SUMMARY

The disclosure provides a TNF family ligand trimer-containing antigen binding molecule comprising
(a) at least one moiety capable of specific binding to a target cell antigen and
(b) a first and a second polypeptide that are linked to each other by a disulfide bond,
wherein the antigen binding molecule is characterized in that the first polypeptide comprises two ectodomains of a TNF ligand family member or two fragments thereof that are connected to each other by a peptide linker and in that the second polypeptide comprises only one ectodomain of said TNF ligand family member or a fragment thereof.

The disclosure provides a TNF family ligand trimer-containing antigen binding molecule comprising
(a) at least one moiety capable of specific binding to a target cell antigen,
(b) a first and a second polypeptide that are linked to each other by a disulfide bond,
wherein the antigen binding molecule is characterized in that the first polypeptide comprises two ectodomains of a TNF ligand family member or two fragments thereof that are connected to each other by a peptide linker and in that the second polypeptide comprises only one ectodomain of said TNF ligand family member or a fragment thereof, and
(c) an Fc domain composed of a first and a second subunit capable of stable association.

The disclosure provides a TNF family ligand trimer-containing antigen binding molecule, comprising
(a) at least one moiety capable of specific binding to a target cell antigen and
(b) a first and a second polypeptide that are linked to each other by a disulfide bond,
wherein the antigen binding molecule is characterized in that

or a fragment thereof connected via a peptide linker to C-terminus of the CH3 domain of said polypeptide, or

(iii) the first polypeptide contains a VH-CL or a VL-CH1 domain and the second polypeptide contains a VL-CH1 domain or a VH-CL domain, respectively, wherein the second polypeptide is linked to the first polypeptide by a disulfide bond between the CH1 and CL domain, and wherein the first polypeptide comprises two ectodomains of a TNF ligand family member or fragments thereof that are connected to each other and to to VH or VL by a peptide linker and wherein the second polypeptide comprises one ectodomain of said TNF ligand family member or a fragment thereof connected via a peptide linker to VL or VH of said polypeptide.

In one aspect, the disclosure provides a tumour necrosis factor (TNF) family ligand trimer-containing antigen binding molecule comprising

(a) at least one Fab molecule capable of specific binding to a target cell antigen and

(b) a first and a second polypeptide that are linked to each other by a disulfide bond,

wherein the antigen binding molecule is characterized in that the first polypeptide comprises two ectodomains of a TNF ligand family member selected from 4-1BBL and OX40L or a fragment thereof that are connected to each other by a peptide linker and in that the second polypeptide comprises only one ectodomain of said TNF ligand family member or a fragment thereof, and further comprising

(c) an Fc domain composed of a first and a second subunit capable of stable association with each other,

wherein the antigen binding molecule is characterized in that

(i) the first polypeptide contains a first heavy chain constant (CH1) domain or first light chain constant (CL) domain and the second polypeptide contains a CL or CH1 domain, respectively, wherein the second polypeptide is linked to the first polypeptide by a disulfide bond between the CH1 and CL domain, and wherein the first polypeptide comprises two ectodomains of a TNF ligand family member or fragments thereof that are connected to each other and to the CH1 or CL domain by a peptide linker and wherein the second polypeptide comprises one ectodomain of said TNF ligand family member or a fragment thereof connected via a peptide linker to the CL or CH1 domain of said second polypeptide, or

(ii) the first polypeptide contains a constant CH3 domain and the second polypeptide contains a constant CH3 domain, respectively, and wherein the first polypeptide comprises two ectodomains of a TNF ligand family member or fragments thereof that are connected to each other and to the C-terminus of the CH3 domain by a peptide linker and wherein the second polypeptide comprises only one ectodomain of said TNF ligand family member or a fragment thereof connected via a peptide linker to C-terminus of the CH3 domain of said second polypeptide, or

(iii) the first polypeptide contains a VH-CL or a VL-CH1 domain and the second polypeptide contains a VL-CH1 domain or a VH-CL domain, respectively, wherein the second polypeptide is linked to the first polypeptide by a disulfide bond between the CH1 and CL domain, and wherein the first polypeptide comprises two ectodomains of a TNF ligand family member or fragments thereof that are connected to each other and to the heavy chain variable domain (VH) or to the light chain variable domain (VL) by a peptide linker and wherein the second polypeptide comprises one ectodomain of said TNF ligand family member or a fragment thereof connected via a peptide linker to VL or VH of said second polypeptide.

