CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP120897

Project Title:
ß-Lapachone Nanotherapeutics for NQO1-Targeted Therapy of Cancer

Award Mechanism:
Bridging the Gap: Early Translational Research Awards

Principal Investigator:
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Entity:
The University of Texas Southwestern Medical Center

Lay Summary:

Making cancer therapies safer, with greater tumor-specificity and little or no drug resistance during treatment, is a major goal of our research. We discovered that ß-lapachone (ß-lap), a novel therapeutic agent, specifically kills cancer cells that over-express a particular enzyme, NAD(P)H:quinone oxidoreductase 1 (NQO1). ß-Lap induces a unique cell death mechanism in which NQO1+ cancer cells specifically kill themselves by trying to metabolize the drug. When metabolized, ß-lap produces hydrogen peroxide and cancer cells literally disinfect themselves. Since NQO1 is over-expressed in most solid cancers of the lung (e.g., nonsmall cell), pancreas, breast, and prostate, and is expressed at low or no levels in normal tissues (even in adjacent normal tissue next to tumors). In mouse tumor models bearing human cancers of the types noted above, we found that efficacious killing of tumors occured without toxic side effects and no long-term consequences to the animals. Complete responses against pancreas, lung, prostate and breast cancers have been observed with this drug. Unfortunately, this agent is really hard to dissolve in water to treat humans. Recently, we discovered that we can load the drug into a polymer nanoparticle that can significantly increase the water solubility of the drug, and specifically deliver the drug to tumor tissue because of the leaky blood vessels that feed tumors. In this application, we will produce ß-lap nanomedicine in a protocol that is compatible for human testing in Phase I trials. The major deliverable at the end of our studies would be a drug that will be used for Phase I clinical trials against specific cancers that have elevated levels of the enzyme, NQO1. In addition to ß-lap therapeutics, we will also establish a biomarker analysis kit that can select patients with the most beneficial safety and antitumor efficacy toward the therapy, as well as determine during therapy that the cancers respond.