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CD28CAR/CD137CAR-expressing T-Lymphocytes

National Cancer Institute

Source

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Third generation, chimeric antigen receptor (CAR) cells composed of T-lymphocytes transduced with a lentiviral vector expressing a CAR consisting of an a single chain variable fragment specific for a particular antigen, coupled to the two co-stimulatory signaling domains Cluster of Differentiation 28 (CD28) and Cluster of Differentiation 137 (CD137; 4-1BB), and the zeta chain of the T-cell receptor (TCR)/CD3 complex (CD3-zeta), with potential immunomodulating and antineoplastic activities. Upon transfusion, CD28CAR/CD137CAR-expressing T-lymphocytes are directed to, and induce selective toxicity in tumor cells expressing the particular antigen. CD28, a T-cell surface-associated co-stimulatory molecule, is required for T-cell activation, proliferation, and survival. The 4-1BB co-stimulatory molecule signaling domain enhances activation and signaling after recognition of the antigen. Furthermore, inclusion of the 4-1BB signaling domain may increase the antitumor activity when compared to the inclusion of the CD28 co-stimulatory domain and CD3-zeta alone.