What is claimed is:

1. A method of making a genetically modified mouse, the method comprising making a genetically modified mouse so that the genetically modified mouse comprises in its germline genome:

(a) a single rearranged human Vκ/Jκ sequence operably linked to a mouse κ constant region, wherein the single rearranged human Vκ/Jκ sequence replaces all endogenous mouse immunoglobulin κ light chain variable region gene segments at the endogenous immunoglobulin κ light chain locus, wherein the single rearranged human Vκ/Jκ sequence is a single rearranged human Vκ1-39/Jκ sequence or a single rearranged human Vκ3-20/Jκ sequence, and wherein the genetically modified mouse lacks an endogenous mouse immunoglobulin κ light chain variable region that is capable of rearranging to form a sequence that encodes a mouse immunoglobulin κ light chain variable domain so that all immunoglobulin kappa light chains expressed by B cells of the genetically modified mouse comprise immunoglobulin kappa light chain variable domains expressed from the single rearranged human Vκ/Jκ sequence or a somatically hypermutated version thereof; and

(b) a plurality of human immunoglobulin heavy chain variable region gene segments operably linked to the endogenous mouse immunoglobulin heavy chain constant region, wherein the plurality of human immunoglobulin heavy chain variable region gene segments replaces endogenous mouse immunoglobulin heavy chain variable region gene segments at the endogenous mouse immunoglobulin heavy chain locus, and the human immunoglobulin heavy chain variable region gene segments are capable of rearranging to form a sequence that encodes a human immunoglobulin heavy chain variable domain.

2. The method of claim 1, wherein the genetically modified mouse has a germline genome that lacks an endogenous mouse immunoglobulin heavy chain variable region capable of rearranging to form a nucleotide sequence that encodes a mouse heavy chain variable domain.

3. The method of claim 1 or 2, wherein the germline genome of the genetically modified mouse comprises a mouse κ intronic enhancer positioned upstream of the mouse κ constant region.

4. The method of any one of claims 1-3, wherein the germline genome of the genetically modified mouse comprises a mouse κ 3' enhancer positioned downstream of the mouse κ constant region.

5. The method of any one of claims 1-4, wherein the plurality of human immunoglobulin heavy chain variable region gene segments comprises a human V_H1-2, V_H1-8, V_H1-18, V_H1-24, V_H2-5, V_H3-7, V_H3-9, V_H3-11, V_H3-13, V_H3-15, V_H3-20, V_H3-23, V_H3-30, V_H3-33, V_H3-43, V_H3-48, V_H4-31, V_H4-39, V_H4-59, V_H5-51, or V_H6-1 gene segment, or a combination thereof.

6. The method of any one of claims 1-5, wherein the plurality of human immunoglobulin heavy chain variable region gene segments comprises a human D1-7, D1-26, D3-3, D3-10, D3-16, D3-22, D5-5, D5-12, D6-6, D6-13, or D7-27 gene segment, or a combination thereof.

7. The method of any one of claims 1-6, wherein the plurality of human immunoglobulin heavy chain variable region gene segments comprises a human J_H1, J_H3, J_H4, J_H5, or J_H6 gene segment, or a combination thereof.

8. The method of any one of claims 1-7, wherein the genetically modified mouse comprises a B cell that comprises a rearranged immunoglobulin heavy chain variable region nucleotide sequence that encodes a human immunoglobulin heavy chain variable domain derived from a human V_H2-5, V_H3-23, V_H3-30, V_H4-39, V_H4-59, or V_H5-51 gene segment, and a human D1-7, D1-26, D3-3, D3-16, D3-10, D3-22, D5-5, D5-12, D6-6, D6-13, or D7-27 gene segment.

9. The method of claim 8, wherein the rearranged immunoglobulin heavy chain variable region sequence is derived from a human J_H1, J_H3, J_H4, J_H5, or J_H6 gene segment.

10. The method of any one of claims 1-9, wherein the mouse κ constant region is the endogenous mouse κ constant region.

11. The method of any one of claims 1-10, wherein the single rearranged human Vκ/Jκ sequence is a single rearranged human Vκ1-39/Jκ sequence.

12. The method of any one of claims 1-11, wherein the single rearranged human Vκ/Jκ sequence is a rearranged human Vκ1-39/Jκ sequence comprising a single human germline Vκ1-39 segment and a single human germline Jκ segment.

13. The method of claim 11 or 12, wherein the single rearranged human Vκ1-39/Jκ sequence comprises a human Jκ5 gene segment.

14. The method of claim 13, wherein the single rearranged human Vκ1-39/Jκ5 sequence comprises the sequence as set forth in nucleotides 2362 through 2686 of SEQ ID NO:1.

15. The method of claim 13 or 14, wherein the plurality of human immunoglobulin heavy chain variable region gene segments comprises a human V_H2-5, V_H3-23, V_H3-30, V_H4-59, and V_H5-51 gene segment.

16. The method of any one of claims 1-10, wherein the single rearranged human Vκ/Jκ sequence is a single rearranged human Vκ3-20/Jκ sequence.

