

Claims

1. A multispecific antibody comprising
 - a. a first antigen-binding region capable of binding human CD123 comprising complementarity determining region (CDR)1 sequence set forth in SEQ ID NO:2, the VH CDR2 sequence set forth in SEQ ID NO:3 and the VH CDR3 sequence set forth in SEQ ID NO:4; and
 - b. a second antigen-binding region capable of binding a human V γ 9V δ 2 T cell receptor.
2. The multispecific antibody of claim 1, wherein
 - i. X₁ in SEQ ID NO: 2 is G;
 - ii. X₂ in SEQ ID NO: 3 is T; and/or
 - iii. X₃ in SEQ ID NO: 4 is Y.
3. The multispecific antibody according to claim 1 or claim 2, wherein the multispecific antibody is a bispecific antibody.
4. The multispecific antibody according to any one of the preceding claims, wherein the first antigen-binding region is a single-domain antibody and/or the second antigen-binding region is a single-domain antibody.
5. The multispecific antibody according to any one of the preceding claims, wherein the first antigen-binding region comprises or consists of a sequence set forth in SEQ ID NO:1 or SEQ ID NO: 33, or a sequence having at least 90%, such as at least 92%, e.g. at least 94%, such as at least 96%, e.g. at least 98% sequence identity to a sequence set forth in SEQ ID NO:1 or SEQ ID NO: 33.
6. The multispecific antibody according to any one of the preceding claims, wherein the multispecific antibody is able to activate human V γ 9V δ 2 T cells.
7. The multispecific antibody according to any one of the preceding claims, wherein the second antigen-binding region comprises the VH CDR1 sequence set forth in SEQ ID NO:18, the VH CDR2 sequence set forth in SEQ ID NO:19 and the VH CDR3 sequence set forth in SEQ ID NO:20, and wherein X₄ in SEQ ID NO: 20 is F,

or

wherein the second antigen-binding region comprises the VH CDR1 sequence set forth in SEQ ID NO:39, the VH CDR2 sequence set forth in SEQ ID NO:40 and the VH CDR3 sequence set forth in SEQ ID NO:41,

or

wherein the second antigen-binding region comprises the VH CDR1 sequence set forth in SEQ ID NO:42, the VH CDR2 sequence set forth in SEQ ID NO:43 and the VH CDR3 sequence set forth in SEQ ID NO:44,

or

wherein the second antigen-binding region comprises the VH CDR1 sequence set forth in SEQ ID NO:45, the VH CDR2 sequence set forth in SEQ ID NO:46 and the VH CDR3 sequence set forth in SEQ ID NO:47.

8. The multispecific antibody according to any one of the preceding claims, wherein the second antigen-binding region comprises or consists of the sequence set forth in SEQ ID NO:17, or a sequence having at least 90%, such as least 92%, e.g. at least 94%, such as at least 96%, e.g. at least 98% sequence identity to the sequence set forth in SEQ ID NO:17,

or

wherein the second antigen-binding region comprises or consists of the sequence set forth in SEQ ID NO:36, or a sequence having at least 90%, such as least 92%, e.g. at least 94%, such as at least 96%, e.g. at least 98% sequence identity to the sequence set forth in SEQ ID NO:36,

or

wherein the second antigen-binding region comprises or consists of the sequence set forth in SEQ ID NO:37, or a sequence having at least 90%, such as least 92%, e.g. at least 94%, such as at least 96%, e.g. at least 98% sequence identity to the sequence set forth in SEQ ID NO:37,

or

wherein the second antigen-binding region comprises or consists of the sequence set forth in SEQ ID NO:38, or a sequence having at least 90%, such as least 92%, e.g. at least 94%, such as at least 96%, e.g. at least 98% sequence identity to the sequence set forth in SEQ ID NO:38.

