Lipid Nanoparticle-Mediated Delivery of mRNA Encoded Synthetic Antigens for CAR T Cell Therapy

CAR T cell immunotherapy is a highly effective cancer treatment that works by modifying a patient's T cells in order to precisely target antigens on the surface of cancer cells. However, there are several limitations to the current technology. While substantial benefit has been seen in application to blood cancers, there has been limited success in use on solid tumors. This is due to both the physical barriers in place surrounding solid tumors and the presence of an immunosuppressive tumor microenvironment. Additionally, CAR T cell therapy relies on targeting specific tumor-associated antigens, which can be expressed inconsistently between different patients or even appear in healthy cells. Thus, attacking these markers can damage an individual's healthy cells in addition to the cancer cells, producing off-target effects.

Researchers at the Georgia Institute of Technology have developed a novel approach to CAR T cell immunotherapy by creating synthetic antigens that sensitize solid tumors for recognition and elimination by using markers that are completely unique from those naturally occurring in the human body. This substantially increases the immunogenicity of viral vectors and significantly reduces the toxicity to surrounding non-tumor cells, resulting in reduced tumor burden, improved survival, improved epitope spread, and protection against tumor recurrence.

Researchers have developed a novel technology that enables targeted cancer therapy via lipid nanoparticles that deliver mRNA-encoded synthetic antigens to tumor cells, guiding CAR T cell attacks. This technology encapsulates synthetic antigen-encoding mRNA within lipid nanoparticles (LNPs) to direct universal CAR T cells towards tumor cells. By expressing these antigens on the surface of tumor cells, the technology enables the body's own immune system to recognize and destroy cancer cells, including those that lack immunogenic antigens, thereby expanding the efficacy and applicability of CAR T cell therapies across various cancer types.

Summary Bullets

- Georgia Tech's novel CAR T cell therapy uses lipid nanoparticles (LNPs) to deliver mRNA-encoded synthetic antigens, improving targeting of solid tumors and reducing off-target effects.

- The technology ensures efficient mRNA delivery, prompting tumor cells to express unique antigens, enhancing immune recognition and destruction of cancer cells.

- This approach broadens CAR T cell therapy applicability, allows repeat dosing, and minimizes off-tumor toxicity, offering significant advantages over traditional methods.

Solution Advantages

- Enables targeting of tumors with low antigen expression or those lacking immunogenic antigens.
- Protects mRNA from degradation in vivo, ensuring efficient delivery and expression of synthetic antigens.
- Low immunogenicity of LNPs allows for repeat dosing, a significant advantage over viral vectors.
- Expands the applicability of CAR T cell therapies to a broader range of cancers.
- Potentially reduces the risk of on-target off-tumor toxicity by precisely directing CAR T cells to tumor cells.

Potential Commercial Applications

- Targeted cancer therapies, particularly for types lacking clear antigen targets.
- Customizable treatment plans for a broad range of hematological malignancies and solid tumors.
- Combinatorial therapies utilizing CAR T cells for enhanced cancer treatment efficacy.
- Research and development in synthetic biology and immunotherapy.

Inventors

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IP Status

Patent application has been filed :

Publications

Sensitizing solid tumors to CAR-mediated cytotoxicity using synthetic antigens, BioRxiv - 2021

Images

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