



CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP100528

Project Title:
Targeting Tumor Microenvironment by NKT Cells

Award Mechanism:
Individual Investigator

Principal Investigator:
Metelitsa, Leonid S

Entity:
Baylor College of Medicine

Lay Summary:

Natural Killer T (NKT) cells are a subset of white blood cells with potent anti-tumor properties. Several years ago our laboratory made the original observation that tumor infiltration with NKT cells was associated with good outcome in children with neuroblastoma, one of the most common and deadly cancer of childhood. Since then similar observations have been made by other scientists in different types of cancer in adults. However, the mechanism by which NKT cells mediate anti-tumor responses has remained largely unknown, precluding a rational design of NKT-based immunotherapies. The role of NKT cells was especially puzzling because these cells could not directly recognize neuroblastoma and the majority of other types of cancer cells in humans. In a recent study that was published by *The Journal of Clinical Investigation*, our group demonstrated that NKT cells selectively target tumor-associated macrophages (TAMs), blood-derived cells that provide essential support for tumor cell growth and their resistance to therapy. TAMs are known to localize to tumor areas that are deprived of adequate oxygen supply (hypoxia). After sensing a hypoxic environment, TAMs initiate the process of new blood vessel formation that re-establishes the oxygen supply to the growing tumor. Our new data suggests that NKT cells chase and kill or inhibit TAMs inside hypoxic tumor tissues and thereby control tumor growth. However, NKT cells themselves are inhibited inside tumors by the oxygen deprivation and tumor-derived factors. The proposed investigation will exploit this novel anti-tumor defense mechanism and apply innovative cell engineering technologies to restore NKT cell function inside hypoxic tissues of neuroblastoma. Our development of NKT-cell therapy will be broadly applicable in diverse types of cancer in children and adults and have a major impact on future cancer therapies.