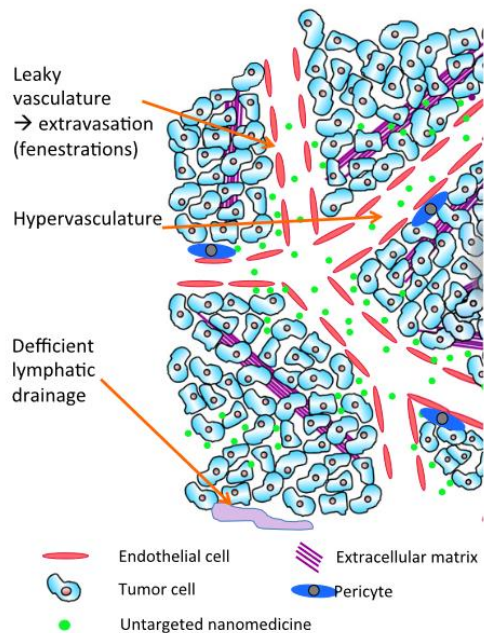


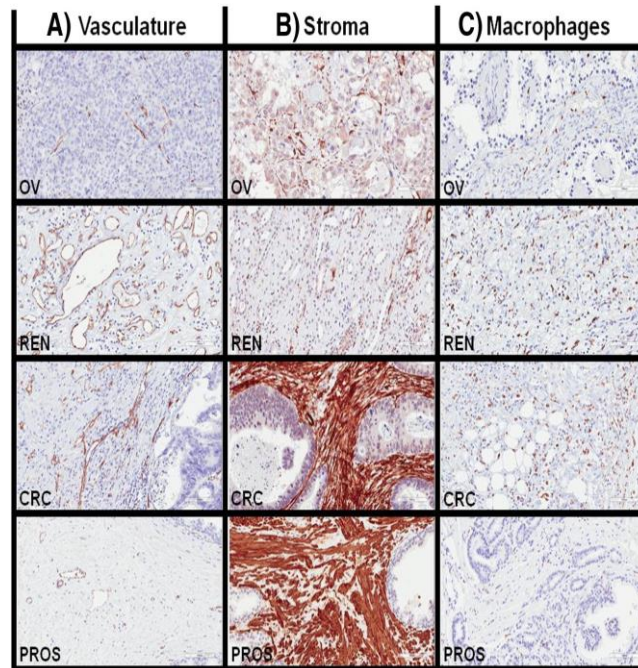
SIZE-TUNABLE THERANOSTICS MICELLES FOR SUBCUTANEOUS DRUG DELIVERY AND SENTINEL LYMPH NODE TARGETING