17. The method of any one of claims 1-10 and 16, wherein the single rearranged human Vκ/Jκ sequence is a single rearranged human Vκ3-20/Jκ sequence comprising a single human germline Vκ3-20 segment and a single human germline Jκ segment.

18. The method of claim 16 or 17, wherein the single rearranged human Vκ3-20/Jκ sequence comprises a human Jκ1 gene segment.

19. The method of claim 18, wherein the single rearranged human Vκ3-20/Jκ1 sequence comprises the sequence as set forth in nucleotides 2373 through 2697 of SEQ ID NO:11.

20. The method of claim 18 or 19, wherein the plurality of human immunoglobulin heavy chain variable region gene segments comprises a human V_H4-39 and V_H5-51 gene segment.

21. A method for making an antibody that binds an antigen of interest, the method comprising:

(i) immunizing the genetically modified mouse made according to the method of any one of claims 1-20 with an antigen of interest,

(ii) obtaining

(a) a human immunoglobulin light chain variable region nucleotide sequence encoding a human immunoglobulin light chain variable domain of an antibody that was generated by the genetically modified mouse in response to the antigen of interest, and/or

(b) a human immunoglobulin heavy chain variable region nucleotide sequence encoding a human immunoglobulin heavy chain variable domain of an antibody that was generated by the genetically modified mouse in response to the antigen of interest, and

(iii) employing the human immunoglobulin light chain variable region nucleotide sequence of (a) and/or the human immunoglobulin heavy chain variable region nucleotide sequence of (b) to produce an antibody that binds the antigen.

22. Use of a genetically modified mouse in making an antibody, wherein the germline genome of said genetically modified mouse comprises:

(a) a single rearranged human Vκ/Jκ sequence operably linked to a mouse κ constant region, wherein the single rearranged human Vκ/Jκ sequence replaces all endogenous mouse immunoglobulin κ light chain variable region gene segments at the endogenous immunoglobulin κ light chain locus, wherein the single rearranged human Vκ/Jκ sequence is a single rearranged human Vκ1-39/Jκ sequence or a single rearranged human Vκ3-20/Jκ sequence, and wherein the genetically modified mouse lacks an endogenous mouse κ immunoglobulin light chain variable region that is capable of rearranging to form a sequence that encodes a mouse immunoglobulin κ light chain variable domain so that all immunoglobulin kappa light chains expressed by B cells of the genetically modified mouse comprise immunoglobulin kappa light chain variable domains expressed from the single rearranged human Vκ/Jκ sequence or a somatically hypermutated version thereof; and

(b) a plurality of human immunoglobulin heavy chain variable region gene segments operably linked to the endogenous mouse immunoglobulin heavy chain constant region, wherein the plurality of human immunoglobulin heavy chain variable region gene segments

replaces endogenous mouse immunoglobulin heavy chain variable region gene segments at the endogenous mouse immunoglobulin heavy chain locus, and the human immunoglobulin heavy chain variable region gene segments are capable of rearranging to form a sequence that encodes a human immunoglobulin heavy chain variable domain.

23. The use of claim 22, wherein the genetically modified mouse has a germline genome that lacks an endogenous mouse immunoglobulin heavy chain variable region capable of rearranging to form a nucleotide sequence that encodes a mouse heavy chain variable domain.

24. The use of claim 22 or 23, wherein the germline genome of the genetically modified mouse comprises a mouse κ intronic enhancer positioned upstream of the mouse κ constant region.

25. The use of any one of claims 22-24, wherein the germline genome of the genetically modified mouse comprises a mouse κ 3' enhancer positioned downstream of the mouse κ constant region.

26. The use of any one of claims 22-25, wherein the plurality of human immunoglobulin heavy chain variable region gene segments comprises a human V_H1-2, V_H1-8, V_H1-18, V_H1-24, V_H2-5, V_H3-7, V_H3-9, V_H3-11, V_H3-13, V_H3-15, V_H3-20, V_H3-23, V_H3-30, V_H3-33, V_H3-43, V_H3-48, V_H4-31, V_H4-34, V_H4-59, or V_H6-1 gene segment, or a combination thereof.

27. The use of any one of claims 22-26, wherein the plurality of human immunoglobulin heavy chain variable region gene segments comprises a human D1-7, D1-26, D3-3, D3-10, D3-16, D3-22, D5-5, D5-12, D6-6, D6-13, or D7-27 gene segment, or a combination thereof.

28. The use of any one of claims 22-27, wherein the plurality of human immunoglobulin heavy chain variable region gene segments comprises a human J_H1, J_H3, J_H4, J_H5, or J_H6 gene segment, or a combination thereof.

29. The use of any one of claims 22-28, wherein the genetically modified mouse comprises a B cell that comprises a rearranged immunoglobulin heavy chain variable region nucleotide

sequence that encodes a human immunoglobulin heavy chain variable domain derived from a human V_H2-5, V_H3-23, V_H3-30, V_H4-39, V_H4-59, or a V_H5-51 gene segment, and a human D1-7, D1-26, D3-3, D3-16, D3-10, D3-22, D5-5, D5-12, D6-6, D6-13, or a D7-27 gene segment.