In a particular embodiment, the TNF ligand family member is one that costimulates human T-cell activation. Thus, the TNF family ligand trimer-containing antigen binding molecule comprises (a) at least one moiety capable of specific binding to a target cell antigen and (b) a first and a second polypeptide that are linked to each other by a disulfide bond, wherein the antigen binding molecule is characterized in that the first polypeptide comprises two ectodomains of a TNF ligand family member or two fragments thereof that are connected to each other by a peptide linker and in that the second polypeptide comprises only one ectodomain of said TNF ligand family member or a fragment thereof, wherein the TNF ligand family member costimulates human T-cell activation. More particularly, the TNF ligand family member is selected from 4-1BBL and OX40L.

In one embodiment, the TNF ligand family member is 4-1BBL.

In a further embodiment, the ectodomain of a TNF ligand family member comprises the amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO: 2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:96, SEQ ID NO: 373, SEQ ID NO:374 and SEQ ID NO:375, particularly the amino acid sequence of SEQ ID NO:1 or SEQ ID NO:96.

In another embodiment, the ectodomain of a TNF ligand family member or fragment thereof comprises the amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3 , SEQ ID NO:4 and SEQ ID NO:96, particularly the amino acid sequence of SEQ ID NO:1 or SEQ ID NO:96. More particularly, the ectodomain of a TNF ligand family member comprises the amino acid sequence of SEQ ID NO:96.

In a further embodiment, the TNF family ligand trimer-containing antigen binding molecule of the disclosure comprises
(a) at least one moiety capable of specific binding to a target cell antigen and
(b) a first and a second polypeptide that are linked to each other by a disulfide bond,

Claims

1. A tumour necrosis factor (TNF) family ligand trimer-containing antigen binding molecule comprising

(a) at least one Fab molecule capable of specific binding to a target cell antigen and

(b) a first and a second polypeptide that are linked to each other by a disulfide bond,

wherein the antigen binding molecule is characterized in that the first polypeptide comprises two ectodomains of a TNF ligand family member selected from 4-1BBL and OX40L or a fragment thereof that are connected to each other by a peptide linker and in that the second polypeptide comprises only one ectodomain of said TNF ligand family member or a fragment thereof, and further comprising

(c) an Fc domain composed of a first and a second subunit capable of stable association with each other,

wherein the antigen binding molecule is characterized in that

(i) the first polypeptide contains a first heavy chain constant (CH1) domain or first light chain constant (CL) domain and the second polypeptide contains a CL or CH1 domain, respectively, wherein the second polypeptide is linked to the first polypeptide by a disulfide bond between the CH1 and CL domain, and wherein the first polypeptide comprises two ectodomains of a TNF ligand family member or fragments thereof that are connected to each other and to the CH1 or CL domain by a peptide linker and wherein the second polypeptide comprises one ectodomain of said TNF ligand family member or a fragment thereof connected via a peptide linker to the CL or CH1 domain of said second polypeptide, or

(ii) the first polypeptide contains a constant CH3 domain and the second polypeptide contains a constant CH3 domain, respectively, and wherein the first polypeptide comprises two ectodomains of a TNF ligand family member or fragments thereof that are connected to each other and to the C-terminus of the CH3 domain by a peptide linker and wherein the second polypeptide comprises only one ectodomain of said TNF ligand family member or a fragment thereof connected via a peptide linker to C-terminus of the CH3 domain of said second polypeptide, or

(iii) the first polypeptide contains a VH-CL or a VL-CH1 domain and the second polypeptide contains a VL-CH1 domain or a VH-CL domain, respectively, wherein the second polypeptide is linked to the first polypeptide by a disulfide bond between the

CH1 and CL domain, and wherein the first polypeptide comprises two ectodomains of a TNF ligand family member or fragments thereof that are connected to each other and to the heavy chain variable domain (VH) or to the light chain variable domain (VL) by a peptide linker and wherein the second polypeptide comprises one ectodomain of said TNF ligand family member or a fragment thereof connected via a peptide linker to VL or VH of said second polypeptide.

