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Combination Therapy of Prostate Cancer Utilizing Functionalized Iron Oxide Nanoparticles carrying TNF- α and Lactonic Sophorolipids

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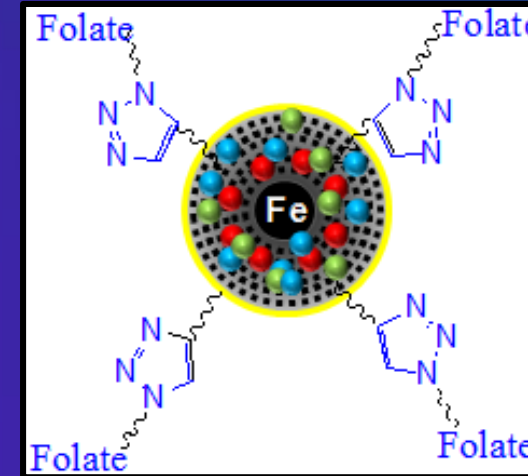
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Outline

- ▶ Introduction
 - ▶ What are nanoparticles?
 - ▶ Tumor Necrosis Factor-alpha (TNF- α) and Lactonic sophorolipids (LSLs)
- ▶ Experimental
 - ▶ Synthesis of IONPs & Surface Ligand Modification
- ▶ Results
 - ▶ Characterizations
 - ▶ Microscopy Images
 - ▶ Biological Assays
- ▶ Conclusion

Introduction: What are Nanoparticles?

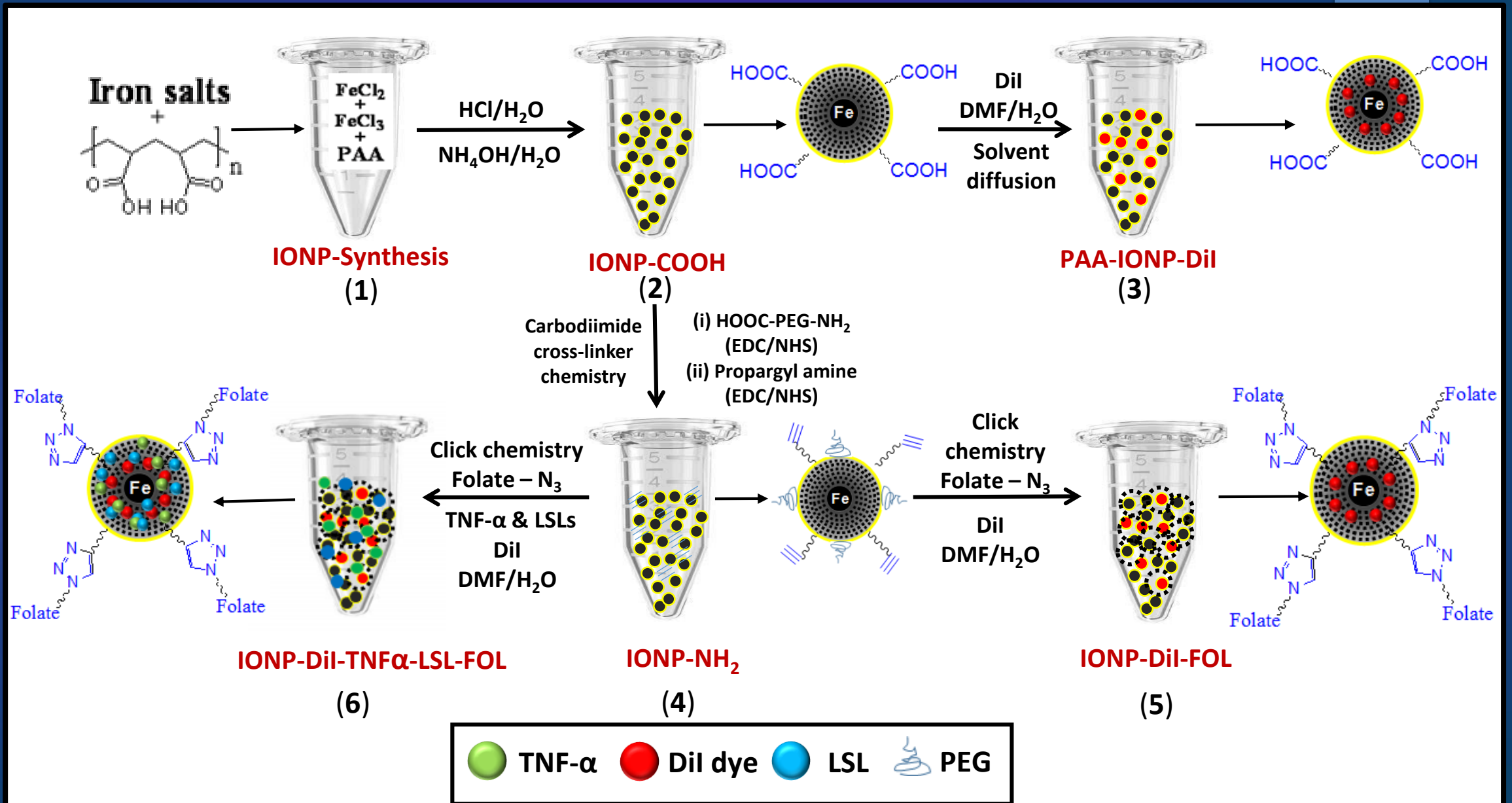
- ▶ Nanoparticles are tiny (1-100 nm) particles that exhibit unique properties and characteristics at nano-scale.
- ▶ Many uses in the field of biomedicine and therapeutics
 - ▶ Targeted drug delivery
 - ▶ Encapsulation of small molecules (drugs, optical dyes)
 - ▶ Dosage control and imaging
 - ▶ Surface ligand modification (folic acid) for receptor specificity
 - ▶ Only treat cells of interest
 - ▶ MRI Contrast Imaging (Iron Oxide nanoparticles)
- ▶ Our Aim: Treat LNCaP strain prostate cancer with a combination therapy of soluble TNF- α and LSLs with folate-functionalized iron oxide nanoparticles (IONPs)



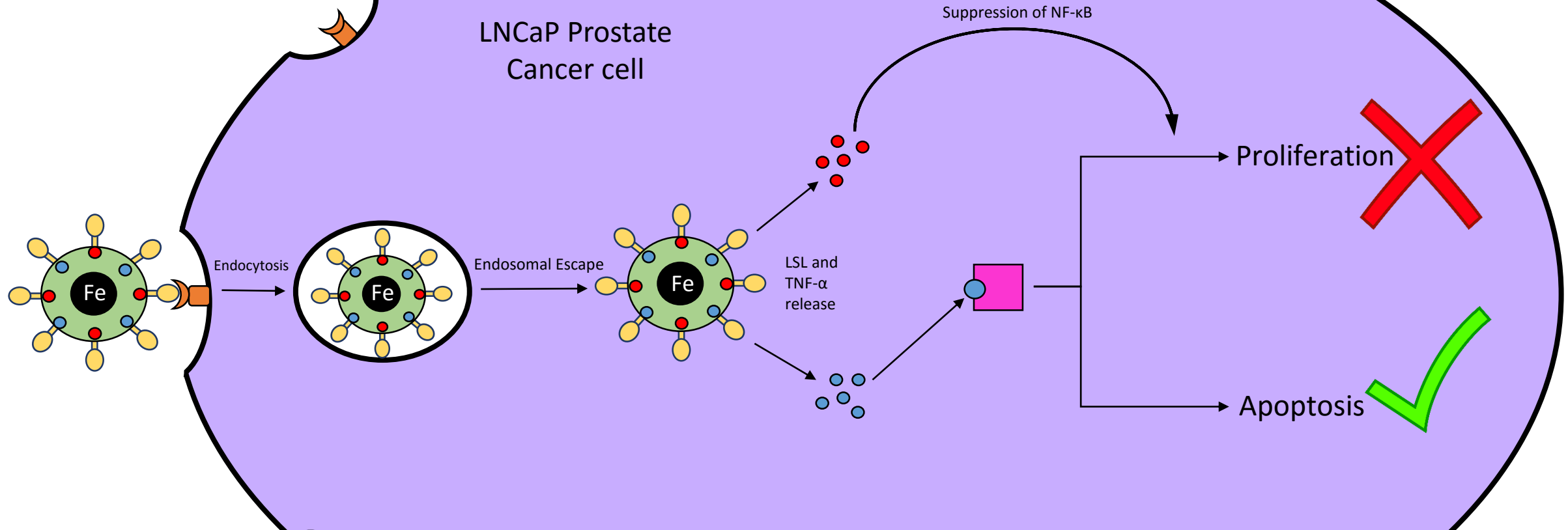
Introduction: Why use TNF- α and LSLs?

