



CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP150416

Project Title:
Translational Investigations On Fenretinide and Safingol For Pediatric
Cancer Use

Award Mechanism:
Individual Investigator Research Awards for Cancer in Children and
Adolescents

Principal Investigator:
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Entity:
Texas Tech University Health Sciences Center

Lay Summary:

We are developing a new kind of chemotherapy to fight pediatric cancers resistant to current therapies. This new chemotherapy uses high doses of a drug, called fenretinide, to increase certain toxic waxes, called dihydroceramides, in cancer cells and kill them. Because these waxes do not increase in normal cells, fenretinide is well-tolerated clinically. Using new formulations of fenretinide, we have been able to reduce, even eliminate, pediatric neuroblastoma cancer cells in some children in early clinical trials. We will now try to further increase the killing power of fenretinide by combining it with an artificial wax, called safingol. In the laboratory, when fenretinide-induced waxes meet safingol in cancer cells, the killing power can increase up to ten-fold. Interestingly, we have determined that feeding cancer cells certain fats at the same time that fenretinide is given causes certain of the toxic waxes to increase even further. This may be clinically useful because some of the waxes are better at killing cancer cells than others. We have also discovered that cancer cells try to protect themselves from fenretinide by revving up a protective process in the cell, called autophagy. We have early evidence that inhibiting autophagy allows the toxic waxes to kill the cancer cells faster and better. In this project, we will make a clinical drug supply of fenretinide and safingol to test in children with relapsed cancers. We will determine which specific fats are the best to combine with fenretinide to increase the toxic waxes in neuroblastoma cancer cells. We will also determine the best ways to go about inhibiting autophagy in neuroblastoma cells for use in a future clinic trial with fenretinide. Lastly, we will try to determine if there are autophagy-related chemicals in cancer cells that may allow us to predict which neuroblastoma cancers are more apt to respond to fenretinide so we better know which patients to treat.