Alec Wang
Uniklinik RWTH Aachen University

Heterogenous Uptake

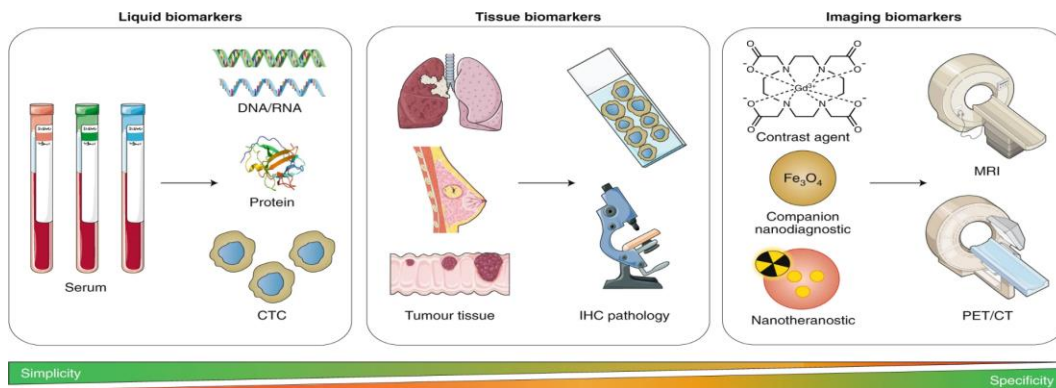


Danhier, F., *Journal of Controlled Release*, 2016

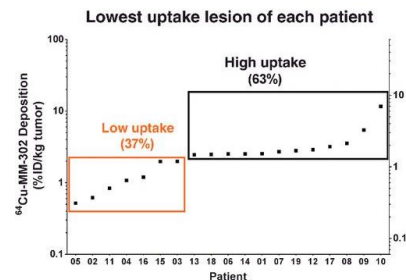


Hare, J.I., et. Al., *Advanced Drug Delivery Reviews*, 2017

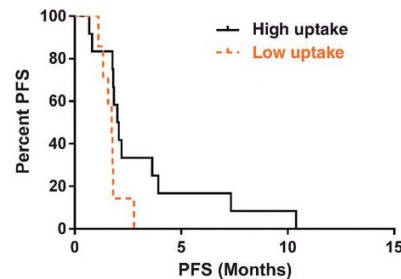
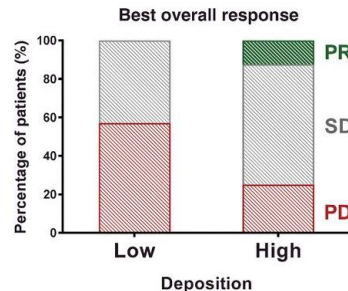
Patient Stratification



van der Meel, R., et al., *Nature Nanotechnology*, 2019



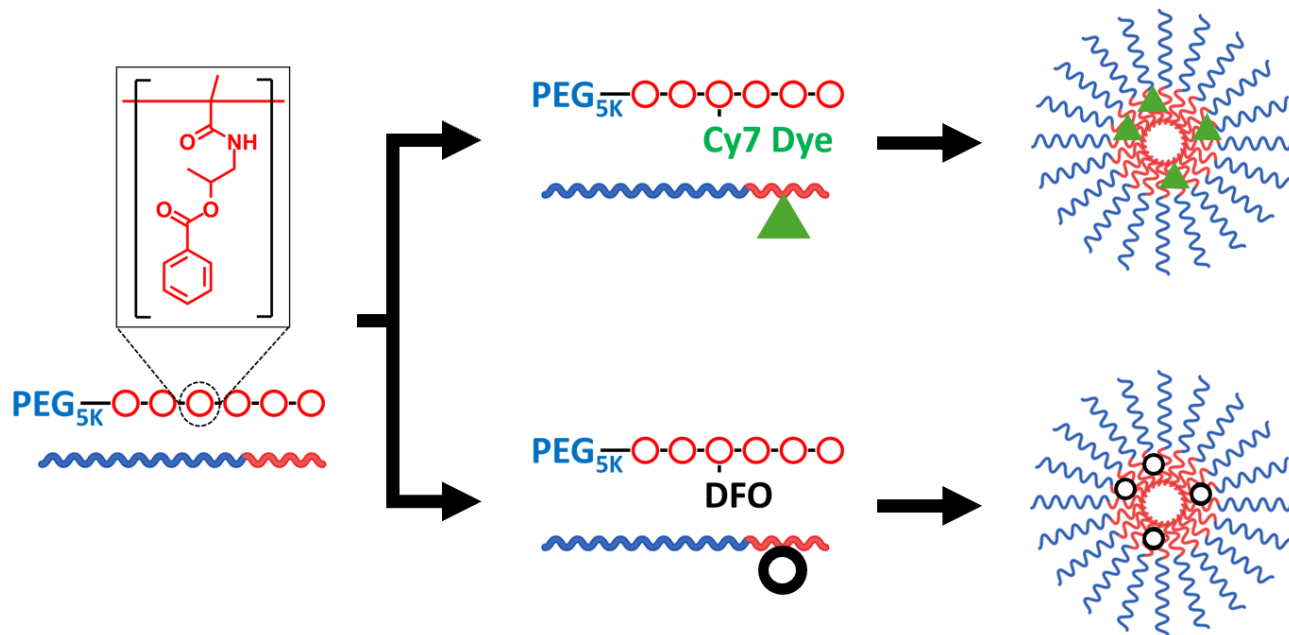
Lee, H., et al., *Clinical Cancer Research*, 2017