- ▶ TNF- α
 - ▶ Cytokine important in many cellular pathways
 - ▶ Apoptosis and proliferation pathways
 - ▶ In cancer cells, TNF- α and associated proteins behave aberrantly
 - ▶ Nuclear factor kappa B (NF- κ B) initiates proliferation unchecked
 - ▶ Binding to its receptor, TNFR-1, does not occur in tumor cells
 - ▶ Solution: Introduction of exogenous soluble TNF- α may help initiate cell death in tumors
 - ▶ Inspired by Aurimmune* (gold nanoparticle)
- ▶ LSLs
 - ▶ Glycolipids extracted from non-pathogenic yeast
 - ▶ Enhance immune response and reduce inflammation
 - ▶ Associated with large decreases in cytokine mRNA
 - ▶ Suspected inhibition of NF- κ B
 - ▶ Implementation inspired by Dr. Richard Gross' research
 - ▶ Hypothesis: Synergy between these two compounds?

Experimental: Nanoparticle Synthesis



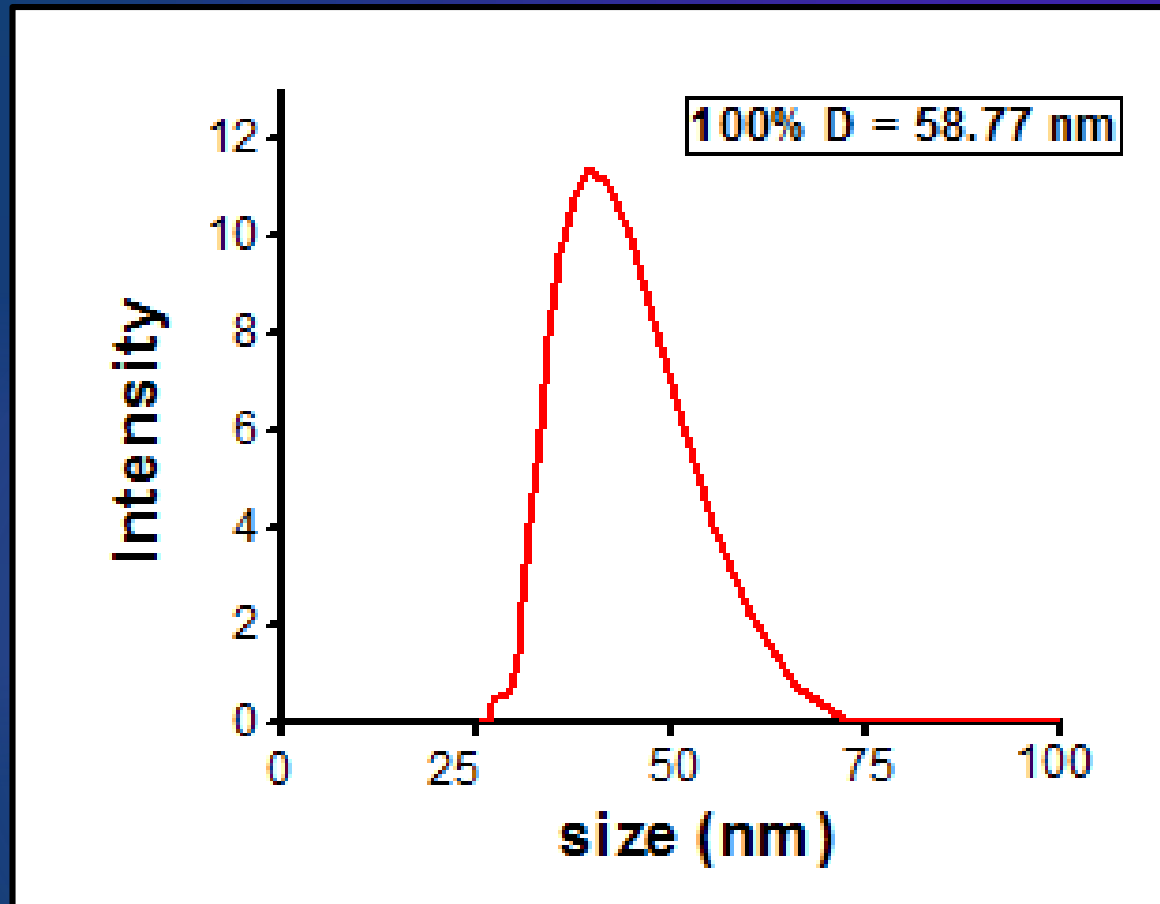
LNCaP Prostate Cancer cell



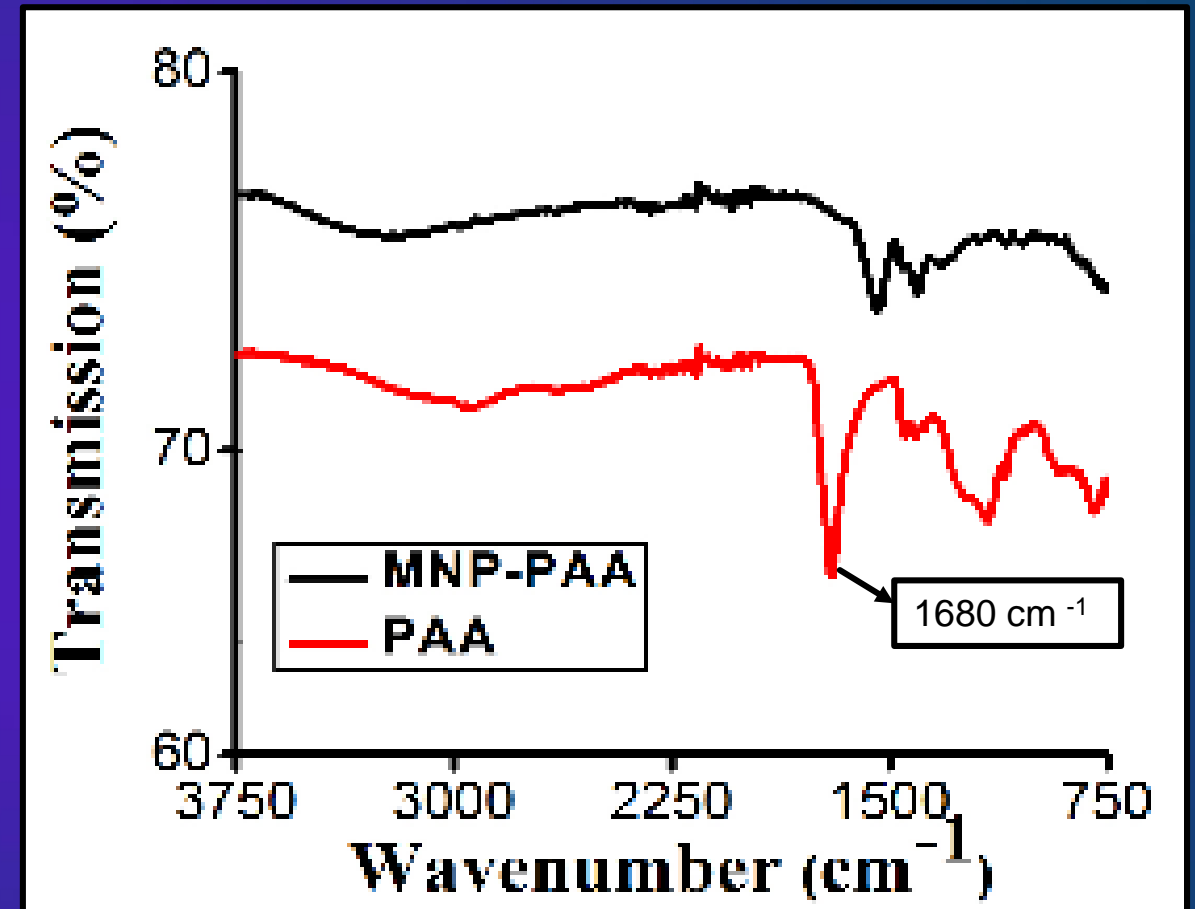
- = sTNFR-1
- = sTNF-α
- = LSLs
- 🍷 = Folic acid receptor
- 🍷 = Folic acid

Results: IONP Characterization

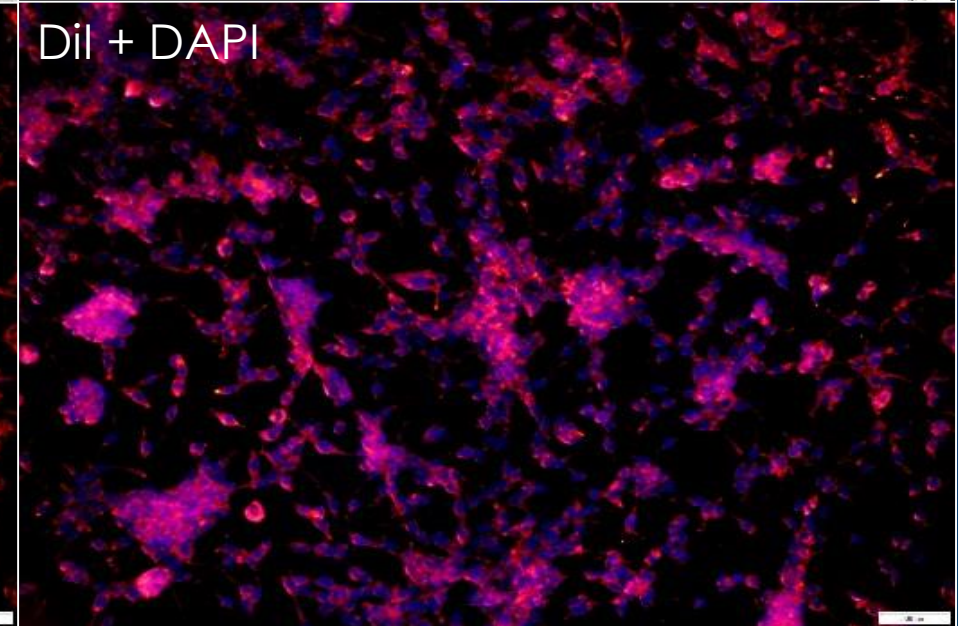
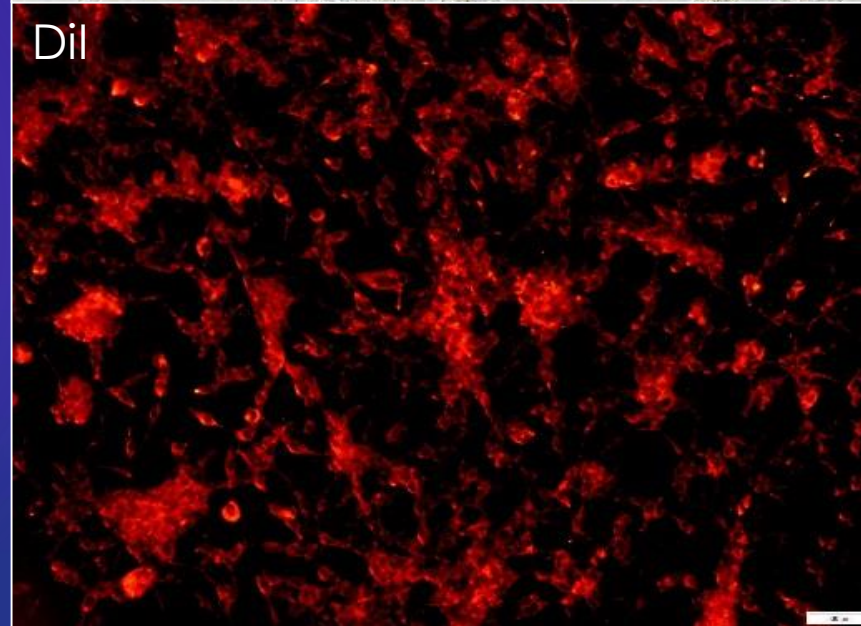
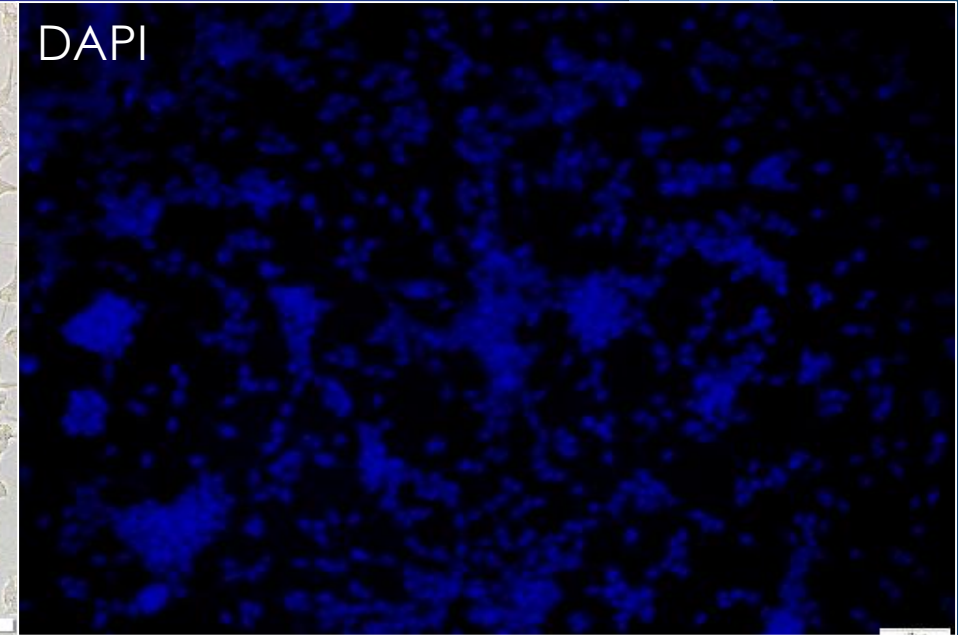
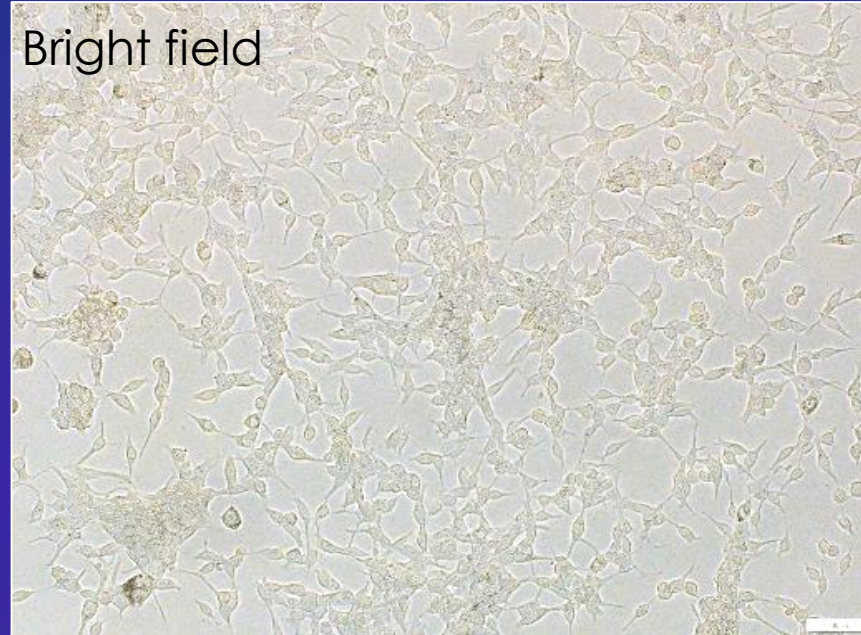
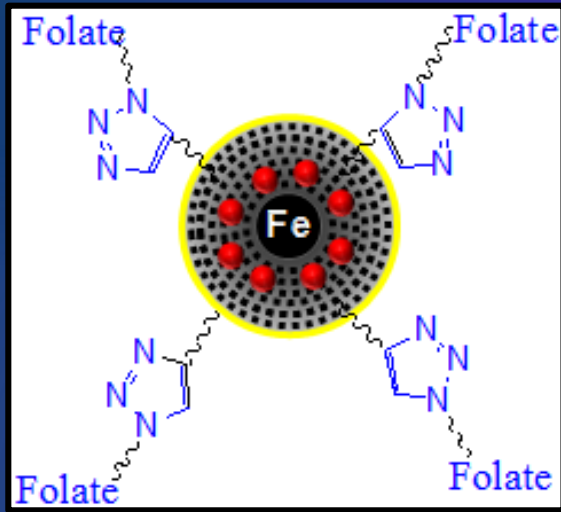
Dynamic Light Scattering



