the immune response is re-directed to the target cells and is independent of peptide antigen presentation by the target cell or the specificity of the T cell as would be relevant for normal MHC-restricted activation of CTLs. In this context it is crucial that CTLs are only activated when a target cell is presenting the bispecific antibody to them, i.e. the immunological synapse is mimicked. Particularly desirable are bispecific antibodies that do not require lymphocyte preconditioning or co-stimulation in order to elicit efficient lysis of target cells.

FOLR1 is expressed on epithelial tumor cells of various origins, e.g., ovarian cancer, lung cancer, breast cancer, renal cancer, colorectal cancer, endometrial cancer. Several approaches to target FOLR1 with therapeutic antibodies, such as farletuzumab, antibody drug conjugates, or adoptive T cell therapy for imaging of tumors have been described (Kandalaft et al., J Transl Med. 2012 Aug 3;10:157. doi: 10.1186/1479-5876-10-157; van Dam et al., Nat Med. 2011 Sep 18;17(10):1315-9. doi: 10.1038/nm.2472; Cliftonet al., Hum Vaccin. 2011 Feb;7(2):183-90. Epub 2011 Feb 1; Kelemen et al., Int J Cancer. 2006 Jul 15;119(2):243-50; Vaitilingam et al., J Nucl Med. 2012 Jul;53(7); Teng et al., 2012 Aug;9(8):901-8. doi: 10.1517/17425247.2012.694863. Epub 2012 Jun 5. Some attempts have been made to target folate receptor-positive tumors with constructs that target the folate receptor and CD3 (Kranz et al., Proc Natl Acad Sci U S A. Sep 26, 1995; 92(20): 9057–9061; Roy et al., Adv Drug Deliv Rev. 2004 Apr 29;56(8):1219-31; Huiting Cui et al Biol Chem. Aug 17, 2012; 287(34): 28206–28214; Lamers et al., Int. J. Cancer. 60(4):450 (1995); Thompson et al., MAbs. 2009 Jul-Aug;1(4):348-56. Epub 2009 Jul 19; Mezzanzanca et al., Int. J. Cancer, 41, 609–615 (1988). However, the approaches taken so far have many disadvantages. The molecules used thus far could not be readily and reliably produced as they require chemical cross linking. Similarly, hybrid molecules cannot be produced at large scale as human proteins and require the use of rat, murine or other proteins that are highly immunogenic when administered to humans and, thus, of limited therapeutic value. Further, many of the existing molecules retained FcgR binding.

Thus, there remains a need for novel, improved bispecific antibodies for targeted T cell mediated immunotherapy. The present invention provides bispecific antigen binding molecules designed for targeted T cell activation, particularly, bispecific antigen binding molecules suitable as effective and safe therapeutics that can be readily produced and dosed.

Summary

The disclosure provides 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; and

(ii) a second antigen binding moiety capable of specific binding to Folate Receptor 1 (FolR1).

In one aspect, the disclosure provides 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 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;

(ii) a second antigen binding moiety capable of specific binding to Folate Receptor 1 (FolR1).

In one embodiment, the T cell activating bispecific antigen binding molecule comprises a first antigen binding moiety that 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. In one embodiment, the T cell activating bispecific antigen binding molecule additionally comprises (iii) a third antigen binding moiety capable of specific binding to FolR1. In one embodiment, the second and third antigen binding moiety capable of specific binding to FolR1 comprise identical heavy chain complementarity determining region (CDR) and light chain CDR sequences. In one embodiment, the third antigen binding moiety is identical to the second antigen binding moiety.

In one embodiment of the T cell activating bispecific antigen binding molecule of the above embodiments, at least one of the second and third antigen binding moiety is a Fab molecule. In one embodiment, the T cell activating bispecific antigen binding molecule of the above embodiments, additionally comprises an Fc domain composed of a first and a second subunit capable of stable association. In some embodiments, the first antigen binding moiety and the second antigen binding moiety are each connected at the C-terminus of the Fab heavy chain to the N-terminus of the first or second subunit of the Fc domain. In some embodiments, a third

antigen binding moiety is fused at the C-terminus of the Fab heavy chain to the N-terminus of the Fab heavy chain of the first antigen binding moiety, optionally via a peptide linker.