Screen for patients who are most likely to respond

Do not treat people who are unlikely to benefit

Imageable Polymeric Micelle Platform



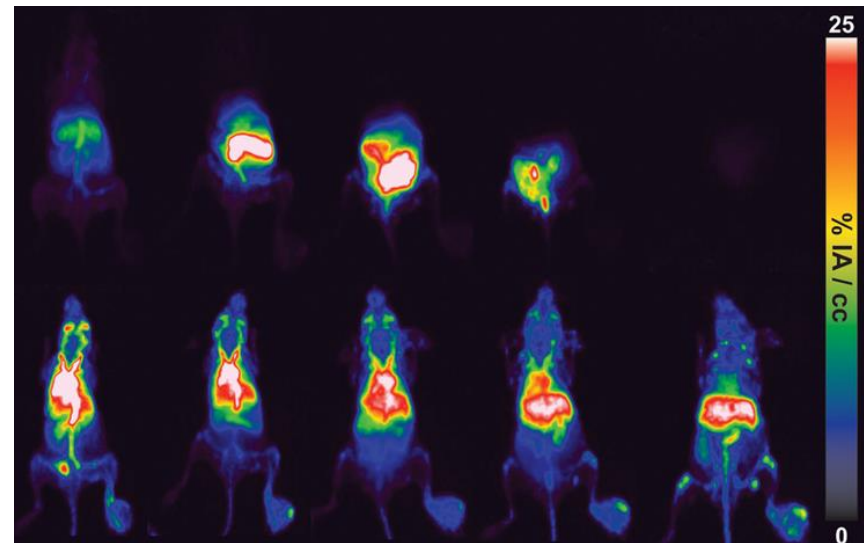
Wang, A., et. al., Manuscript in Revision

But Where Does the Drug Go?

- We're following the nanoparticle
- But can we be certain the drug ends up in the same place?

Drug

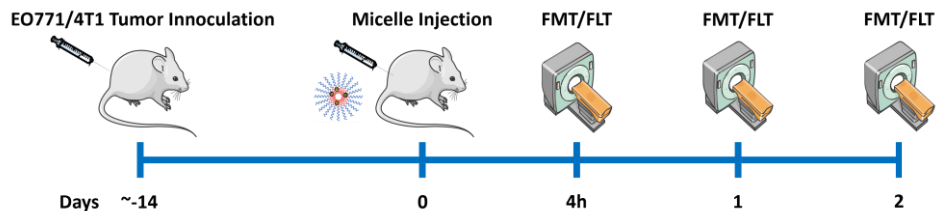
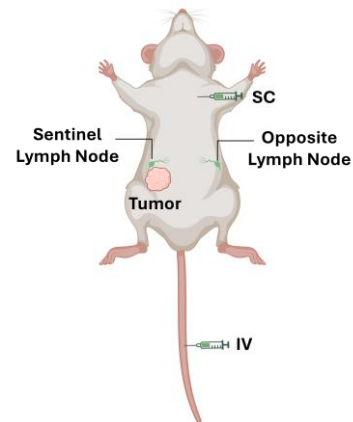
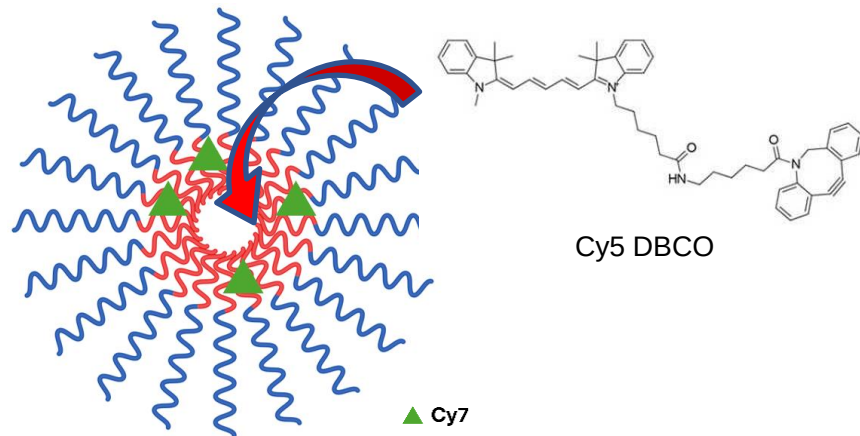
Carrier



