CANCER PREVENTION & RESEARCH INSTITUTE OF TEXAS

Award ID:
RP180810

Project Title:
Controlling the Activity of Anticancer T Cells by Inducing Replicative Senescence

Award Mechanism:
High Impact/High Risk

Principal Investigator:
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Entity:
Baylor College of Medicine

Lay Summary:

Certain cancers can be effectively treated — and even cured — by enhancing cells from a patient's own body. Changing these specialized immune cells, called "T cells," to enable them recognize and kill tumor cells has a number of advantages over conventional cancer drugs. For instance, T cells can easily find tumors, multiply and remain in the body until the tumor is cleared. One downside to these powerful "living drugs" is that their long-term activity in patients hard to control or even predict, which sometimes results in unwanted toxicities. For example, T cells trained to recognize leukemia cells also attack normal blood cells responsible for preventing infections, among other functions. As a consequence, many of these patients require numerous additional treatments to fill the gap left by these cells. Sometimes when a patient doesn't have enough healthy T cells to make this living drug, they receive T cells from another person. Unfortunately, even if these cells effectively kill the cancer, they may also attack other, healthy parts of the patient's body — a dangerous condition called "graft-versus-host disease". In order for these anti-cancer T cells to be used more widely, we must find a way to make their behavior safer and more predictable overtime.

In this project, we will create and test a safety system for these cells. We found that artificially turning on certain genes in T cells can make them age faster than usual, which should prevent their long-term survival. Because these T cells must be able to clear cancer cells to be helpful for patients, we made sure our aging genes do not change the cells' ability to kill tumor cells in the short-term. Here, we will make the T cells age a little bit each time they kill a cancer cell in patients, thus stopping them from doing long-term damage to the body after the tumor is gone. This system should allow these T cells to be safe while retaining their desired anti-tumor properties.