

Chemical Engineering Thesis Defense

Aminoglycoside Polymers and Combination Treatments in Triple Negative Breast Cancer Studies

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abstract

In the United States, 12% of women are typically diagnosed with breast cancer, where 20-30% of these cases are identified as Triple Negative Breast Cancer (TNBC). In the state of Arizona, 810 deaths occur due to breast cancer and more than 4,600 cases are diagnosed every year (American Cancer Society). The lack of estrogen, progesterone, and HER2 receptors in TNBC makes discovery of targeted therapies further challenging. To tackle this issue, a novel multi-component drug vehicle is presented. Previously, we have shown that mitoxantrone, a DNA damaging drug, can sensitize TNBC cells to TRAIL, which is a protein that can selectively kill cancer cells. In this current study, we have formulated aminoglycoside-derived nanoparticles (liposomes) loaded with mitoxantrone, PARP inhibitors, for delivery to cancer cells. PARP inhibitors are helpful in preventing cancer cells from repairing their DNA following damage from other drugs (e.g. mitoxantrone). Various treatment liposome groups, consisting of lipid-containing polymers (lipopolymers) synthesized in our laboratory, were formulated and characterized for their size, surface charge, and stability. PARP inhibitors and treatment of cells for in-vitro with these liposomes resulted in synergistic death of cancer cells. Finally, we are initiating studies for evaluating the pre-clinical efficacy of these approaches using immunodeficient mouse models of TNBC disease.

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