No, the drug doesn't always end up in the same place

Pratt, E.C., et. al., Nature Biomedical Engineering, 2024

In Vivo Biodistribution of Both Drug and Nanocarrier

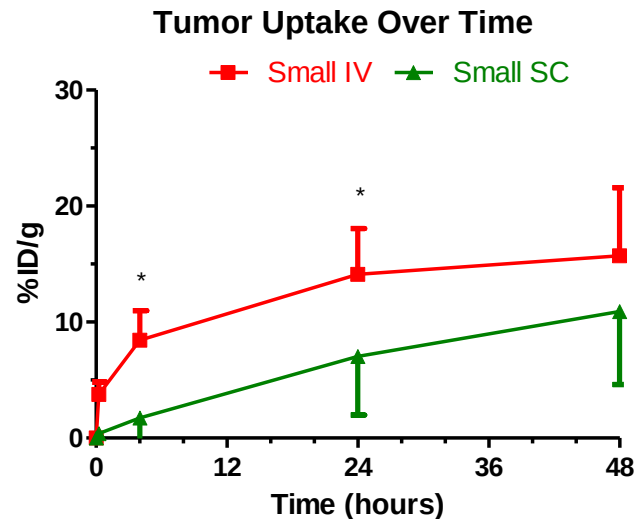
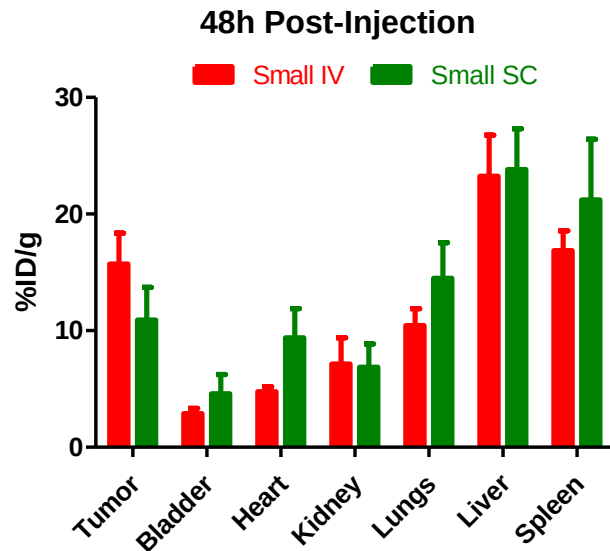
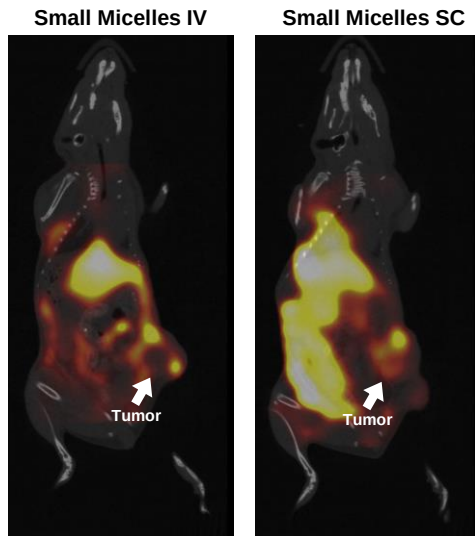


Biodistribution of the nanoparticle and the payload

Do they co-localize on a cellular level?