In one embodiment of the T cell activating bispecific antigen binding molecule of the above embodiments, the antigen binding moiety capable of specific binding to Folate Receptor 1 (FolR1) comprises at least one heavy chain complementarity determining region (CDR) amino acid sequence selected from the group consisting of SEQ ID NO: 16, SEQ ID NO: 17 and SEQ ID NO: 18 and at least one light chain CDR selected from the group of SEQ ID NO: 32, SEQ ID NO: 33, SEQ ID NO: 34. In one embodiment, the antigen binding moiety capable of specific binding to Folate Receptor 1 (FolR1) comprises a variable heavy chain comprising an amino

the T cell activating bispecific antigen binding molecule of any of the above embodiments has an affinity (monovalent binding) of 1 μM or greater. In one embodiment, the affinity is around 1.4 μM for human FolR1. In one embodiment, the T cell activating bispecific antigen binding molecule of any of the above embodiments has an avidity (bivalent binding) of about 1-100nM or lower. In one embodiment, the avidity is about 10 nM or less. In one embodiment, the avidity is 10 nM.

In one embodiment, the T cell activating bispecific antigen binding molecule of any of the above embodiments binds to FolR1 expressed on a human tumor cell. In one embodiment, the T cell activating bispecific antigen binding molecule of any of the above embodiments binds to a conformational epitope on human FolR1. In one embodiment, the T cell activating bispecific antigen binding molecule of any of the above embodiments does not bind to human Folate Receptor 2 (FolR2) or to human Folate Receptor 3 (FolR3). In one embodiment of the T cell activating bispecific antigen binding molecule of any of the above embodiments, the antigen binding moiety binds to a FolR1 polypeptide comprising the amino acids 25 to 234 of human FolR1 (SEQ ID NO:227). In one embodiment of the T cell activating bispecific antigen binding molecule of any of the above embodiments, the FolR1 antigen binding moiety binds to a FolR1 polypeptide comprising the amino acid sequence of SEQ ID NOs:227, 230 and 231, and wherein the FolR1 antigen binding moiety does not bind to a FolR polypeptide comprising the amino acid sequence of SEQ ID NOs:228 and 229.

The disclosure provides for a bispecific antibody comprising a) a first antigen-binding site that competes for binding to human FolR1 with a reference antibody comprising a variable heavy chain domain (VH) of SEQ ID NO: 49 and a variable light chain domain of SEQ ID NO: 51; and b) a second antigen-binding site that competes for binding to human CD3 with a reference antibody comprising a variable heavy chain domain (VH) of SEQ ID NO: 36 and a variable light chain domain of SEQ ID NO: 31, wherein binding competition is measured using a surface plasmon resonance assay.

In another aspect, the disclosure provides for a bispecific antibody comprising a) a first antigen-binding site that competes for binding to human FolR1 with a reference antibody comprising a variable heavy chain domain (VH) of SEQ ID NO: 274 and a variable light chain domain of SEQ ID NO: 31; and b) a second antigen-binding site that competes for binding to human CD3 with a reference antibody comprising a variable heavy chain domain (VH) of SEQ ID NO: 36 and a variable light chain domain of SEQ ID NO: 31, wherein binding competition is measured using a surface plasmon resonance assay.

The disclosure provides for a T cell activating bispecific antigen binding molecule comprising a first antigen binding moiety capable of specific binding to CD3, and a second antigen binding moiety capable of specific binding to Folate Receptor 1 (FolR1), wherein the T cell activating bispecific antigen binding molecule binds to the same epitope on human FolR1 as a first reference antibody comprising a variable heavy chain domain (VH) of SEQ ID NO: 49 and a variable light chain domain of SEQ ID NO: 51; and wherein the T cell activating bispecific antigen binding molecule binds to the same epitope on human CD3 as a second reference antibody comprising a variable heavy chain domain (VH) of SEQ ID NO: 36 and a variable light chain domain of SEQ ID NO: 31.

