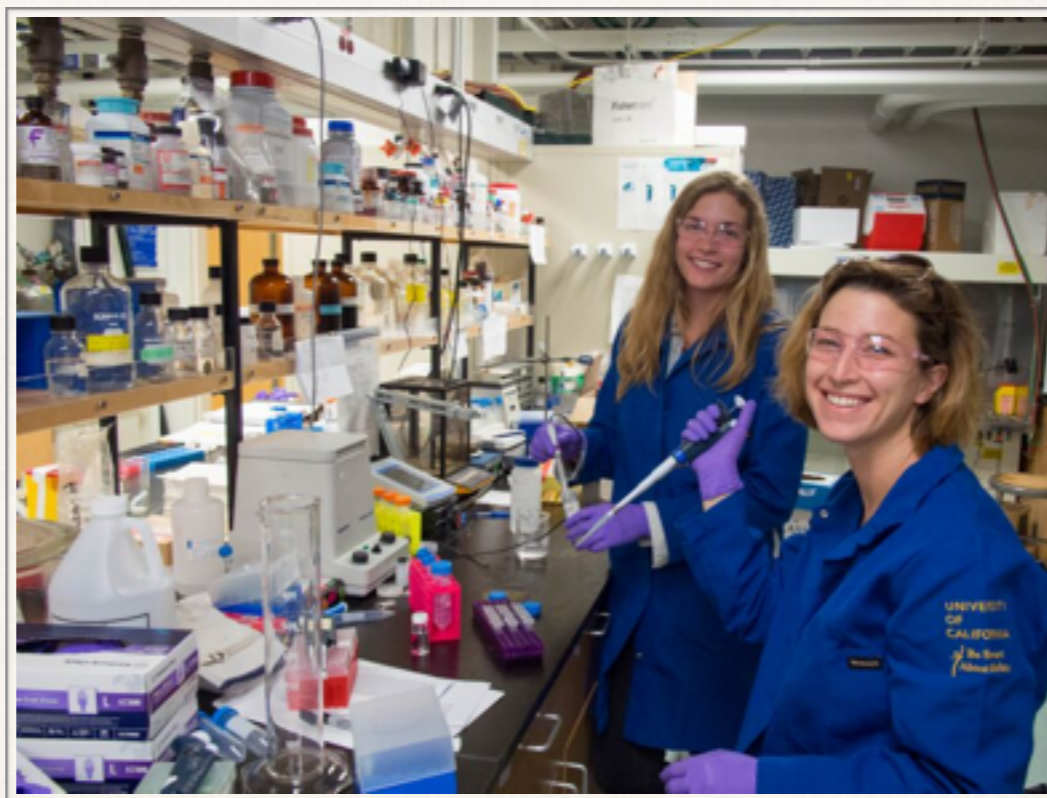
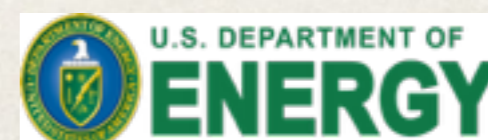
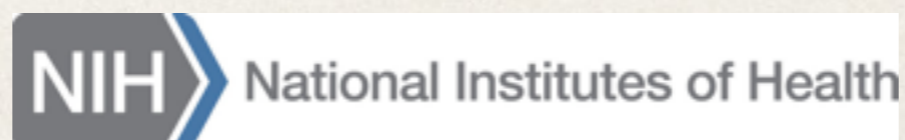


Optimizing a Lipid-Nanocarrier for Efficient Loading and Delivery of a Hydrophobic Drug: Paclitaxel



