separate cycle and with surface regeneration between the cycles. The concentration series are indicated as an overlay plot aligned at the start of the injection (time 0). Fitting models for kinetics considered 1:1 binding. Temperature: 298 K.

Summary

In one aspect, the present disclosure provides a humanized CD1a targeting moiety, wherein the CD1a targeting moiety is an antibody, F(ab')2, Fab, scFab or scFv, comprising a VL domain consisting of SEQ ID NO: 1 and a VH domain consisting of SEQ ID NO: 2.

Preferably, the CD1a targeting moiety is a scFv comprising a VL domain consisting of SEQ ID NO: 1 and a VH domain consisting of SEQ ID NO: 2. More preferably, the CD1a targeting moiety is a scFv consisting of SEQ ID NO:3

In a further aspect, the present disclosure provides a chimeric antigen receptor (CAR) comprising:

a) an extracellular domain comprising a CD1a targeting moiety, wherein the CD1a targeting moiety is a scFv comprising a VL domain consisting of SEQ ID NO: 1 and a VH domain consisting of SEQ ID NO: 2;

b) a transmembrane domain; and

c) an intracellular signaling domain.

Preferably the transmembrane domain comprises the transmembrane domain of CD28, CD3, CD45, CD4, CD8, CD9, CD16, CD22, CD33, CD37, CD64, CD80, CD86, CD134, CD137, or CD154. Preferably, the intracellular domain of CD3ζ, FcRγ, CD3γ, CD3δ, CD3ε, CD5, CD22, CD79a, CD79b or CD66b. Preferably, the CAR further comprises a costimulatory signaling domain, preferably the costimulatory signaling domain comprises the intracellular domain of CD27, CD28, CD137, CD134, CD30, CD40, lymphocyte function-associated antigen-1 (LFA-1), CD2, CD7, LIGHT, NKG2C, or CD276. Most preferably, the CAR consists of SEQ ID NO: 13.

In a further example, the present disclosure provides a nucleic acid encoding the CAR according to the previous example. In a further aspect, the present disclosure provides a nucleic acid encoding the CAR as disclosed herein.

In one example, the present disclosure provides a cell comprising the nucleic acid according to the previous example. Preferably, the cell is a T-cell. In one aspect, the present disclosure provides a cell comprising the nucleic acid as disclosed herein and/or the CAR as disclosed herein.

In another example, the present disclosure provides a pharmaceutical composition comprising a plurality of cells according to the previous example and a pharmaceutically acceptable carrier or diluent. In another aspect, the present disclosure provides a pharmaceutical composition comprising a plurality of cells as disclosed herein and a pharmaceutically acceptable carrier or diluent.

In another example, the present disclosure provides a cell according to the previous example for use as a medicament. In one aspect, the present disclosure provides the cell as disclosed herein or the pharmaceutical composition as disclosed herein for use as a medicament. Preferably, the use is in a method of treating a CD1a-positive cancer, wherein the method comprises administering the cell or composition to a patient in need thereof. Preferably, the CD1a-positive cancer is cortical T-cell acute lymphoblastic leukemia, preferably, relapsed/refractory cortical T-cell acute lymphoblastic leukemia. In one aspect, the present disclosure provides use of the cell as disclosed herein or the pharmaceutical composition as disclosed herein in the manufacture of a medicament for treating a CD1a-positive cancer in a patient in need thereof.

Definitions

“Administering” or “administration of” a medicament to a patient (and grammatical equivalents of this phrase) refers to direct administration, which may be administration to a patient by a medical professional or may be self-administration, and/or indirect administration, which may be the act of prescribing a drug. E.g., a physician who instructs a patient to self-administer a medicament or provides a patient with a prescription for a drug is administering the drug to the patient.

The term “affibody” refers to a protein that is derived from the Z domain of protein A and that been engineered to bind to a specific target (see Frejd & Kim, 2017. Exp Mol Med. 49(3): e306).

The term "antibody" refers to a molecule comprising at least one immunoglobulin domain that binds to, or is immunologically reactive with, a particular target. The term includes whole antibodies and any antigen binding portion or single chains thereof and combinations thereof; for instance, the term “antibody” in particular includes bivalent antibodies and bivalent bispecific antibodies.

A typical type of antibody comprises at least two heavy chains ("HC") and two light chains ("LC") interconnected by disulfide bonds.

Each "heavy chain" comprises a "heavy chain variable domain" (abbreviated herein as "VH") and a "heavy chain constant domain" (abbreviated herein as "CH"). The heavy chain constant domain typically comprises three constants domains, CH1, CH2, and CH3.

Each "light chain" comprises a "light chain variable domain" (abbreviated herein as "VL") and a "light chain constant domain" ("CL"). The light chain constant domain (CL) can be of the kappa type or of the lambda type. The VH and VL domains can be further subdivided into regions of hypervariability, termed Complementarity Determining Regions ("CDR"), interspersed with regions that are more conserved, termed "framework regions" ("FW").

Each VH and VL is composed of three CDRs and four FWs, arranged from amino-terminus to carboxy-terminus in the following order: FW1, CDR1, FW2, CDR2, FW3, CDR3, FW4. The