CLAIMS:

1. A polypeptide library comprising a plurality of different polypeptides, which comprise:

i) an antibody heavy chain variable region (V_H) comprising a scaffold region which is at least 90% identical to the scaffold region of IGHV3-23 as set out in SEQ ID NO: 3; and

ii) an antibody light chain variable region (V_L) comprising a scaffold region which is at least 90% identical to the scaffold region of any one of IGLV1-40 (as set out in SEQ ID NO: 18), IGLV1-44 (as set out in SEQ ID NO: 21), IGLV1-47 (as set out in SEQ ID NO: 24), IGLV1-51 (as set out in SEQ ID NO: 15), IGLV3-1 (as set out in SEQ ID NO: 6), IGLV3-19 (as set out in SEQ ID NO: 27), IGLV3-21 (as set out in SEQ ID NO: 9), IGLV6-57 (as set out in SEQ ID NO: 12);wherein the V_H and the V_L are capable of forming an antigen-binding site; and

wherein at least two of the polypeptides differ from one another in the sequence of amino acids present in one or more complementarity determining regions (CDRs) in the V_H and/or V_L variable regions.

2. The library of claim 1, wherein the sequence of amino acids in one or more of the CDRs of the V_H and/or V_L variable domains is random or semi-random or is derived from a human antibody.

3. A method of constructing a polypeptide library, the method comprising preparing a plurality of different polypeptides, which comprise:

i) an antibody heavy chain variable region (V_H) comprising a scaffold region which is at least 90% identical to the scaffold region of IGHV3-23 as set out in SEQ ID NO: 3; and

ii) an antibody light chain variable region (V_L) comprising a scaffold region which is at least 90% identical to the scaffold region of any one of IGLV1-40 (as set out in SEQ ID NO: 18), IGLV1-44 (as set out in SEQ ID NO: 21), IGLV1-47 (as set out in SEQ ID NO: 24), IGLV1-51 (as set out in SEQ ID NO: 15), IGLV3-1 (as set out in SEQ ID NO: 6), IGLV3-19 (as set out in SEQ ID NO: 27), IGLV3-21 (as set out in SEQ ID NO: 9), IGLV6-57 (as set out in SEQ ID NO: 12); wherein the V_H and the V_L are capable of forming an antigen-binding site; and

wherein at least two of the polypeptides differ from one another in the sequence of amino acids present in one or more CDRs in the V_H and/or V_L variable regions.

4. A polynucleotide library comprising a plurality of different polynucleotides, wherein each polynucleotide encodes a polypeptide comprising:

i) an antibody heavy chain variable region (V_H) comprising a scaffold region which is at least 90% identical to the scaffold region of IGHV3-23 as set out in SEQ ID NO: 3; and

ii) an antibody light chain variable region (V_L) comprising a scaffold region which is at least 90% identical to the scaffold region of any one of IGLV1-40 (as set out in SEQ ID NO: 18), IGLV1-44 (as set out in SEQ ID NO: 21), IGLV1-47 (as set out in SEQ ID NO: 24), IGLV1-51 (as set out in SEQ ID NO: 15), IGLV3-1 (as set out in SEQ ID NO: 6), IGLV3-19 (as set out in SEQ ID NO: 27), IGLV3-21 (as set out in SEQ ID NO: 9), IGLV6-57 (as set out in SEQ ID NO: 12); wherein the V_H and the V_L are capable of forming an antigen-binding site; and

wherein at least two of the polynucleotides differ from one another by encoding polypeptides comprising one or more different CDRs in the V_H and/or V_L variable regions.

5. The library of claim 4, wherein the polynucleotides encode a sequence of amino acids in one or more of the CDRs of the V_H and/or V_L variable domains that is random or semi-random or is derived from a human antibody.

6. A method of constructing a polynucleotide library, the method comprising preparing a plurality of different polynucleotides encoding a polypeptide, which comprises:

i) an antibody heavy chain variable region (V_H) comprising a scaffold region which is at least 90% identical to the scaffold region of IGHV3-23 as set out in SEQ ID NO: 3; and

ii) an antibody light chain variable region (V_L) comprising a scaffold region which is at least 90% identical to the scaffold region of any one of IGLV1-40 (as set out in SEQ ID NO: 18), IGLV1-44 (as set out in SEQ ID NO: 21), IGLV1-47 (as set out in SEQ ID NO: 24), IGLV1-51 (as set out in SEQ ID NO: 15), IGLV3-1 (as set out in SEQ ID NO: 6), IGLV3-19 (as set out in SEQ ID NO: 27), IGLV3-21 (as set out in SEQ ID NO: 9), IGLV6-57 (as set out in SEQ ID NO: 12);wherein the V_H and the V_L are capable of forming an antigen-binding site; and

wherein at least two of the polynucleotides differ from one another by encoding polypeptides comprising one or more different CDRs in the V_H and/or V_L variable regions.