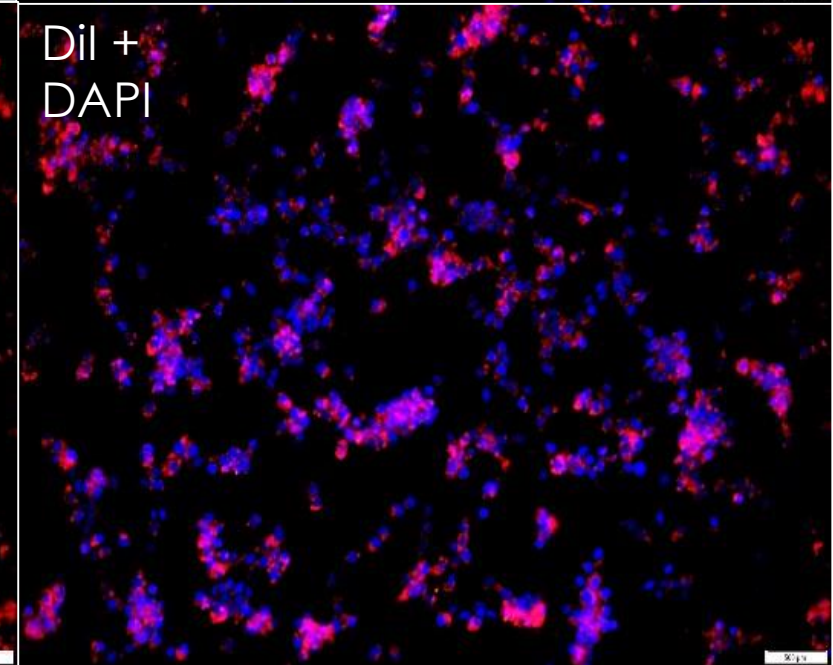
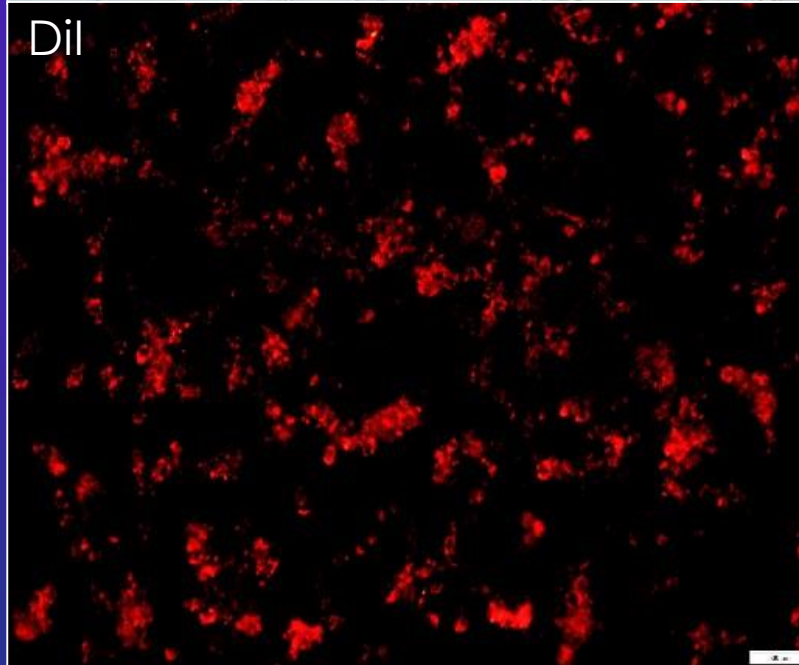
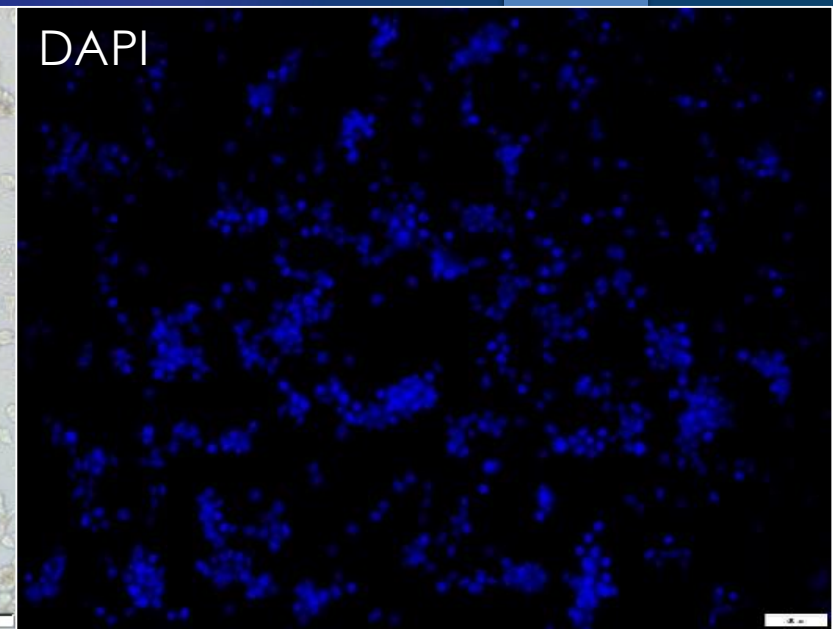
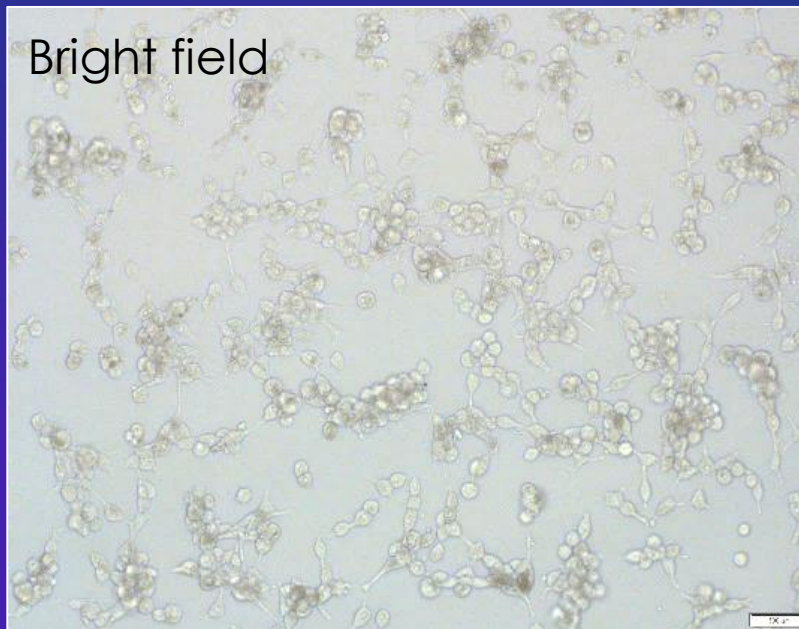
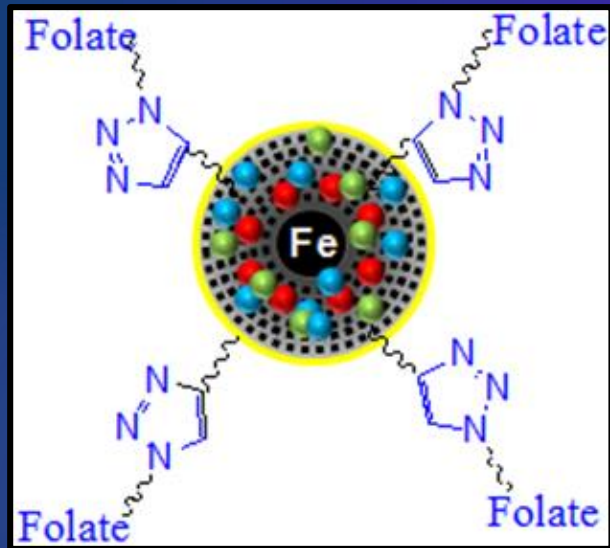
FT-IR