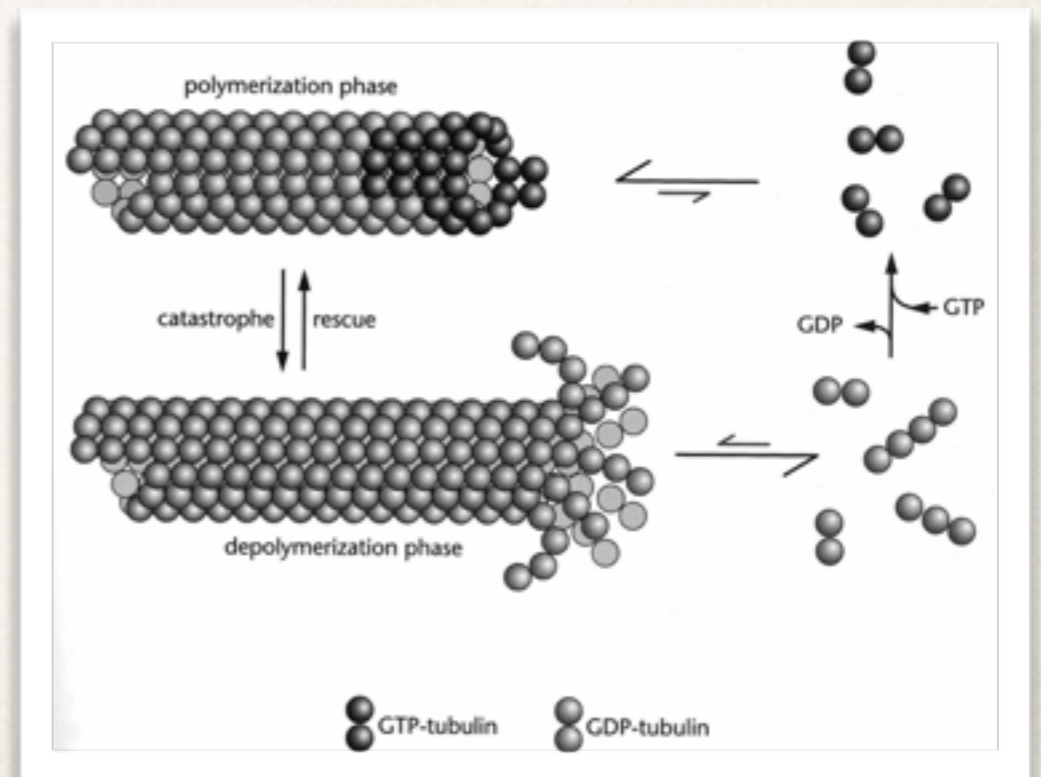
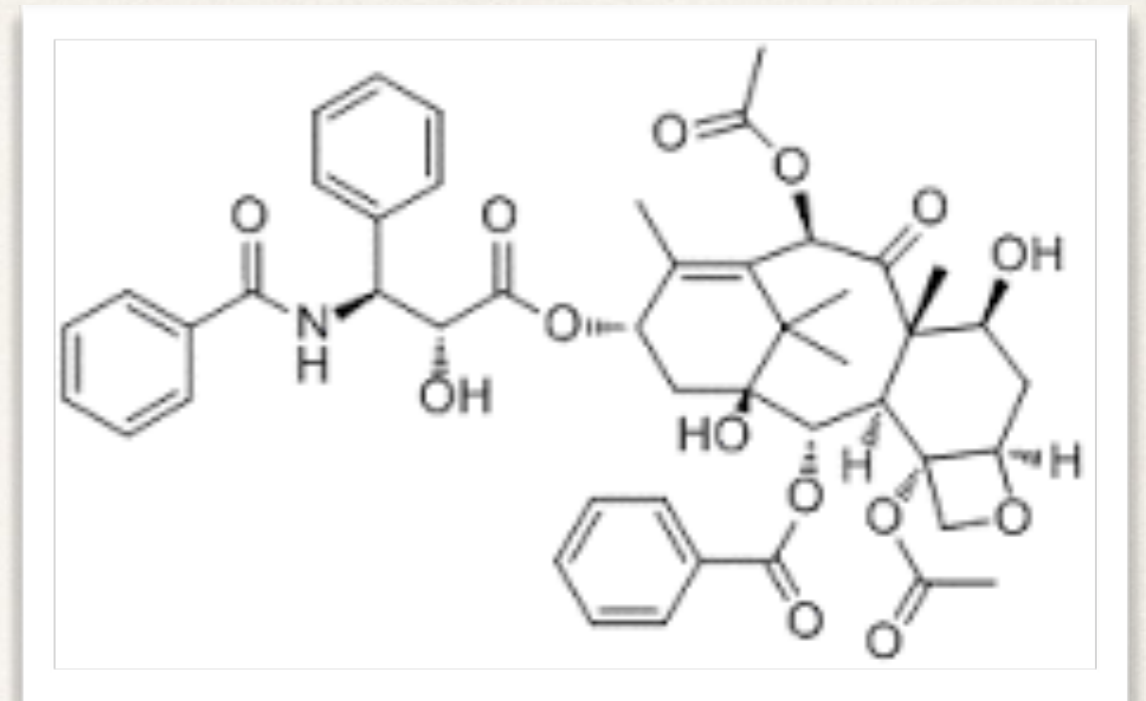
Lauren Galvin, MRL RET Program Participant

Victoria Steffes, PhD Candidate
Safinya Group



Paclitaxol

- ❖ Standard of Care:
 - ❖ Solubilized in Cremophor & ethanol
 - ❖ Causes hypersensitivity reactions
 - ❖ Reduces potential therapeutic index

