Targeted Drug Delivery for Charge-Based Biomaterials

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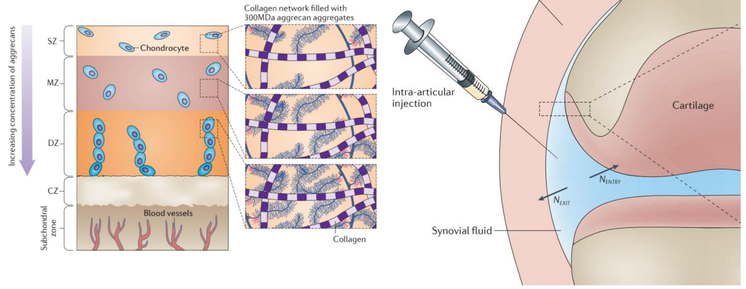
Abstract

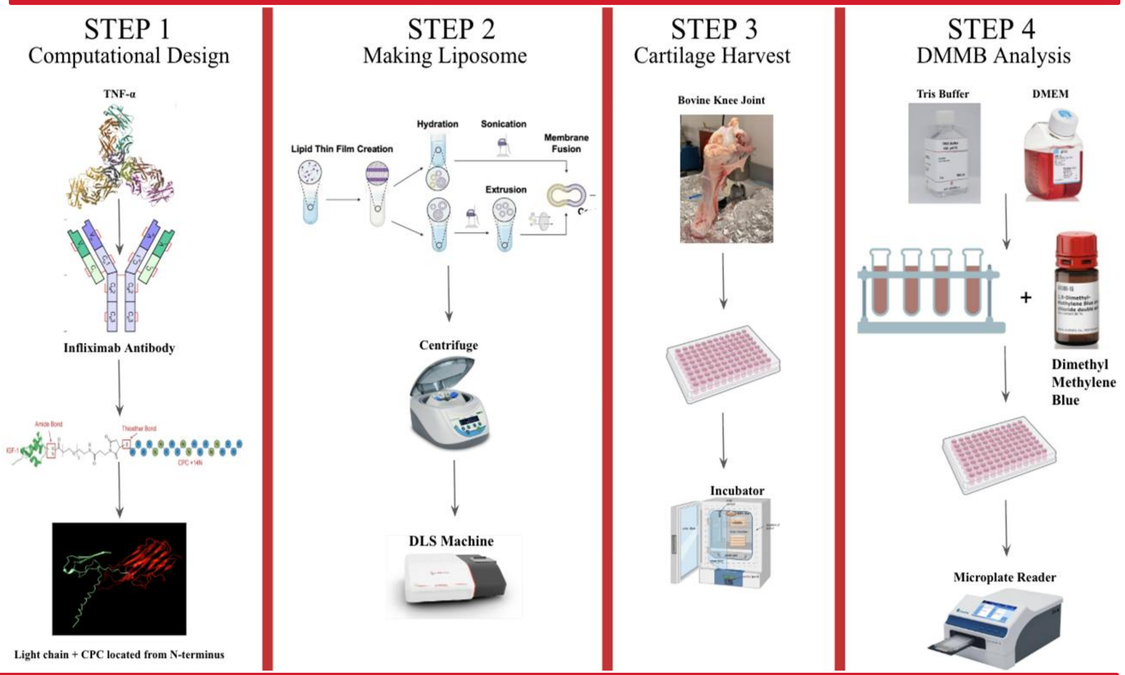
Osteoarthritis is a joint disease linked with severe pain and inflammation. Due to factors such as age, injuries, and obesity, osteoarthritis can develop in a variety of patients, limiting their mobility. The goal of the Bajpayee Lab is to develop a method of drug delivery that allows an osteoarthritis treatment to fully penetrate through the cartilage and retain there for an effective amount of time. This process involves taking advantage of charge-based drug delivery. The goal of the YSP students is to understand how to computationally design therapeutics for osteoarthritis treatment, while also learning the basics of delivering such drugs. In the lab, we have made liposomes and worked with cartilage explants, while computationally, we have been designing protein inhibitors.

Background

Due to the tissue's dense composition of collagen fibers and proteoglycans, the ability for drugs to penetrate into the cartilage is limited. As the cartilage contains negatively-charged glycosaminoglycans (GAGs), one promising solution is to engineer positively-charged drug carriers which may be injected into the surroundings of the tissue and are attracted to the negatively-charged GAGs, allowing for drug retainment. This research investigates computationally designed cationic protein therapeutics and drug transport through the cartilage matrix. We hypothesize that positively charged drug carriers will improve drug penetration and retention in the cartilage, leading to more effective treatment of cartilage-related diseases.



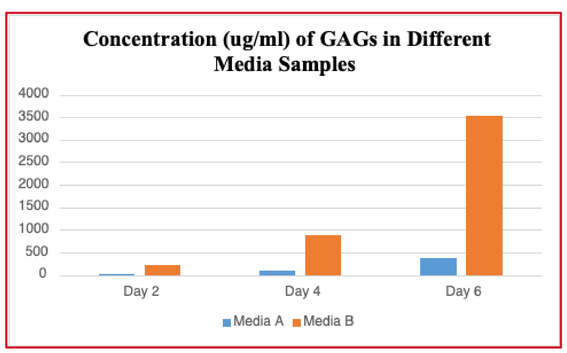
Experimental Methods



Results

Liposome Size Characterization by Dynamic Light Scattering

Inspired By	CPC Position	Clashes	RMSD
Light Chain	C - Terminus	511	43 pruned atom pairs is 0.692 angstroms
Light Chain	N -Terminus	101	43 pruned atom pairs is 0.692 angstroms
Heavy Chain	C - Terminus	107	67 pruned atom pairs is 0.562 angstroms
Heavy Chain	N - Terminus	123	69 pruned atom pairs is 0.445 angstroms



Conclusion and Future Steps

Conclusion

- Positively charged carriers are able to penetrate deep enough into the cartilage
- Successfully modeled new anti-TNF-α biologics
- Developed liposomal carriers capable of navigating dense cartilage structures
- Sterilizing and cultivating bovine knee cartilage for cells to culture
- Validated final treatment success via DMMB assay metrics

Future Steps: Building on our current results, testing how positively charged carriers can overcome the cartilage barrier to deliver the new TNF-*a* drugs. Given that damaged cartilage is packed with negatively charged molecules, using a positive charge acts like a magnet, pulling the drug deep into the tissue rather than letting it wash away in joint fluid.

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