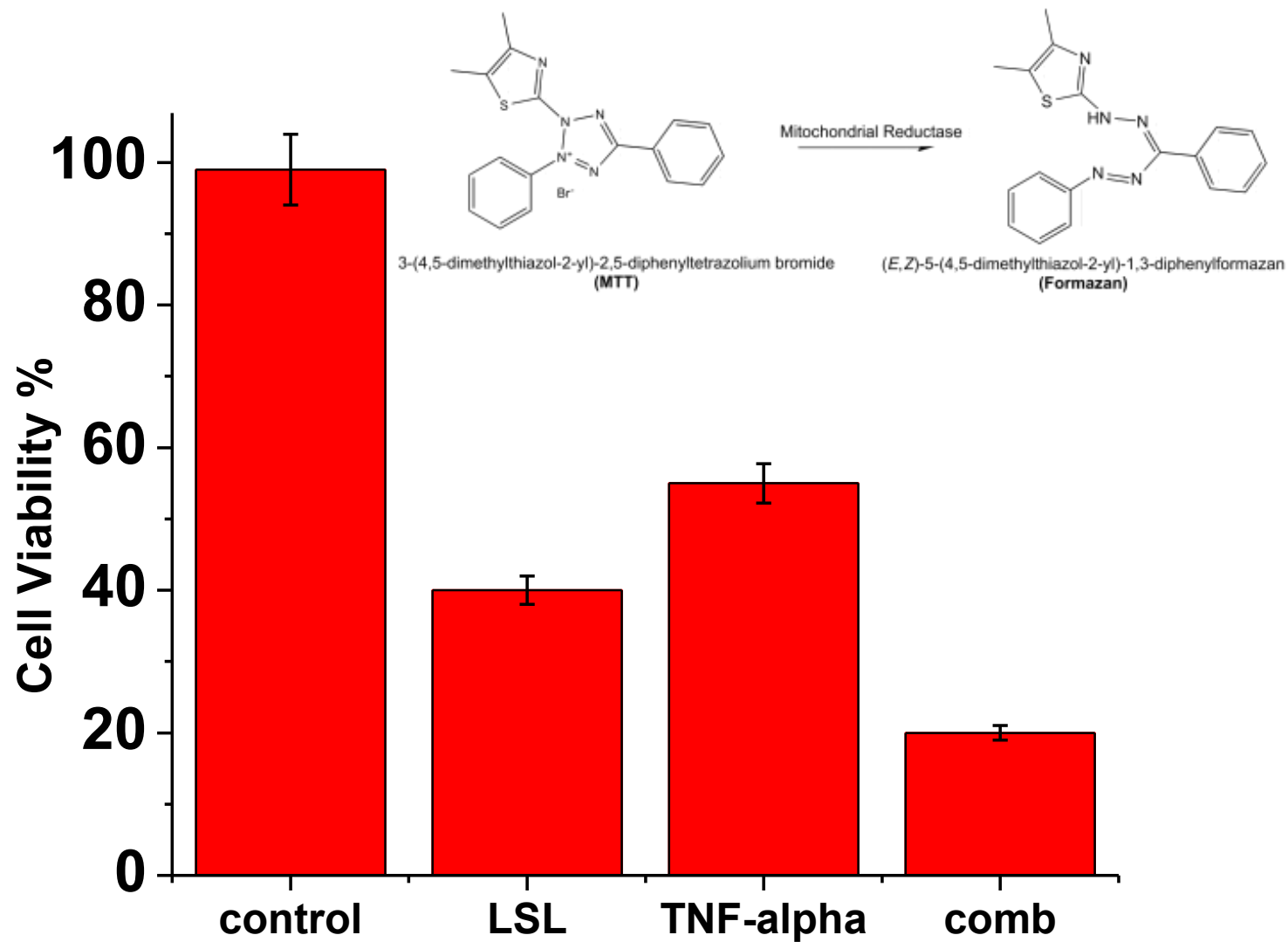
Results: Fluorescence Microscopy – Dye Internalization