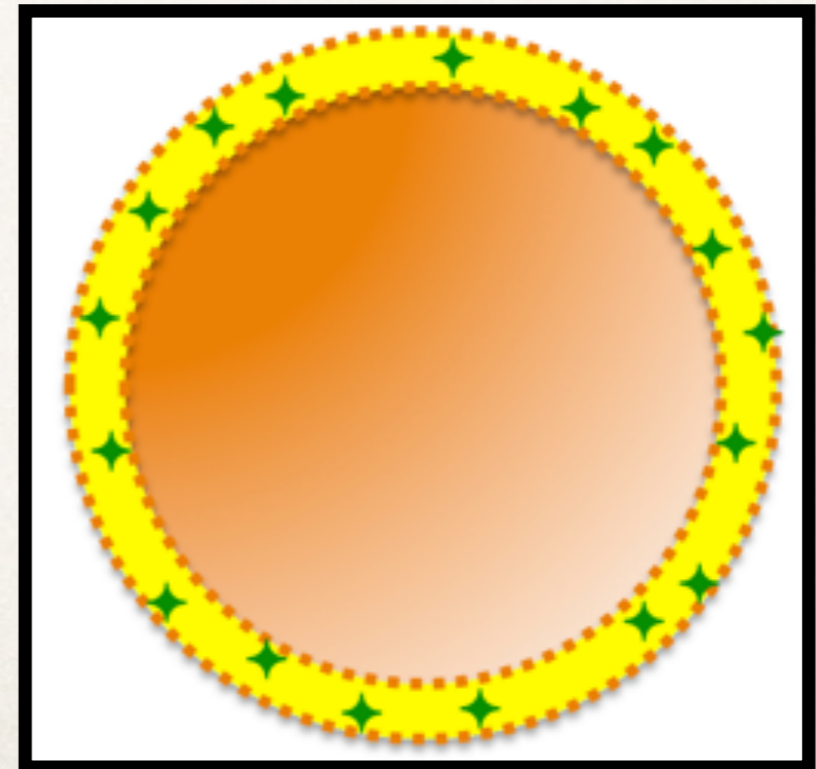
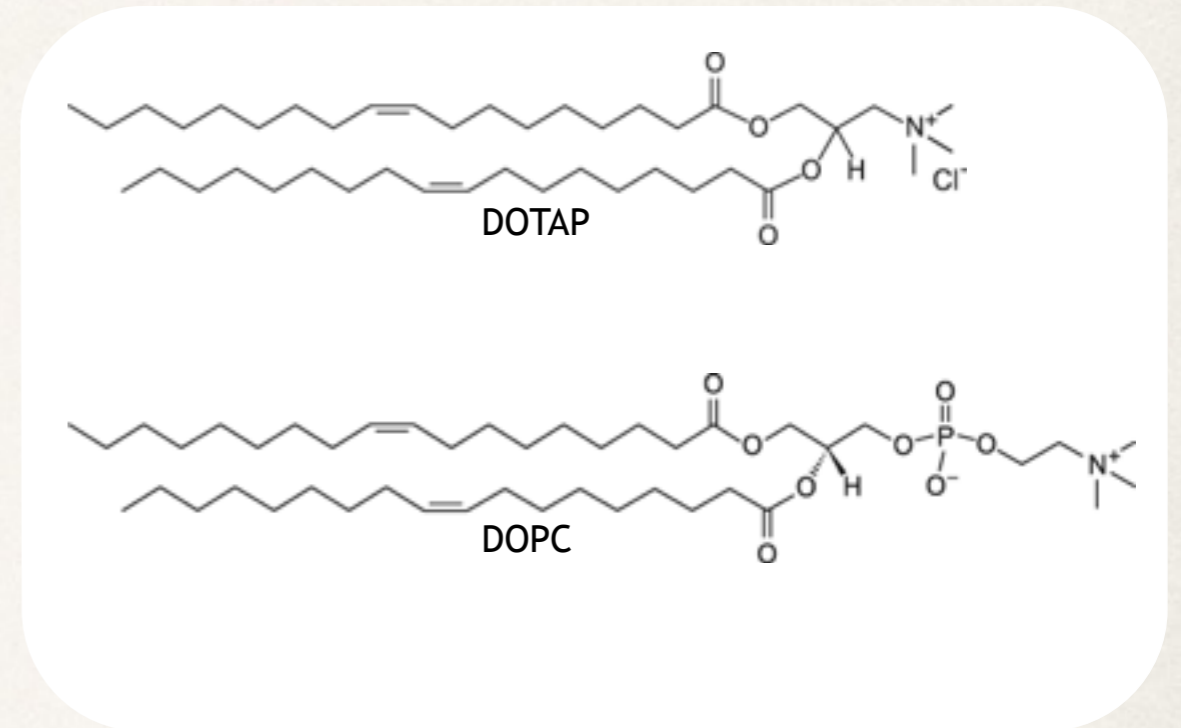