7. An isolated and/or recombinant polypeptide comprising:

i) an antibody heavy chain variable region (V_H) comprising a scaffold region which is at least 90% identical to the scaffold region of IGHV3-23 as set out in SEQ ID NO: 3; and

ii) an antibody light chain variable region (V_L) comprising a scaffold region which is at least 90% identical to the scaffold region of any one of IGLV1-40 (as set out in SEQ ID NO: 18), IGLV1-44 (as set out in SEQ ID NO: 21), IGLV1-47 (as set out in SEQ ID NO: 24), IGLV1-51 (as set out in SEQ ID NO: 15), IGLV3-1 (as set out in SEQ ID NO: 6), IGLV3-19 (as set out in SEQ ID NO: 27), IGLV3-21 (as set out in SEQ ID NO: 9), IGLV6-57 (as set out in SEQ ID NO: 12);wherein the V_H and the V_L are capable of forming an antigen-binding site.

8. The polypeptide of claim 7, wherein the V_L comprises a scaffold region which is at least 90% identical to the scaffold region of IGLV3-1 as set out in SEQ ID NO.6.

9. The polypeptide of claim 7 or claim 8, which is a variable fragment (Fv).

10. The polypeptide of any one of clamis 7-9, which is a Fab fragment, a Fab' fragment, a F(ab') fragment, a scFv, a diabody, a triabody, a tetrabody or higher order polypeptide complex.

11. The polypeptide of claim 10, wherein the polypeptide is a scFv and the V_H and the V_L are linked together via a peptide linker.

12. The polypeptide of any one of claims 7-11, wherein the scaffold region of the V_H and/or V_L variable regions is at least 95%, 96%, 97%, 98% or 99% identical to the scaffold region of any of the given sequences.

13. The polypeptide of any one of claims 7-12, which is soluble under reducing conditions.

14. The polypeptide of any one of claims 7-13, which is soluble and capable of stably forming an antigen-binding site when produced under reducing conditions.

15. The polypeptide of any one of claims 7-14, which is conjugated to a compound.

16. The polypeptide of claim 15, wherein the compound is selected from the group consisting of a radioisotope, a detectable label, a therapeutic compound, a colloid, a toxin, a nucleic acid, a peptide, a protein, a compound that increases the half life of the polypeptide in a subject, and mixtures thereof.

17. An isolated and/or exogenous polynucleotide encoding the polypeptide of any one of claims 7-16, or a heavy or light chain variable region thereof.

18. A vector comprising the polynucleotide of claim 17.

19. A host cell comprising the polypeptide of any one of claims 7-16, the polynucleotide of claim 17, or the vector of claim 18.

20. A method of screening for a polypeptide that binds to a target molecule, the method comprising contacting a polypeptide of any one of claims 7-16 or the library of any one of claims 1, 2, 4 and 5 with the target molecule, and determining whether the polypeptide of any one of claims 7-16 binds to the target molecule.

21. The method of claim 20, wherein a polynucleotide encoding the polypeptide of any one of claims 7-16 is expressed in a host cell or in a cell-free expression system to produce the polypeptide of any one of claims 7-16.

22. The method of claim 21, wherein the polynucleotide is expressed in the cytoplasm and/or periplasm of a host cell.

23. The method of claim 22, wherein the host cell is a bacterial cell, a yeast cell or a mammalian cell.

24. The method of claim 23, wherein the host cell is a bacterial cell and the method comprises:

a) culturing a bacterial cell comprising a polynucleotide encoding the polypeptide of any one of claims 7-16 such that the polypeptide is produced,

b) permeabilising the bacterial cell, wherein the polynucleotide and the polypeptide is retained inside the permeabilised bacterial cell,

c) contacting the permeabilised bacterial cell with the target molecule such that it diffuses into the permeabilised bacterial cell, and

d) determining whether the polypeptide of any one of claims 7-16 binds to the target molecule.

25. The method of claim 21, wherein the cell-free expression system comprises a ribosome display system, an mRNA display system, or a cis-display system.

