CLAIMS

1. A CD16a-binding polypeptide which comprises at least one motif that binds to CD16a, in which the polypeptide comprises the following structure:

[N-terminal portion]-[Helix 1]-[Separating portion]-[Helix 2]-[C-terminal portion]

the CD16a-binding motif being the portion [Helix 1]-[Separating portion]-[Helix 2].

2. A CD16a-binding polypeptide according to Claim 1, in which:

Helix 1 comprises the sequence $X_9X_{10}X_{11}AX_{13}X_{14}EIX_{17}X_{18}$ and Helix 2 comprises the sequence $X_{24}X_{25}QX_{27}X_{28}AFX_{31}X_{32}$ $X_{33}LX_{35}$, [SEQ ID NO 120] in which,

(a) X_9 is A, D, F, H, I, K, L, Q, R, T, V or Y;

X_{10} is Q;

X_{11} is A, D, E, F, H, I, K, L, M, N, Q, R, S, T, V, W or Y;

X_{13} is A, Q or V;

X_{14} is A, F, H, I, K, L, N, Q, R, S, T, V, W or Y;

X_{17} is Q or R;

X_{18} is A, D, E, F, H, I, K, N, Q, R, S, T or V;

X_{24} is H;

X_{25} is A or H;

X_{27} is A, I, K, Q, R, S, T or V;

X_{28} is F or Y;

X_{31} is I or L;

X_{32} is A, E, H, K, L, N, Q or R;

X_{33} is K or S;

and X_{35} is A, H, I, L, M, R or S; or

(b) X_9 is V; X_{10} is Q; X_{11} is M; X_{13} is Q; X_{14} is F; X_{17} is R; X_{18} is K; X_{24} is H; X_{25} is H; X_{27} is S; X_{28} is F; X_{31} is I; X_{32} is K; X_{33} is S and X_{35} is M, and optionally in which within Helix 1 and Helix 2, at least 1 and no more than 5 (for example at least 1 and no more than 3) of the X_n residues are replaced by an alternative residue, and/or at least at

least 1 and no more than 5 (for example 1 and no more than 3) of the residues not labelled as X_n are replaced by an alternative residue; or

(c) X_9 is Q; X_{10} is F; X_{11} is Y; X_{13} is R; X_{14} is D; X_{17} is D; X_{18} is L; X_{24} is E; X_{25} is D; X_{27} is K; X_{28} is W; X_{31} is Y; X_{32} is M; X_{33} is S and X_{35} is I, and optionally in which within Helix 1 and Helix 2, at least 1 and no more than 5 (for example at least 1 and no more than 3) of the X_n residues are replaced by an alternative residue, and/or at least 1 and no more than 5 (for example at least 1 and no more than 3) of the residues not labelled as X_n are replaced by an alternative residue; or

(d) X_9 is F; X_{10} is W; X_{11} is I; X_{13} is E; X_{14} is S; X_{17} is E; X_{18} is S; X_{24} is I; X_{25} is Y; X_{27} is K; X_{28} is W; X_{31} is K; X_{32} is Y; X_{33} is S and X_{35} is A, and optionally in which within Helix 1 and Helix 2, at least 1 and no more than 5 (for example at least 1 and no more than 3) of the X_n residues are replaced by an alternative residue, and/or at least 1 and no more than 5 (for example at least 1 and no more than 3) of the residues not labelled as X_n are replaced by an alternative residue.

3. A CD16a-binding polypeptide according to Claim 1 or 2, in which:

Helix 1 comprises the sequence $X_9X_{10}X_{11}AX_{13}X_{14}EIX_{17}X_{18}$ [SEQ ID NO 127] and Helix 2 comprises the sequence $X_{24}X_{25}QX_{27}X_{28}AFX_{31}X_{32}$ $X_{33}LX_{35}$, [SEQ ID NO 120] in which,

X_9 is A, D, F, H, I, K, L, Q, R, T, V or Y; X_{10} is Q; X_{11} is A, D, E, F, H, I, K, L, M, N, Q, R, S, T, V, W or Y; X_{13} is A, Q or V; X_{14} is A, F, H, I, K, L, N, Q, R, S, T, V, W or Y; X_{17} is Q or R; X_{18} is A, D, E, F, H, I, K, N, Q, R, S, T or V; X_{24} is H; X_{25} is A or H; X_{27} is A, I, K, Q, R, S, T or V; X_{28} is F or Y; X_{31} is I or L; X_{32} is A, E, H, K, L, N, Q or R; X_{33} is K or S; and X_{35} is A, H, I, L, M, R or S.

4. A CD16a-binding polypeptide according to Claim 1, 2 or 3, in which:

X_9 is K, Q or Y; X_{10} is Q; X_{11} is I or Q; X_{13} is Q;X_{14} is W or Y; X_{17} is R; X_{18} is H, K or R; X_{24} is H; X_{25} is H; X_{27} is A, K or T; X_{28} is F; X_{31} is I; X_{32} is A, K or Q; X_{33} is K or S; and X_{35} is I or L.

5. A CD16a-binding polypeptide according to Claim 2, 3 or 4, in which the CD16a binding efficacy is at least 10% of SEQ ID NO: 1; and/or in which the CD16a-binding polypeptide competes with SEQ ID NO: 1.

6. A CD16a-binding polypeptide according to any preceding claim, in which the separating portion is a sequence of 1 to 5 (preferably 2 to 5, for example 2, 3, 4 or 5; or for example 3 to 5, for example 3, 4 or 5, and more preferably 3) naturally occurring amino acids.

7. A CD16a-binding polypeptide according to any preceding claim, in which the N-terminal portion is absent or is a sequence of 1 to 15 (preferably 1 to 10 or 1 to 8, more preferably 1 to 5, for example 1, 2, 3 4 or 5) naturally occurring amino acids.

