Solid tumor CAR-T cell therapy

Solid tumor CAR-T cell therapy has so far yielded limited results, in terms of therapeutic effects, as compared to the dramatic results observed for hematological malignancies. Many factors involve both the tumor cells and the microenvironment.

The researchers conducted experiments with CAR T cells that specifically target CD70, a protein found on the surface of certain tumor cells. They used a unique experimental setup involving a 3D microchannel network within a substance described as “bio-conjugated liquid-like solid (LLS) medium.” This setup was designed to mimic the complex environment within solid tumors.

Successful Migration: The experiments yielded positive results, showing that the CD70-specific CAR T cells were able to migrate effectively within the 3D microchannel network in the LLS medium.

Anti-Tumor Activity: Importantly, the CAR T cells demonstrated anti-tumor activity against glioblastoma and osteosarcoma tumors that expressed CD70. Immune Recruitment Mechanism: Through a comprehensive analysis of cytokines and chemokines (chemical signals involved in immune responses) and in situ imaging (observing processes in their natural environment), the researchers determined that the recruitment of immune cells occurred through a process known as chemotaxis. This means that the CAR T cells were drawn toward the tumor cells by specific chemical signals.

Importance of Effector to Target Ratio: The researchers found that the ratio of CAR T cells to tumor cells (effector to target ratio) played a crucial role in the overall effectiveness of the anti-tumor response. This suggests that having the right balance of CAR T cells is important for their function.

Single-Cell Analysis: To gain deeper insights, the researchers collected individual immune cells and analyzed their gene expression at the single-cell level. This allowed them to identify differences in gene expression patterns among different immune cell subpopulations.

The findings of this study are significant because they shed light on the complex interactions between CAR T cells and solid tumors, particularly in the context of brain and bone cancers. This research provides valuable insights that can inform future studies and the development of more effective CAR T cell therapies for solid tumors.

In summary, this study used a specialized experimental setup to study how CAR T cells function in solid tumors, focusing on their migration, anti-tumor activity, and the molecular mechanisms involved. The results offer important insights into improving CAR T cell-based treatments for challenging solid tumors [1)].

The lack of specific target antigens and severe, potentially fatal, toxicities caused by on-target off-tumor toxicities constitute major hurdles. Furthermore, the tumor microenvironment is usually characterized by chronic inflammation, the presence of immunosuppressive molecules, and immune cells that can reduce CAR T cell efficacy and facilitate antigen escape. Nonetheless, solid tumors are under investigation as possible targets despite their complexity, which represents a significant challenge. In preclinical mouse models, CAR T cells are able to efficiently recognize and kill several

tumor xenografts. Overall, in the next few years, there will be intensive research into optimizing novel cell therapies to improve their effector functions and keep untoward effects in check [2].

Target selection is the most critical aspect in determining the prognosis of patients receiving this treatment [3]

CAR-modified T cells can mediate long-term durable remissions in B cell malignancies, but expanding this platform to solid tumors requires the discovery of surface targets with limited expression in normal tissues.

CAR therapy has shown promise in treating cancer, but at the cost of unexpected toxicity against normal tissues, not predicted by preclinical testing. Johnson et al. are working to generate more physiologically relevant models for preclinical CAR toxicity testing, and in doing so, have discovered that CAR therapy induces immunogenic cell death, with the potential for cures [4].

see EGFRvIII targeted chimeric antigen receptor T.

Glioblastoma CAR-T cell therapy

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1)
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