9. The multispecific antibody according to any one of the preceding claims, wherein the first antigen-binding region capable of binding human CD123 is located N-terminally of the second antigen-binding region capable of binding the human V δ 2 chain.
10. The multispecific antibody according to any one of the preceding claims, wherein the multispecific antibody further comprises a half-life extension domain, such as an Fc region, preferably a human Fc region.
11. The multispecific antibody according claim 10, wherein the Fc region is a heterodimer comprising two Fc polypeptides, wherein the first antigen-binding region is fused to the first Fc polypeptide and the second antigen-binding region is fused to the second Fc polypeptide and wherein the first and second Fc polypeptides comprise asymmetric amino acid mutations that favor the formation of heterodimers over the formation of homodimers, wherein preferably the first Fc polypeptide comprises a T366W substitution and the second Fc polypeptide comprises T366S, L368A and Y407V substitutions, or vice versa, wherein the amino acid positions correspond to human IgG1 according to the EU numbering system.
12. The multispecific antibody according any one of claims 10 or 11, wherein the cysteine residues at position 220 in the first and second Fc polypeptides have been deleted or substituted, wherein the amino acid position corresponds to human IgG1 according to the EU numbering system.
13. The multispecific antibody according any one of claims 10 to 12, wherein the first and second Fc polypeptides further comprise a mutation at position 234 and/or 235, preferably wherein the first and second Fc polypeptide comprise an L234F and an L235E substitution, wherein the amino acid positions correspond to human IgG1 according to the EU numbering system.
14. The multispecific antibody according to any one of claims 10 to 13, wherein the first Fc polypeptide comprises the sequence set forth in SEQ ID NO:21 and the second Fc polypeptide comprises the sequence set forth in SEQ ID NO:22, or vice versa.

15. The multispecific antibody according to any one of the preceding claims, wherein the multispecific antibody is capable of mediating killing of CD123-expressing cells, such as C1r-neo cells or THP-1 cells, by V γ 9V δ 2 T cells.
16. The multispecific antibody according to any one of the preceding claims wherein
- the first antigen-binding region is a single-domain antibody comprising VH CDR1 sequence set forth in SEQ ID NO:2, wherein X₁ in SEQ ID NO: 2 is G, the VH CDR2 sequence set forth in SEQ ID NO:3, wherein X₂ in SEQ ID NO: 3 is T and the VH CDR3 sequence set forth in SEQ ID NO:4, wherein X₃ in SEQ ID NO: 4 is Y; and
 - the second antigen-binding region is a single-domain antibody comprising an amino acid sequence that is at least 94% identical to SEQ ID NO: 17.
17. The multispecific antibody of claim 16, wherein the first antigen binding region comprises an amino acid sequence that is at least 94% identical to SEQ ID NO: 1.
18. An antibody comprising a first antigen-binding region capable of binding human CD123, wherein the first antigen-binding region is a single-domain antibody comprising:
- VH CDR1 sequence set forth in SEQ ID NO:2, the VH CDR2 sequence set forth in SEQ ID NO:3 and the VH CDR3 sequence set forth in SEQ ID NO:4, wherein preferably the first antigen-binding region comprises or consists of: a sequence selected from the group of sequences set forth in SEQ ID NO:1, 25 to 34, or a sequence having at least 90%, such as least 92%, e.g. at least 94%, such as at least 96%, e.g. at least 98% sequence identity to a sequence selected from the group of sequences set forth in SEQ ID NO:1, 25 to 34, or
 - the VH CDR1 sequence set forth in SEQ ID NO:10, the VH CDR2 sequence set forth in SEQ ID NO:11 and the VH CDR3 sequence set forth in SEQ ID NO:12, wherein preferably the first antigen-binding region comprises or consists of: the sequence set forth in SEQ ID NO:9, or a sequence having at least 90%, such as least 92%, e.g. at least 94%, such as at least 96%, e.g. at least 98% sequence identity to the sequence set forth in SEQ ID NO:9.
19. A pharmaceutical composition comprising a multispecific antibody according to any one of claims 1-17 or the antibody according to claim 18 and a pharmaceutically-

acceptable excipient.

20. The multispecific antibody according to any one of claims 1 to 17 or the antibody according to claim 18 for use as a medicament, preferably for use in the treatment of cancer, more preferably for use in the treatment of acute myeloid leukemia, B-cell acute lymphoblastic leukemia, hairy cell leukemia, Hodgkin lymphoma, blastic plasmacytoid dendritic neoplasm, chronic myeloid leukemia, chronic lymphocytic leukemia, B-cell chronic lymphoproliferative disorders or myelodysplastic syndrome.
21. A nucleic acid construct comprising a nucleotide sequence encoding the multispecific antibody of claims 1-17 or the antibody according to claim 18 or a host cell comprising one or more nucleic acid constructs encoding multispecific antibody of claims 1-17 or the antibody according to claim 18.
22. Use of the antibody according to any one of claims 1 to 18 or the antibody according to claim 19 in the manufacture of a medicament for the treatment of cancer, more preferably for use in the treatment of acute myeloid leukemia, B-cell acute lymphoblastic leukemia, hairy cell leukemia, Hodgkin lymphoma, blastic plasmacytoid dendritic neoplasm, chronic myeloid leukemia, chronic lymphocytic leukemia, B-cell chronic lymphoproliferative disorders or myelodysplastic syndrome.