Halts cell division via microtubule stabilization

EndoTAG

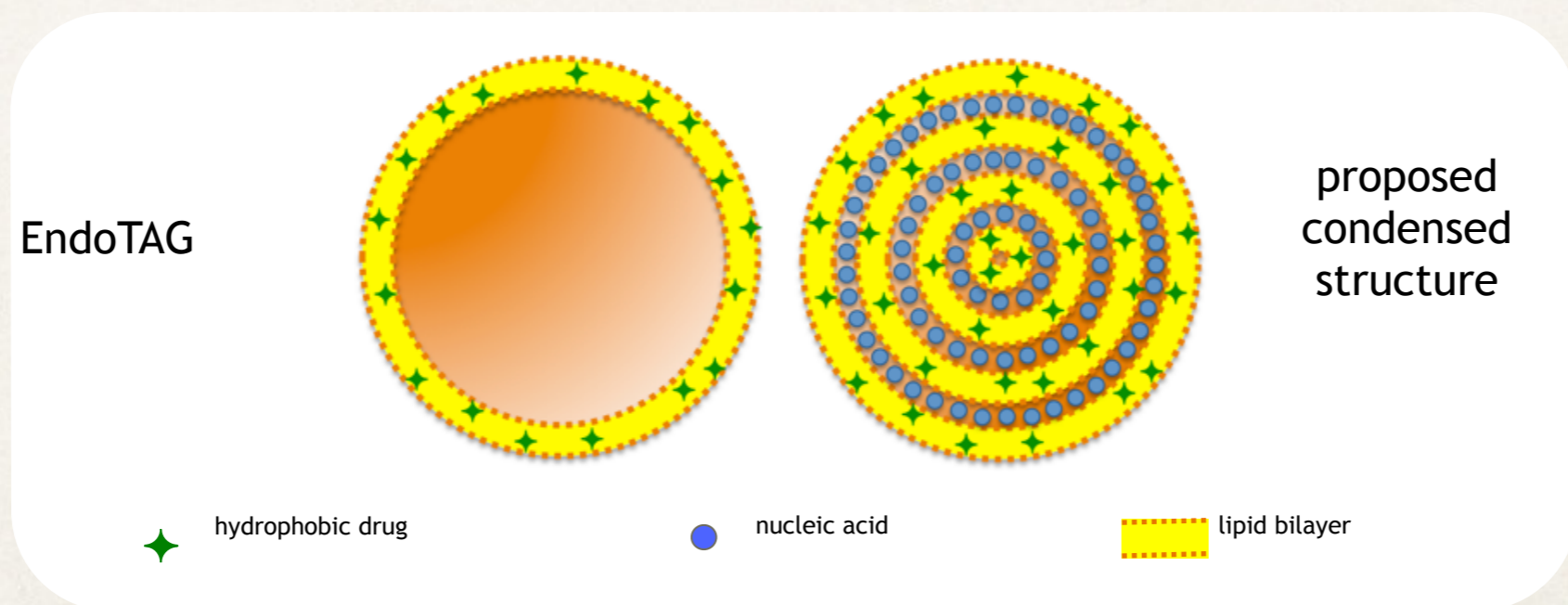
Stage III Trials

- ❖ 3 Component system:
 - ❖ DOTAP, DOPC & Paclitaxol
- ❖ Unilamellar Structure
- ❖ Passive Targeting , EPR and electrostatic favorability
- ❖ No systematic understanding of factors controlling:
 - ❖ Drug loading
 - ❖ Intracellular drug delivery

