CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP121071

Project Title:
Development Of Multistage Vectored siRNA Therapeutics For The Treatment Of Breast Cancer

Award Mechanism:
Bridging the Gap: Early Translational Research Awards

Principal Investigator:
Ferrari, Mauro

Entity:
The Methodist Hospital Research Institute

Lay Summary:

While substantial progress has been recorded in the fight against breast cancer, the burden of death and suffering inflicted upon society by this disease remain unacceptably high. In 2010, an estimated 207,090 newcases of invasive breast cancer are expected in women in the U. S. About 39,840 women in U. S. are expected to die from breast cancer this year. Accounting for around 15% of total breast cancer cases, triple negative breast cancer (TNBC) primarily affects younger women – untypical for breast cancer in general – women with African-American descent and women carrying a BRCA1 mutation and others. The current treatments with chemotherapy drugs are not very effective. Major reasons for the ineffectiveness are 1) tumor tissues do not receive enough drugs to reach a therapeutic dose; 2) the majority of drugs are stuck in the filtering organs such as liver and lung, causing severe side effects; and 3) no targeted therapy is available for TNBC. As a result, the TNBC patients have the highest mortality rate among all breast cancer patients. The nanotechnology-based new drug in this application will overcome these problems. Tumor cell killing is triggered by blockage of the DNA damage repair pathways that are essential to keep integrity of the genome.Efficient delivery of therapeutics is achieved with the multistage vector drug delivery system, which has been shown to be very effective for breast cancer and ovarian cancer treatment. Therapeutic efficacy is assessed in the human-tumor-in-mouse models generated by implanting human tumor biopsies into immunodeficient mice. Biodistribution and pharmacokinetics are evaluated in mouse tumor models and in Sprague-Dawley rats. Toxicity of the multistage vector delivered therapeutics will also be monitored in Sprague-Dawley rats. These studies are required by the US Food and Drug Administration (FDA) for application of a investigational new drug status before the new drug can used in clinic.