The disclosure provides for a T cell activating bispecific antigen binding molecule comprising a first antigen binding moiety capable of specific binding to CD3, and a second antigen binding moiety capable of specific binding to Folate Receptor 1 (FolR1), wherein the T cell activating bispecific antigen binding molecule binds to the same epitope on human FolR1 as a first reference antibody comprising a variable heavy chain domain (VH) of SEQ ID NO: 274 and a variable light chain domain (VL) of SEQ ID NO: 31; and wherein the T cell activating bispecific antigen binding molecule binds to the same epitope on human CD3 as a second reference antibody comprising a variable heavy chain domain (VH) of SEQ ID NO: 36 and a variable light chain domain (VL) of SEQ ID NO: 31.

The disclosure relates to an antibody or an antigen-binding fragment thereof that competes for binding to human FolR1 with an antibody that comprises a variable heavy chain domain (VH) of SEQ ID NO: 274 and a variable light chain domain of SEQ ID NO: 31, wherein binding competition is measured using a surface plasmon resonance assay.

The disclosure provides for a T cell activating bispecific antigen binding molecule, wherein the antigen binding molecule comprises a first, second, third, fourth and fifth polypeptide chain that form a first, a second and a third antigen binding moiety, wherein the first antigen binding moiety is capable of binding CD3 and the second and the third antigen binding moiety each are capable of binding Folate Receptor 1 (FolR1), wherein a) the first and the second polypeptide chain comprise, in amino (N)-terminal to carboxyl (C)-terminal direction, VLD1 and CLD1; b) the third polypeptide chain comprises, in N-terminal to C-terminal direction, VLD2 and CH1D2; c) the fourth polypeptide chain comprises, in N-terminal to C-terminal direction, VHD1, CH1D1, CH2D1 and CH3D1; d) the fifth polypeptide chain comprises VHD1, CH1D1, VHD2, CLD2, CH2D2 and CH3D2; wherein VLD1 is a first light chain variable domain, VLD2 is a second light chain variable domain, CLD1 is a first light chain

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 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 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 sequence of SEQ ID NO:309.

In one aspect, the disclosure provides for a T cell activating bispecific antigen binding molecule comprising the amino acid sequence of SEQ ID NO:276. 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: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 disclosure provides for an isolated polynucleotide encoding the T cell activating bispecific antigen binding molecule as disclosed herein or a fragment thereof. 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: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 activating bispecific antigen binding molecule comprising the nucleotide sequence of SEQ ID NO:97. 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:198.

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:287. 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:288. 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:289.

The disclosure provides for an isolated polypeptide encoded by the polynucleotide of the above embodiment. In one aspect, the disclosure provides for a polypeptide encoded by the polynucleotide as disclosed herein. The disclosure provides for a vector, particularly an expression vector, comprising the polynucleotide encoding the T cell activating bispecific antigen binding molecule of any one of the embodiments disclosed herein. In another aspect, the disclosure provides a vector, particularly an expression vector, comprising the polynucleotide as disclosed herein. In another aspect, the disclosure provides for a host cell comprising a polynucleotide or a vector as disclosed herein.

In one aspect, the disclosure provides for 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 as disclosed herein 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.

In one aspect, the disclosure provides for a T cell activating bispecific antigen binding molecule produced by the method as disclosed herein.

In one aspect, the disclosure provides for a pharmaceutical composition comprising the T cell activating bispecific antigen binding molecule as disclosed herein and a pharmaceutically acceptable carrier. In one aspect, the disclosure provides for the T cell activating bispecific antigen binding molecule as disclosed herein of any one of the above embodiments or the pharmaceutical composition as disclosed herein for use as a medicament.

The disclosure provides for the T cell activating bispecific antigen binding molecule of any one of the above embodiments or the pharmaceutical composition of any one of the above embodiments for use in the treatment of a disease in an individual in need thereof. In some embodiments, the disease is cancer. In another aspect, the disclosure provides for the T cell activating bispecific antigen binding molecule as disclosed herein or the pharmaceutical composition as disclosed herein for use in the treatment of cancer. The disclosure provides for a use of the T cell activating bispecific antigen binding molecule of any one of the above embodiments for the manufacture of a medicament for the treatment of a disease in an individual in need thereof. In another aspect, the disclosure provides for use of the T cell activating bispecific antigen binding molecule as disclosed herein for the manufacture of a medicament for the treatment of cancer.