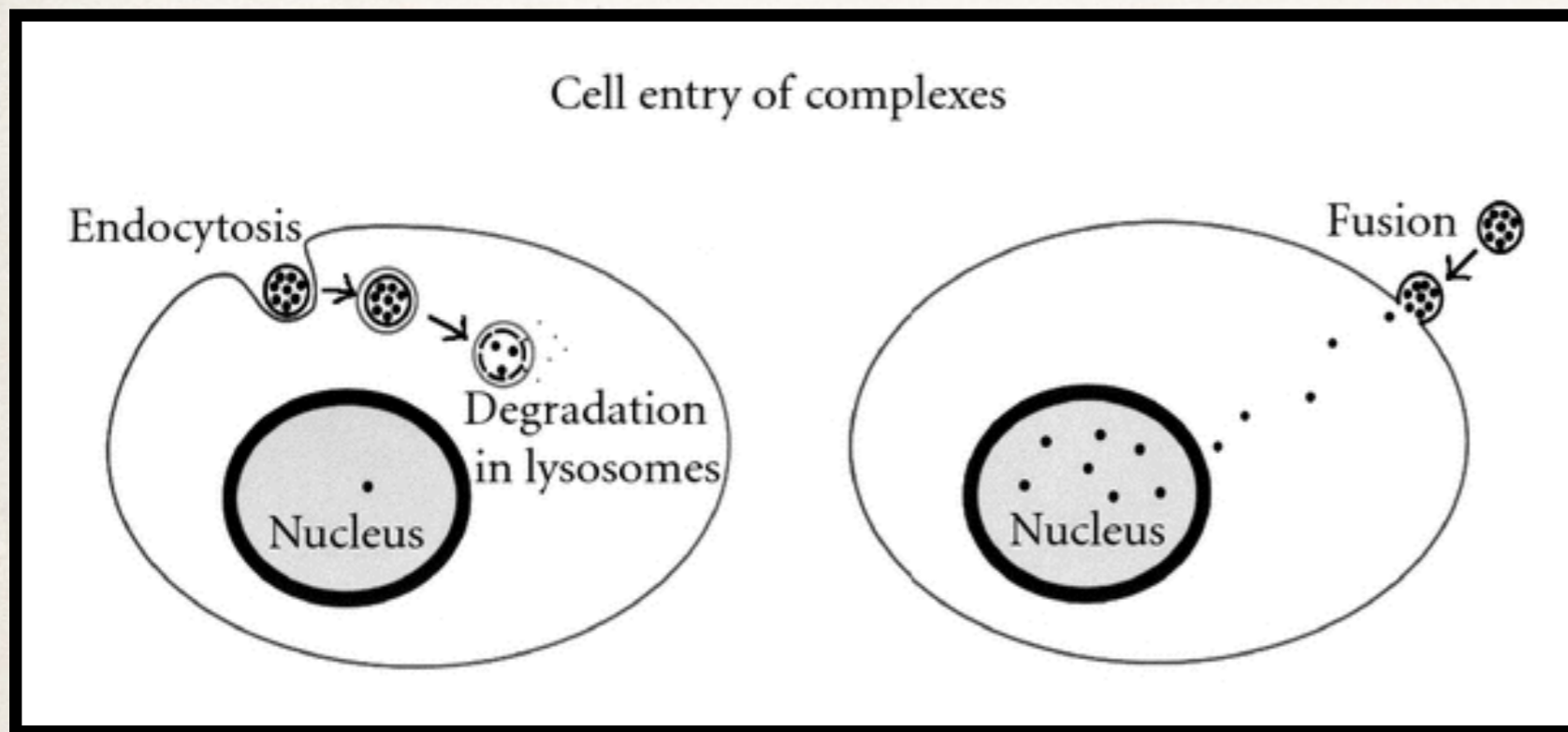


Proposed Methods to Improve Drug Loading and Delivery

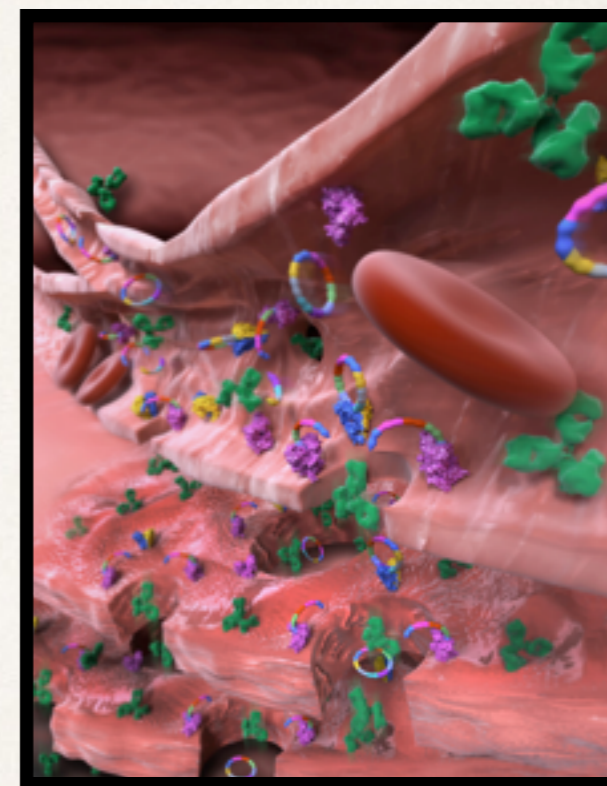
- ❖ Unilamellar vs Multilamellar
 - ❖ Achieve more drug / particle