30. The use of claim 29, wherein the rearranged immunoglobulin heavy chain variable region nucleotide sequence is derived from a human J_H1, J_H3, J_H4, J_H5, or J_H6 gene segment.

31. The use of any one of claims 22-30, wherein the mouse κ constant region is the endogenous mouse κ constant region.

32. The use of any one of claims 22-31, wherein the single rearranged human Vκ/Jκ sequence is a single rearranged human Vκ1-39/Jκ sequence.

33. The use of any one of claims 22-32, wherein the single rearranged human Vκ/Jκ sequence is a single rearranged human Vκ1-39/Jκ sequence comprising a single human germline Vκ1-39 segment and a single human germline Jκ segment.

34. The use of claim 32 or 33, wherein the single rearranged human Vκ1-39/Jκ sequence comprises a human Jκ5 gene segment.

35. The use of claim 34, wherein the single rearranged human Vκ1-39/Jκ5 sequence comprises the sequence as set forth in nucleotides 2362 through 2686 of SEQ ID NO:1.

36. The use of claim 34 or 35, wherein the plurality of human immunoglobulin heavy chain variable region gene segments comprises a V_H2-5, V_H3-23, V_H3-30, V_H4-59, and V_H5-51 gene segment.

37. The use of any one of claims 22-31, wherein the single rearranged human Vκ/Jκ sequence is a single rearranged human Vκ3-20/Jκ sequence.

38. The use of any one of claims 22-31 and 37, wherein the single rearranged human Vκ/Jκ sequence is a single rearranged human Vκ3-20/Jκ sequence comprising a single human germline Vκ3-20 segment and a single human germline Jκ segment.

39. The use of claim 37 or 38, wherein the single rearranged human Vκ3-20/Jκ sequence comprises a human Jκ1 gene segment.

40. The use of claim 39, wherein the single rearranged human Vκ3-20/Jκ1 sequence comprises the sequence as set forth in nucleotides 2373 through 2697 of SEQ ID NO:11.

41. The use of claim 39 or 40, wherein the plurality of human immunoglobulin heavy chain variable region gene segments comprises a V_H4-39 and V_H5-51 gene segment.

42. The use of any one of claims 22-41, wherein the antibody is a bispecific antibody.

43. A method for selecting a nucleotide sequence encoding a human immunoglobulin heavy chain variable region, said method comprising the steps of:

(a) immunizing a genetically modified mouse with an antigen of interest, wherein the germline genome of the genetically modified mouse comprises:

(i) a single rearranged human Vκ/Jκ sequence operably linked to a mouse κ constant region, wherein the single rearranged human Vκ/Jκ sequence replaces all endogenous mouse immunoglobulin κ light chain variable region gene segments at the endogenous immunoglobulin κ light chain locus, wherein the single rearranged human Vκ/Jκ sequence is a single rearranged human Vκ1-39/Jκ sequence or a single rearranged human Vκ3-20/Jκ sequence, and wherein the genetically modified mouse lacks an endogenous mouse κ immunoglobulin light chain variable region that is capable of rearranging to form a sequence that encodes a mouse immunoglobulin κ light chain variable domain so that all immunoglobulin kappa light chains expressed by B cells of the genetically modified mouse comprise immunoglobulin kappa light chain variable domains expressed from the single rearranged human Vκ/Jκ sequence or a somatically hypermutated version thereof; and

(ii) a plurality of human immunoglobulin heavy chain variable region gene segments operably linked to the endogenous mouse immunoglobulin heavy chain constant region, wherein the plurality of human immunoglobulin heavy chain variable region gene segments replaces endogenous mouse immunoglobulin heavy chain variable region gene segments at the endogenous mouse immunoglobulin heavy chain locus, and the human immunoglobulin heavy chain variable region gene segments are capable of rearranging to form a sequence that encodes a human immunoglobulin heavy chain variable domain;

(b) allowing the genetically modified mouse to develop an immune response to the antigen of interest; and

(c) identifying a clonally selected lymphocyte of the genetically modified mouse that expresses an antibody that specifically binds the antigen of interest, and obtaining from the lymphocyte or the antibody a nucleotide sequence that encodes a human immunoglobulin heavy chain variable region that specifically binds the antigen of interest.

44. The method of claim 43, wherein the genetically modified mouse has a germline genome that lacks an endogenous mouse immunoglobulin heavy chain variable region capable of rearranging to form a nucleotide sequence that encodes a mouse heavy chain variable domain.

45. The method of claim 43 or 44, wherein the germline genome of the genetically modified mouse comprises a mouse κ intronic enhancer positioned upstream of the mouse κ constant region.

46. The method of any one of claims 43-45, wherein the germline genome of the genetically modified mouse comprises a mouse κ 3' enhancer positioned downstream of the mouse κ constant region.

