

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.

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 : GIIPIFGSITYAQKFQD;
 CDR3 : RGNWNPFD; or

comprising the amino acid sequence:

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

wherein

X₁₃ = or L or F.

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
 TIADKSTNTAYMELSSLRSEDTAVYYCARRGNWNPFDPWGQGTTLTVSS;

QVQLVQSGAEVKKPGSSVKVSKASGDAFKSKTFTISWVRQAPGQGLEWLGGIIPFGTITYAQKFQGRV
 TITADKSTNTAFMELSSLRSEDTAMYYCTRRGNWNPFDPWGQGTTLTVSS; or

EVQLVQSGSELKKPGSSVKVSKASGVTFNSRTFTISWVRQAPGQGLEWLGSIIPIFGTITYAQKFQGRVT
 ITADKSTSTAFMELTSLRSEDTAIYYCTRRGNWNPFDPWGQGTTLTVSS; or

QVQLVQSGAEVKKPGSSVKVSCASGGTFRGSGISWVRQAPGQGLEWVGGFIPFFGSANYAQKFRDR
VTITADKSATTAYMELSSLRSEDTAIYYCAKRGWNPLDPWGQGTTLVTVSS; or

QVQLVQSGAEVKKPGSSVKVSCASGVTFKSKTLTISWVRQAPGQGLEWLGGIIPFGSITYAQKFQDRV
SITADKSTNTAYLELNSLRSEDTAIYYCARRGNWNPFDLPWGQGTTLVTVSS; or

EVQLVQSGAEVKKPGSSVKVSCASGGTFRGSGISWVRQAPGQGLEWVGGFIPFFGSANYAQKFRDRV
TITADKSATTAYMELSSLRSEDTAIYYCAKRGWNPNPFDLPWGQGTTLVTVSS;

with 0-10, preferably 0-5 amino acid variations, insertions, deletions, substitutions, additions or a combination thereof at one or more positions other than the CDRs.

5. The antigen-binding protein of any one of claims 1-4, wherein said light chain variable region comprises a common light chain variable region.
6. The antigen-binding protein of any one of claims 1-5, wherein said common light chain variable region comprises an IgVκ1-39 light chain variable region.
7. The antigen-binding protein of any one of claims 1-6, wherein said light chain variable region is a germline IgVκ1-39*01 variable region.
8. The antigen-binding protein of any one of claims 1-7, wherein the light chain variable region comprises the kappa light chain IgVκ1-39*01/IGJκ1*01 or IgVκ1-39*01/IGJκ5*01.
9. The antigen-binding protein of any one of claims 1-8, wherein the light chain variable region comprises the germline kappa light chain IgVκ1-39*01/IGJκ1*01 or IgVκ1-39*01/IGJκ5*01.
10. The antigen-binding protein of any one of claims 1-9, wherein said light chain variable region comprises the amino acid sequence.
DIQMT QSPSS LSASV GDRVT ITCRA SQSIS SYLNW YQQKP GKAPK LLIYA ASSLQ SGVPS RFSGS
GSGTD FTLTI SSLQP EDFAT YYCQQ SYSTP PTFGQ GTKVE IK or DIQMT QSPSS LSASV GDRVT
ITCRA SQSIS SYLNW YQQKP GKAPK LLIYA ASSLQ SGVPS RFSGS GSGTD FTLTI SSLQP EDFAT
YYCQQ SYSTP PITFG QGTRL EIK
with 0-5 amino acid variations, insertions, deletions, substitutions, additions or a combination thereof.
11. The antigen-binding protein of any one of claims 1-10, which is an antibody, preferably a bispecific antibody.
12. The bispecific antibody of claim 11, comprising a H/L chain combination of any one of claims 1-10, 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, PSMA protein or a variant thereof.
13. The antibody or bispecific antibody of claim 11 or 12, which is a human or humanized antibody.
14. The bispecific antibody of any one of claims 11-13, comprising two different immunoglobulin heavy chains with compatible heterodimerization domains.

15. The bispecific antibody of claim 14, wherein said compatible heterodimerization domains are compatible immunoglobulin heavy chain CH3 heterodimerization domains.
16. The bispecific antibody of any one of claims 11-15, 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.
17. The bispecific antibody of any one of claims 11-16, comprising a common light chain.
18. The antigen-binding protein or antibody of any one of claims 1-17, for use in the treatment of a subject in need thereof, in particular wherein the subject has cancer or is treated for cancer.
19. The antigen-binding protein or antibody for use of claim 18, wherein the treatment comprises the local administration and/or local release of the antigen-binding protein or antibody of claims 1-3.
20. The antigen-binding protein or antibody for use of claim 18, wherein the treatment comprises the administration of the antigen-binding protein or antibody of claims 4 to a subject with an over-active immune system, in particular wherein the subject has an auto-immune disease.