CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP120314

Project Title:
Engineering and Preliminary Evaluation of a Fully Human, Non-Immunogenic Asparaginase For the Treatment of L-Asn Auxotrophic Cancers

Award Mechanism:
High Impact/High Risk

Principal Investigator:
Georgiou, George

Entity:
The University of Texas at Austin

Lay Summary:

Many cancers have genetic defects that lead them to lose the ability to synthesize certain amino acids. Unlike non-malignant cells the cancer cells have to take up these amino acids from the blood supply. Drug treatments that lead to depletion of the required amino acid from the blood supply starve the tumor leading to cancer cell killing while non-malignant cells that can synthesize that amino acid are unaffected. The most effective way to deplete a specific amino acid in the blood supply is by injection of an enzyme that selectively destroys it. This approach has proven to be highly efficacious in the treatment of leukemias and other tumors that cannot synthesize the amino acid L-Asparagine. The bacterial enzyme asparaginase is in clinical use under the trade name Oncospar® and has proved to be extremely effective for the treatment of a variety of leukemias. However, because Oncospar® is a bacterial enzyme, it is recognized as a foreign substance by the immune system. Adverse immune responses preclude the use of Oncospar® in 30% of pediatric leukemia patients, on patients that relapse and need a second round of treatment and in cancers that require prolonged administration of the drug. Here we propose to develop a fully human enzyme therapeutic, which by definition will not be foreign to the immune system. Because humans do not produce an asparaginase we will use modern protein engineering technologies to convert a different human enzyme into an asparaginase. In addition to developing an important new drug, other major benefits from this research include: (1) The results of the present study will provide critical preliminary results for future grant applications to support clinical development of the new drug. (3) This grant will serve as a catalyst to spur the development of a new approach in protein therapeutics, e.g. engineering human enzymes for the depletion of other amino acids important in cancer (L-Tyrosine, L-Methionine, etc).