

CLAIMS

WHAT IS CLAIMED IS:

1. An antibody or antibody fragment comprising a CDRH1 comprising an amino acid sequence at least about 90% identical to that set forth in SEQ ID NOs: 152 or 155, a CDRH2 comprising an amino acid sequence at least about 90% identical to that set forth in SEQ ID NOs: 153 or 156, and a CDRH3 comprising an amino acid sequence at least about 90% identical to that set forth in SEQ ID NOs: 154 or 157.
2. The antibody or antibody fragment of claim 1, further comprising a CDRL1 comprising an amino acid sequence at least about 90% identical to that set forth in SEQ ID NOs: 158 or 161, a CDRL2 comprising an amino acid sequence at least about 90% identical to that set forth in SEQ ID NOs: 159 or 162, and a CDRL3 comprising an amino acid sequence at least about 90% identical to that set forth in SEQ ID NOs: 160 or 163.
3. A method of treating cancer comprising administering the antibody or antibody fragment of any one of claims 1-2.
4. A method of treating a viral infection comprising administering the antibody or antibody fragment of any one of claims 1-2.
5. A nucleic acid library comprising: a plurality of sequences comprising nucleic acids that when translated encode for an antibody or antibody fragment, wherein each sequence of the plurality of sequences comprises a variant sequence encoding for a CDR1, CDR2, or CDR3 on a variable region of a heavy chain (VH) or a CDR1, CDR2, or CDR3 on a variable region of a light chain (VL); wherein the library comprises at least 30,000 variant sequences; and wherein the antibody or antibody fragments bind to its antigen with a K_D of less than 100 nM.
6. The nucleic acid library of claim 5, wherein the antibody is a single domain antibody.
7. The nucleic acid library of claim 6, wherein the single domain antibody is a VHH antibody.
8. The nucleic acid library of claim 5, wherein the antibody binds to TIGIT.
9. The nucleic acid library of claim 5, wherein the variable region of the heavy chain when translated comprises an amino acid sequence at least about 90% identical to that set forth in SEQ ID NOs: 84-100.
10. The nucleic acid library of claim 5, wherein the variable region of the light chain when translated comprises an amino acid sequence at least about 90% identical to that set forth in SEQ ID NOs: 101-117.
11. The nucleic acid library of claim 5, wherein the CDR1, CDR2, or CDR3 on the variable region of the heavy chain comprises an amino acid sequence at least about 90% identical to that set forth in any one of SEQ ID NOs: 67-83 or 118-128.

12. The nucleic acid library of claim 5, wherein the CDR1, CDR2, or CDR3 on the variable region of the light chain comprises an amino acid sequence at least about 90% identical to that set forth in any one of SEQ ID NOs: 129-137.
13. The nucleic acid library of claim 5, wherein the antibody binds to CD47.
14. The nucleic acid library of claim 5, wherein the antibody binds to CD3 epsilon.
15. The nucleic acid library of claim 5, wherein the variable region of the heavy chain when translated comprises an amino acid sequence at least about 90% identical to that set forth in SEQ ID NOs: 138-141.
16. The nucleic acid library of claim 5, wherein the variable region of the light chain when translated comprises an amino acid sequence at least about 90% identical to that set forth in SEQ ID NOs: 142-145.
17. The nucleic acid library of claim 5, wherein the nucleic acid library comprises at least 50,000 variant sequences.
18. The nucleic acid library of claim 5, wherein the nucleic acid library comprises at least 100,000 variant sequences.
19. The nucleic acid library of claim 5, wherein the nucleic acid library comprises at least 10^5 non-identical nucleic acids.
20. The nucleic acid library of claim 5, wherein the nucleic acid library has a theoretical diversity of at least 10^9 sequences.
21. A nucleic acid library comprising: a plurality of sequences comprising nucleic acids that when translated encode for a single domain antibody, wherein each sequence of the plurality of sequences comprises a variant sequence encoding for CDR1, CDR2, or CDR3 on a variable region of a heavy chain (VH); wherein the library comprises at least 30,000 variant sequences; and wherein the antibody or antibody fragments bind to its antigen with a K_D of less than 100 nM.
22. The nucleic acid library of claim 21, wherein a length of the VH when translated is about 90 to about 100 amino acids.
23. The nucleic acid library of claim 21, wherein a length of the VH when translated is about 100 to about 400 amino acids.
24. The nucleic acid library of claim 21, wherein a length of the VH is about 270 to about 300 base pairs.
25. The nucleic acid library of claim 21, wherein a length of the VH is about 300 to about 1200 base pairs.
26. The nucleic acid library of claim 21, wherein the single domain antibody is a VHH antibody.

