

Claims

1. An antigen-binding protein that binds human CD3 comprising an antibody variable domain comprising a heavy chain variable region and a light chain variable region wherein the heavy chain variable region comprises a CDR1, CDR2 and CDR3 comprising the amino acid sequence:

CDR1 : SFGIS
 CDR2 : GFIPVLGTANYAQKFQG
 CDR3 : RGNWNPFD; or

comprising the amino acid sequence:

CDR1 : SX₁TFTIS;
 CDR2 : GIIPX₂FGTITYAQKFQG;
 CDR3 : RGNWNPFD;

wherein

X₁ = K or R;
 X₂ = L or I, and

wherein the light chain variable region comprises the CDR1, CDR2 and CDR3 of IGKV1-39.

2. The antigen-binding protein of claim 1 wherein;

X₁ = K; and X₂ = L; or

X₁ = R; and X₂ = I.

3. An antigen-binding protein that binds human CD3 comprising an antibody variable domain comprising a heavy chain variable region and a light chain variable region wherein the heavy chain variable region comprises a CDR1, CDR2 and CDR3 comprising the amino acid sequence:

CDR1 : SKTLTIS;
 CDR2 : GIIFIQSITYAQKFQD;
 CDR3 : RGNWNPFD; or

comprising the amino acid sequence:

CDR1 : GSGIS;
 CDR2 : GFIPFFGSANYAQKFRD;
 CDR3 : RGNWNPX₁₃DP;

wherein

X₁₃ = or L or F, and

wherein the light chain variable region comprises the CDR1, CDR2 and CDR3 of IGKV1-39.

4. An antigen-binding protein that binds human CD3 comprising an antibody variable domain comprising a heavy chain variable region and a light chain variable region wherein the heavy chain variable region comprises the amino acid sequence:

EVQLVQSGAEVKKPGSSVKVSKASGGTFRSFGISWVRQAPGQGLEWMGGFIPVLGTANYAQKFQGRV
 TIADKSTNTAYMELSSLRSEDTAVYYCARRGNWNPFDPWGQGTLTVSS; or

QVQLVQSGAEVKKPGSSVKVSKASGDAFKSKTFTISWVRQAPGQGLEWLGGIIPFGTITYAQKFQGRV
 TITADKSTNTAFMELSSLRSEDTAMYYCTRRGNWNPFDPWGQGTLTVSS; or

EVQLVQSGSELKKPGSSVKVSKASGVTFNSRTFTISWVRQAPGQGLEWLGSIIPIFGTITYAQKFQGRV
 ITADKSTSTAFMELTSLRSEDTAIYYCTRRGNWNPFDPWGQGTLTVSS; or

QVQLVQSGAEVKKPGSSVKVSCASGGTFRGSGISWVRQAPGQGLEWVGGFIPFFGSANYAQKFRDR
VTITADKSATTAYMELSSLRSEDTAIYYCAKRGNNPLDPWGQGTLVTVSS; or

QVQLVQSGAEVKKPGSSVKVSCASGVTFKSKTLTISWVRQAPGQGLEWLGGIPIFGSITYAQKFQDRV
SITADKSTNTAYLELNSLRSEDTAIYYCARRGNWNPFDLPWGQGTLVTVSS; or

EVQLVQSGAEVKKPGSSVKVSCASGGTFRGSGISWVRQAPGQGLEWVGGFIPFFGSANYAQKFRDRV
TITADKSATTAYMELSSLRSEDTAIYYCAKRGNNPFDLPWGQGTLVTVSS;

with 0-10 amino acid variations at one or more positions other than the CDRs, and
wherein said light chain variable region comprises the amino acid sequence:

DIQMT QSPSS LSASV GDRVIT ITCRA SQSIS SYLNW YQQKP GKAPK LLIYA ASSLQ SGVPS RFSGS
GSGTD FTLTI SSLQP EDFAT YYCQQ SYSTP PTFGQ GTKVE IK or DIQMT QSPSS LSASV GDRVIT
ITCRA SQSIS SYLNW YQQKP GKAPK LLIYA ASSLQ SGVPS RFSGS GSGTD FTLTI SSLQP EDFAT
YYCQQ SYSTP PITFG QGTRL EIK

with 0-5 amino acid variations at one or more positions other than the CDRs.

5. The antigen-binding protein of claim 4, wherein the heavy chain variable region comprises 0-5 amino acid variations at one or more positions other than the CDRs.
6. The antigen-binding protein of any one of claims 1-5, wherein the antigen-binding protein is an antibody.
7. The antigen-binding protein of claim 6, wherein the antibody is a bispecific antibody.
8. The antigen-binding protein of claim 6 or 7, wherein the antigen-binding protein is a bispecific antibody comprising a H/L chain combination of any one of claims 1-4, and a H/L chain combination that binds a tumor-antigen, in particular wherein said H/L chain combination that binds a tumor-antigen binds human BCMA, CD19, CD20, CD30, CD33, CD38, CD44, CD123, CD138, CEA, CLEC12A, CS-1, EGFR, EGFRvIII, EPCAM, DLL3, LGR5, MSLN, FOLR1, FOLR3, HER2, HM1.24, MCSP, PD-L1 or PSMA protein.
9. The antigen-binding protein of any one of claims 6-8, wherein the antibody is a human or humanized antibody.
10. The antigen-binding protein of any one of claims 6-9, wherein the antibody comprises two different immunoglobulin heavy chains with compatible heterodimerization domains.
11. The antigen-binding protein antibody of claim 10, wherein said compatible heterodimerization domains are compatible immunoglobulin heavy chain CH3 heterodimerization domains.
12. The antigen-binding protein of any one of claims 7-11, wherein said bispecific antibody is an IgG antibody with a mutant CH2 and/or lower hinge domain such that interaction of the bispecific IgG antibody to a Fc-gamma receptor is reduced, in particular wherein the mutant CH2 and/or lower hinge domain comprise an amino substitution at position 235 and/or 236 (according to EU numbering), preferably an L235G and/or G236R substitution.

13. The antigen-binding protein of any one of claims 6-12, wherein the antibody comprises a common light chain.
14. The antigen-binding protein of any one of claims 1-13, for use in therapy.
15. The antigen-binding protein of claim 15, wherein the therapy is cancer therapy.
16. Use of an antigen-binding protein of any one of claims 1-13 in the manufacture of a medicament for the treatment of cancer in a subject.
17. The use of claim 16, wherein the medicament is formulated for local administration and/or local release of the antigen-binding protein.
18. The use of claim 16, wherein the subject has an auto-immune disease.