47. The method of any one of claims 43-46, wherein the plurality of human immunoglobulin heavy chain variable region gene segments comprises a human V_H1-2, V_H1-8, V_H1-24, V_H2-5, V_H3-7, V_H3-9, V_H3-11, V_H3-13, V_H3-15, V_H3-20, V_H3-23, V_H3-30, V_H3-33, V_H3-48, V_H4-31, V_H4-39, V_H4-59, V_H5-51, or V_H6-1 gene segment, or a combination thereof.

48. The method of any one of claims 43-47, wherein the plurality of human immunoglobulin heavy chain variable region gene segments comprises a human D1-7, D1-26, D3-3, D3-10, D3-16, D3-22, D5-5, D5-12, D6-6, D6-13, or D7-27 gene segment, or a combination thereof.

49. The method of any one of claims 43-48, wherein the plurality of human immunoglobulin heavy chain variable region gene segments comprises a human J_H1, J_H3, J_H4, J_H5, or J_H6 gene segment, or a combination thereof.

50. The method of any one of claims 43-49, wherein the genetically modified mouse comprises a B cell that comprises a rearranged immunoglobulin heavy chain variable region nucleotide sequence that encodes a human immunoglobulin heavy chain variable domain derived from a human V_H2-5, V_H3-23, V_H3-30, V_H4-39, V_H4-59, or a V_H5-51 gene segment, and a human D1-7, D1-26, D3-3, D3-16, D3-10, D3-22, D5-5, D5-12, D6-6, D6-13, or a D7-27 gene segment.

51. The method of claim 50, wherein the rearranged immunoglobulin heavy chain variable region nucleotide sequence is derived from a human J_H1, J_H3, J_H4, J_H5, or J_H6 gene segment.

52. The method of any one of claims 43-51, wherein the mouse κ constant region is the endogenous mouse κ constant region.

53. The method of any one of claims 43-52, wherein the single rearranged human Vκ/Jκ sequence is a single rearranged human Vκ1-39/Jκ sequence.

54. The method of any one of claims 43-53, wherein the single rearranged human Vκ/Jκ sequence is a single rearranged human Vκ1-39/Jκ sequence comprising a single human germline Vκ1-39 segment and a single human germline Jκ segment.

55. The method of claim 53 or 54, wherein the single rearranged human Vκ1-39/Jκ sequence comprises a human Jκ5 gene segment.

56. The method of claim 55, wherein the single rearranged human Vκ1-39/Jκ5 sequence comprises the sequence as set forth in nucleotides 2362 through 2686 of SEQ ID NO:1.

57. The method of claim 55 or 56, wherein the plurality of human immunoglobulin heavy chain variable region gene segments comprises a human V_H2-5, V_H3-23, V_H3-30, V_H4-59, and V_H5-51 gene segment.

58. The method of any one of claims 43-52, wherein the single rearranged human Vκ/Jκ sequence is a single rearranged human Vκ3-20/Jκ sequence.

59. The method of any one of claims 43-52 and 58, wherein the single rearranged human Vκ/Jκ sequence is a rearranged human Vκ3-20/Jκ sequence comprising a single human germline Vκ3-20 segment and a single human germline Jκ segment.

60. The method of claim 58 or 59, wherein the single rearranged human Vκ3-20/Jκ sequence comprises a human Jκ1 gene segment.

61. The method of claim 60, wherein the single rearranged human Vκ3-20/Jκ1 sequence comprises the sequence as set forth in nucleotides 2373 through 2697 of SEQ ID NO:11.

62. The method of claim 60 or 61, wherein the plurality of human immunoglobulin heavy chain variable region gene segments comprises a human V_H4-39 and V_H5-51 gene segment.

63. The method of any one of claims 43-62, wherein steps (a) through (c) are performed a first time for a first antigen of interest to generate a first human immunoglobulin heavy chain variable region nucleotide sequence encoding a first human heavy chain variable domain, and steps (a) through (c) are performed a second time for a second antigen of interest to generate a second human immunoglobulin heavy chain variable region nucleotide sequence encoding a second human heavy chain variable domain.

64. The method of claim 63, further comprising

(i) joining the first human immunoglobulin heavy chain variable region nucleotide sequence with a first human immunoglobulin heavy chain constant region nucleotide sequence, which encodes a first human immunoglobulin heavy chain constant domain, to form a first human immunoglobulin heavy chain sequence, and

(ii) joining the second human immunoglobulin heavy chain variable region nucleotide sequence with a second human immunoglobulin heavy chain constant region nucleotide sequence, which encodes a second human immunoglobulin heavy chain constant domain, to form a second human immunoglobulin heavy chain sequence;

wherein the first human immunoglobulin heavy chain constant domain encoded by the first human immunoglobulin heavy chain constant region nucleotide sequence comprises a modification that eliminates or substantially reduces the affinity of the first human immunoglobulin heavy chain constant domain to protein A, and the second human immunoglobulin heavy chain constant domain retains the ability to bind protein A.

65. The method of claim 64, wherein the modification that eliminates or substantially reduces affinity of the first human immunoglobulin heavy chain constant domain to protein A is selected from a 95R (EU 435R), a 96F (EU 436F), or a combination thereof.

