



## CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:  
RP130258

Project Title:  
Tumor cell lytic peptoids that target exposed phosphatidylserine

Award Mechanism:  
Individual Investigator

Principal Investigator:  
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Entity:  
University of Houston

### Lay Summary:

New drugs that target cancer cells specifically promise to revolutionize cancer medicine. Because they are cancer-specific, they spare the rest of the body from toxic side effects. However, scientists quickly realized that protein targets for those drugs are not found in every cancer type and no universal cancer specific protein targets are available. We believe we have identified a global marker of cancer. The lipid phosphatidylserine (PS) is universally present in the tumor microenvironment and absent from healthy normal tissues. To target PS specifically, we selected a peptide-like molecule, called a peptoid, from a large library. The dimeric version of the peptoid potently killed cancer cells by bursting their outer membrane. The peptoids have no effect on normal cells. The overall goal of this proposal is to develop different versions of this peptoid to identify even more effective compounds. We will make changes in molecular structure and test the derivatives for specific lytic activity on cancer cells. Then, we will validate the chosen peptoids by testing them for anti-tumor activity in several different cancer models; breast, prostate, leukemia, glioma and lung. Next, we shall determine the mechanism of action of the PS-targeting peptoids. We expect to see that the peptoids act by destroying the tumor's blood supply by killing the cells that line the vessels, resulting in vascular shutdown and death of tumor cells through starvation of oxygen and nutrients. In addition, the cancer cells themselves carry PS and should also be lysed by the drug. Peptoids are inexpensive to prepare, serum stable, and can be rapidly refined for optimal efficacy. Therefore, our peptoids could rapidly and cost effectively be transformed into a new class of drugs with the potential to make a major impact on cancer treatment. Since PS is a universal target, the peptoids could have extraordinary breadth of application in multiple cancer types.