T-cell engagers

In neurosurgery

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- Targeting Dual Immune Checkpoints PD-L1 and HLA-G by Trispecific T Cell Engager for Treating Heterogeneous Lung Cancer
- An oncolytic adenovirus co-expressing a bi-specific T cell engager and IL-2 for the treatment of ovarian cancer
- CD87-targeted BiTE and CAR-T cells potently inhibit invasive nonfunctional pituitary adenomas
- Improved antitumor effects elicited by an oncolytic HSV-1 expressing a novel B7H3nb/CD3 BsAb
- Enhanced CD1d phosphatidylserine presentation using a single-domain antibody promotes immunomodulatory CD1d-TIM-3 interactions
- Nanobody-based trispecific T cell engager (Nb-TriTE) enhances therapeutic efficacy by overcoming tumor-mediated immunosuppression

T-cell engagers, also known as bispecific T-cell engagers or BiTEs, are a class of immunotherapy drugs designed to harness the immune system's T cells to target and destroy cancer cells. They are a form of immunotherapy that has gained significant attention and shown promise in the treatment of certain types of cancer, particularly hematologic malignancies.

Here's how T-cell engagers work:

Bispecific Design: T-cell engagers are engineered molecules with a bispecific design, meaning they have two binding sites. One binding site is designed to attach to a specific antigen on the surface of cancer cells, while the other binding site is designed to attach to T cells. This dual targeting capability brings cancer cells and T cells into close proximity.

Bringing T Cells and Cancer Cells Together: By binding to both T cells and cancer cells simultaneously, T-cell engagers physically bridge the two cell types. This interaction helps overcome some of the immune system's limitations in recognizing and attacking cancer cells, as cancer cells can sometimes evade detection.

T-cell Activation: Once T-cell engagers bring T cells close to cancer cells, they activate the T cells. This activation triggers a powerful immune response, causing the T cells to release cytotoxic substances, such as perforin and granzyme, which can directly kill the cancer cells. T-cell activation can also induce the release of cytokines, which further enhance the immune response.

T-cell engagers have been particularly effective in the treatment of certain types of blood cancers, such as acute lymphoblastic leukemia (ALL) and non-Hodgkin lymphoma. One of the most well-known T-cell engagers is blinatumomab, which has been approved for the treatment of B-cell precursor ALL. Another example is CD19-targeting CAR-T cell therapies, which can be considered a form of T-cell engager because they also bring T cells into contact with cancer cells through the targeting of the CD19 antigen.

Advantages of T-cell engagers include their specificity for cancer cells (reducing the risk of off-target effects) and their potential to induce rapid and potent immune responses. However, they may be

associated with side effects, including cytokine release syndrome (CRS) and neurologic toxicities, which need to be monitored and managed.

Research in this field is ongoing, with efforts to develop and refine T-cell engagers for the treatment of various cancers. These therapies represent an exciting advancement in cancer immunotherapy and offer hope for patients with certain types of cancer that were previously difficult to treat.

A novel bispecific T-cell engager (BiTE) has been developed as an efficient immunotherapeutic molecule specifically bringing the T-cell and the tumor target together for enhanced immunotherapy. The general BiTE construct consists of two single-chain variable antibody fragments (scFvs) targeting a tumor-associated antigen (TAA) and a T-cell marker in tandem. The binding of BiTEs to tumor antigens induces immediate T-cells' cytotoxicity against tumor cells without involving any typical costimulatory signals, specific TCR and MHC recognition [1)]

1)
Yang XM, Lin XD, Shi W, Xie SX, Huang XN, Yin SH, Jiang XB, Hammock BD, Xu ZP, Lu XL. Nanobody-based bispecific T-cell engager (Nb-BiTE): a new platform for enhanced T-cell immunotherapy. Signal Transduct Target Ther. 2023 Sep 4;8(1):328. doi: 10.1038/s41392-023-01523-3. PMID: 37661200.