66. A method of making an antibody, said method comprising:

(a) immunizing a genetically modified mouse with an antigen of interest, wherein the genetically modified mouse comprises in its germline genome:

(i) an engineered mouse immunoglobulin kappa light chain locus comprising a single rearranged human Vκ/Jκ sequence operably linked to a mouse κ constant region, wherein the engineered mouse immunoglobulin kappa light chain locus comprises in order: a human promoter sequence, a mouse leader sequence, and the single rearranged human Vκ/Jκ sequence and replaces all endogenous mouse immunoglobulin κ light chain variable region gene segments at the endogenous immunoglobulin κ light chain locus, wherein the single rearranged human Vκ/Jκ sequence is a single rearranged human Vκ1-39/Jκ sequence or a single rearranged human Vκ3-20/Jκ sequence, and wherein the genetically modified mouse lacks an endogenous mouse κ immunoglobulin light chain variable region that is capable of rearranging to form a sequence that encodes a mouse immunoglobulin κ light chain

variable domain so that all immunoglobulin kappa light chains expressed by B cells of the genetically modified mouse comprise immunoglobulin kappa light chain variable domains expressed from the single rearranged human Vκ/Jκ sequence or a somatically hypermutated version thereof; and

(ii) a plurality of human immunoglobulin heavy chain variable region gene segments operably linked to the endogenous mouse immunoglobulin heavy chain constant region, wherein the plurality of human immunoglobulin heavy chain variable region gene segments replaces endogenous mouse immunoglobulin heavy chain variable region gene segments at the endogenous mouse immunoglobulin heavy chain locus, and the human immunoglobulin heavy chain variable region gene segments are capable of rearranging to form a sequence that encodes a human immunoglobulin heavy chain variable domain;

(b) allowing the genetically modified mouse to develop an immune response to the antigen of interest, wherein the genetically modified mouse expresses a population of antibodies in response to the antigen of interest;

(c) identifying a clonally selected lymphocyte of the genetically modified mouse, wherein the lymphocyte expresses an antibody that specifically binds the antigen of interest;

(d) obtaining from the lymphocyte a human immunoglobulin heavy chain variable region nucleotide sequence that encodes a human immunoglobulin heavy chain variable domain that, when paired with a human immunoglobulin light chain variable domain encoded by the single rearranged human Vκ/Jκ sequence, specifically binds to the antigen of interest from the population of antibodies; and

(e) employing the human immunoglobulin heavy chain variable region nucleotide sequence of (d) in making an antibody, wherein the antibody comprises a human immunoglobulin light chain variable domain derived from the single rearranged human Vκ/Jκ sequence and a human immunoglobulin heavy chain variable domain encoded by the human immunoglobulin heavy chain variable region nucleotide sequence of (d) that pairs with said human immunoglobulin light chain variable domain.

67. The method of claim 66, wherein the genetically modified mouse has a germline genome that lacks an endogenous mouse immunoglobulin heavy chain variable region capable of rearranging to form a nucleotide sequence that encodes a mouse heavy chain variable domain.

68. The method of claim 66 or 67, wherein the germline genome of the genetically modified mouse comprises a mouse κ intronic enhancer positioned upstream of the mouse κ constant region.

69. The method of any one of claims 66-68, wherein the germline genome of the genetically modified mouse comprises a mouse κ 3' enhancer positioned downstream of the mouse κ constant region.

70. The method of any one of claims 66-69, wherein the plurality of human immunoglobulin heavy chain variable region gene segments comprises a human V_H1-2, V_H1-8, V_H1-24, V_H2-5, V_H3-7, V_H3-9, V_H3-11, V_H3-13, V_H3-15, V_H3-20, V_H3-23, V_H3-30, V_H3-33, V_H3-48, V_H4-31, V_H4-39, V_H4-59, V_H5-51, or V_H6-1 gene segment, or a combination thereof.

71. The method of any one of claims 66-70, wherein the plurality of human immunoglobulin heavy chain variable region gene segments comprises a human D1-7, D1-26, D3-3, D3-10, D3-16, D3-22, D5-5, D5-12, D6-6, D6-13, or D7-27 gene segment, or a combination thereof.

72. The method of any one of claims 66-71, wherein the plurality of human immunoglobulin heavy chain variable region gene segments comprises a human J_H1, J_H3, J_H4, J_H5, or J_H6 gene segment, or a combination thereof.

73. The method of any one of claims 66-72, wherein the genetically modified mouse comprises a B cell that comprises a rearranged immunoglobulin heavy chain variable region nucleotide sequence that encodes a human immunoglobulin heavy chain variable domain derived from a human V_H2-5, V_H3-23, V_H3-30, V_H4-39, V_H4-59, or a V_H5-51 gene segment, and a human D1-7, D1-26, D3-3, D3-16, D3-10, D3-22, D5-5, D5-12, D6-6, D6-13, or a D7-27 gene segment.

74. The method of claim 73, wherein the rearranged immunoglobulin heavy chain variable region nucleotide sequence is derived from a human J_H1, J_H3, J_H4, J_H5, or J_H6 gene segment.