2. The TNF family ligand trimer-containing antigen binding molecule of claim 1, wherein the TNF ligand family member costimulates human T-cell activation.

3. The TNF family ligand trimer-containing antigen binding molecule of claims 1 or 2, wherein the TNF ligand family member is 4-1BBL.

4. The TNF family ligand trimer-containing antigen binding molecule of any one of claims 1 to 3, wherein the ectodomain of a TNF ligand family member comprises the amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO: 2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:96, SEQ ID NO: 373, SEQ ID NO:374 and SEQ ID NO:375, particularly the amino acid sequence of SEQ ID NO:1 or SEQ ID NO:96.

5. The TNF family ligand trimer-containing antigen binding molecule of any one of claims 1 to 4, wherein the ectodomain of a TNF ligand family member comprises the amino acid sequence of SEQ ID NO:96.

6. The TNF family ligand trimer-containing antigen binding molecule of any one of claims 1 to 5, comprising
(a) at least one moiety capable of specific binding to a target cell antigen and
(b) a first and a second polypeptide that are linked to each other by a disulfide bond, wherein the antigen binding molecule is characterized in that the first polypeptide comprises the amino acid sequence selected from the group consisting of SEQ ID NO:5, SEQ ID NO:97, SEQ ID NO:98 and SEQ ID NO:99 and in that the second polypeptide comprises the amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:96, SEQ ID NO:3 and SEQ ID NO:4.

7. The TNF family ligand trimer-containing antigen binding molecule of any one of claims 1 to 6, comprising
(a) at least one moiety capable of specific binding to a target cell antigen, and

(b) a first polypeptide containing a CH1 or CL domain and a second polypeptide containing a CL or CH1 domain, respectively, wherein the second polypeptide is linked to the first polypeptide by a disulfide bond between the CH1 and CL domain, and wherein the antigen binding molecule is characterized in that the first polypeptide comprises two ectodomains of a TNF ligand family member or fragments thereof that are connected to each other and to the CH1 or CL domain by a peptide linker and in that the second polypeptide comprises only one ectodomain of said TNF ligand family member or a fragment thereof connected via a peptide linker to the CL or CH1 domain of said polypeptide.

8. The TNF family ligand trimer-containing antigen binding molecule of any one of claims 1 to 7, wherein the target cell antigen is selected from the group consisting of Fibroblast Activation Protein (FAP), Melanoma-associated Chondroitin Sulfate Proteoglycan (MCSP), Epidermal Growth Factor Receptor (EGFR), Carcinoembryonic Antigen (CEA), CD19, CD20 and CD33.

9. The TNF family ligand trimer-containing antigen binding molecule of any one of claims 1 to 8, wherein the target cell antigen is Fibroblast Activation Protein (FAP).

10. The TNF family ligand trimer-containing antigen binding molecule of any one of claims 1 to 9, wherein the moiety capable of specific binding to FAP comprises a VH domain comprising (i) CDR-H1 comprising the amino acid sequence of SEQ ID NO:7 or SEQ ID NO:100, (ii) CDR-H2 comprising the amino acid sequence of SEQ ID NO:8 or SEQ ID NO:101, and (iii) CDR-H3 comprising the amino acid sequence of SEQ ID NO:9 or SEQ ID

NO:102, and a VL domain comprising (iv) CDR-L1 comprising the amino acid sequence of SEQ ID NO:10 or SEQ ID NO:103, (v) CDR-L2 comprising the amino acid sequence of SEQ ID NO:11 or SEQ ID NO:104, and (vi) CDR-L3 comprising the amino acid sequence of SEQ ID NO:12 or SEQ ID NO:105.

11. The TNF family ligand trimer-containing antigen binding molecule of any one of claims 1 to 10, wherein the moiety capable of specific binding to FAP comprises a variable heavy chain comprising an amino acid sequence of SEQ ID NO:16 and a variable light chain comprising an amino acid sequence of SEQ ID NO:17 or wherein the moiety capable of specific binding to FAP comprises a variable heavy chain comprising an amino acid sequence of SEQ ID NO:106 and a variable light chain comprising an amino acid sequence of SEQ ID NO:107.

