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**Treatment of Her-2 Overexpressing Breast Cancer with Targeted Immunoliposomes**

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Awarded: $180,000  
Grant Mechanism: Post Doctoral Fellowship - Translational Research  
Research Focus: Treatment

Public Abstract:  
Almost 25 percent of breast tumors are composed of cells that have an increased number of growth receptors (Her-2) on their surface. The increase in Her-2 receptors correlates with an aggressive cancer that often metastasizes, resulting in a low chance of patient survival. Current chemotherapeutic techniques lack specificity for the tumor cells, resulting in dose-limiting side effects that prevent effective treatment of the cancer. The goal of our research is to significantly enhance selective delivery of chemotherapeutic drugs to Her-2 overexpressing tumors using a nanoparticle (liposome) delivery system and a novel two component strategy. The liposomes used in this therapy are attached to a targeting antibody which allows the liposomes to bind Her-2 overexpressing cells with high specificity. Once the liposomes bind to the cell surface, they are internalized into the cell. During this process, a vesicle, called an endosome, invaginates from the outer cell membrane and travels into the cell. A pore forming protein is attached to the liposomes which breaks down the endosome membrane, allowing drug released from the liposomes to pass directly into the target cell cytoplasm. Many modern chemotherapeutic agents are larger molecules such as DNA, RNA and cytotoxic proteins whose function is dependent on crossing over the endosome. This liposomal based method of delivery improves on current liposome techniques by offering a possible method for delivering large quantities of these chemotherapeutic molecules to breast tumor cells. A principal focus of our research will be on the development of a two-component targeting strategy. Under this approach, the pore forming protein and the encapsulated drug will be split into two different groups of liposomes. Only when these two kinds of liposomes interact within a cell will the drug be effectively delivered to the target cell cytoplasm. The probability of overlap is much greater in a Her-2 overexpressing cell and in theory, will amplify targeting specificity by as much as an order of magnitude. After maximizing the one- and two-component drug delivery using cell culture, we will target Her-2 overexpressing tumors in an immunocompetent mouse model to test the effectiveness of these approaches in vivo.

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