

CDR1, CDR2, and CDR3 sequences as described herein. The invention further relates to antigen binding molecules to FLT3 comprising both variable heavy chain CDR1, CDR2, CDR3, and variable light chain CDR1, CDR2, and CDR3 sequences as described herein.

[0038] Additional heavy and light chain variable domains and CDR polynucleotide and amino acid sequences suitable for use in FLT3-binding molecules according to the present invention are found in U.S. Provisional Application Number 62/199,944, filed on July 31, 2015.

[0039] The invention further relates to methods of treating a disease or disorder in a subject in need thereof comprising administering to the subject the antigen binding molecules, the CARs, TCRs, polynucleotides, vectors, cells, or compositions according to the invention. Suitable diseases for treatment include, but are not limited to, acute myeloid leukemia (AML), chronic myelogenous leukemia (CML), chronic myelomonocytic leukemia (CMML), juvenile myelomonocytic leukemia, atypical chronic myeloid leukemia, acute promyelocytic leukemia (APL), acute monoblastic leukemia, acute erythroid leukemia, acute megakaryoblastic leukemia, myelodysplastic syndrome (MDS), myeloproliferative disorder, myeloid neoplasm, myeloid sarcoma), or combinations thereof. Additional diseases include inflammatory and/or autoimmune diseases such as rheumatoid arthritis, psoriasis, allergies, asthma, Crohn's disease, IBD, IBS, fibromyalgia, mastocytosis, and Celiac disease.

BRIEF DESCRIPTION OF THE FIGURES

[0040] FIG. 1, depicts flow cytometric analysis of FLT3 cell surface expression on human cell lines.

[0041] FIG. 2, depicts CAR expression in primary human T cells electroporated with mRNA encoding for various CARs.

[0042] FIGs. 3A to 3H, depict cytolytic activity of electroporated CAR T cells against multiple cell lines following 16 hours of coculture.

[0043] FIG. 4, comprising of FIGs. 4A to 4X, depicts IFN γ , IL-2, and TNF α production by electroporated CAR T cells following 16 hours of coculture with the indicated target cell lines.

[0044] FIGs. 5A and 5B, depict CAR expression in lentivirus transduced primary human T cells from two healthy donors.

[0045] FIGs. 6A to 6D, depict the average cytolytic activity over time from two healthy donors expressing the indicated CARs cocultured with various target cell lines.

[0046] FIG. 7, comprising of FIGS. 7A to 7F, depicts IFN γ , TNF α , and IL-2 production by lentivirus transduced CAR T cells from two healthy donors following 16 hours of coculture with the indicated target cell lines.

[0047] FIGs. 8A and 8B, depict proliferation of CFSE-labeled lentivirus transduced CAR T cells from two healthy donors following 5 days of coculture with CD3-CD28 beads or the indicated target cell lines.

[0048] FIG. 9, depicts CAR expression in lentivirus transduced primary human T cells used for in vivo studies.

[0049] FIGs. 10A to 10C, depict bioluminescence imaging of labeled acute myeloid leukemia cells following intra-venous injection of CAR T cells in a xenogeneic model.

[0050] FIG. 11, depicts survival curves of mice injected with CAR T cells.

[0051] FIG. 12, depicts the pGAR vector map.

DETAILED DESCRIPTION OF THE INVENTION

[0052] It will be appreciated that chimeric antigen receptors (CARs or CAR-Ts) and T cell receptors (TCRs) are genetically engineered receptors. These engineered receptors can be readily inserted into and expressed by immune cells, including T cells in accordance with techniques known in the art. With a CAR, a single receptor can be programmed to both recognize a specific antigen and, when bound to that antigen, activate the immune cell to attack and destroy the cell bearing that antigen. When these antigens exist on tumor cells, an immune cell that expresses the CAR can target and kill the tumor cell.

[0053] CARs can be engineered to bind to an antigen (such as a cell-surface antigen) by incorporating an antigen binding molecule that interacts with that targeted antigen. Preferably, the antigen binding molecule is an antibody fragment thereof, and more preferably one or more single chain antibody fragment ("scFv"). An scFv is a single chain antibody fragment having the variable regions of the heavy and light chains of an antibody linked together. See U.S. Patent Nos. 7,741,465, and 6,319,494 as well as Eshhar *et al.*, Cancer Immunol Immunotherapy (1997) 45: 131-136. An scFv retains the parent antibody's ability to specifically interact with