8. A CD16a-binding polypeptide according to any preceding claim, in which the C-terminal portion is absent or is a sequence of 1 to 50 (for example 1 to 35, 1 to 30, 15 to 25 or 18 to 22) naturally occurring amino acids.

9. A CD16a-binding polypeptide according to Claim 1, 2 or 3, in which the sequence of the CD16a-binding polypeptide is selected from:

VDNKFNKEVQMAQFEIRKLPNLNHHQSFAFIKSLMDDPSQSANLLAEAKKLNDAQAPK [SEQ ID NO: 1] or

VDNKFNKEQQIAQYEIRKLPNLNHHQTFAFIKSLLDDPSQSANLLAEAKKLNDAQAPK [SEQ ID NO:51]

10. A CD16a-binding oligomer, which comprises at least two CD16a-binding polypeptides as defined in any preceding claim, for example 2, 3, 4, or 5 CD16a-binding polypeptides as defined in any preceding claim.

11. A CD16a-binding polypeptide according to any of Claims 2 to 9, or CD16a-binding oligomer according to Claim 10, which further comprises an additional functional portion (for example at least one, at least two, or at least three; for example 1, 2, 3, 4 or 5 additional functional portions).

12. A CD16a-binding polypeptide or CD16a-binding oligomer according to Claim 11, in which the CD16a-binding polypeptide or CD16a-binding oligomer comprises at least two (for example 2, 3, 4 or 5) additional functional portions,

in which a first additional functional portion comprises an additional binding moiety (for example an additional binding moiety specific for a cancer cell surface target, for example a myeloma cell surface antigen, for example BCMA, or is specific for a NK

cell target); and in which the second additional functional portion comprises an immune signalling molecule, for example a cytokine, for example IL-15 or derivatives thereof; or

in which a first additional functional portion comprises an additional binding moiety (for example an additional binding moiety specific for a cancer cell surface target, for example a myeloma cell surface antigen, for example BCMA, or is specific for a NK cell target); and in which the second additional functional portion comprises an additional binding moiety (for example an additional binding moiety specific for a cancer cell surface target, for example a myeloma cell surface antigen, for example BCMA, or is specific for a NK cell target).

13. A CD16a-binding polypeptide or CD16a-binding oligomer according to Claim 11 or 12, in which the additional functional portion(s) is/are separated from the CD16a-binding polypeptide or the or CD16a-binding oligomer by a linker, for example in which the linker is a sequence of 1 to 50 naturally occurring amino acids, preferably 1 to 25 (for example 1 to 20), naturally occurring amino acids selected from the group consisting of G, S and T (preferably G and S).

14. A nucleic acid molecule, an expression vector or a host cell, the nucleic acid molecule being one encoding the CD16a-binding polypeptide according to any of Claims 1 to 9 or 11 to 13; or encoding a CD16a-binding oligomer according to any of Claims 10 to 13; the expression vector being one comprising such a nucleic acid molecule; the host cell being one comprising such a nucleic acid molecule or such an expression vector.

15. A method of making the CD16a-binding polypeptide according to any of Claims 1 to 9 or 11 to 13, or a CD16a-binding oligomer according to any of Claims 10 to 13, the method comprising maintaining a host cell according to Claim 14 under optimal conditions for expression of the nucleic acid and isolating the CD16a-binding polypeptide.

16. A CD16a binder-drug conjugate comprising the CD16a-binding polypeptide according to any of Claims 1 to 9 or 11 to 13, or a CD16a-binding oligomer according to any of Claims 10 to 13, and an additional therapeutic agent, preferably in which the additional therapeutic agent is a cytotoxic drug, for example MMAF, MMAE, doxorubicin, pyrrolobenzodiazepine, amanitin, maytansinoids, duostatins, mitomycin C, desmethyltopotecan or SN-38.

17. A pharmaceutical composition comprising the CD16a-binding polypeptide as defined in any of Claims 1 to 9 or 11 to 13, a CD16a-binding oligomer according to any of Claims 10 to 13, or a nucleic acid molecule or expression vector according to Claim 14.

18. A CD16a-binding polypeptide according to any of Claims 1 to 9 or 11 to 13, a CD16a-binding oligomer according to any of Claims 10 to 13, the nucleic acid molecule or expression vector according to Claim 14, a CD16a binder-drug conjugate according to Claim 16, and/or a pharmaceutical composition according to Claim 17, for use in medicine.

19. A kit comprising the CD16a-binding polypeptide according to any of Claims 1 to 9 or 11 to 13, a CD16a-binding oligomer according to any of Claims 10 to 13, a CD16a binder-drug conjugate according to Claim 16, or a pharmaceutical composition according to Claim 17 and, optionally, one or more further therapeutic agent(s), preferably in which the one or more further therapeutic agent(s) is selected from a proteasome inhibitor (for example carlfizomib or bortezomib), an immunomodulatory agent (for example lenalidomide or thalidomide), an alkylator (for example melphalan or melflufen), a steroid (for example dexamethasone or prednisone), an anti-CD38 agent (for example daratumumab), an immune checkpoint inhibitor (for example a CTLA-4 inhibitor, a PD-1 inhibitor, or a PD-L1 inhibitor), and an ADAM17 inhibitor.

20. A CD16a-binding polypeptide according to any of Claims 1 to 9 or 11 to 13, a CD16a-binding oligomer according to any of Claims 10 to 13, a nucleic acid molecule or expression vector according to Claim 14, a CD16a binder-drug conjugate according to Claim 16, a pharmaceutical composition according to Claim 17, and/or a kit according to Claim 19 for use in the treatment of cancer, preferably in which the cancer is multiple myeloma.