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NURF Project Summary 2012

Briefly describe any new skills you acquired during your summer research:

- Fluorescence-quenching titrations to determine binding affinity of ligands to an antibody

Please briefly share a practical application/end use of your research:

- Treatment of multiple myeloma with minimal side effects from therapeutic cancer drugs.

Multiple myeloma is a malignancy of the plasma cells, which is characterized by tumor development in the bone marrow. Unfortunately, because of interactions with the bone marrow environment, the tumor develops resistance to cancer drugs such as doxorubicin. This resistance, known as cell adhesion mediated drug resistance, makes multiple myeloma presently incurable.

The goal of my research summer was to help create a nanoparticle that has the ability to overcome this cell adhesion mediated drug resistance and destroy the tumor. In order to achieve this goal, it was necessary to synthesize a peptide sequence that is specific to the alpha-4 beta-1 (VLA-4) receptors on the tumor surface and incorporate it into a micellar nanoparticle loaded with doxorubicin. Hopefully, this would allow for the nanoparticle to be taken up into the tumor so that the cancer drug would be delivered more effectively to only the tumor. When I began my fellowship this summer, our lab group was beginning a large-scale *in vivo* mouse trial with the drug nanoparticles. During the summer, I synthesized the required targeting peptide and conjugated it to a lipid to be included in the micellar nanoparticle using solid support peptide synthesis and Fmoc chemistry.

During my fellowship I also worked on developing "immuno-liposomes," which are liposomes that have antibodies conjugated to the surface, to be used for tumor treatment. Due to an antibody's high binding affinity to its specific epitope or receptor, immuno-liposomes can be used to efficiently deliver cancer therapeutics to a tumor. Throughout the summer, I aided in testing the ability several methods to conjugate the antibodies to a liposome. Furthermore, I developed a new method to purify unconjugated antibodies away from the new immuno-liposome. Finally, I tested and modified a method of isolating antibodies from biological fluids using ammonium sulfate precipitation.

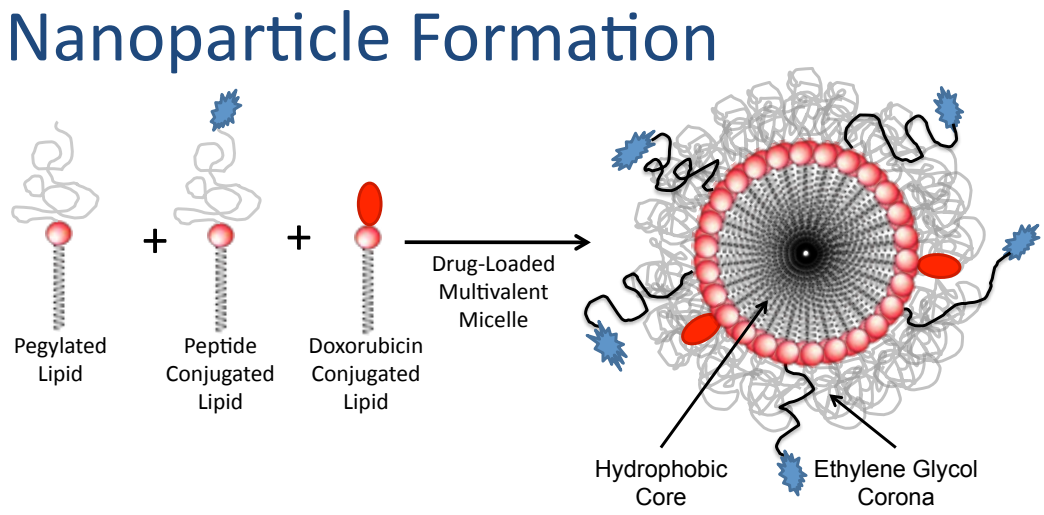

Fig. 1. Cartoon of micellar nanoparticle to be injected into mice that consists of a Peptide-conjugated lipid, a Doxorubicin-conjugated lipid, and a pegylated lipid.