The disclosure provides for a method of treating a disease in an individual, comprising administering to said individual a therapeutically effective amount of a composition comprising the T cell activating bispecific antigen binding molecule of any one of the above embodiments in a pharmaceutically acceptable form. In some embodiments, said disease is a cancer.

The disclosure provides for a method for inducing lysis of a target cell, comprising contacting a target cell with the T cell activating bispecific antigen binding molecule of any one of the above embodiments in the presence of a T cell. In one aspect, the disclosure provides for a method for inducing lysis of a FolR1$^+$ target cell, comprising contacting a target cell with the T cell activating bispecific antigen binding molecule as disclosed herein in the presence of a CD3$^+$ T cell.

Brief Description of the Drawings

Figures 1A-I illustrate exemplary configurations of the T cell activating bispecific antigen binding molecules (TCBs) of the invention. All constructs except the kappa-lambda format in (Fig. 1I) have P329G LALA mutations and comprise knob-into-hole Fc fragments with knob-into-hole modifications. (Fig. 1A) Illustration of the "FolR1 TCB 2+1 inverted (common light chain)". The FolR1 binder is fused at the C-terminus of the Fab heavy chain to the N-terminus of the first subunit of the Fc domain comprising the knob modification. These constructs are not crossed and have three times the same VLCL light chain. (Fig. 1B) Illustration of the "FolR1 TCB 1+1 head-to-tail (common light chain)". These constructs are not crossed and have two times the same VLCL light chain. (Fig. 1C) Illustration of the "FolR1 TCB 1+1 classical (common light chain)". These constructs are not crossed and have two times the same VLCL light chain. (Fig. 1D) Illustration of the "FolR1 TCB 2+1 classical (common light chain)". The CD3 binder is fused at the C-terminus of the Fab heavy chain to the N-terminus of the first subunit of the Fc domain comprising the knob modification. These constructs are not crossed and have three times the same VLCL light chain. (Fig. 1E) Illustration of the "FolR1 TCB 2+1 crossfab classical". These constructs comprise a Ck-VH chain for the CD3 binder instead of the conventional CH1-VH chain. The CD3 binder is fused at the C-terminus of the Fab heavy chain to the N-terminus of the first subunit of the Fc domain comprising the knob modification. (Fig. 1F) Illustration of the "FolR1 TCB 2+1 crossfab inverted". These constructs comprise a Ck-VH chain for the CD3 binder instead of the conventional CH1-VH chain. The FolR1 binder is fused at the C-terminus of the Fab heavy chain to the N-terminus of the first subunit of the Fc domain comprising the knob modification. (Fig. 1G) Illustration of the "FolR1 TCB 1+1 crossfab head-

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 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;
   (ii) a second antigen binding moiety capable of specific binding to Folate Receptor 1 (FolR1).

2. The T cell activating bispecific antigen binding molecule of claim 1, 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.

3. The T cell activating bispecific antigen binding molecule of claim 1 or 2, additionally comprising
   (iii) a third antigen binding moiety capable of specific binding to FolR1.

4. The T cell activating bispecific antigen binding molecule of claim 1 to 3, wherein at least one of the second and third antigen binding moiety is a Fab molecule.

5. The T cell activating bispecific antigen binding molecule of any of claims 1 to 4, additionally comprising

(iv) an Fc domain composed of a first and a second subunit capable of stable association.

6. The T cell activating bispecific antigen binding molecule of any of the preceding claims, wherein the antigen binding moiety capable of specific binding to FolR1 comprises 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.

7. The T cell activating bispecific antigen binding molecule of claim 6, 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 of claims 1 to 5, wherein the antigen binding moiety capable of specific binding to FolR1 comprises 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.

9. The T cell activating bispecific antigen binding molecule of claim 8, 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.