12. The TNF family ligand trimer-containing antigen binding molecule of any one of claims 1 to 11, wherein the Fc domain is an IgG, particularly an IgG1 Fc domain or an IgG4 Fc domain.

13. The TNF family ligand trimer-containing antigen binding molecule of any one of claims 1 to 12, wherein the Fc domain is an IgG1 Fc domain comprising the amino acid substitutions at positions 234 and 235 (EU numbering) and/or 329 (EU numbering).

14. The TNF family ligand trimer-containing antigen binding molecule of any one of claims 1 to 13, wherein the antigen binding molecule comprises
a first heavy chain and a first light chain, both comprising a Fab molecule capable of specific binding to a target cell antigen,
a first peptide comprising two ectodomains of a TNF ligand family member or fragments thereof connected to each other by a first peptide linker fused at its C-terminus by a second peptide linker to a second heavy or light chain,
and a second peptide comprising one ectodomain of said TNF ligand family member fused at its C-terminus by a third peptide linker to a second light or heavy chain, respectively.

15. The TNF family ligand trimer-containing antigen binding molecule of any one of claims 1 to 14, wherein the first peptide comprising two ectodomains of a TNF ligand family member or fragments thereof connected to each other by a first peptide linker is fused at its C-terminus by a second peptide linker to a CH1 domain that is part of a heavy chain,
and the second peptide comprising one ectodomain of said TNF ligand family member or a fragment thereof is fused at its C-terminus by a third peptide linker to a CL domain that is part of a light chain.

16. The TNF family ligand trimer-containing antigen binding molecule of any one of claims 1 to 14, wherein the first peptide comprising two ectodomains of a TNF ligand family member or fragments thereof connected to each other by a first peptide linker is fused at its C-terminus by a second peptide linker to a CL domain that is part of a heavy chain, and the second peptide comprising one ectodomain of said TNF ligand family member or a fragment thereof is fused at its C-terminus by a third peptide linker to a CH1 domain that is part of a light chain.

17. The TNF family ligand trimer-containing antigen binding molecule of claims 15 or 16, wherein in the CL domain adjacent to the TNF ligand family member the amino acid at position 123 (EU numbering) has been replaced by arginine (R) and the amino acid at position 124 (EU numbering) has been substituted by lysine (K), and wherein in the CH1 domain adjacent to the TNF ligand family member the amino acids at position 147 (EU numbering) and at position 213 (EU numbering) have been substituted by glutamic acid (E).

18. The TNF family ligand trimer-containing antigen binding molecule of any one of claims 1 to 17, wherein the antigen binding molecule comprises
(a) a first heavy chain and a first light chain, both comprising a Fab molecule capable of specific binding to a target cell antigen,
(b) a second heavy chain comprising an amino acid sequence selected from the group consisting of SEQ ID NO:5, SEQ ID NO:97, SEQ ID NO:98 and SEQ ID NO:99, and a second light chain comprising an amino acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:96, SEQ ID NO:3 and SEQ ID NO:4.

19. The TNF family ligand trimer-containing antigen binding molecule of any one of claims 1 to 15, wherein the antigen binding molecule comprises
(i) a first heavy chain comprising the VH domain comprising the amino acid sequence of SEQ ID NO:16 and a first light chain comprising the VL domain comprising the amino acid sequence of SEQ ID NO:17 or
a first heavy chain comprising the VH domain comprising the amino acid sequence of SEQ ID NO:106 and a first light chain comprising the VL domain comprising the amino acid sequence of SEQ ID NO:107,
(ii) a second heavy chain comprising the amino acid sequence selected from the group consisting of SEQ ID NO:14, SEQ ID NO:108, SEQ ID NO:111 and SEQ ID NO:113, and
(iii) a second light chain comprising the amino acid sequence of SEQ ID NO:15, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:112 and SEQ ID NO:114.