What cell populations take-up the particle and payload?

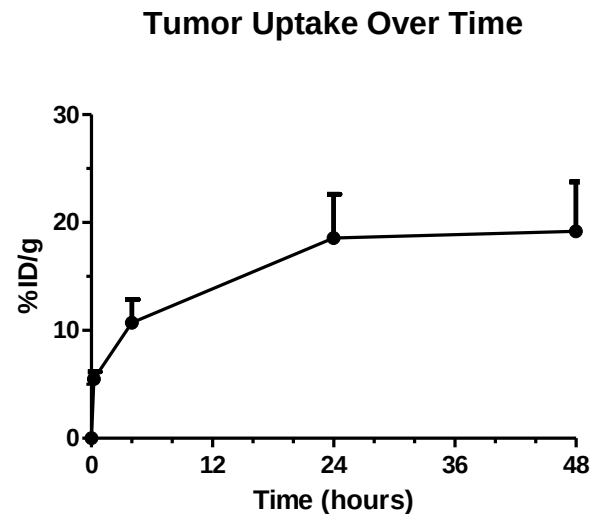
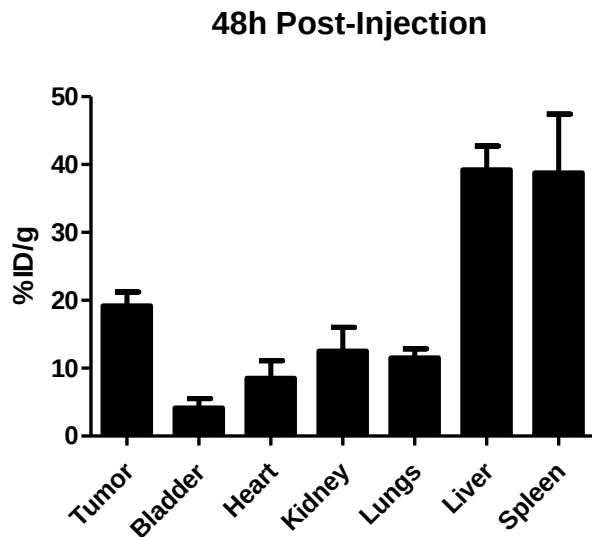
Biodistribution – EO771 Triple Negative Breast Cancer



Subcutaneously administered polymeric micelles still behave like PEGylated nanoparticles

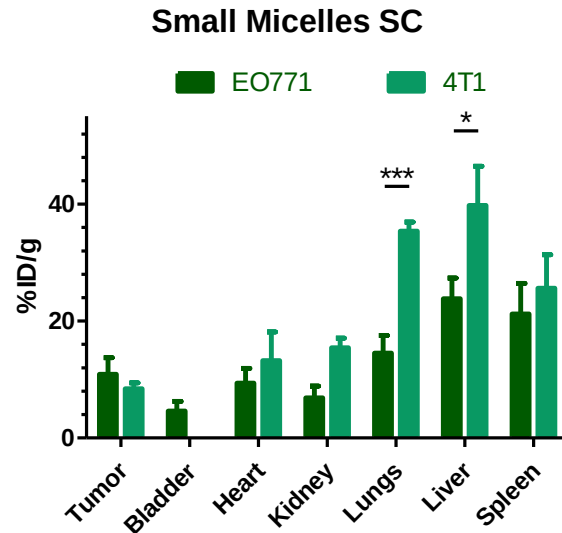
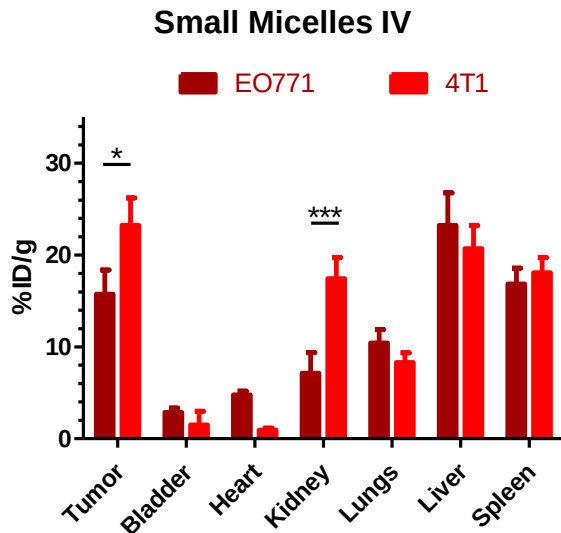
Tumor uptake is delayed compared to intravenous administration

