NDnano
Notre Dame Nanoscience and Technology

NDnano Summer Undergraduate Research
2021 Project Summary

1. Student name & home university:
Qinxiao Wu, University of Notre Dame

2. ND faculty name & department:
Dr. Prakash Nallathamby, Department of Aerospace and Mechanical Engineering
Dr. Paul Helquist, Department of Chemistry and Biochemistry

3. Summer project title:
Magnetic Nanocarrier based, Precision Combinatorial Chemotherapeutics Treatment Against Metastatic Cancer Cells

4. Briefly describe new skills you acquired during your summer research:
Over the summer, I learned cell subculturing techniques to properly bring up various cell lines from liquid nitrogen storage and maintain their growth through appropriate media and buffers. In addition, I also learned how to apply treatment to the cells in order to selectively permeabilize cancer cells under an external magnetic field. At the same time, I learned to synthesize gold magneto-silica nanoparticles (Au-MagSiNs) with and without fluorescence (rhodamine - RITC) The fluorescence was visible on the AMI machine which I learned to operate and analyze data from. The data allowed me to determine whether the amount of gold on the nanoparticles were sufficient and if not, I could modify the amount accordingly. After synthesizing various types of nanoparticles, I learned to use a transmission electron microscopy to image them. To contribute to the ongoing research project from past summers, I also observed tail vein and retro-orbital drug injections into mice and was able to sacrifice them to obtain various organs which were used for histopathology and MRI imaging.

5. Briefly share a practical application/end use of your research:
The leading cause of fatalities in breast cancer is metastasis. To increase the success rate of metastasis-free survival, there is a need to tackle therapy-resistant metastatic forms of the disease with novel, patient-friendly, and combinatorial treatment regimens. At present, doxorubicin (Dox) regimens are the standard of care for tumor debulking although it does not stop metastatic recurrence and presents cardiotoxicity. Vacuolar ATPase (V-ATPase) H + pump inhibitors such as diphyllins prevent metastasis, but the ubiquitous occurrence of this target raises concerns of off-target toxicity. A solution is targeted delivery of therapeutics to reduce the off-target effects while minimizing drug dose side-effects. So by magnetically permeabilizing MagSiNs formulations into the cancer cells, the active form of the drugs can be released through a magnetic trigger. The drugs can then be selectively compartmentalized into the cancer cells, and the V-ATPase inhibitor will work synergistically with the doxorubicin to reduce cancer cell numbers and inhibit cancer metastasis. Further tests to make MagSiNs into a platform technology will mitigate the side effects in chemotherapeutics for a variety of cancers.

6. 50- to 75-word abstract of your project:

This project aims to target cancer cells by tuning the magnetic field-induced force exerted by label-free magnetic nanomaterials at the cell membrane to selectively permeabilize the more compliant cancer cell membranes but not the stiff healthy cell membranes.

7. References for papers, posters, or presentations of your research:

N/A

One-page project summary that describes problem, project goal and your activities / results:

Due to the side effects and induced cardiotoxicity of anthracyclines (e.g. doxorubicin), oncologic treatments need to be improved to lower these risks. The purpose of the project is to test the biocompatibility of the magneto silica nanoparticles (MAgSiNs) and doxorubicin-loaded MAgSiNs in cell cultures and a mouse model. Primarily, human umbilical vein endothelial cells(HUVEC) was used as the control cell line, whereas breast epithelial cancer cells (MDA-MB-231), prostate cancer cells (PC3), ovarian cancer cells (A2780 and SK-OV-3) were used to test the effectiveness of the proposed design. For the mouse model, we conducted a biodistribution of the MAgSiNs and doxorubicin-loaded MAgSiNs along with histopathology of organs to confirm that the nanoparticles did not cause inflammation.

Recently developed magneto-silica nanoparticles (Mag-Si-Ns of ~5-8 nm) in the Nallathamby lab have been tuned to selectively permeabilize cancer cells under an external magnetic field, followed by a triggered release of a drug cocktail through an external alternating-current electromagnetic field. The MagSiNs possess a cobalt ferrite core and a piezoelectric fused silica shell. Anticancer drugs (Dox and Diph) encapsulated on MagSiNs are co-administered to specifically inhibit cancer growth and metastasis in the cell lines tested, while avoiding toxic side-effects on healthy control endothelial cells (HUVEC). In conclusion, the drugs@MagSiNs formulations were magnetically permeabilized into the cancer cells. The active form of the drugs were released through a magnetic trigger. The drugs were selectively compartmentalized into the cancer cells, and the V-ATPase inhibitor worked synergistically with doxorubicin to reduce cancer cell numbers and inhibit cancer metastasis.

Prior to the initialization of the project, OE19 and OE33(oesophageal cancer) cells were used to teach me proper sterile handling and cell subculturing techniques. I washed the cells in Dulbecco's phosphate-buffered saline (DPBS), detached with 0.25% trypsin, centrifuged at 280G, and then resuspended in proper growth media (RPMI1600). This process was altered slightly to thaw cells from liquid nitrogen. To apply the treatment of MAgSiNs, a hemocytometer was used to count the number of cells in solution. This allowed for the solution to be diluted properly so each well in the plates contained an approximately equal amount of cells. After MAgSiNs were applied under a magnetic field, assays were conducted in order to determine cell viability.

After the MAgSiNs were properly synthesized, the nanoparticles (NPs) were injected into the tail veins of each mouse (200 uL of 0.5 mg/mL NPs). In order to trace the movement of the NPs, I sacrificed the mice and took out specific organs (e.g., heart, liver, lungs, feces pellets, kidney, and spleen). Then using the AMI machine, I was able to detect the amounts of NPs in each organ at different times (4hr, 8hr, and 24hr) in order to determine where they accumulated.

In conclusion, this project was based on extending the research done in previous years and finalizing the platform technology of MAgSiNs.