75. The method of any one of claims 66-74, wherein the mouse κ constant region is the endogenous mouse κ constant region.

76. The method of any one of claims 66-75, wherein the single rearranged human Vκ/Jκ sequence is a single rearranged human Vκ1-39/Jκ sequence.

77. The method of any one of claims 66-76, wherein the single rearranged human Vκ/Jκ sequence is a rearranged human Vκ1-39/Jκ sequence comprising a single human germline Vκ1-39 segment and a single human germline Jκ segment.

78. The method of claim 76 or 77, wherein the single rearranged human Vκ1-39/Jκ sequence comprises a human Jκ5 gene segment.

79. The method of claim 78, wherein the single rearranged human Vκ1-39/Jκ5 sequence comprises the sequence as set forth in nucleotides 2362 through 2686 of SEQ ID NO:1.

80. The method of claim 78 or 79, wherein the plurality of human immunoglobulin heavy chain variable region gene segments comprises a human V_H2-5, V_H3-23, V_H3-30, V_H4-59, and V_H5-51 gene segment.

81. The method of any one of claims 66-75, wherein the single rearranged human Vκ/Jκ sequence is a single rearranged human Vκ3-20/Jκ sequence.

82. The method of any one of claims 66-75 and 81, wherein the single rearranged human Vκ/Jκ sequence is a rearranged human Vκ3-20/Jκ sequence comprising a single human germline Vκ3-20 segment and a single human germline Jκ segment.

83. The method of claims 81 or 82, wherein the human Vκ3-20/Jκ sequence comprises a human Jκ1 gene segment.

84. The method of claim 83, wherein the single rearranged human Vκ3-20/Jκ1 sequence comprises the sequence as set forth in nucleotides 2373 through 2697 of SEQ ID NO:11.

85. The method of claim 83 or 84, wherein the plurality of human immunoglobulin heavy chain variable region gene segments comprises a human V_H4-39, and V_H5-51 gene segment.

86. The method of claim 64, wherein the first and second human immunoglobulin heavy chain variable region nucleotide sequence are used to make a bispecific antibody.

87. A method of making a bispecific antigen-binding protein, the method comprising:

(a) expressing in a host cell a first human immunoglobulin heavy chain comprising a first human immunoglobulin heavy chain variable domain encoded by a first human immunoglobulin heavy chain variable region nucleotide sequence identical to a human immunoglobulin heavy chain variable region nucleotide sequence of a B cell of a first genetically engineered mouse that has been immunized with a first antigen of interest that comprises a first epitope, wherein the first genetically engineered mouse comprises in its germline genome:

(i) a single rearranged human Vκ/Jκ sequence operably linked to a mouse κ constant region, wherein the single rearranged human Vκ/Jκ sequence replaces all endogenous mouse immunoglobulin κ light chain variable region gene segments at the endogenous immunoglobulin κ light chain locus, wherein the single rearranged human Vκ/Jκ sequence is a single rearranged human Vκ1-39/Jκ sequence or a single rearranged human Vκ3-20/Jκ sequence, and wherein the first genetically engineered mouse lacks an endogenous mouse κ immunoglobulin light chain variable region that is capable of rearranging to form a sequence that encodes a mouse immunoglobulin κ light chain variable domain so that all immunoglobulin kappa light chains expressed by B cells of the first genetically modified mouse comprise immunoglobulin kappa light chain variable domains expressed from the single rearranged human Vκ/Jκ sequence or a somatically hypermutated version thereof; and

(ii) a plurality of human immunoglobulin heavy chain variable region gene segments operably linked to the endogenous mouse immunoglobulin heavy chain constant region, wherein the plurality of human immunoglobulin heavy chain variable region gene segments replaces endogenous mouse immunoglobulin heavy chain variable region gene segments at the endogenous mouse immunoglobulin heavy chain

locus, and the human immunoglobulin heavy chain variable region gene segments are capable of rearranging to form a sequence that encodes a human immunoglobulin heavy chain variable domain;

wherein the first genetically engineered mouse comprises a population of B cells, wherein each B cell in the population expresses a human immunoglobulin light chain variable domain derived from the single rearranged human Vκ/Jκ sequence and expresses a human immunoglobulin heavy chain variable domain derived from the plurality of human immunoglobulin heavy chain variable region gene segments of (a)(ii); and

(b) expressing in the same host cell a second human immunoglobulin heavy chain comprising a second human immunoglobulin heavy chain variable domain encoded by a second human immunoglobulin heavy chain variable region nucleotide sequence identical to a human immunoglobulin heavy chain variable region nucleotide sequence of a B cell of a second genetically engineered mouse that has been immunized with a second antigen of interest that comprises a second epitope, wherein the second genetically engineered mouse comprises in its germline genome:

(i) a single rearranged human Vκ/Jκ sequence operably linked to a mouse κ constant region, wherein the single rearranged human Vκ/Jκ sequence replaces all endogenous mouse immunoglobulin κ light chain variable region gene segments at the endogenous immunoglobulin κ light chain locus, wherein the single rearranged human Vκ/Jκ sequence is identical or substantially identical to the single rearranged human Vκ/Jκ sequence inserted at the endogenous mouse immunoglobulin κ light chain variable region locus of the first genetically engineered mouse, and wherein the second genetically engineered mouse lacks an endogenous mouse κ immunoglobulin light chain variable region that is capable of rearranging to form a sequence that encodes a mouse immunoglobulin κ light chain variable domain; and

(ii) a plurality of human immunoglobulin heavy chain variable region gene segments operably linked to the endogenous mouse immunoglobulin heavy chain constant region, wherein the plurality of human immunoglobulin heavy chain variable region gene segments replaces endogenous mouse immunoglobulin heavy chain variable region gene segments at the endogenous mouse immunoglobulin heavy chain

locus, and the human immunoglobulin heavy chain variable region gene segments are capable of rearranging to form a sequence that encodes a human immunoglobulin heavy chain variable domain;

wherein the second genetically engineered mouse comprises a population of B cells, wherein each B cell in the population expresses a human immunoglobulin light chain variable domain derived from the single rearranged human Vκ/Jκ sequence and expresses a human immunoglobulin heavy chain variable domain derived from the plurality of human immunoglobulin heavy chain variable region gene segments of (b)(ii); and

(c) expressing in the same host cell a human immunoglobulin light chain comprising a human immunoglobulin light chain variable domain derived from a single rearranged human Vκ/Jκ sequence that is identical or substantially identical to the single rearranged human Vκ/Jκ sequence inserted at the endogenous mouse immunoglobulin κ light chain variable region locus of the genetically engineered first and/or second mouse,

wherein the expressed first human immunoglobulin heavy chain, which comprises the first variable domain encoded by the first human immunoglobulin heavy chain variable region, pairs with the expressed second human immunoglobulin heavy chain, which comprises the second variable domain encoded by the second human immunoglobulin heavy chain variable region, and wherein the first and second human immunoglobulin heavy chains each pair with the human immunoglobulin light chain comprising the human immunoglobulin light chain variable domain, thereby making a bispecific antigen-binding protein.

88. The method of claim 87, wherein the plurality of human immunoglobulin heavy chain variable region gene segments of the first and/or second mouse comprises a human V_H1-2, V_H1-8, V_H1-24, V_H2-5, V_H3-7, V_H3-9, V_H3-11, V_H3-13, V_H3-15, V_H3-20, V_H3-23, V_H3-30, V_H3-33, V_H3-48, V_H4-31, V_H4-39, V_H4-59, V_H5-51, or V_H6-1 gene segment, or a combination thereof.

89. The method of claim 87 or 88, wherein the germline genome of the first and/or the second genetically modified mouse comprises each of human V_H1-2, V_H1-8, V_H1-24, V_H2-5, V_H3-7, V_H3-9, V_H3-11, V_H3-13, V_H3-15, V_H3-20, V_H3-23, V_H3-30, V_H3-33, V_H3-48, V_H4-31, V_H4-39, V_H4-59, V_H5-51, and V_H6-1 gene segments.

90. The method of any one of claims 87-89, wherein the plurality of human immunoglobulin heavy chain variable region gene segments of the first and/or second mouse comprises a human D1-7, D1-26, D3-3, D3-10, D3-16, D3-22, D5-5, D5-12, D6-6, D6-13, or D7-27 gene segment, or a combination thereof.

91. The method of any one of claims 87-90, wherein the plurality of human immunoglobulin heavy chain variable region gene segments of the first and/or second mouse comprises a human J_H1, J_H3, J_H4, J_H5, or J_H6 gene segment, or a combination thereof.

92. The method of any one of claims 87-91, wherein the first and/or second human immunoglobulin heavy chain variable domain is encoded by a immunoglobulin heavy chain variable region nucleotide sequence that is derived from a human $V_H/D/J_H$ rearrangement comprising a human 2-5/6-6/1, 3-23/3-3/4, 3-23/3-10/4, 3-30/6-6/1, 3-30/6-6/3, 3-30/1-7/4, 3-30/5-12/4, 3-30/6-13/4, 3-30/6-6/4, 3-30/7-27/4, 3-30/3-22/5, 3-30/6-6/5, 3-30/7-27/5, 4-39/1-26/3, 4-59/3-16/3, 4-59/3-22/3, 4-59/3-16/4, 5-51/5-5/3, 5-51/6-13/5, or a 5-51/3-16/6 $V_H/D/J_H$ rearrangement.

93. The method of any one of claims 87-92, wherein the single rearranged human Vκ/Jκ sequence of the first and second mouse comprises a single rearranged human Vκ1-39/Jκ sequence.

94. The method of any one of claims 87-92, wherein the single rearranged human Vκ/Jκ sequence of the first and second mouse comprises a single rearranged human Vκ1-39/Jκ sequence comprising a single human germline Vκ1-39 segment and a single human germline Jκ segment.

95. The method of claim 93 or 94, wherein the single rearranged human Vκ1-39/Jκ sequence comprises a human Jκ5 gene segment.