Results: Fluorescence Microscopy – Dye and Combination Therapy

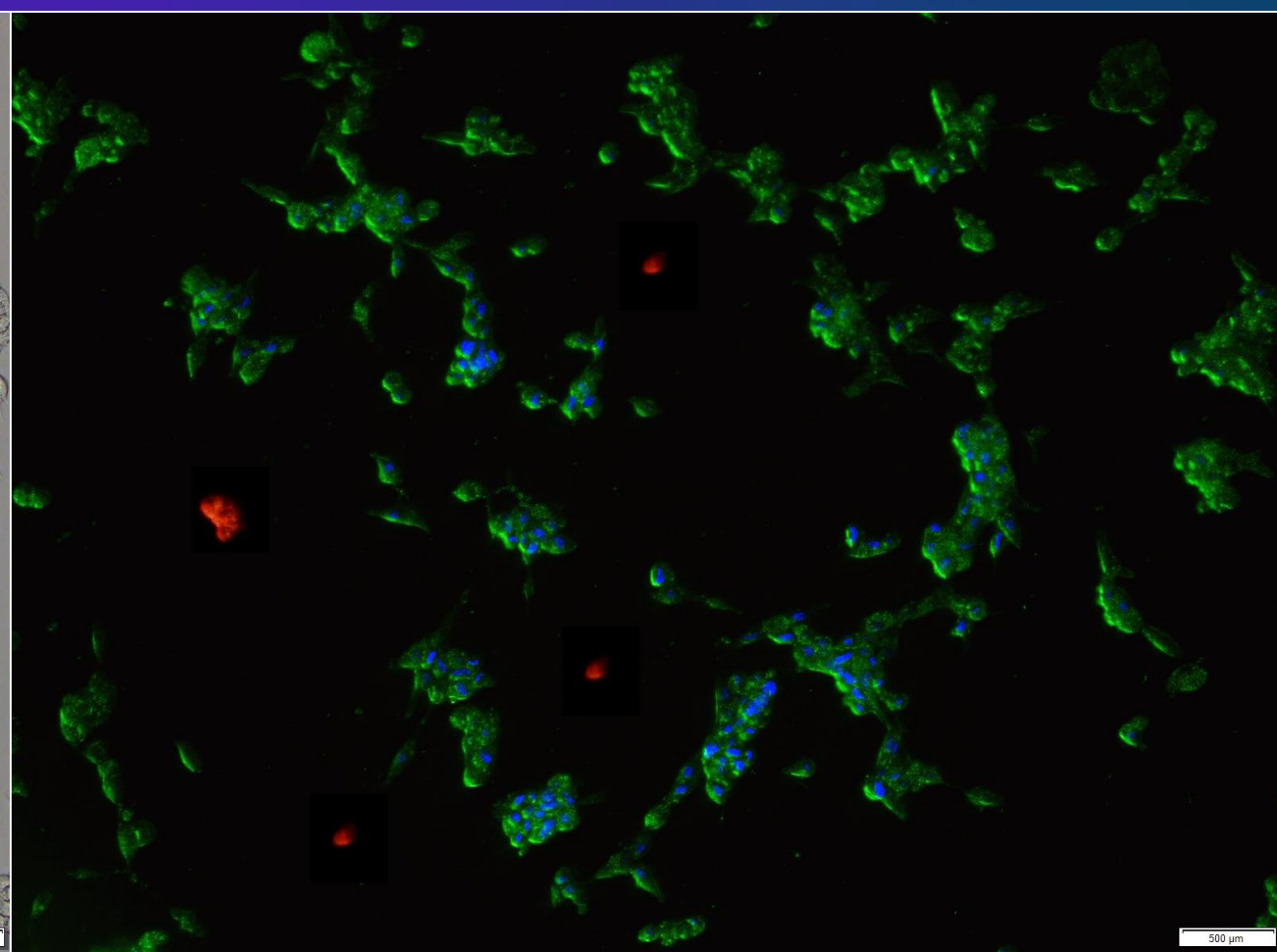


Results: MTT Assay