20. The TNF family ligand trimer-containing antigen binding molecule of any one of claims 1 to 14 and 16, wherein the antigen binding molecule comprises
(i) a first heavy chain comprising the VH domain comprising the amino acid sequence of SEQ ID NO:16 and a first light chain comprising the VL domain comprising the amino acid sequence of SEQ ID NO:17 or
a first heavy chain comprising the VH domain comprising the amino acid sequence of SEQ ID NO:106 and a first light chain comprising the VL domain comprising the amino acid sequence of SEQ ID NO:107,
(ii) a second heavy chain comprising the amino acid sequence selected from the group consisting of SEQ ID NO:115, SEQ ID NO:117, SEQ ID NO:119 and SEQ ID NO:173, and
(iii) a second light chain comprising the amino acid sequence selected from the group consisting of SEQ ID NO:116, SEQ ID NO:118, SEQ ID NO:120 and SEQ ID NO:174.

21. The TNF family ligand trimer-containing antigen binding molecule of any one of claims 1 to 14, 16 and 20, selected from the group consisting of:
a) a molecule comprising a first heavy chain comprising the amino acid sequence of SEQ ID NO:164, a first light chain comprising the amino acid sequence of SEQ ID NO:125, a second heavy chain comprising the amino acid sequence of SEQ ID NO:115 and a second light chain comprising the amino acid sequence of SEQ ID NO:116;
b) a molecule comprising a first heavy chain comprising the amino acid sequence of SEQ ID NO:164, a first light chain comprising the amino acid sequence of SEQ ID NO:125, a second heavy chain comprising the amino acid sequence of SEQ ID NO:117 and a second light chain comprising the amino acid sequence of SEQ ID NO:118;
c) a molecule comprising two light chains comprising the amino acid sequence of SEQ ID NO:125, a first heavy chain comprising the amino acid sequence of SEQ ID NO:123 and a second heavy chain comprising the amino acid sequence of SEQ ID NO:124;
d) a molecule comprising a first heavy chain comprising the amino acid sequence of SEQ ID NO:164, a first light chain comprising the amino acid sequence of SEQ ID NO:125, a second heavy chain comprising the amino acid sequence of SEQ ID NO:119 and a second light chain comprising the amino acid sequence of SEQ ID NO:120;
e) a molecule comprising a first heavy chain comprising the amino acid sequence of SEQ ID NO:164, a first light chain comprising the amino acid sequence of SEQ ID NO:125, a second heavy chain comprising the amino acid sequence of SEQ ID NO:173 and a second light chain comprising the amino acid sequence of SEQ ID NO:174; and
f) a molecule comprising two light chains comprising the amino acid sequence of SEQ ID NO:125, a first heavy chain comprising the amino acid sequence of SEQ ID NO:126 and a second heavy chain comprising the amino acid sequence of SEQ ID NO:127.

22. The TNF family ligand trimer-containing antigen binding molecule of any one of claims 1 to 13, comprising
(a) at least one moiety capable of specific binding to a target cell antigen, and
(b) a first and a second polypeptide that are linked to each other by a disulfide bond, wherein the antigen binding molecule is characterized in that the first polypeptide contains a CH3 domain and the second polypeptide contains a CH3 domain, respectively, and wherein the first polypeptide comprises two ectodomains of a TNF ligand family member or fragments thereof that are connected to each other and to the C-terminus of the CH3 domain by a peptide linker and wherein the second polypeptide comprises one ectodomain of said

TNF ligand family member or a fragment thereof connected via a peptide linker to C-terminus of the CH3 domain of said polypeptide.

23. The TNF family ligand trimer-containing antigen binding molecule of claim 22, comprising two Fab molecules capable of specific binding to a target cell antigen.

24. The TNF family ligand trimer-containing antigen binding molecule of claim 22, wherein the antigen binding molecule comprises
(i) a first heavy chain comprising the amino acid sequence of SEQ ID NO:121, a second heavy chain comprising the amino acid sequence of SEQ ID NO:122, and two light chains comprising the amino acid sequence of SEQ ID NO:19, or
(ii) a first heavy chain comprising the amino acid sequence of SEQ ID NO:123, a second heavy chain comprising the amino acid sequence of SEQ ID NO:124, and two light chains comprising the amino acid sequence of SEQ ID NO:125, or
(iii) a first heavy chain comprising the amino acid sequence of SEQ ID NO:126, a second heavy chain comprising the amino acid sequence of SEQ ID NO:127, and two light chains comprising the amino acid sequence of SEQ ID NO:125.

