



CANCER PREVENTION & RESEARCH
INSTITUTE OF TEXAS

Award ID:
RP130166

Project Title:
Engineering membrane toxic C-type lectins for tumor targeting

Award Mechanism:
High Impact/High Risk

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

Lay Summary:

An important strategy for cancer therapy is the specific targeting of toxic agents to cancerous cells in vivo without damage to non-cancerous tissues. In this proposal, we aim to develop engineered membrane-toxic lectins that will specifically target and destroy tumor cells. Our strategy will take advantage of our discovery of the RegIII lectins, a unique family of membrane toxic C-type lectins. These proteins have the ability to bind to cell surface sugars and then destroy the membranes of the targeted cell. Although these membrane toxic lectins evolved to target microorganisms, we propose to reengineer their sugar binding function so that they specifically bind to tumor cells and destroy their targets by membrane attack. First, we will use protein engineering to alter the RegIII lectin sugar binding specificity so that it recognizes carbohydrate structures that are found on the surfaces of tumor cells. This will be followed by in vitro selection to achieve specific, high affinity binding to the tumor-specific sugars. Second, we will test the effectiveness of lectin-mediated tumor targeting in cell culture models. Together, these experiments represent an innovative approach to developing tumor-targeting therapeutics that leverages our discovery of a unique group of membrane toxic lectins. These studies offer the promise of novel therapeutics to treat many types of cancers.