

Targeting cancer with engineered T cells

April 20 2016

Dr. Philip Greenberg, head of immunology and a member of the Clinical Research Division at Seattle's Fred Hutchinson Cancer Research Center and a leader in cancer immunology, will describe how he and colleagues are genetically engineering T cells to seek out cancer cells, penetrate their defenses and kill them.

In a presentation at the American Association for Cancer Research Annual Meeting 2016 in New Orleans, he also will provide a preview of next-generation strategies and upcoming clinical trials for a variety of cancers. The [presentation](#) will be from 10:55 to 11:20 a.m. CDT April 20 as part of a symposium on the function of T cells and their therapeutic application in cancer.

T cells are [white blood cells](#) that attack [abnormal cells](#) in our bodies, including those infected by viruses and other foreign invaders. T cells can also target cancer cells, but they sometimes fail to recognize cancer cells as the enemy. Many [cancer cells](#) produce proteins that suppress nearby T cell activity, rendering the immune response futile.

Among Greenberg's topics will be:

- Research to discover antigens that are good targets for T [cell receptors](#) (TCRs). For example, an appropriate target would be plentiful in [tumor cells](#) but absent or nearly so in normal tissues. As will be discussed, WT1 is a targetable tumor antigen for leukemia and potentially some other cancers. T cell receptors are molecules on the surfaces of T cells that are responsible for

recognizing and binding to antigens.

- Preliminary data from a clinical trial for patients with acute myeloid leukemia (AML) in which T cells are being engineered with a receptor selected for its ability to target the WT1 antigen.
- Other current or planned trials using TCR-engineered T cells to target tumors. These include non-small cell lung cancer and mesothelioma, pancreatic cancer, high-grade serous ovarian cancer and additional studies on AML.
- An update on a mesothelioma study in which three patients with advanced, treatment-resistant disease have received the experimental T cell therapy. One now has stable disease and one has experienced significant tumor regression.
- Next-generation strategies, which include designing better, more targeted synthetic T cell receptors and manipulating other factors, such as elements of the tumor environment, to improve antitumor activity.
- Engineering T cells to treat solid tumors. Mouse studies using pancreatic [cancer](#) as a model are providing numerous insights. Among them: T cell therapy using TCR-engineered T cells induces tumor cell death, but this is only temporary as the tumor ultimately turns the T [cells](#) off. However, anti-tumor activity can be sustained by administering multiple infusions, and if repeated every two weeks the infusions significantly prolong survival in mice. This strategy is in the process of being translated to human clinical trials.

Greenberg is a founder of and consultant to [Juno Therapeutics](#). He is a stockholder in the company and he receives grant and research support from it. Juno Therapeutics was initially formed on technology from researchers at Fred Hutch, Memorial Sloan Kettering Cancer Center and Seattle Children's Research Institute to commercialize promising immunotherapies.

Provided by Fred Hutchinson Cancer Research Center

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