25. The TNF family ligand trimer-containing antigen binding molecule of any one of claims 1 to 8, 12 to 18and 22 to 23, wherein the target cell antigen is CD19.

26. The TNF family ligand trimer-containing antigen binding molecule of any one of claims 1 to 8, 12 to 18, 22 to 23 and 25, wherein the moiety capable of specific binding to CD19 comprises a VH domain comprising (i) CDR-H1 comprising the amino acid sequence of SEQ ID NO:195 or SEQ ID NO:252, (ii) CDR-H2 comprising the amino acid sequence of SEQ ID NO:196 or SEQ ID NO:253, and (iii) CDR-H3 comprising the amino acid sequence of SEQ ID NO:197 or SEQ ID NO:254, and a VL domain comprising (iv) CDR-L1 comprising the amino acid sequence of SEQ ID NO:198 or SEQ ID NO:249, (v) CDR-L2 comprising the amino acid sequence of SEQ ID NO:199 or SEQ ID NO:250, and (vi) CDR-L3 comprising the amino acid sequence of SEQ ID NO:200 or SEQ ID NO:251.

27. The TNF family ligand trimer-containing antigen binding molecule of any one of claims 1 to 8, 12 to 18, 22 to 23, 25 and 26, wherein the moiety capable of specific binding to CD19 comprises a variable heavy chain comprising an amino acid sequence of SEQ ID NO:201 and a variable light chain comprising an amino acid sequence of SEQ ID NO:202 or wherein the moiety capable of specific binding to FAP comprises a variable heavy chain comprising an amino acid sequence of SEQ ID NO:357 and a variable light chain comprising an amino acid sequence of SEQ ID NO:358.

28. The TNF family ligand trimer-containing antigen binding molecule of any one of claims 1 to 8, 12 to 18 and 25 to 27, wherein the antigen binding molecule comprises
(i) a first heavy chain comprising the VH domain comprising the amino acid sequence of SEQ ID NO:201 and a first light chain comprising the VL domain comprising the amino acid sequence of SEQ ID NO:202 or
a first heavy chain comprising the VH domain comprising the amino acid sequence of SEQ ID NO:357 and a first light chain comprising the VL domain comprising the amino acid sequence of SEQ ID NO:358,
(ii) a second heavy chain comprising the amino acid sequence selected from the group consisting of SEQ ID NO:14, SEQ ID NO:108, SEQ ID NO:111 and SEQ ID NO:113, and
(iii) a second light chain comprising the amino acid sequence of SEQ ID NO:15, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:112 and SEQ ID NO:114.

29. The TNF family ligand trimer-containing antigen binding molecule of any one of claims 1 to 8, 12 to 18 and 25 to 28, wherein the antigen binding molecule comprises
(i) a first heavy chain comprising the VH domain comprising the amino acid sequence of SEQ ID NO:201 and a first light chain comprising the VL domain comprising the amino acid sequence of SEQ ID NO:202 or
a first heavy chain comprising the VH domain comprising the amino acid sequence of SEQ ID NO:357 and a first light chain comprising the VL domain comprising the amino acid sequence of SEQ ID NO:358,
(ii) a second heavy chain comprising the amino acid sequence selected from the group consisting of SEQ ID NO:115, SEQ ID NO:117, SEQ ID NO:119 and SEQ ID NO:173, and
(iii) a second light chain comprising the amino acid sequence selected from the group consisting of SEQ ID NO:116, SEQ ID NO:118, SEQ ID NO:120 and SEQ ID NO:174.

