Award ID:
RP130588

Project Title:
Targeting Tumor and Tumor-Supportive Stroma by NKT Cells

Award Mechanism:
Individual Investigator

Principal Investigator:
Metelitsa, Leonid S

Entity:
Baylor College of Medicine

Lay Summary:

The overall goal of this proposal is to develop an effective immunotherapy of cancer using certain white blood cells called Natural Killer T cells (NKTs). We will engineer these cells to increase their ability to attack both tumor-cells and the tissues that support their growth. Our group recently showed that NKTs localize to the tumor site in neuroblastoma patients and attack non-malignant cells called tumor-associated macrophages, which provide critical support for the survival and growth of the tumor cells. To work well, NKTs must survive in the hostile environment and our published and preliminary results suggest that upon genetic engineering with a survival factor called IL-15 and with a cancer -targeting molecule called CAR.GD2, NKTs will survive at the tumor site and have antitumor efficacy both by killing the cancer directly and by disrupting the supporting environment. In order to prove this, we will use NKTs from neuroblastoma patients and engineer them so that they make IL-15 and have on their surface new components (CAR.GD2) that can recognize the tumor cells directly. The anti-tumor potential of these engineered NKTs will be tested using in vitro and in vivo experimental systems. The best construct will be selected and can be produced to clinical standards at our GMP facility for subsequent phase I clinical trial of gene-modified NKTs in neuroblastoma patients. Thus, the proposed investigation will translate the accumulated knowledge in the biology and function of human NKTs into a novel cancer immunotherapy with a major potential impact on cancer treatment.