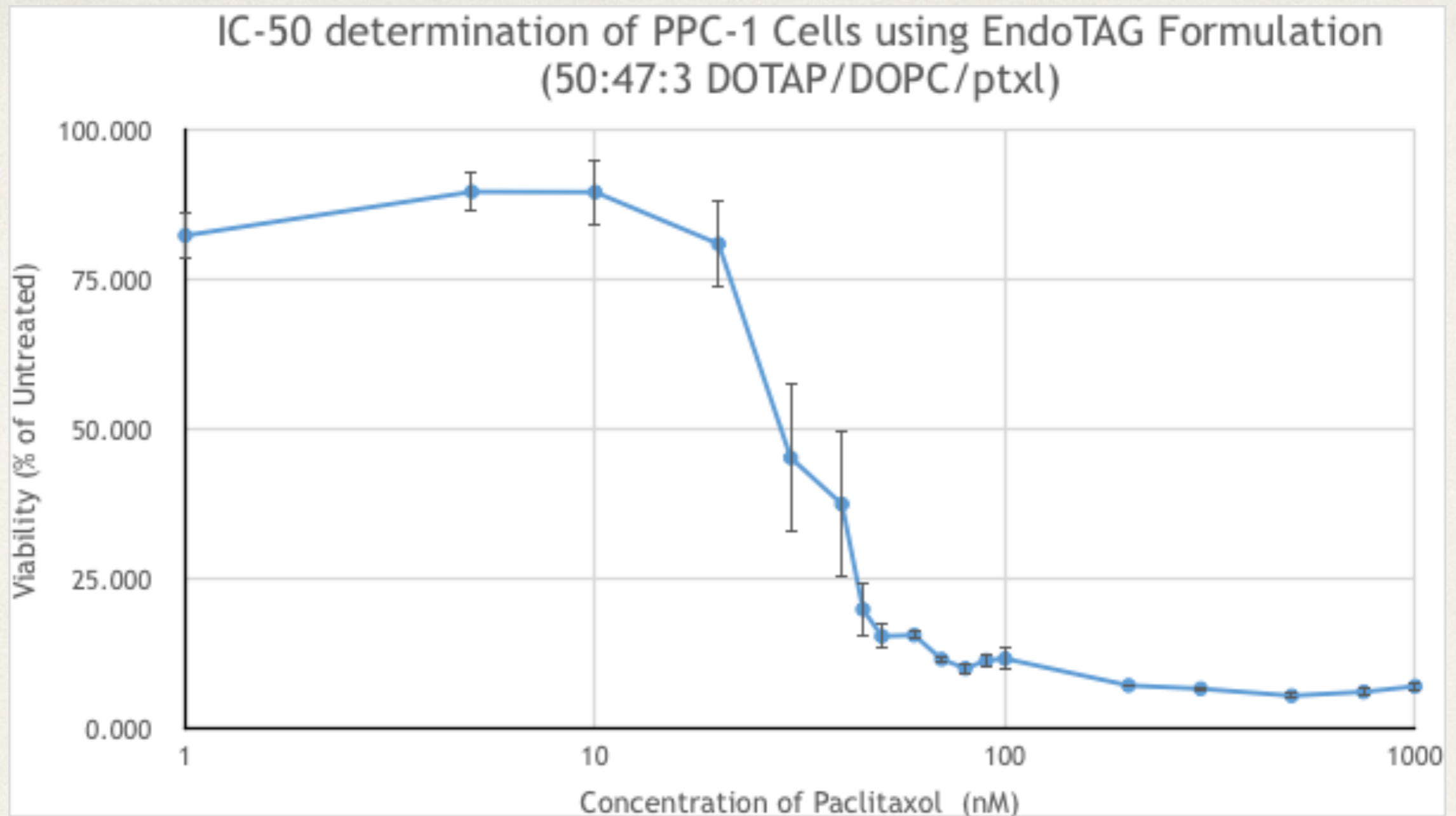
Cell Uptake and Drug Delivery



Endosomal uptake: endocytosis, fusion or endosomal rupture



EPR: enhanced permeation and retention effect through “leaky” tumor vasculature



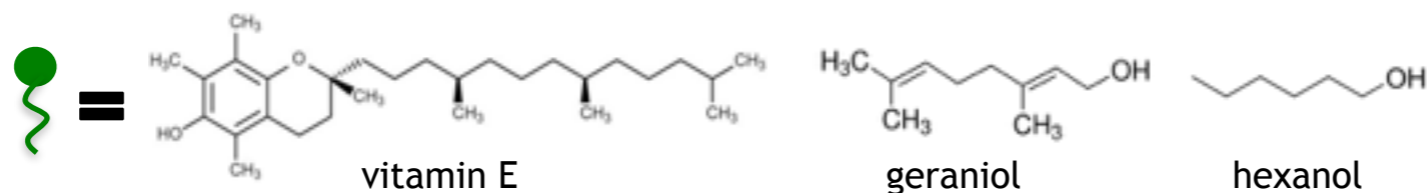
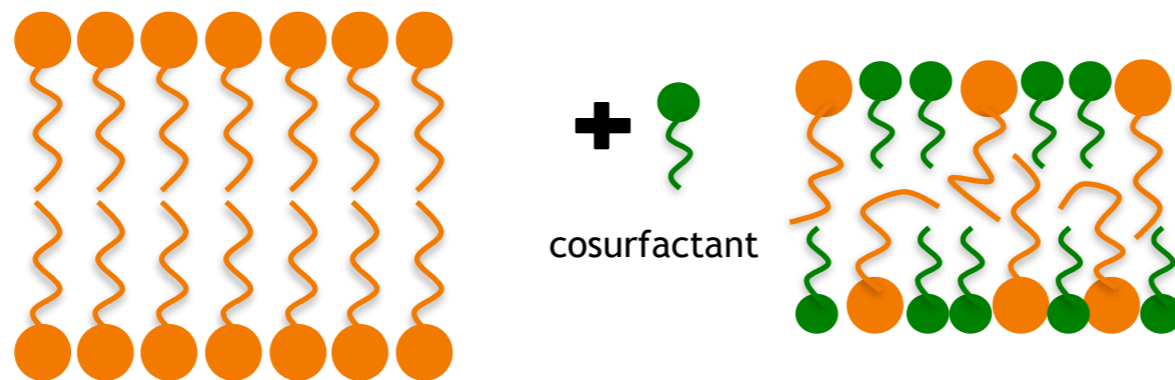
IC50 EndoTAG