30. The TNF family ligand trimer-containing antigen binding molecule of any one of claims 1 to 8, 22, 23 and 25 to 27, wherein the antigen binding molecule comprises
(i) a first heavy chain comprising the amino acid sequence of SEQ ID NO:209, a second heavy chain comprising the amino acid sequence of SEQ ID NO:210, and two light chains comprising the amino acid sequence of SEQ ID NO:206, or
(ii) a first heavy chain comprising the amino acid sequence of SEQ ID NO:213, a second heavy chain comprising the amino acid sequence of SEQ ID NO:214, and two light chains comprising the amino acid sequence of SEQ ID NO:206, or
(iii) a first heavy chain comprising the amino acid sequence of SEQ ID NO:309, a second heavy chain comprising the amino acid sequence of SEQ ID NO:310, and two light chains comprising the amino acid sequence of SEQ ID NO:279, or
(iv) a first heavy chain comprising the amino acid sequence of SEQ ID NO:313, a second

heavy chain comprising the amino acid sequence of SEQ ID NO:314, and two light chains comprising the amino acid sequence of SEQ ID NO:279.

31. The TNF family ligand trimer-containing antigen binding molecule of any one of claims 1 to 8, 12 to 18 and 22 to 23, wherein the target cell antigen is CEA.

32. The TNF family ligand trimer-containing antigen binding molecule of any one of claims 1 to 8, 12 to 18, 22 to 23 and 31, wherein the moiety capable of specific binding to CEA comprises a VH domain comprising (i) CDR-H1 comprising the amino acid sequence of SEQ ID NO:321, (ii) CDR-H2 comprising the amino acid sequence of SEQ ID NO:322, and (iii) CDR-H3 comprising the amino acid sequence of SEQ ID NO:323, and a VL domain comprising (iv) CDR-L1 comprising the amino acid sequence of SEQ ID NO:324, (v) CDR-L2 comprising the amino acid sequence of SEQ ID NO:325, and (vi) CDR-L3 comprising the amino acid sequence of SEQ ID NO:326.

33. The TNF family ligand trimer-containing antigen binding molecule of any one of claims 1 to 8, 12 to 18, 22 to 23, 31 and 32, wherein the moiety capable of specific binding to CEA comprises a variable heavy chain comprising an amino acid sequence of SEQ ID NO:329 and a variable light chain comprising an amino acid sequence of SEQ ID NO:330.

34. The TNF family ligand trimer-containing antigen binding molecule of any one of claims 1 to 8, 12 to 18 and 31 to 33, wherein the antigen binding molecule comprises
(i) a first heavy chain comprising the VH domain comprising the amino acid sequence of SEQ ID NO:329 and a first light chain comprising the VL domain comprising the amino acid sequence of SEQ ID NO:330,
(ii) a second heavy chain comprising the amino acid sequence selected from the group consisting of SEQ ID NO:14, SEQ ID NO:108, SEQ ID NO:111 and SEQ ID NO:113, and
(iii) a second light chain comprising the amino acid sequence of SEQ ID NO:15, SEQ ID NO:109, SEQ ID NO:110, SEQ ID NO:112 and SEQ ID NO:114.

35. The TNF family ligand trimer-containing antigen binding molecule of any one of claims 1 to 9, 12 to 18 and 31 to 34, wherein the antigen binding molecule comprises
(i) a first heavy chain comprising the VH domain comprising the amino acid sequence of SEQ ID NO:329 and a first light chain comprising the VL domain comprising the amino acid sequence of SEQ ID NO:330,
(ii) a second heavy chain comprising the amino acid sequence selected from the group consisting of SEQ ID NO:115, SEQ ID NO:117, SEQ ID NO:119 and SEQ ID NO:173, and

(iii) a second light chain comprising the amino acid sequence selected from the group consisting of SEQ ID NO:116, SEQ ID NO:118, SEQ ID NO:120 and SEQ ID NO:174.

36. The TNF family ligand trimer-containing antigen binding molecule of any one of claims 1 to 8, 22, 23 and 31 to 33, wherein the antigen binding molecule comprises
(i) a first heavy chain comprising the amino acid sequence of SEQ ID NO:337, a second heavy chain comprising the amino acid sequence of SEQ ID NO:338, and two light chains comprising the amino acid sequence of SEQ ID NO:334, or
(ii) a first heavy chain comprising the amino acid sequence of SEQ ID NO:341, a second heavy chain comprising the amino acid sequence of SEQ ID NO:342, and two light chains comprising the amino acid sequence of SEQ ID NO:334.

