Using Nanoparticles for Drug Delivery

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Introduction

I worked with my mentor L. Sebastian Ojeda to investigate the use of Reticuloendothelial System (RES) Blockade as a means to improve nanoparticle (NP) circulation time and delivery to tumors. Drugs passively targeting tumors rely on NPs & the EPR effect to improve circulation time; however, only a 0.7% median of administered NPs utilizing the EPR effect reach their target tumor[1].

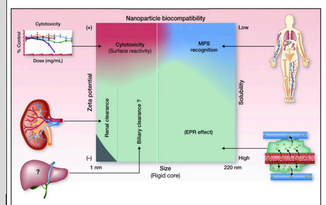


Figure 1: Distribution of nanoparticles based on size, solubility, and charge

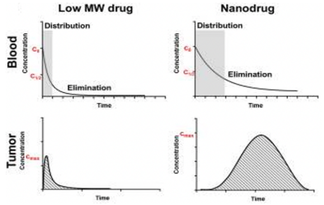


Figure 2: Circulation times and tumor accumulation for free drugs vs. encapsulated drugs

Objective & Impact of Professor's Research

RES Blockade is the theory that administering an inert pre-dosage of a nanoparticle (i.e., biodegradable empty liposomes) can saturate your RES prior to a secondary administration of therapeutic NPs leading to fewer therapeutic NPs being picked up by RES cells, increases circulation time, and decreases the accumulation of toxic NPs to RES organs (liver, spleen).

To investigate the use of RES Blockade to improve drug delivery, we first characterized important microscope parameters:

1. Determining the Nikon A1R system limits.
2. Assess real time NP tracking capabilities under physiologically relevant conditions

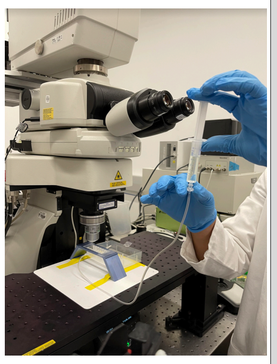


Figure 3: Tracking NPs in real time w/ Nikon A1R & microchannel

Skills Learned

Characterization of Nanoparticles

Utilized the Nanosight system to verify that the correct concentration and size of liposome NPs after they had been diluted into solutions for microchannel flow experiments.

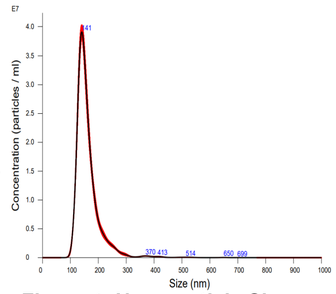


Figure 4: Nanoparticle Size Distribution

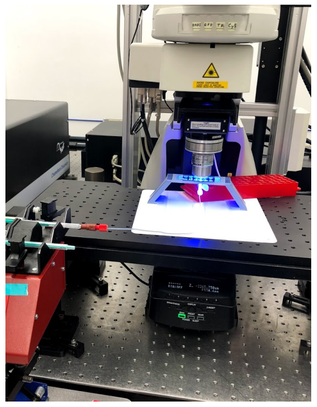


Figure 5: Nikon A1R Microchannel Flow Setup

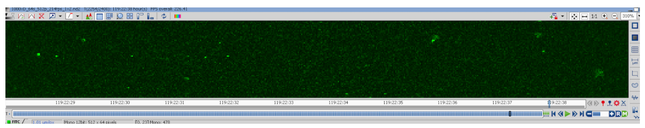
Defining Nikon Imaging Limitations

Tested Nikon A1R system boundaries to find optimal frame rate vs. resolution, zoom level, scan size, and pixel height that could be used to track particles

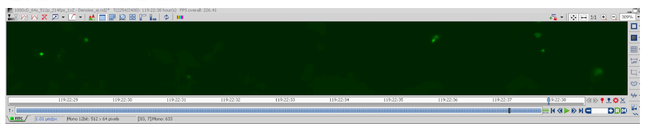
Determining Denoising Method

Using the Nikon A1R particle tracking software we tested different denoising methods to determine which one led to the most accurate particle concentration count.

A. Raw Data



B. Denoised Data



C. Particle Tracking

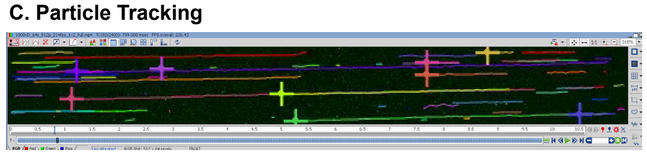


Figure 6: Denoising process to filter out unwanted noise and accurately track particle concentration and flow rate across microchannel length

What's Next for the Z lab

The next step in this research is to conduct in-vivo modeling with the defined Nikon A1R imaging setup. Afterwards, they will test the RES Blockade Strategy in an orthotopic tumor model to determine if there is an improvement in delivery to the tumor.

My STEM Course Work

- Being a part of SHINE has taught me that it is okay to not know everything down to the bone. What matters is the reason behind it and overall concept.
- This will help me not beat myself up over not being the best at memorizing every detail of different biological and technical concepts.
- SHINE has introduced me to an amazing community of scientists who have shown me compassion and patience. I can say I have ended SHINE which much more confidence than I had prior to participating.

Advice for Future SHINE Students

My advice for future students would be to embrace the free-fall at the beginning of SHINE. The overall experience will be rewarding. It's okay to not have much background in STEM, this is what SHINE is for, to provide you with experience. Being part of SHINE and Professor's Zavaleta's lab I can say I feel empowered to become an Engineer. #womeninstem

Figure 7: USC MICHELSON CENTER FOR CONVERGENT BIOSCIENCE

References

Reference 1: Wilhelm, S., Tavares, A., Dai, Q. *et al.* Analysis of nanoparticle delivery to tumours. *Nat Rev Mater* **1,** 16014 (2016). https://doi.org/10.1038/natrevmats.2016.14
Figure 1: Zamboni, W.C., et al. "Best Practices in Cancer Nanotechnology: Perspective from NCI Nanotechnology Alliance". Clinical Cancer Research. 2012
Figure 2: Zamboni, W.C., et al. "Best Practices in Cancer Nanotechnology: Perspective from NCI Nanotechnology Alliance". Clinical Cancer Research. 2012
Figure 3: Ammey Corrales
Figure 4: L. Sebastian Ojeda
Figure 5: L. Sebastian Ojeda
Figure 6: L. Sebastian Ojeda
Figure 7: Ammey Corrales

Acknowledgements

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