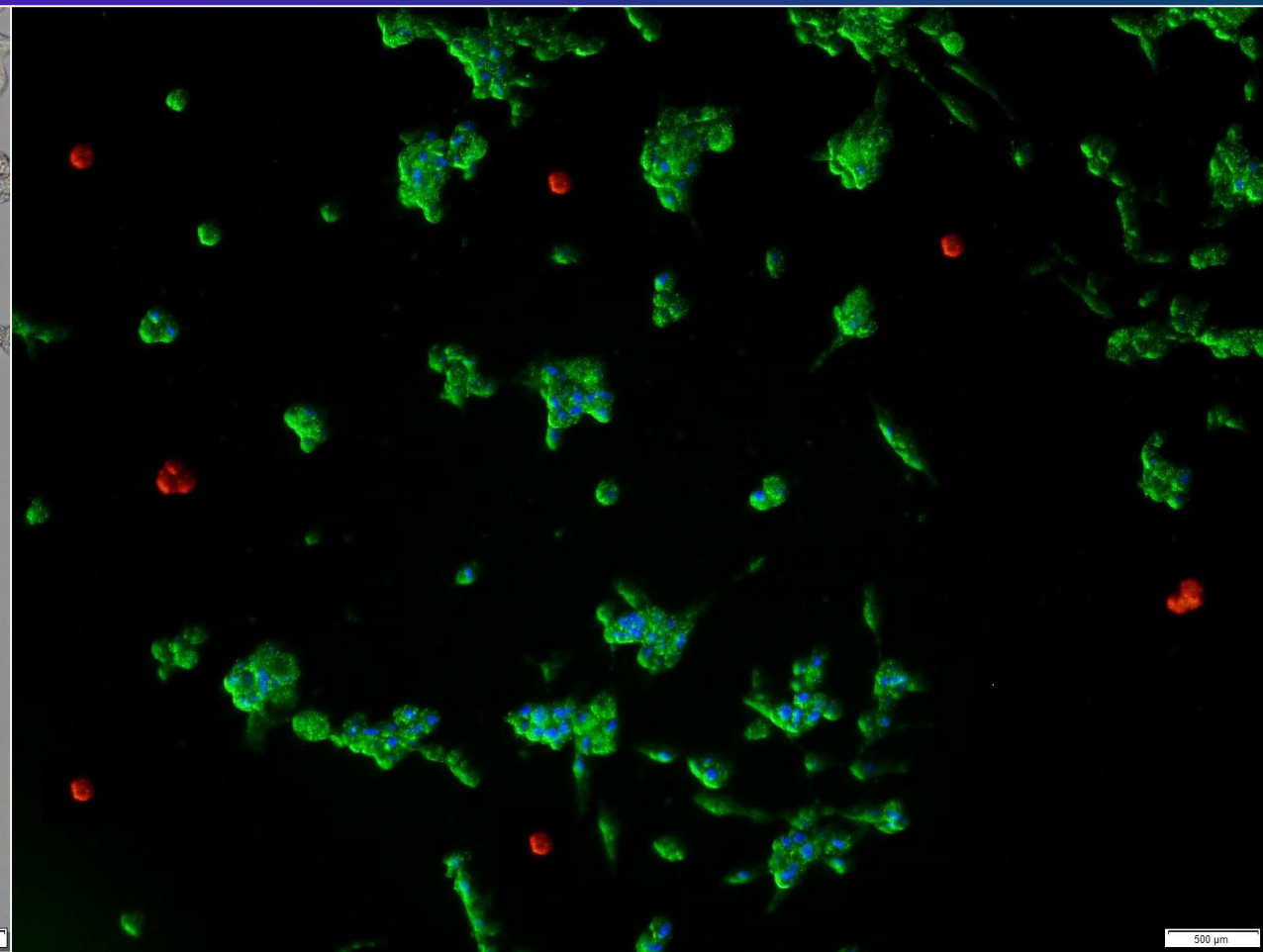
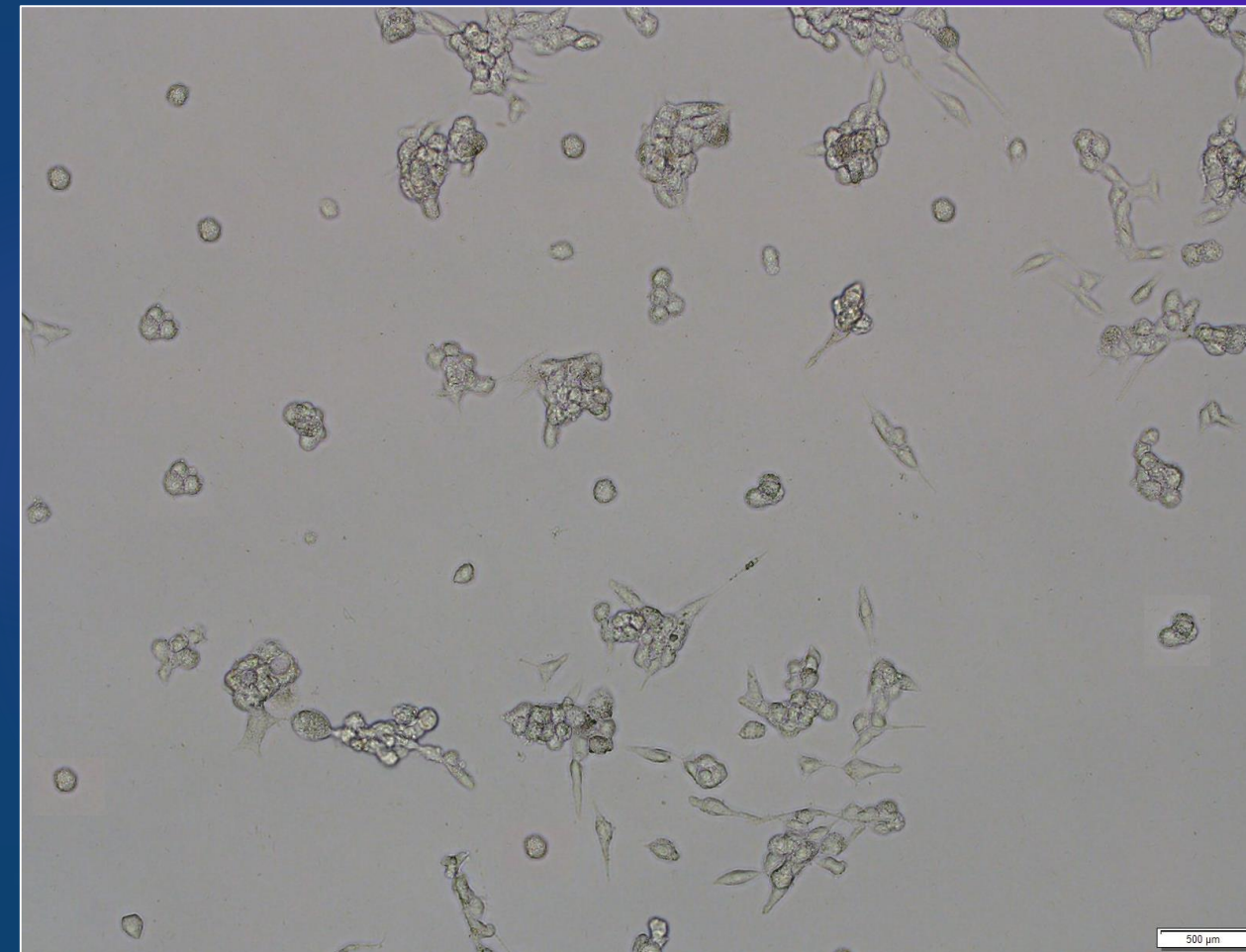
Results: Apoptosis/Necrosis Assay (TNF- α)