Biodistribution – Large Micelles EO771



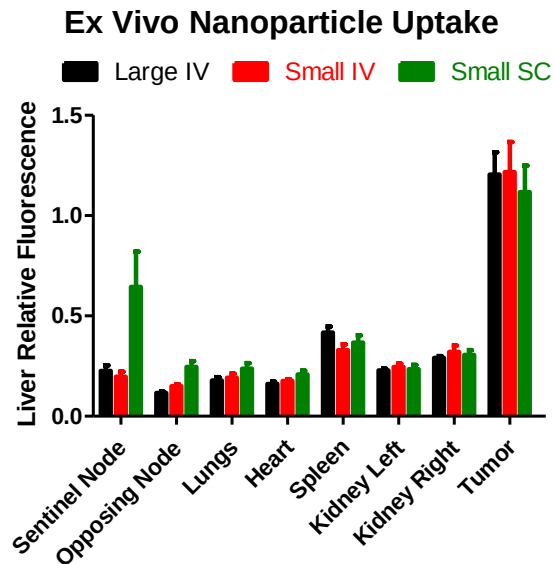
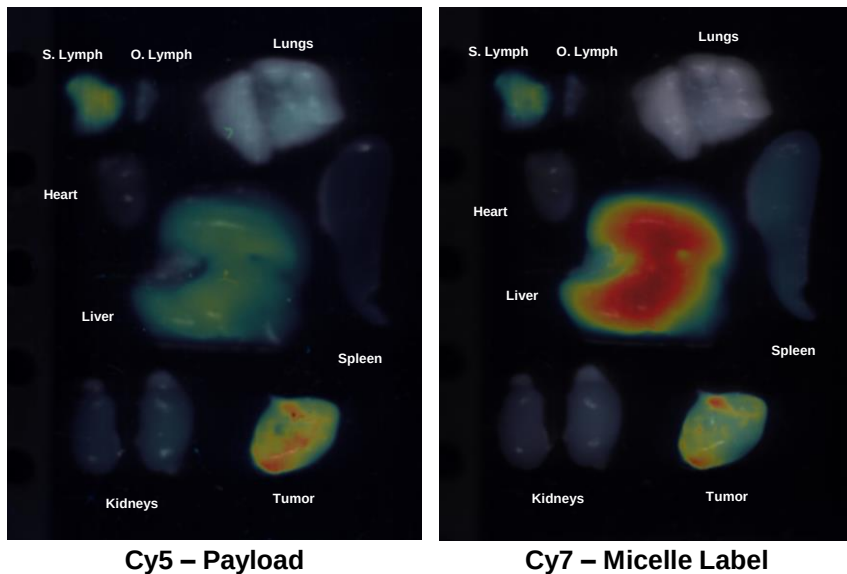
Large particles show much higher off-target accumulation in the liver and spleen