10. The T cell activating bispecific antigen binding molecule of any one of claims 1 to 5, wherein the antigen binding moiety capable of specific binding to FolR1 comprises:

(a) a complementarity determining region heavy chain 1 (CDR-H1) amino acid sequences of SEQ ID NO: 8;
(b) a CDR-H2 amino acid sequence of SEQ ID NO: 9;
(c) a CDR-H3 amino acid sequence of SEQ ID NO: 50;
(d) a complementarity determining region light chain 1 (CDR-L1) amino acid sequence of SEQ ID NO: 52;
(e) a CDR-L2 amino acid sequence of SEQ ID NO: 53, and
(f) a CDR-L3 amino acid sequence of SEQ ID NO: 54.

11. The T cell activating bispecific antigen binding molecule of claim 10, 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: 49 and a variable light chain comprising an amino acid sequence of SEQ ID NO: 51.

12. The T cell activating bispecific antigen binding molecule of any one of claims 1 to 5, wherein the antigen binding moiety capable of specific binding to FolR1 comprises:

(a) a complementarity determining region heavy chain 1 (CDR-H1) amino acid sequences of SEQ ID NO: 16;

(b) a CDR-H2 amino acid sequence of SEQ ID NO: 275;

(c) a CDR-H3 amino acid sequence of SEQ ID NO: 315;

(d) a complementarity determining region light chain 1 (CDR-L1) amino acid sequence of SEQ ID NO: 32;

(e) a CDR-L2 amino acid sequence of SEQ ID NO: 33, and

(f) a CDR-L3 amino acid sequence of SEQ ID NO: 34.

13. The T cell activating bispecific antigen binding molecule of claim 12, 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.

14. The T cell activating bispecific antigen binding molecule of claim 1 to 5 or 9 to 11, 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.

15. The T cell activating bispecific antigen binding molecule of any one of claims 5 to 14, wherein the Fc domain is an IgG class immunoglobulin, specifically an IgG_1 or IgG_4, Fc domain.

16. The T cell activating bispecific antigen binding molecule of any one of claims 5 to 15, wherein the Fc domain is a human Fc domain.

17. The T cell activating bispecific antigen binding molecule of any one of claims 5 to 16, wherein the Fc domain comprises a modification promoting the association of the first and the second subunit of the Fc domain.

18. The T cell activating bispecific antigen binding molecule of claim 17, 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.

19. The T cell activating bispecific antigen binding molecule of any one of claims 5 to 18, 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 IgG_1 Fc domain.

20. The T cell activating bispecific antigen binding molecule of claim 19, 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).

21. The T cell activating bispecific antigen binding molecule of any one of claims 1 to 5 and 12 to 13, 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).

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22. A bispecific antibody comprising a) a first antigen-binding site that competes for binding to human FolR1 with a reference antibody comprising a variable heavy chain domain (VH) of SEQ ID NO: 274 and a variable light chain domain (VL) of SEQ ID NO: 31; and b) a second antigen-binding site that competes for binding to human CD3 with a reference antibody comprising a variable heavy chain domain (VH) of SEQ ID NO: 36 and a variable light chain domain (VL) of SEQ ID NO: 31, wherein binding competition is measured using a surface plasmon resonance assay.

23. A T cell activating bispecific antigen binding molecule comprising the amino acid sequence of SEQ ID NO:276.

24. An isolated polynucleotide encoding the T cell activating bispecific antigen binding molecule of any one of claims 1 to 23 or a fragment thereof.

25. A polypeptide encoded by the polynucleotide of claim 24.

26. A vector, particularly an expression vector, comprising the polynucleotide of claim 24.

27. A host cell comprising the polynucleotide of claim 24 or the vector of claim 26.

28. 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 27 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.

29. A T cell activating bispecific antigen binding molecule produced by the method of claim 28.

30. A pharmaceutical composition comprising the T cell activating bispecific antigen binding molecule of any one of claims 1 to 23 and a pharmaceutically acceptable carrier.

31. The T cell activating bispecific antigen binding molecule of any one of claims 1 to 23 or the pharmaceutical composition of claim 30 for use as a medicament.

32. The T cell activating bispecific antigen binding molecule of any one of claims 1 to 23 or the pharmaceutical composition of claim 30 for use in the treatment of cancer.

33. Use of the T cell activating bispecific antigen binding molecule of any one of claims 1 to 23 for the manufacture of a medicament for the treatment of cancer.

34. A 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 23 in the presence of a $CD3^+$ T cell.