Annexin-V/Fluorescein
Hoescht
Ethidium homodimer

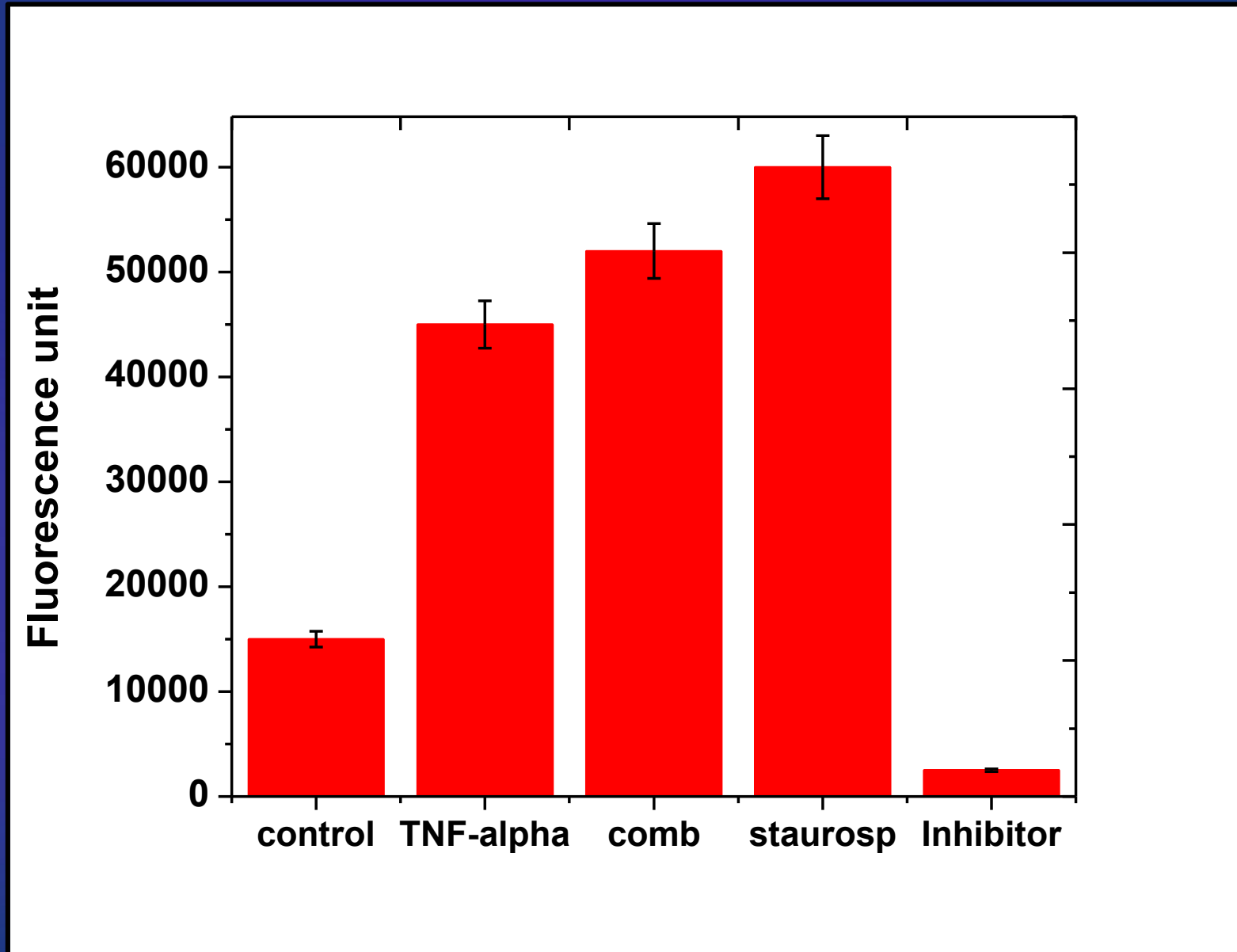


Results: Apoptosis/Necrosis Assay (Combination)

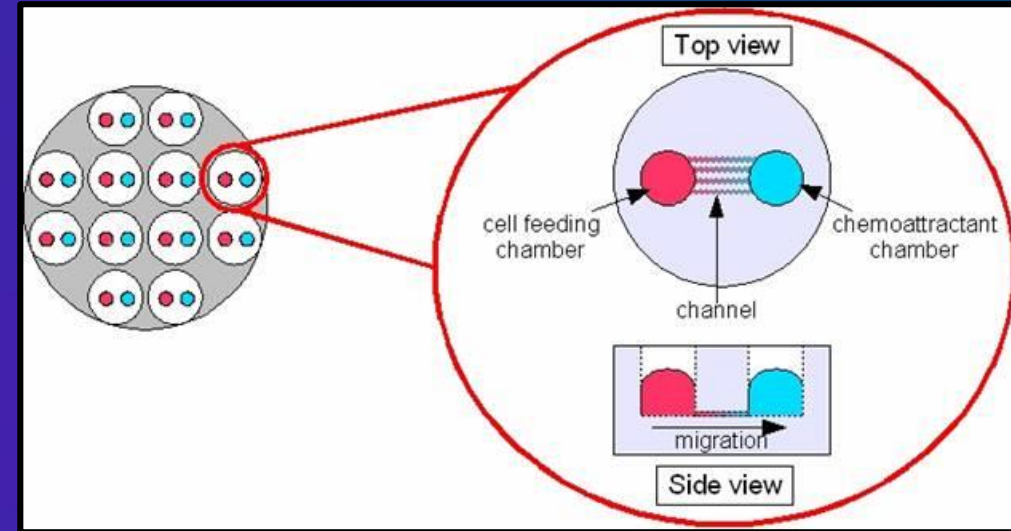
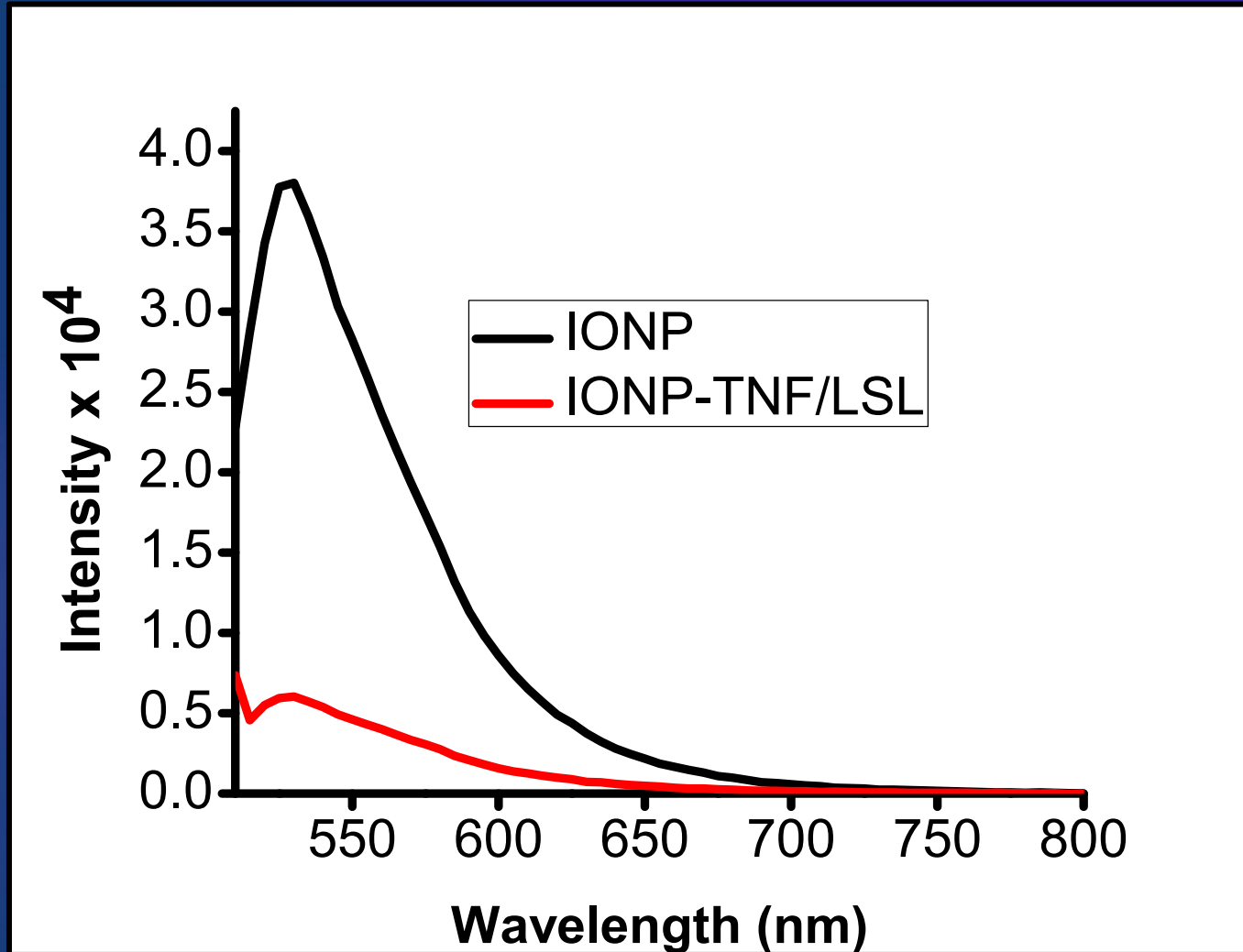
Annexin-V/Fluorescein
Hoescht
Ethidium homodimer



Results: Apoptosis/Necrosis Assay Results



Results: Migration Assay



Conclusions

- ▶ Successful synthesis of folate-conjugated IONPs and encapsulation of TNF- α and LSLs
- ▶ Results of cytotoxicity assays show up to 80% cell death with combined treatment after 24 hrs
- ▶ Significant increase in apoptotic initiation following 24 hr. incubation with TNF- α and combination treatment
- ▶ Our results support our hypothesis the synergistic combined therapy
- ▶ Next step: Look to in-vivo mouse models for treatment

Thank You!

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