Biodistribution – EO771 vs 4T1



4T1 cancer model shows higher uptake vs EO771 for IV micelles

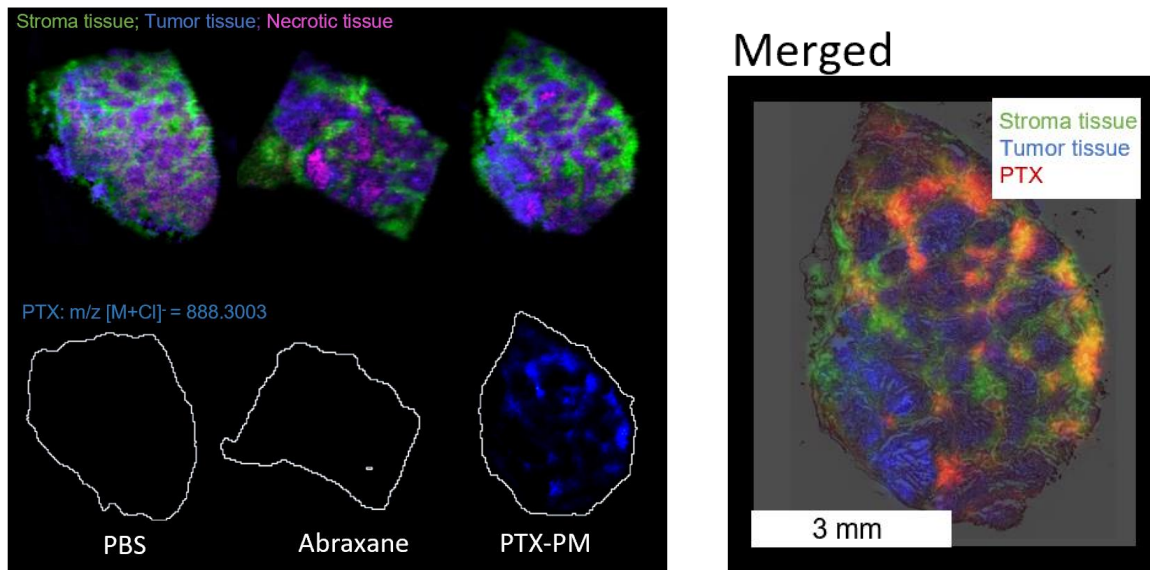
Sentinel Lymph Node Delivery



Micelles can be injected subcutaneously to enhance accumulation in sentinel lymph nodes

No enhancement in other lymph nodes – including lymph nodes draining the injection site

