

Application of Peptide Amphiphile Micelles in Atherosclerosis Diagnosis

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Introduction & Objective

Cardiovascular disease (CVD) is currently the leading cause of death worldwide

- almost 18 million deaths/year
- Atherosclerosis: formation of plaques in arteries
- buildup of cholesterol, fat, and calcium, or hydroxyapatite (HA), on arterial walls
- prone to rupture, which can result in myocardial infarction

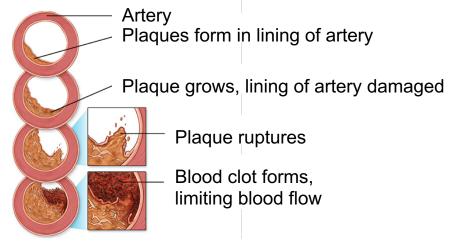


Figure 1. Development of atherosclerotic plaques (Source: Mayo Clinic)

Project Objective: synthesize self-assembling micelles with hydroxyapatite binding peptide (HABP) that can target and bind to HA within plaques

Summer Objectives:

- purify HABP samples
- confirm conjugation of peptide using MALDI mass spectrometry

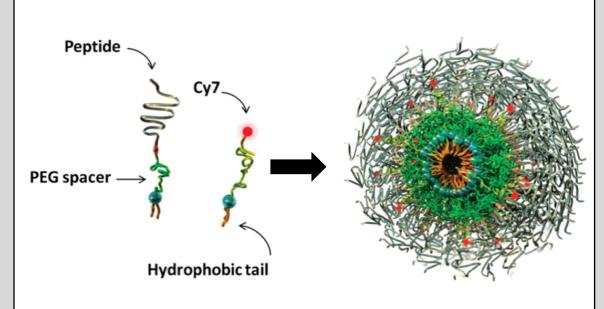


Figure 2. Model of self-assembling micelle (right) and amphiphile subunits. One subunit is a peptide amphiphile (left) and the other is an amphiphile fluorescently labeled with Cyanine-7 (middle). (Source: Chung, et al. Adv. Healthcare Mater. 2015)

Techniques & Skills Learned

High Performance Liquid Chromatography (HPLC)

A technique used to identify, purify, and collect the separate constituents of a sample based on the interactions of the particles with the column they are run through.

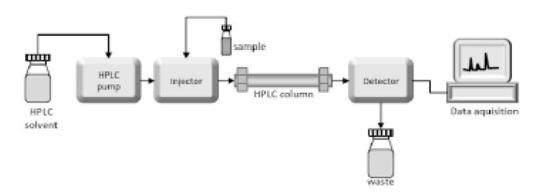


Figure 3. Instrumentation of HPLC (Source: LaboratoryInfo)

Matrix-Assisted Laser Desorption/Ionization (MALDI) Mass Spectrometry

A method of determining the mass of a particle by vaporizing a sample and creating ions that travel to a detector, where their mass is determined.

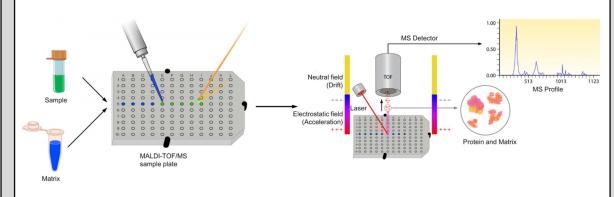


Figure 4. The process of MALDI-TOF mass spectroscopy (Source: Creative Proteomics)

Dynamic Light Scattering (DLS)

A method of determining the size of nanoparticles suspended in solution by sending a laser through the sample and analyzing the diffraction patterns.

Tissue Sample Imaging

The procedure of imaging stained tissue samples from various mouse organs using a compound light microscope.

Transmission Electron Microscopy (TEM)

A form of microscopy involving the transmission of electrons through a specimen to form an image (results in a 2D image).

Flash Freezing

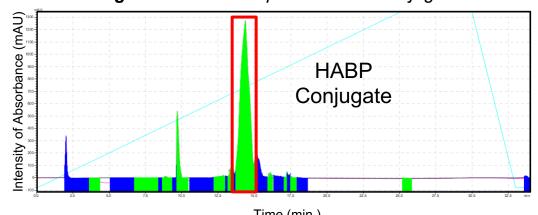
A technique of rapidly freezing tissue samples to -80°C and below temperatures using liquid nitrogen.

Methods and Results

Purification of HABP Conjugate

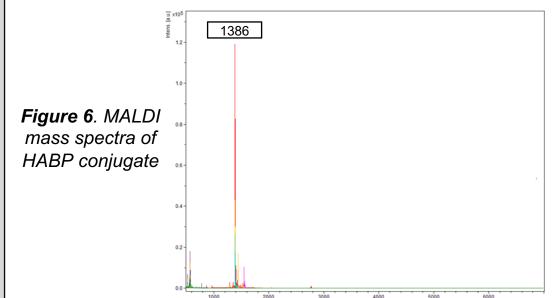
- The conjugate sample was purified using HPLC.
- The conjugate elutes within the 13-15 minute

Figure 5. HPLC Graph for HABP Conjugate



Matrix-Assisted Laser Desorption/Ionization (MALDI) Mass Spectrometry

• MALDI mass spec. confirmed the presence of the conjugate and identified its mass as 1386.



Transmission Electron Microscopy (TEM)

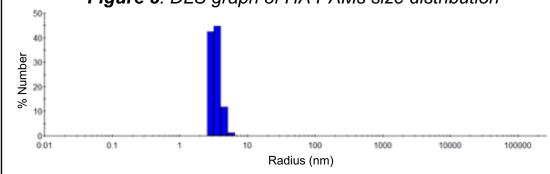
TEM was used to view the formation of HA PAMs.

Figure 7. TEM imaging of hydroxyapatite peptide amphiphile micelles (HA PAMs). PC: Deborah Chin

Dynamic Light Scattering (DLS)

DLS was used to measure the radius of HA PAMs as 16 nm.

Figure 8. DLS graph of HA PAMs size distribution



Impact of Professor's Research

The Chung Lab focuses on the research of nanoparticles, specifically self-assembled micelle systems, to improve the clinical diagnosis and/or treatment of various diseases. Researchers in the lab work to develop peptide amphiphile-based micelles that can target specific locations within the body, furthering the potential for theranostic applications, including noninvasive diagnostic procedures and more efficient/effective drug delivery. Research currently being conducted in the lab investigates the applications of nanoparticles in diseases such as atherosclerosis, kidney disease, and cancer.

Next Steps for You & Advice for Future SHINE Students

Being a part of the SHINE program this summer has affirmed my interest in biomedical engineering and in research. I hope to further explore BME research in the rest of my high school career and in college.

My advice to any future SHINE students is:

- Ask plenty of questions
- Do not be afraid to ask for help
- Be patient (research takes time!)

Acknowledgements

I am incredibly grateful to Dr. Chung for welcoming me into her lab, to my mentor Deborah Chin for all of her guidance and instruction, and to all of the members of the Chung Lab, to whom I could always go with my questions. A final thank you to Dr. Mills and the SHINE team as a whole for their efforts to make SHINE such an educational and rewarding experience.