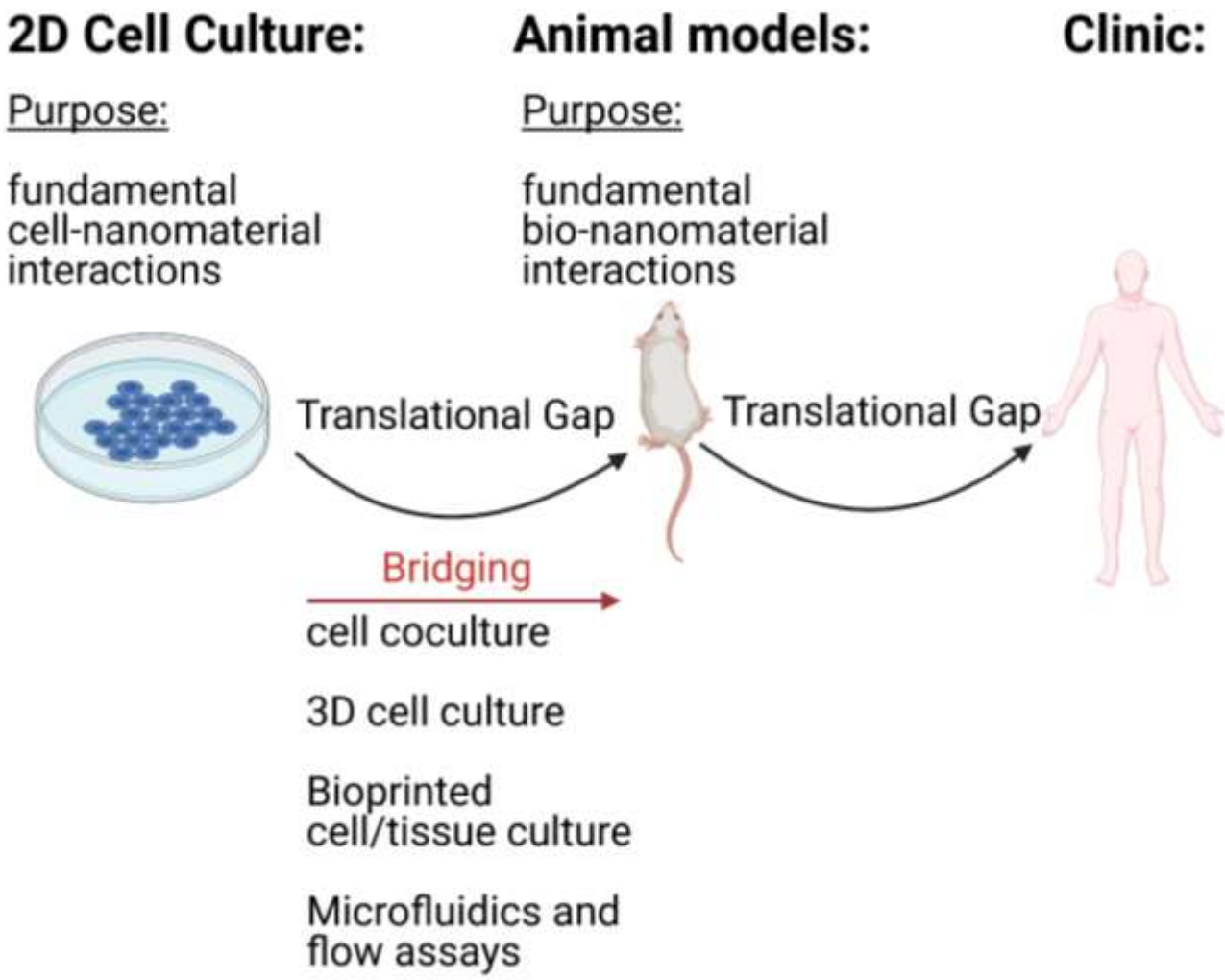
Nanoparticle accumulation in macrophages



Summary and future directions:

Large translational gap exists between cellular and animal studies

Can bridge this gap by creating a more complex *in vitro* system



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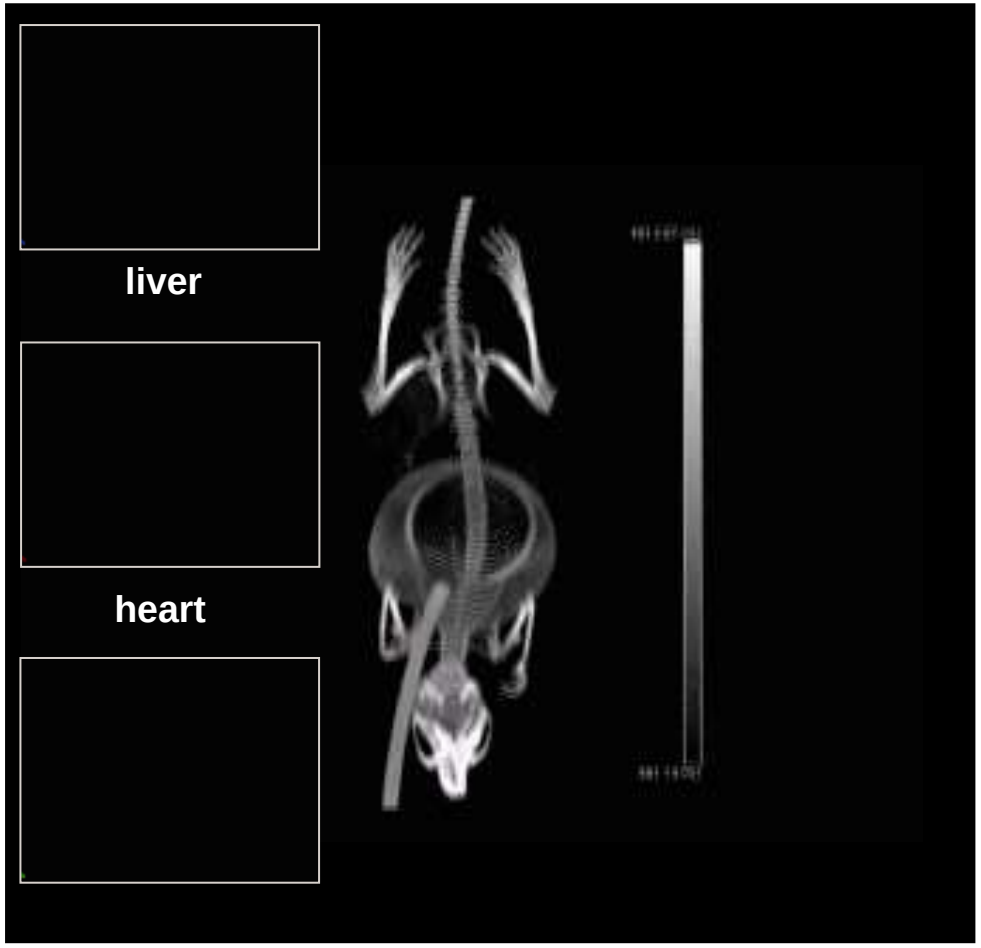
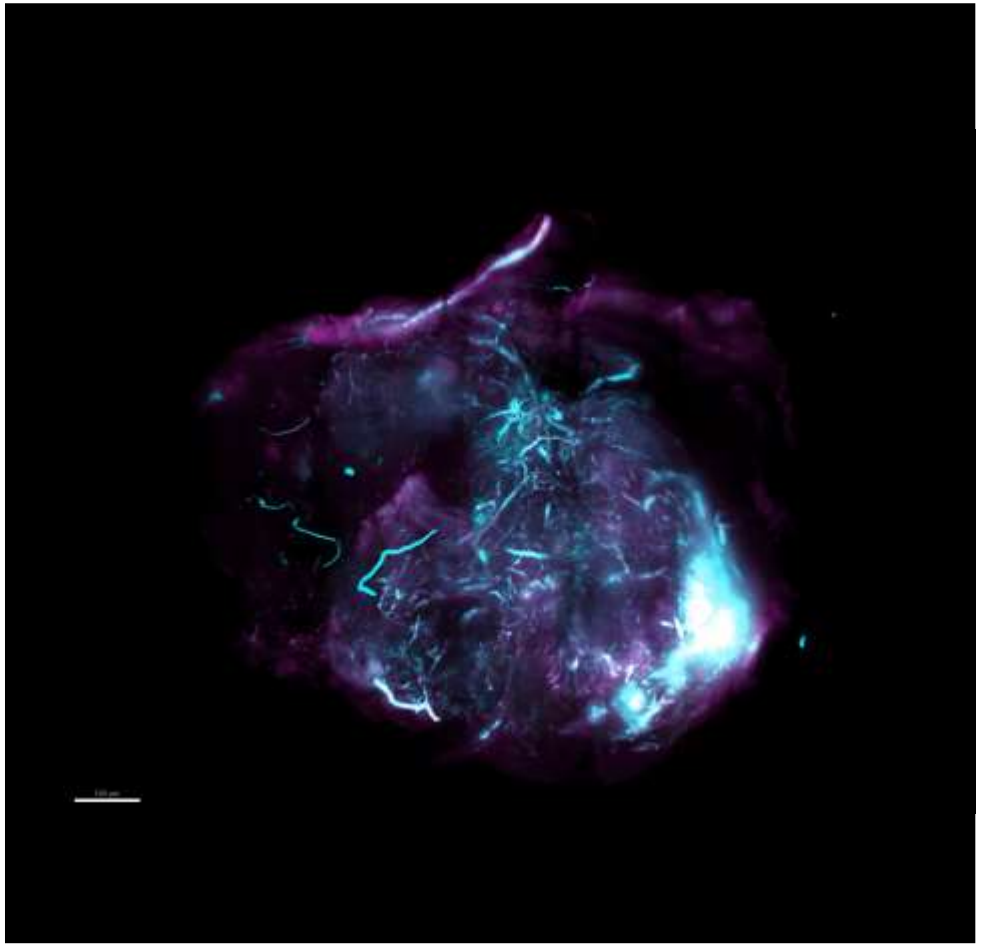


Match polymer concentration with *in vivo* blood circulation



Investigate *in vivo* tumour accumulation and penetration of NPs

Acknowledgments:

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Dr. Nick Fletcher
Assoc. Prof. Chun-Xia Zhao

Thurecht group members

CRICOS code 00025B

National Imaging Facility

THE UNIVERSITY OF QUEENSLAND AUSTRALIA | QBI
Queensland Brain Institute

THE UNIVERSITY OF QUEENSLAND AUSTRALIA

AIBN Australian Institute for Bioengineering and Nanotechnology

CAI Centre for Advanced Imaging

ANFF Queensland Node