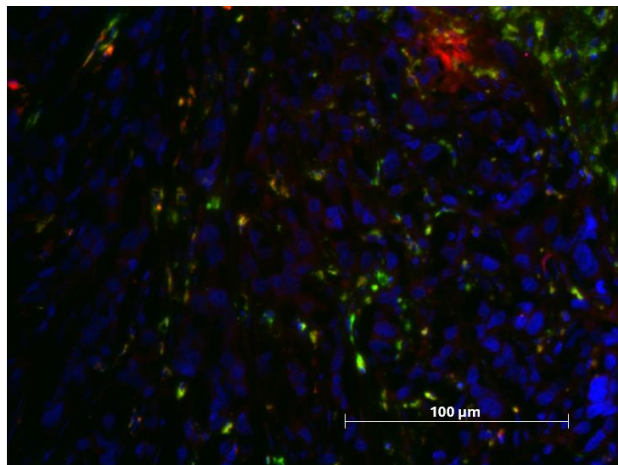
Drug Delivery in Tissues



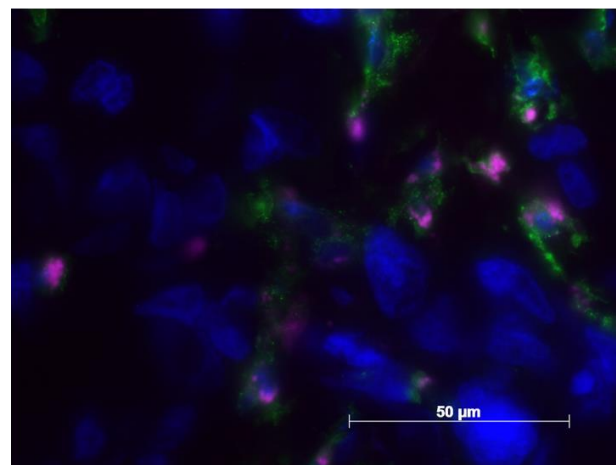
Micelles can deliver much more drug to tumors than other nanostructures

Pena, Q., et. al., Manuscript in Preparation

What cells do we get to?



Nuclei Blood Vessel Polymer



Nuclei Macrophage Polymer

Fluorescent-labeling allows for tissue and cell level imaging of micelles

Co-localization of nanoparticles inside tumor-associated macrophages

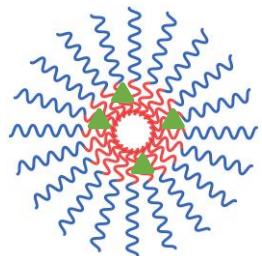


Laura Schäfer

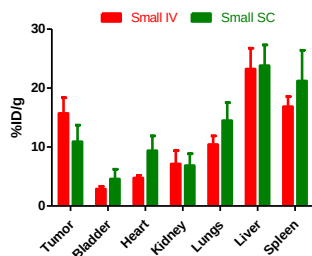
Outlook

Conclusions

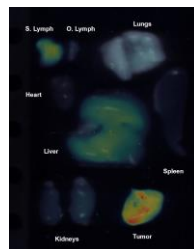
Fluorescence-Imageable Micelles



Efficient Tumor Delivery

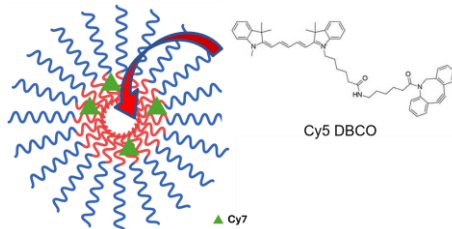


Sentinel Lymph Node Targeting

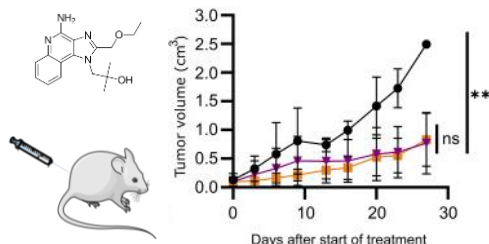


What's Next?

Following the Drug In Vivo



Immunomodulation Therapy



Key Take-Aways

- Imageable micelles can act as patient-specific biomarkers for accumulation
- Our polymeric micelles are a versatile platform for imaging
- Excellent tumor uptake across multiple models of triple negative breast cancer
- Micelles can be administered subcutaneously and still achieve high tumor uptake
- Subcutaneous injection drives accumulation of polymeric micelles in sentinel lymph nodes
- Potential for potent immunotherapy at both the tumor and the lymph node

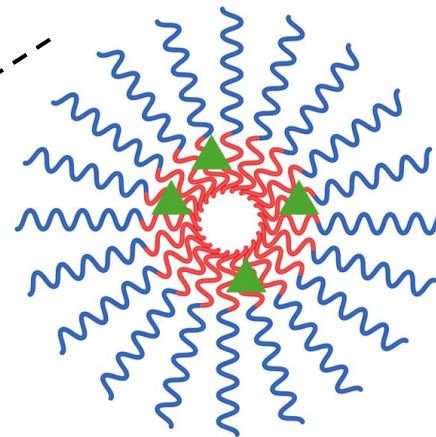
Maybe?



Maybe?



Maybe?



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DELIVERY INNOVATIONS**