

chain comprises the amino acid sequence of SEQ ID NO:309. In one of the above embodiments of the T cell activating bispecific antigen binding molecule, the fifth polypeptide chain comprises the amino acid sequence of SEQ ID NO:308. In one of the above embodiments of the T cell activating bispecific antigen binding molecule, the first and second polypeptide chain
5 comprise the amino acid sequence of SEQ ID NO:230; the third polypeptide chain comprises the amino acid sequence of SEQ ID NO:86; the fourth polypeptide chain comprises the amino acid sequence of SEQ ID NO:309; and the fifth polypeptide chain comprise the amino acid sequence of SEQ ID NO:308.

The disclosure provides for a T cell activating bispecific antigen binding molecule comprising
10 the amino acid sequence of SEQ ID NO:308. In one embodiment, the T cell activating bispecific antigen binding molecule of the above embodiment further comprises the amino acid sequence of SEQ ID NO:230 and of SEQ ID NO:86.

The disclosure provides for an isolated polypeptide comprising the amino acid sequence of SEQ ID NO:308. The disclosure provides for an isolated polypeptide comprising the amino acid
15 sequence of SEQ ID NO:309.

The disclosure provides for a T cell activating bispecific antigen binding molecule comprising the amino acid sequence of SEQ ID NO:276. The T cell activating bispecific antigen binding molecule of the disclosure further comprises the amino acid sequence of SEQ ID NO:277 and of SEQ ID NO:35. Thus, in one aspect, the disclosure provides for a T cell activating bispecific antigen binding molecule
20 comprising the amino acid sequence of SEQ ID NO:276 and further comprising the amino acid sequence of SEQ ID NO: 277 and of SEQ ID NO: 35.

The disclosure provides for an isolated polypeptide comprising the amino acid sequence of SEQ ID NO:277. The disclosure provides for an isolated polypeptide comprising the amino acid sequence of SEQ ID NO:276.

~~In one aspect, the~~
25 The disclosure provides for an isolated polynucleotide encoding the T cell activating bispecific antigen binding molecule as disclosed herein or a fragment thereof. In one aspect, the disclosure provides for an isolated polynucleotide encoding the T cell activating bispecific antigen binding molecule as disclosed herein. In one embodiment, the disclosure provides for an isolated polynucleotide encoding a T cell activating bispecific antigen binding molecule comprising the nucleotide
30 sequence of SEQ ID NO:169. In one embodiment, the disclosure provides for an isolated polynucleotide encoding a T cell activating bispecific antigen binding molecule comprising the nucleotide sequence of SEQ ID NO:246. In one embodiment, the disclosure provides for an isolated polynucleotide encoding a T cell activating bispecific antigen binding molecule comprising the nucleotide sequence of SEQ ID NO:247. In one embodiment, the disclosure provides for an isolated polynucleotide encoding a T cell
35 activating bispecific antigen binding molecule comprising the nucleotide sequence of SEQ ID NO:97. In one embodiment, the disclosure provides for an isolated

Claims

1. A T cell activating bispecific antigen binding molecule comprising
 - (i) a first antigen binding moiety which is a Fab molecule capable of specific binding to CD3, and which comprises at least one heavy chain complementarity determining region (CDR) amino acid sequence selected from the group consisting of SEQ ID NO: 37, SEQ ID NO: 38 and SEQ ID NO: 39 and at least one light chain CDR selected from the group of SEQ ID NO: 32, SEQ ID NO: 33, SEQ ID NO: 34;
 - (ii) a second antigen binding moiety capable of specific binding to Folate Receptor 1 (FolR1) which comprises:
 - a) the heavy chain CDR1 of SEQ ID NO: 16, the heavy chain CDR2 of SEQ ID NO: 17, the heavy chain CDR3 of SEQ ID NO: 18, the light chain CDR1 of SEQ ID NO: 32, the light chain CDR2 of SEQ ID NO: 33, and the light chain CDR3 of SEQ ID NO: 34;
 - b) the heavy chain CDR1 of SEQ ID NO: 8, the heavy chain CDR2 of SEQ ID NO: 56, the heavy chain CDR3 of SEQ ID NO: 57, the light chain CDR1 of SEQ ID NO: 59, the light chain CDR2 of SEQ ID NO: 60, and the light chain CDR3 of SEQ ID NO: 65; or
 - c) a complementarity determining region heavy chain 1 (CDR-H1) amino acid sequences of SEQ ID NO: 16, a CDR-H2 amino acid sequence of SEQ ID NO: 275, a CDR-H3 amino acid sequence of SEQ ID NO: 315, a complementarity determining region light chain 1 (CDR-L1) amino acid sequence of SEQ ID NO: 32, a CDR-L2 amino acid sequence of SEQ ID NO: 33, and, a CDR-L3 amino acid sequence of SEQ ID NO: 34.
2. The T cell activating bispecific antigen binding molecule of claim 1, wherein the first antigen binding moiety comprises the heavy chain CDR1 of SEQ ID NO: 37, the heavy chain CDR2 of SEQ ID NO: 38, the heavy chain CDR3 of SEQ ID NO: 39, the light chain CDR1 of SEQ ID NO: 32, the light chain CDR2 of SEQ ID NO: 33, and the light chain CDR3 of SEQ ID NO: 34.
3. The T cell activating bispecific antigen binding molecule of claim 1 or 2, wherein the first antigen binding moiety comprises a variable heavy chain comprising an amino acid

sequence of SEQ ID NO: 36 and a variable light chain comprising an amino acid sequence of SEQ ID NO: 31.