26. A host cell library comprising a plurality of host cells comprising a polypeptide of any one of claims 7-16, wherein at least one host cell comprises a polypeptide that differs from a polypeptide present in another host cell in the library in the sequence of amino acids present in one or more CDRs in the V_H and/or V_L variable domains.

27. A composition comprising the polypeptide of any one of claims 7-16, the polynucleotide of claim 17 and/or the vector of claim 18, and a pharmaceutically acceptable carrier.

28. A kit comprising the polypeptide of any one of claims 7-16, the polynucleotide of claim 17 and/or the vector of claim 18, and an agent capable of permeabilising a bacterial cell.

29. Use of the polypeptide of any one of claims 7-16 in therapeutic or diagnostic applications.

CLAIMS:

1. A polypeptide library comprising a plurality of different polypeptides, which comprise:

i) an antibody heavy chain variable region (V_H) comprising a scaffold region which is at least 90% identical to the scaffold region of IGHV3-23 as set out in SEQ ID NO: 3; and

ii) an antibody light chain variable region (V_L) comprising a scaffold region which is at least 90% identical to the scaffold region of any one of IGLV1-40 (as set out in SEQ ID NO: 18), IGLV1-44 (as set out in SEQ ID NO: 21), IGLV1-47 (as set out in SEQ ID NO: 24), IGLV3-1 (as set out in SEQ ID NO: 6), IGLV3-19 (as set out in SEQ ID NO: 27), IGLV6-57 (as set out in SEQ ID NO: 12); wherein the V_H and the V_L are capable of forming an antigen-binding site; and

wherein at least two of the polypeptides differ from one another in the sequence of amino acids present in one or more complementarity determining regions (CDRs) in the V_H and/or V_L variable regions, and wherein the polypeptides are soluble under reducing conditions.

2. The library of claim 1, wherein the sequence of amino acids in one or more of the CDRs of the V_H and/or V_L variable domains is random or semi-random or is derived from a human antibody.

3. A method of constructing a polypeptide library that is soluble under reducing conditions, the method comprising preparing a plurality of different polypeptides, which comprise:

i) an antibody heavy chain variable region (V_H) comprising a scaffold region which is at least 90% identical to the scaffold region of IGHV3-23 as set out in SEQ ID NO: 3; and

ii) an antibody light chain variable region (V_L) comprising a scaffold region which is at least 90% identical to the scaffold region of any one of IGLV1-40 (as set out in SEQ ID NO: 18), IGLV1-44 (as set out in SEQ ID NO: 21), IGLV1-47 (as set out in SEQ ID NO: 24), IGLV3-1 (as set out in SEQ ID NO: 6), IGLV3-19 (as set out in SEQ ID NO: 27), IGLV6-57 (as set out in SEQ ID NO: 12); wherein the V_H and the V_L are capable of forming an antigen-binding site; and

wherein at least two of the polypeptides differ from one another in the sequence of amino acids present in one or more CDRs in the V_H and/or V_L variable regions.

4. A polynucleotide library comprising a plurality of different polynucleotides, wherein each polynucleotide encodes a polypeptide comprising:

i) an antibody heavy chain variable region (V_H) comprising a scaffold region which is at least 90% identical to the scaffold region of IGHV3-23 as set out in SEQ ID NO: 3; and

ii) an antibody light chain variable region (V_L) comprising a scaffold region which is at least 90% identical to the scaffold region of any one of IGLV1-40 (as set out in SEQ ID NO: 18), IGLV1-44 (as set out in SEQ ID NO: 21), IGLV1-47 (as set out in SEQ ID NO: 24), IGLV3-1 (as set out in SEQ ID NO: 6), IGLV3-19 (as set out in SEQ ID NO: 27), IGLV6-57 (as set out in SEQ ID NO: 12); wherein the V_H and the V_L are capable of forming an antigen-binding site; and

wherein at least two of the polynucleotides differ from one another by encoding polypeptides comprising one or more different CDRs in the V_H and/or V_L variable regions, and wherein the polypeptides are soluble under reducing conditions.

5. The library of claim 4, wherein the polynucleotides encode a sequence of amino acids in one or more of the CDRs of the V_H and/or V_L variable domains that is random or semi-random or is derived from a human antibody.

