



CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
DP150083

Project Title:
NKT Cell Platform for Cancer Immunotherapy

Award Mechanism:
Bridging the Gap: Early Translational Research Awards

Principal Investigator:
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Entity:
Baylor College of Medicine

Lay Summary:

The goal of this project is to develop a new class of cancer immunotherapy that exploits natural and engineered properties of Natural Killer T cells (NKTs) to target tumor-supportive stroma. Increasing numbers of clinical trials using adoptive T cell therapies are showing anti-tumor activity against a broad range of malignancies. However, tumor growth creates a highly immunosuppressive stroma which impairs T-cell homing to the tumor site or their anti-tumor function. This represents a major and as yet unsolved critical challenge to the development of effective adoptive immunotherapy of cancer. The proposed project will develop banked or "off-the-shelf" NKTs engineered to express the cytokine IL-15, which is a survival factor for both NKTs and T cells. Because NKT cell receptor, CD1d is identical in all individuals, NKTs derived and ex-vivo expanded from one healthy donor can be used to treat multiple patients. To ensure safety we will co-express IL-15 with an iC9-based suicide gene, which has proved safe and effective in a recent phase-I clinical trial. Therefore, we hypothesize that the natural and engineered abilities of NKTs to localize to tumor sites, neutralize immunosuppressive stroma, and rescue tumor-specific T cells can be exploited to create a universal NKT-cell based cellular product for enabling anti-tumor activity of tumor-specific cell therapy products in a wide range of tumors. The following specific aims will test our hypotheses: 1) to screen PBMC from healthy donors and select candidates with highly functional NKTs; 2) to express IL-15/iC9 in NKTs expanded from 5 selected donors and test their therapeutic potential in combination with tumor-specific T cells in models of neuroblastoma and lymphoma; 3) to produce a clinical grade master cell bank of IL-15.iC9 NKTs. This NKT-cell bank could become a platform technology to augment the therapeutic efficacy of tumor-specific T cell products applicable to a broad range of malignancies.