27. The nucleic acid library of claim 21, wherein the antibody binds to TIGIT.
28. The nucleic acid library of claim 21, wherein the CDR1, CDR2, or CDR3 comprises an amino acid sequence at least about 90% identical to that set forth in any one of SEQ ID NOs: 67-83 or 118-128.
29. The nucleic acid library of claim 21, wherein the variable region of the heavy chain when translated comprises an amino acid sequence at least about 90% identical to that set forth in any one of SEQ ID NOs: 84-100.
30. The nucleic acid library of claim 21, wherein the CDR3 on the variable region of the heavy chain comprises an amino acid sequence at least about 90% identical to that set forth in any one of SEQ ID NOs: 101-117.
31. The nucleic acid library of claim 21, wherein the antibody binds to CD47.
32. The nucleic acid library of claim 21, wherein the antibody binds to CD3 epsilon.
33. The nucleic acid library of claim 21, wherein the variable region of the heavy chain when translated comprises an amino acid sequence at least about 90% identical to that set forth in SEQ ID NOs: 138-141.
34. The nucleic acid library of claim 21, wherein the nucleic acid library comprises at least 50,000 variant sequences.
35. The nucleic acid library of claim 21, wherein the nucleic acid library comprises at least 100,000 variant sequences.
36. The nucleic acid library of claim 21, wherein the nucleic acid library comprises at least 10^5 non-identical nucleic acids.
37. The nucleic acid library of claim 21, wherein the nucleic acid library has a theoretical diversity of at least 10^9 sequences.
38. A method for generating a nucleic acid library encoding for a single domain antibody comprising:
 - (a) providing predetermined sequences encoding for:
 - i. a first plurality of polynucleotides, wherein each polynucleotide of the first plurality of polynucleotides encodes for at least 1000 variant sequences encoding for CDR1 on a heavy chain;
 - ii. a second plurality of polynucleotides, wherein each polynucleotide of the second plurality of polynucleotides encodes for at least 1000 variant sequences encoding for CDR2 on a heavy chain;

iii. a third plurality of polynucleotides, wherein each polynucleotide of the third plurality of polynucleotides encodes for at least 1000 variant sequences encoding for CDR3 on a heavy chain; and

(b) mixing the first plurality of polynucleotides, the second plurality of polynucleotides, and the third plurality of polynucleotides to form the nucleic acid library of variant nucleic acids encoding for the single domain antibody, and wherein at least about 70% of the variant nucleic acids encode for a single domain antibody that binds to its antigen with a K_D of less than 100 nM.

39. The method of claim 38, wherein the single domain antibody comprises one heavy chain variable domain.
40. The method of claim 38, wherein the single domain antibody is a VHH antibody.
41. The method of claim 38, wherein the single domain antibody binds to TIGIT.
42. The method of claim 38, wherein the single domain antibody comprises an amino acid sequence at least about 90% identical to that set forth in any one of SEQ ID NOs: 84-100 or 138-141.
43. The method of claim 38, wherein the single domain antibody binds to CD47.
44. The method of claim 38, wherein the nucleic acid library comprises at least 50,000 variant sequences.
45. The method of claim 38, wherein the nucleic acid library comprises at least 100,000 variant sequences.
46. The method of claim 38, wherein the nucleic acid library comprises at least 10^5 non-identical nucleic acids.
47. The method of claim 38, wherein the nucleic acid library comprises at least one sequence encoding for the single domain antibody that binds to an antigen with a K_D of less than 75 nM.
48. The method of claim 38, wherein the nucleic acid library comprises at least one sequence encoding for the single domain antibody that binds to an antigen with a K_D of less than 50 nM.
49. The method of claim 38, wherein the nucleic acid library comprises at least one sequence encoding for the single domain antibody that binds to an antigen with a K_D of less than 25 nM.
50. The method of claim 38, wherein the nucleic acid library comprises at least one sequence encoding for the single domain antibody that binds to an antigen with a K_D of less than 10 nM.
51. The method of claim 38, wherein the nucleic acid library has a theoretical diversity of at least 10^9 sequences.