Award ID:
RP110129

Project Title:
Genetic Engineering of Universal NKT Cells for Cancer Immunotherapy

Award Mechanism:
High Impact/High Risk

Principal Investigator:
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Entity:
Baylor College of Medicine

Lay Summary:

Natural Killer T cells (NKTs) are a unique subset of white blood cells with anti-tumor properties that have been demonstrated in diverse types of cancer. Our group recently revealed a mechanism of NKT-cell anti-tumor activity by demonstrating that NKTs localize to the tumor site and attack non-malignant cells called tumor-associated macrophages (TAMs) which provide critical support for tumor cells and enable tumor growth in many types of cancer. The molecule recognized by NKTs on TAMs is identical in all individuals so that NKTs from unrelated healthy people could be prepared to treat cancer patients if we prevent rejection of these donated NKTs by the patient's immune system. Using an innovative technology with designer zinc finger nucleases (ZFNs), we have modified human white blood cells from one individual so that they can no longer be rejected by the immune system of other persons. In aim-1 of the proposed investigation, we will apply ZFN technology to NKTs obtained from healthy individuals and generate universal NKTs (uNKTs). These engineered uNKTs will be tested for the resistance to killing by immune cells of unrelated individuals. Aim 2 will evaluate the anti-tumor potential of uNKTs using established in vitro and in vivo experimental approaches. The results will generate the first anti-cancer cell therapy product that can be uniformly standardized and used on-demand as an "off-the-shelf" therapy. Therefore, our successful development of uNKT cell therapy may have a major impact on future cell therapies of cancer.