



## CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:  
RP121060

Project Title:  
Manufacture, Formulation, and IND-directed Toxicology of the  
Multifunctional Ceramide Catabolism Inhibitor D-threo-PPMP to enable  
Phase I Clinical Trials

Award Mechanism:  
Bridging the Gap: Early Translational Research Awards

Principal Investigator:  
Maurer, Barry J

Entity:  
Texas Tech University Health Sciences Center

### Lay Summary:

We have demonstrated that certain cellular waxes, called 'long chain dihydroceramides', can kill a variety of adult and pediatric cancer cells in the laboratory. We have determined that a drug, called fenretinide (4-HPR), causes cancer cells, but not normal cells, to increase their levels of certain dihydroceramide waxes up to a hundred-fold. We have determined that a second drug, called D-threo-PPMP, can maintain high levels of these dihydroceramide waxes in cancer cells by preventing the cells from changing them into other types of nontoxic waxes. We have shown that tumors growing in mice respond better to fenretinide + PPMP than they do to fenretinide-alone, and that fenretinide + PPMP is very well tolerated in mice. We have formulated fenretinide for high-dose clinical delivery using new oral and intravenous formulations and have completed early clinical studies that have produced multi-year, cancer-free responses in the childhood neuroblastoma cancer and in adult T-cell lymphoma cancers. We now seek CPRIT support to make pharmacy-grade PPMP and put it into a specially-made oral powder for clinical use in combination with fenretinide. We will test this oral powder for its ability to produce good PPMP levels in the blood and the ability of the new oral fenretinide + PPMP combination to shrink tumors growing in mice. If these experiments are successful, we will carefully test the combination of oral fenretinide + PPMP for blood drug levels and side effects in rats and dogs. These studies, if successful, will enable us to ask the U.S. Food and Drug Administration (FDA) for permission to open new early phase clinical trials of fenretinide + PPMP in adult and pediatric cancers in Texas.

The use of 'long chain dihydroceramide waxes' to kill cancer cells in patients is a totally new way to attack cancer cells and may produce better results, with many fewer side effects, in a variety of different adult and pediatric cancer types, than do current therapies.