6. A method of constructing a polynucleotide library, the method comprising preparing a plurality of different polynucleotides encoding a polypeptide, which comprises:

i) an antibody heavy chain variable region (V_H) comprising a scaffold region which is at least 90% identical to the scaffold region of IGHV3-23 as set out in SEQ ID NO: 3; and

ii) an antibody light chain variable region (V_L) comprising a scaffold region which is at least 90% identical to the scaffold region of any one of IGLV1-40 (as set out in SEQ ID NO: 18), IGLV1-44 (as set out in SEQ ID NO: 21), IGLV1-47 (as set out in SEQ ID NO: 24), IGLV3-1 (as set out in SEQ ID NO: 6), IGLV3-19 (as set out in SEQ ID NO: 27), IGLV6-57 (as set out in SEQ ID NO: 12);wherein the V_H and the V_L are capable of forming an antigen-binding site; and

wherein at least two of the polynucleotides differ from one another by encoding polypeptides comprising one or more different CDRs in the V_H and/or V_L variable regions, and wherein the polypeptides are soluble under reducing conditions.

7. An isolated and/or recombinant polypeptide comprising:

i) an antibody heavy chain variable region (V_H) comprising a scaffold region which is at least 90% identical to the scaffold region of IGHV3-23 as set out in SEQ ID NO: 3; and

ii) an antibody light chain variable region (V_L) comprising a scaffold region which is at least 90% identical to the scaffold region of any one of IGLV1-40 (as set out in SEQ ID NO: 18), IGLV1-44 (as set out in SEQ ID NO: 21), IGLV1-47 (as set out in SEQ ID NO: 24), IGLV3-1 (as set out in SEQ ID NO: 6), IGLV3-19 (as set out in SEQ ID NO: 27), IGLV6-57 (as set out in SEQ ID NO: 12);wherein the V_H and the V_L are capable of forming an antigen-binding site, and wherein the polypeptide is soluble under reducing conditions.

8. The polypeptide of claim 7, wherein the V_L comprises a scaffold region which is at least 90% identical to the scaffold region of IGLV3-1 as set out in SEQ ID NO.6.

9. The polypeptide of claim 7 or claim 8, which is a variable fragment (Fv).

10. The polypeptide of any one of clamis 7-9, which is a Fab fragment, a Fab' fragment, a F(ab') fragment, a scFv, a diabody, a triabody, a tetrabody or higher order polypeptide complex.

11. The polypeptide of any one of claims 7-10, wherein the scaffold region of the V_H and/or V_L variable regions is at least 95% identical to the scaffold region of any of the given sequences.

12. The polypeptide of any one of claims 7-11, which is soluble and capable of stably forming an antigen-binding site when produced under reducing conditions.

13. An isolated and/or exogenous polynucleotide encoding the polypeptide of any one of claims 7-12, or a heavy or light chain variable region thereof.

14. A vector comprising the polynucleotide of claim 13.

15. A method of screening for a polypeptide that binds to a target molecule, the method comprising contacting a polypeptide of any one of claims 7-12 or the library of any one of claims 1, 2, 4 and 5 with the target molecule, and determining whether the polypeptide of any one of claims 7-12 binds to the target molecule.

16. The method of claim 15, wherein a polynucleotide encoding the polypeptide of any one of claims 7-12 is expressed in a host cell or in a cell-free expression system to produce the polypeptide of any one of claims 7-12.

17. The method of claim 16, wherein the polynucleotide is expressed in the cytoplasm and/or periplasm of a host cell, and wherein the host cell is a bacterial cell, a yeast cell or a mammalian cell.

18. The method of claim 17, wherein the host cell is a bacterial cell and the method comprises:

a) culturing a bacterial cell comprising a polynucleotide encoding the polypeptide of any one of claims 7-12 such that the polypeptide is produced,

b) permeabilising the bacterial cell, wherein the polynucleotide and the polypeptide is retained inside the permeabilised bacterial cell,

c) contacting the permeabilised bacterial cell with the target molecule such that it diffuses into the permeabilised bacterial cell, and

d) determining whether the polypeptide of any one of claims 7-12 binds to the target molecule.

19. A host cell library comprising a plurality of host cells comprising a polypeptide of any one of claims 7-12, wherein at least one host cell comprises a polypeptide that differs from a polypeptide present in another host cell in the library in the sequence of amino acids present in one or more CDRs in the V_H and/or V_L variable domains.

20. A composition comprising the polypeptide of any one of claims 7-12, the polynucleotide of claim 13 and/or the vector of claim 14, and a pharmaceutically acceptable carrier.

21. A kit comprising the polypeptide of any one of claims 7-12, the polynucleotide of claim 13 and/or the vector of claim 14, and an agent capable of permeabilising a bacterial cell.