Copper-Diethyldithiocarbamate Complex Loaded and DSPE-PEG-c(RGD) Surface Functionalized Liposomes for Treating Glioblastoma

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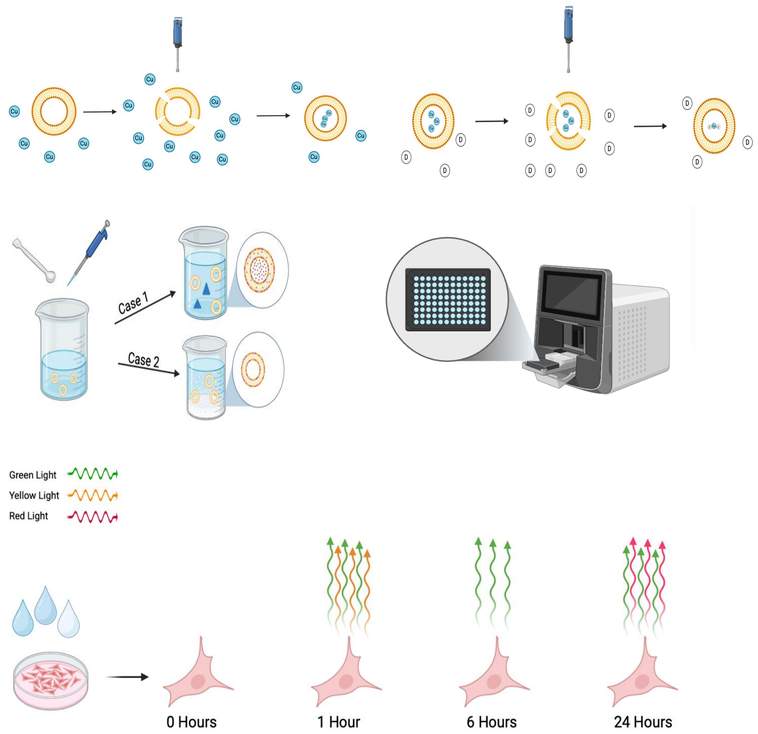
Research Questions

- Does surface functionalization of liposomes using cyclic RGD increase targeting efficacy on U87 glioblastoma cells?
- Does Cu-DDC_2 trigger controlled cell apoptosis on U87 glioblastoma cells?
- Can surface functionalized and drug loaded nanoparticles achieve higher U87 specific apoptosis rates?.

Background

Malignant Glioblastoma Multiforme is among the most aggressive and treatment-resistant form of brain cancer. Despite advancements in cancer therapies, the median patient survival time remains under 15 months [1]. New treatment methods using metal ions show promise, but are limited by instability within physiological conditions, off-target toxicity, and low blood-brain barrier penetration. To overcome these drawbacks, many researchers have examined the use of liposomes and other synthetic nanocarriers for delivering therapeutic molecules. However, the use of extracellular vesicles, a naturally produced cellular nanocarrier alternative has not been examined for many of these therapies. This research project seeks to engineer U87 GMB extracellular vesicles though the loading of $Cu(DDC)_2$, a studied anticancer compound, and DSP-PEG-c(RGD) for surface functionalization. The optimization of this procedure aims produce a new insight on a target-specific delivery strategy for delivering $Cu(DDC)_2$ into GBM cancer cells, while testing Copper ion induced apoptosis.

Methods



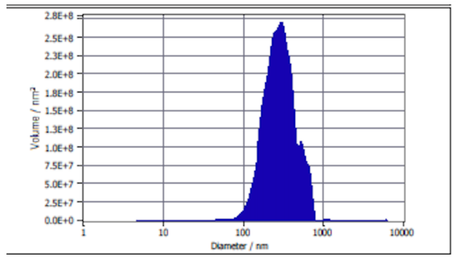
Future Direction

These results suggest that surface functionalization of liposomes increases Cu-DDC_2 delivery and glioblastoma cell apoptosis in vitro. Further studies should aim to characterize blood brain barrier passage, efficacy against 3D tumors, and undesired off-target toxicity using in vivo models.

Acknowledgements

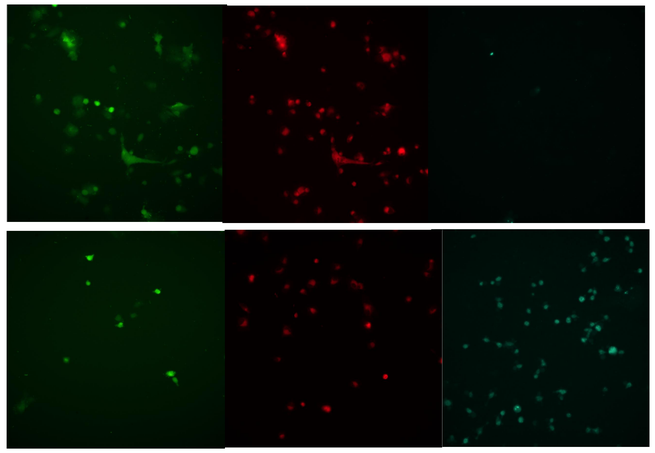
I thank Dr. Yan Li and Danyele Berry for their unparalleled guidance and support. This work was supported by the Bess H. Ward Honors Thesis Award. Finally, I want to acknowledge the FAMU-FSU College of Engineering and FSU Honors Program for their resources and mentorship.

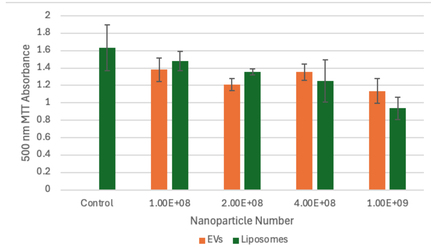
Preliminary Results



- Nanoparticle tracking analysis (NTA) shows normal extracellular vesicle (EV) size distributions between 100nm -800 nm. Some large size is likely due to aggregation during preparation.

- Triple fluorescent microscopy 30 minutes after treatment and 12 hours after treatment. Initial green emittance indicated successful ROS formation. High red emittance followed by decreased red emittance indicated successful mitochondrial depolarization. Increase in blue emittance indicates increased caspase activity 12 hours after treatment.





- MTT viability assay indicates both drug loaded liposomes and EVs achieved similar degrees of apoptosis over 24-hour period. Both forms of treatment induced apoptosis more effectively than negative control treatment.

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