4. The T cell activating bispecific antigen binding molecule of any one of claims 1 to 3,
5 additionally comprising
(iii) a third antigen binding moiety capable of specific binding to FolR1.

5. The T cell activating bispecific antigen binding molecule of claim 4, wherein at least one
10 of the second and third antigen binding moiety is a Fab molecule.

6. The T cell activating bispecific antigen binding molecule of any of claims 1 to 5,
15 additionally comprising
(iv) an Fc domain composed of a first and a second subunit capable of stable
association.

7. The T cell activating bispecific antigen binding molecule of any one of claims 1 to 6,
20 wherein the antigen binding moiety capable of specific binding to FolR1 comprises a
variable heavy chain comprising an amino acid sequence of SEQ ID NO: 15 and a
variable light chain comprising an amino acid sequence of SEQ ID NO: 31.

8. The T cell activating bispecific antigen binding molecule of any one of claims 1 to 6,
25 wherein the antigen binding moiety capable of specific binding to FolR1 comprises a
variable heavy chain comprising an amino acid sequence of SEQ ID NO: 55 and a
variable light chain comprising an amino acid sequence of SEQ ID NO: 64.

9. The T cell activating bispecific antigen binding molecule of any one of claims 1 to 6,
30 wherein the antigen binding moiety capable of specific binding to FolR1 comprises a
variable heavy chain comprising an amino acid sequence of SEQ ID NO: 274 and a
variable light chain comprising an amino acid sequence of SEQ ID NO: 31.

10. The T cell activating bispecific antigen binding molecule of any one of claims 1 to 6 or 8,
35 wherein the first antigen binding moiety is a crossover Fab molecule wherein either the
variable or the constant regions of the Fab light chain and the Fab heavy chain are
exchanged.

11. The T cell activating bispecific antigen binding molecule of any one of claims 6 to 10, wherein the Fc domain is an IgG class immunoglobulin, specifically an IgG₁ or IgG₄, Fc domain.

5 12. The T cell activating bispecific antigen binding molecule of any one of claims 6 to 11, wherein the Fc domain is a human Fc domain.

10 13. The T cell activating bispecific antigen binding molecule of any one of claims 6 to 12, wherein the Fc domain comprises a modification promoting the association of the first and the second subunit of the Fc domain.

15 14. The T cell activating bispecific antigen binding molecule of claim 13, wherein in the CH3 domain of the first subunit of the Fc domain an amino acid residue is replaced with an amino acid residue having a larger side chain volume, thereby generating a protuberance within the CH3 domain of the first subunit which is positionable in a cavity within the CH3 domain of the second subunit, and in the CH3 domain of the second subunit of the Fc domain an amino acid residue is replaced with an amino acid residue having a smaller side chain volume, thereby generating a cavity within the CH3 domain of the second subunit within which the protuberance within the CH3 domain of the first subunit is positionable.

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25 15. The T cell activating bispecific antigen binding molecule of any one of claims 6 to 14, wherein the Fc domain comprises at least one amino acid substitution that reduces binding to an Fc receptor and/or effector function, as compared to a native IgG₁ Fc domain.

30 16. The T cell activating bispecific antigen binding molecule of claim 15, wherein each subunit of the Fc domain comprises three amino acid substitutions that reduce binding to an activating Fc receptor and/or effector function wherein said amino acid substitutions are L234A, L235A and P329G (Kabat numbering).

17. The T cell activating bispecific antigen binding molecule of any one of claims 1 to 16, wherein the T cell activating bispecific antigen binding molecule does not bind to human Folate Receptor 2 (FolR2) or to human Folate Receptor 3 (FolR3).

18. A T cell activating bispecific antigen binding molecule comprising the amino acid sequence of SEQ ID NO:276 and further comprising the amino acid sequence of SEQ ID NO: 277 and of SEQ ID NO: 35.

5 19. An isolated polynucleotide encoding the T cell activating bispecific antigen binding molecule of any one of claims 1 to 18 ~~or a fragment thereof~~.

20. A polypeptide encoded by the polynucleotide of claim 19.

10 21. A vector, particularly an expression vector, comprising the polynucleotide of claim 19.

22. A host cell comprising the polynucleotide of claim 19 or the vector of claim 21.

15 23. A method of producing the T cell activating bispecific antigen binding molecule capable of specific binding to CD3 and a target cell antigen, comprising the steps of a) culturing the host cell of claim 22 under conditions suitable for the expression of the T cell activating bispecific antigen binding molecule and b) recovering the T cell activating bispecific antigen binding molecule.

20 24. A pharmaceutical composition comprising the T cell activating bispecific antigen binding molecule of any one of claims 1 to 18 and a pharmaceutically acceptable carrier.

25 25. The T cell activating bispecific antigen binding molecule of any one of claims 1 to 18 or the pharmaceutical composition of claim 24 for use as a medicament.

26. The T cell activating bispecific antigen binding molecule of any one of claims 1 to 18 or the pharmaceutical composition of claim 24 for use in the treatment of cancer.

30 27. Use of the T cell activating bispecific antigen binding molecule of any one of claims 1 to 18 for the manufacture of a medicament for the treatment of cancer.

28. An *in vitro* method for inducing lysis of a FolR1⁺ target cell, comprising contacting a target cell with the T cell activating bispecific antigen binding molecule of any one of claims 1 to 18 in the presence of a CD3⁺ T cell.