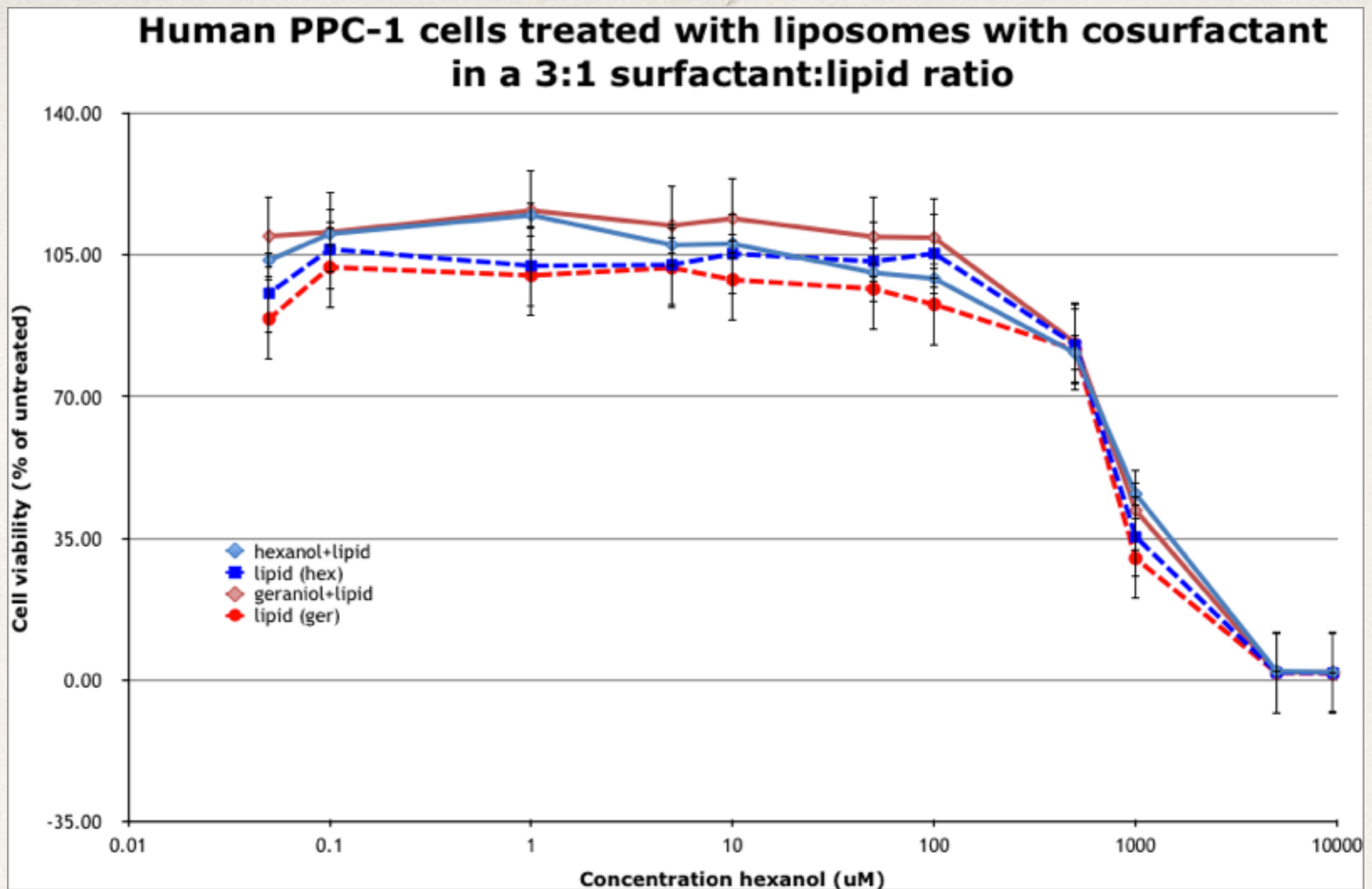
Preliminary step to compare to for studies

Results: Inhibitory Concentration at 50%: value at 50nM to serve as control for future experiments

Inquiry

Will more flexible membranes (achieved by adding cosurfactant) effectively accommodate more drug?





IC50 of Cosurfactants

Hexanol and Geraniol

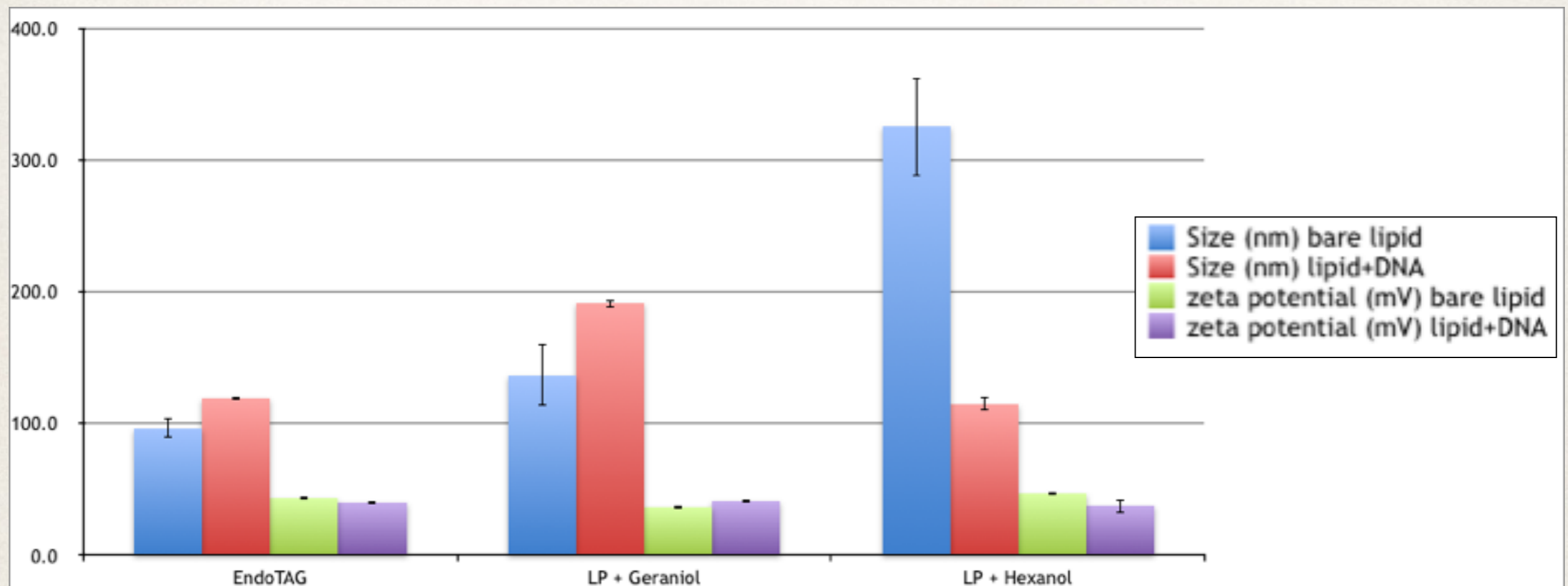
Results: Hexanol nor Geraniol are not toxic at the proposed concentrations. Both surfactants seem comparable at this time.

