T-cell therapy

T-cell therapy, also known as T-cell immunotherapy, is a type of cancer treatment that utilizes the body's own immune system to fight cancer cells.

There are several approaches to T-cell therapy, but one of the most promising and well-known methods is CAR-T cell therapy (Chimeric Antigen Receptor T-cell therapy). In CAR-T cell therapy, T-cells are extracted from the patient's blood and genetically modified to express chimeric antigen receptors (CARs) on their surface. These CARs are designed to recognize specific proteins found on the surface of cancer cells. Once modified, the T-cells are multiplied in the laboratory and infused back into the patient's bloodstream.

When CAR-T cells encounter cancer cells in the body, they recognize and bind to the specific protein targeted by the CAR. This binding activates the CAR-T cell, triggering it to attack and kill the cancer cell. CAR-T cell therapy has shown remarkable success in treating certain types of blood cancers, such as certain types of leukemia and lymphoma, even in cases where other treatments have failed.

Another type of T-cell therapy involves using tumor-infiltrating lymphocytes (TILs), which are T-cells that have naturally migrated into a tumor. These TILs are extracted from a patient's tumor, expanded in the laboratory, and then reinfused into the patient. TIL therapy has shown promise in treating certain solid tumors, such as melanoma.

T-cell therapy is a rapidly evolving field with ongoing research aimed at improving its effectiveness, reducing side effects, and expanding its applicability to a broader range of cancers. While it has shown significant promise, there are still challenges to overcome, including managing potential side effects such as cytokine release syndrome and neurotoxicity, as well as ensuring the long-term persistence of the engineered T-cells.

Limitations

Adoptive T-cell therapy for cancer does face limitations related to both in vitro T-cell expansion and the ability of these expanded T-cells to infiltrate tumors effectively once infused back into the patient's body.

Inefficiency of in vitro T-cell expansion: One limitation is the challenge of expanding T-cells in vitro (outside the body) to generate a sufficient number of cells for therapy. This process can be time-consuming and costly. Additionally, not all T-cells expand equally well, and some patients may have T-cells that are more difficult to expand than others. Improving the efficiency of T-cell expansion techniques is an ongoing area of research to address this limitation.

In vivo T-cell infiltration into tumors: Even after successful expansion and infusion of T-cells into the patient, there's the challenge of ensuring these T-cells effectively infiltrate tumors once they're in the body. Tumors can create a hostile microenvironment that makes it difficult for T-cells to penetrate and attack cancer cells. Factors such as immunosuppressive molecules, lack of proper chemokine signals, and physical barriers within the tumor can hinder T-cell infiltration. Strategies to enhance T-cell trafficking and penetration into tumors are actively being explored, including combining T-cell therapy with other treatments such as checkpoint inhibitors or therapies targeting the tumor microenvironment.

Addressing these limitations is crucial for improving the effectiveness of adoptive T-cell therapy and expanding its applicability to a wider range of cancers. Ongoing research efforts are focused on developing novel techniques and strategies to overcome these challenges and enhance the therapeutic potential of T-cell therapy for cancer.

Adoptive T-cell therapy for cancer therapy is limited by the inefficiency ofin vitroT-cell expansion and the ability ofin vivoT-cells to infiltrate tumors. The construction of multifunctional artificial antigen-presenting cells is a promising but challenging approach to achieve this goal. In this study, a multifunctional artificial antigen-presenting gel droplet (AAPGD) was designed. Its surface provides regulated T-cell receptor (TCR) stimulation and co-stimulation signals and is capable of slow release of mitogenic cytokines and collagen mimetic peptide. The highly uniform AAPGD are generated by a facile method based on standard droplet microfluidic devices. The results of the study indicate that, T-cell proliferatedin vitroutilizing AAPGD have a fast rate and high activity. AAPGD increased the proportion ofin vitroproliferating T cells low differentiation and specificity. The starting number of AAPGDs and the quality ratio of TCR-stimulated and co-stimulated signals on the surface have a large impact on the rapid proliferation of low-differentiated T cellsin vitro. During reinfusion therapy, AAPGD also enhanced T-cell infiltration into the tumor site. In experiments using AAPGD for adoptive T cell therapy in melanoma mice, tumor growth was inhibited, eliciting a potent cytotoxic T-lymphocyte immune response and improving mouse survival. In conclusion, AAPGD promotes rapid low-differentiation proliferation of T cellsin vitroand enhances T cell infiltration of tumorsin vivo. It simplifies the preparation steps of adoptive cell therapy, improves the therapeutic effect, and provides a new pathway for overdosing T cells to treat solid tumors [1)].

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Tian Y, Chen W, Du G, Gao J, Zhao Y, Wang Z, Su M, Hu R, Han F. Microfluidic-based preparation of artificial antigen-presenting gel droplets for integrated and minimalistic adoptive cell therapy strategies. Biofabrication. 2024 Mar 15;16(2). doi: 10.1088/1758-5090/ad2fd4. PMID: 38437712.