NDnano Summer Undergraduate Research
2016 Project Summary

1. Student name: Andrea Oviedo

2. Faculty mentor name: Dr. Tiffanie Stewart

3. Project title: Magnetoelectric Nanoparticles to Specifically Target Cancer Cells *in vitro*

4. Briefly describe any new skills you acquired during your summer research: During my summer research, I learned how to tissue culture using several lines of cells including ovarian cancer cells (DOV-13) and brain tumor cancer cells, in both monolayer and spheroid cultures. In addition, I learned how to fabricate magnetoelectric nanoparticles, also known as MENs, and how to image them using AFM and fluorescent microscopy.

5. Briefly share a practical application/end use of your research: The end goal of our research is to create non-invasive, targeted drug delivery systems for cancer treatments. Our project consisted of studying the specificity of magnetoelectric nanoparticles intake in several cancer cell and healthy cell lines to understand how these particles can be functionalized to *only* target cancer cells while sparing the surrounding healthy tissue during cancer treatments.

To this day, targeted drug delivery systems in cancer treatment remain a formidable challenge. However, nanomedicine is paving the way for externally controlled, on-demand release of drugs using magneto-electric nanoparticles, or MENs. These unique nanoparticles exhibit a nonzero magnetoelectric effect, which can not only amplify a low intensity external magnetic field but also generate an additional local electric field. MENs take advantage of the different membrane electric properties between cancer cells and healthy cells. By remotely applying a weak magnetic field, MENs create an external electric field that changes the nanoporosity of the cell membrane, allowing them to penetrate into the cancer cells (a process known as nanoelectroporation) while leaving the healthy cells undisturbed. Tumor cells have a substantially lower electric potential and therefore display a lower threshold for nanoelectroporation. Therefore, MENs are capable of specifically "targeting" cancer cells as drug delivery carriers, while sparing healthy cells in the process.

Our study focused on the specificity of $CoFe_2O_4$@$BaTiO_3$ MENs intake using four different cell lines, two healthy and two cancer cell lines, under the application of externally applied d.c. magnetic fields of varying intensities. All cell lines were treated with fluorescently functionalized MENs with varying magnetic field gradients. One experiment compared DOV-13 ovarian cancer cells versus LP9 cells, which mimic the healthy lining of the intraperitoneal cavity. The other experiment showed specificity between glioblastoma brain tumor cells and HUVEC endothelial cells that mimic cells lining the blood brain barrier. The final experiment consisted of co-culturing ovarian cancer spheroids in a collagen matrix with healthy LP9 cells and treating both cells lines under the same variables. As we anticipated, MENs successfully

penetrated into both DOV-13 and glioblastoma cells in monolayers and had little penetration in the healthy cell lines. However, the MENs were not effective in penetrating into spheroids with 6 hours of 1500 Oe magnetic field exposure. Overall, the experiment was a success, but if we were to do this experiment again, we would increase the concentration of MENs and the treatment time in the spheroid cultures to see if that would increase the MENs penetration.

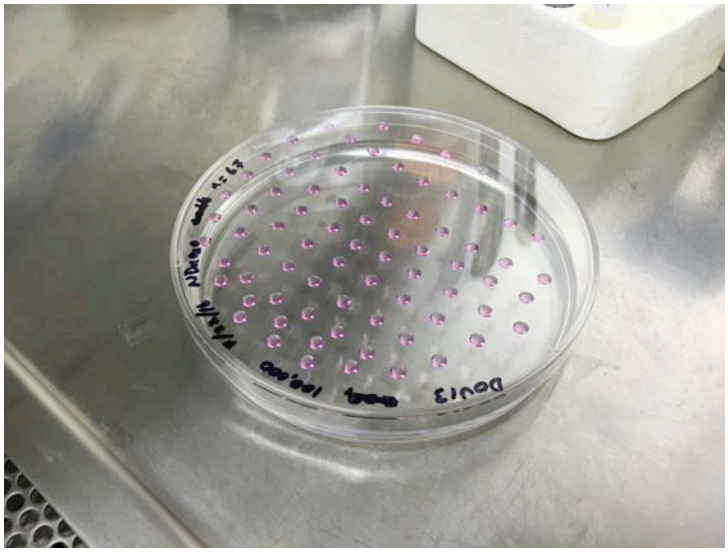

Figure 1: Spheroid culture of DOV-13 ovarian cancer cell line.

Publications (papers/posters/presentations): Magnetoelectric Nanoparticles to Specifically Target Cancer Cells *in vitro* (Poster presentation, July 27th 2016).