IC50: Drug and Surfactants in both Unilamellar and Multilamellar Liposomes

- ❖ Determine the effectiveness of liposomes with drug and surfactants, both bare (unilamellar) and with DNA (multilamellar).
- ❖ Currently waiting on results!

Zetasizer

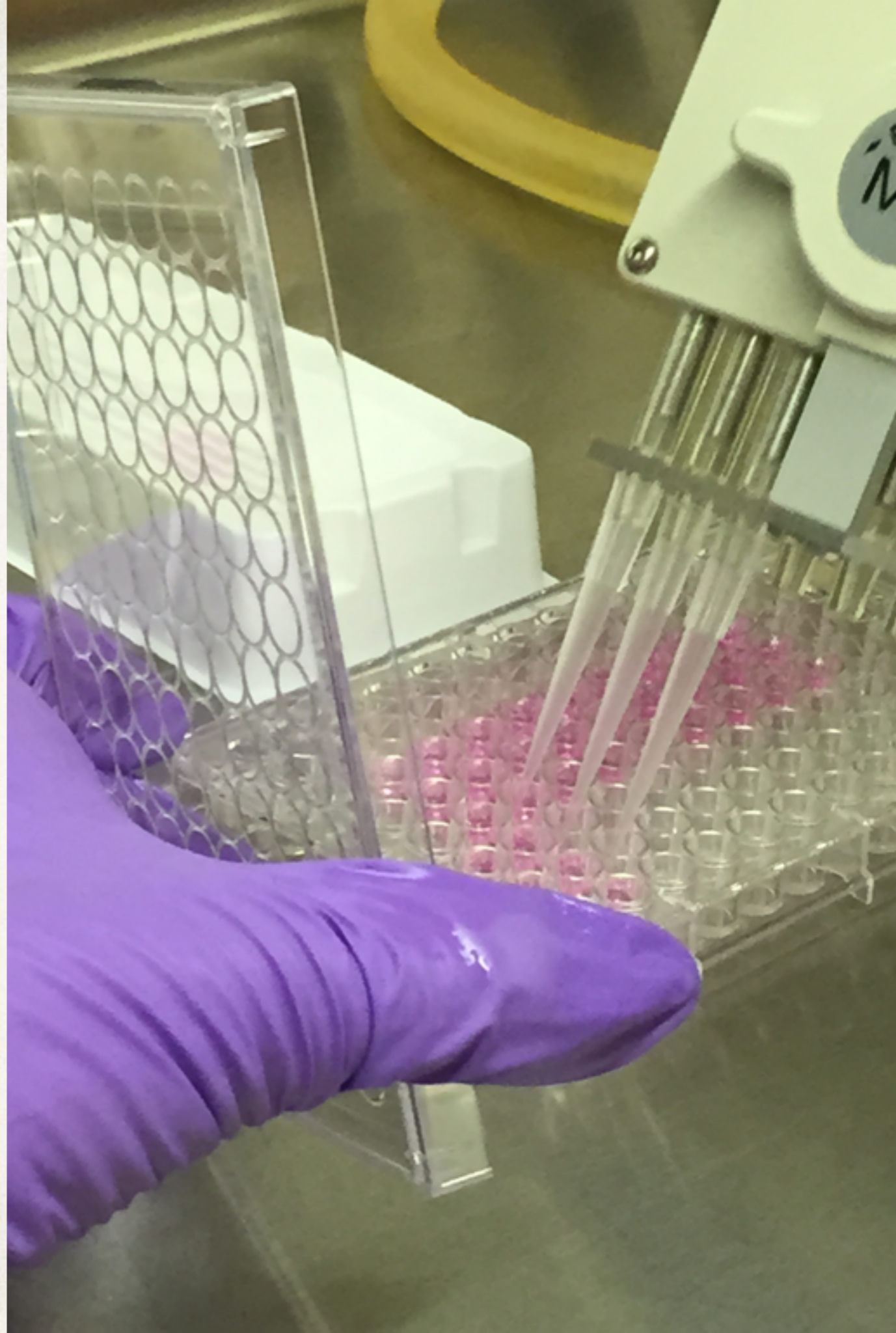
- ❖ One of the methods we use to characterize the physical properties of our liposomes.



Next Step

Cell Viability Assay Comparing:

- ❖ Consurfactants Geraniol vs Hexanol
- ❖ Unilamellar vs Multilamellar
- ❖ Control With and Without Cosurfactant (with and without drug)



Thank You

- ❖ MRL, Research Experience for Teachers Program
- ❖ Frank Kinnaman, RET Coordinator
 - ❖ Mary McGuan, Education Programs Assistant
- ❖ Victoria Steffes, Mentor / PhD Candidate
 - ❖ Safinya Group