37. The TNF family ligand trimer-containing antigen binding molecule of any one of claims 1 to 2, 7 to 17, 22, 23, 25 to 27 and 31 to 33, wherein the TNF ligand family member is OX40L.

38. The TNF family ligand trimer-containing antigen binding molecule of any one of claims 1 to 2, 7 to 17, 22, 23, 25 to 27, 31 to 33 and 37, wherein the ectodomain of a TNF ligand family member comprises the amino acid sequence of SEQ ID NO:53 or SEQ ID NO:54, particularly the amino acid sequence of SEQ ID NO:53.

39. The TNF family ligand trimer-containing antigen binding molecule of any one of claims 1 to 2, 7 to 17, 23, 24, 26 to 28, 32 to 34, 38 and 39, comprising
(a) at least one moiety capable of specific binding to a target cell antigen and
(b) a first and a second polypeptide that are linked to each other by a disulfide bond,
wherein the antigen binding molecule is characterized in that the first polypeptide comprises the amino acid sequence of SEQ ID NO:371 or SEQ ID:372 and in that the second polypeptide comprises the amino acid sequence of SEQ ID NO:53 or SEQ ID NO:54.

40. The TNF family ligand trimer-containing antigen binding molecule of any one of claims 1 to 2, 7 to 17, 22, 23 and 37 to 39, wherein the target cell antigen is Fibroblast Activation Protein (FAP) and the moiety capable of specific binding to FAP comprises a VH domain comprising (i) CDR-H1 comprising the amino acid sequence of SEQ ID NO:7 or SEQ ID NO:100, (ii) CDR-H2 comprising the amino acid sequence of SEQ ID NO:8 or SEQ ID NO:101, and (iii) CDR-H3 comprising the amino acid sequence of SEQ ID NO:9 or SEQ ID NO:102, and a VL domain comprising (iv) CDR-L1 comprising the amino acid sequence of SEQ ID NO:10 or SEQ ID NO:103, (v) CDR-L2 comprising the amino acid sequence of SEQ ID NO:11 or SEQ ID NO:104, and (vi) CDR-L3 comprising the amino acid sequence of SEQ ID NO:12 or SEQ ID NO:1050.

41. The TNF family ligand trimer-containing antigen binding molecule of any one of claims 1 to 2, 7 to 17, 22, 23 and 37 to 40, wherein the antigen binding molecule comprises
(i) a first heavy chain comprising the VH domain comprising the amino acid sequence of SEQ ID NO:16 and a first light chain comprising the VL domain comprising the amino acid sequence of SEQ ID NO:17 or
a first heavy chain comprising the VH domain comprising the amino acid sequence of SEQ ID NO:106 and a first light chain comprising the VL domain comprising the amino acid sequence of SEQ ID NO:107,
(ii) a second heavy chain comprising the amino acid sequence selected from the group consisting of SEQ ID NO:355, and
(iii) a second light chain comprising the amino acid sequence of SEQ ID NO:356.

42. An isolated polynucleotide encoding the TNF family ligand trimer-containing antigen binding molecule of any one of claims 1 to 41.

43. A vector, particularly an expression vector, comprising the isolated polynucleotide of claim 42.

44. A host cell comprising the isolated polynucleotide of claim 42 or the vector of claim 43.

45. A method for producing the TNF family ligand trimer-containing antigen binding molecule of any one of claims 1 to 41, comprising the steps of
(i) culturing the host cell of claim 44 under conditions suitable for expression of the antigen binding molecule, and
(ii) recovering the antigen binding molecule.

46. A pharmaceutical composition comprising the TNF family ligand trimer-containing antigen binding molecule of any one of claims 1 to 41 and at least one pharmaceutically acceptable excipient.

47. The TNF family ligand trimer-containing antigen binding molecule of any one of claims 1 to 41, or the pharmaceutical composition of claim 46, for use as a medicament.

48. The TNF family ligand trimer-containing antigen binding molecule of any one of claims 1 to 41, or the pharmaceutical composition of claim 46, for use in the treatment of cancer.

49. Use of the TNF family ligand trimer-containing antigen binding molecule of any one of claims 1 to 41 for the manufacture of a medicament for the treatment of cancer.