96. The method of claim 95, wherein the human Vκ1-39/Jκ5 sequence comprises the sequence as set forth in nucleotides 2362 through 2686 of SEQ ID NO:1.

97. The method of claim 95 or 96, wherein the plurality of human immunoglobulin heavy chain variable region gene segments of the first and/or second mouse comprises a human V_H2-5, V_H3-23, V_H3-30, V_H4-59, and V_H5-51 gene segment.

98. The method of any one of claims 87-92, wherein the replacement at the endogenous mouse immunoglobulin κ light chain variable region locus of the first and/or second mouse comprises the single rearranged human Vκ3-20/Jκ sequence.

99. The method of any one of claims 87-92 and 98, wherein the replacement at the endogenous mouse immunoglobulin κ light chain variable region locus of the first and/or second mouse comprises the single rearranged human Vκ3-20/Jκ sequence comprising a single human germline Vκ3-20 segment and a single human germline Jκ segment.

100. The method of claim 98 or 99, wherein the single rearranged human Vκ3-20/Jκ sequence comprises a human Jκ1 gene segment.

101. The method of claim 100, wherein the single rearranged human Vκ3-20/Jκ1 sequence comprises the sequence as set forth in nucleotides 2373 through 2697 of SEQ ID NO:11.

102. The method of claim 100 or 101, wherein the plurality of human immunoglobulin heavy chain variable region gene segments of the first and/or second mouse comprises a V_H4-39 and V_H5-51 gene segment.

103. The method of any one of claims 87-102, wherein the first genetically modified mouse and/or the second genetically modified mouse lack an endogenous mouse immunoglobulin heavy chain variable region capable of rearranging to form a sequence that encodes a mouse heavy chain variable domain.

104. The method of any one of claims 87-103, wherein the first and the second antigens are:
two different antigens; or
the same antigen;

and if the first and the second antigens are the same antigen, then the first and the second human immunoglobulin heavy chains bind to different epitopes of the same antigen.

105. The method of claim 104, wherein the first and the second antigens are the same antigen and the binding response of the bispecific antigen-binding protein to said same antigen is at least 2-fold higher than the binding response of a monospecific antigen-binding protein having only the first human immunoglobulin heavy chain and/or a monospecific antigen-binding protein having only the second human immunoglobulin heavy chain.

106. The method of any one of claims 87-105, wherein the first or the second human immunoglobulin heavy chain of the bispecific antigen-binding protein, but not both, bears an amino acid modification that reduces its affinity to protein A, wherein the modification is selected from a 95R (EU 435R), 96F (EU 436F), or a combination thereof.

107. The method of any one of claims 87-106, wherein the mouse κ constant region of the first and/or second mouse is the endogenous mouse κ constant region.

108. The method of any one of claims 87-107, wherein the first mouse and second mouse are the same mouse or separate mice.

109. An isolated B cell from a genetically modified mouse, wherein the genetically modified mouse comprises in its germline genome:

(a) a single rearranged human Vκ/Jκ sequence operably linked to a mouse κ constant region, wherein the single rearranged human Vκ/Jκ sequence replaces all endogenous mouse immunoglobulin κ light chain variable region gene segments at the endogenous immunoglobulin κ light chain locus, wherein the single rearranged human Vκ/Jκ sequence is a single rearranged human Vκ1-39/Jκ sequence or a single rearranged human Vκ3-20/Jκ sequence, and wherein the genetically modified mouse lacks an endogenous mouse κ immunoglobulin light chain variable region that is capable of rearranging to form a sequence that encodes a mouse immunoglobulin κ light chain variable domain; and

(b) a plurality of human immunoglobulin heavy chain variable region gene segments operably linked to the endogenous mouse immunoglobulin heavy chain constant region, wherein the plurality of human immunoglobulin heavy chain variable region gene segments replaces endogenous mouse immunoglobulin heavy chain variable region gene segments at the endogenous mouse immunoglobulin heavy chain locus, and the human immunoglobulin heavy chain variable region gene segments are capable of rearranging to form a sequence that encodes a human immunoglobulin heavy chain variable domain, and

wherein the isolated B cell expresses an immunoglobulin kappa light chain variable domain expressed from the single rearranged human Vκ/Jκ sequence or a somatically hypermutated version thereof.

110. The isolated B cell of claim 109, wherein the genome of the B cell comprises a mouse κ intronic enhancer positioned upstream of the mouse κ constant region.

111. The isolated B cell of any one of claims 109 or 110, wherein the genome of the B cell comprises a mouse κ 3' enhancer positioned downstream of the mouse κ constant region.

112. The isolated B cell of any one of claims 109-111, wherein the mouse κ constant region is the endogenous mouse κ constant region.

113. The isolated B cell of any one of claims 109-112, wherein the single rearranged human Vκ/Jκ sequence is a single rearranged human Vκ1-39/Jκ sequence.

114. The isolated B cell of any one of claims 110-113, wherein the single rearranged human Vκ/Jκ sequence is a single rearranged human Vκ1-39/Jκ sequence comprising a single human germline Vκ1-39 segment and a single human germline Jκ segment.

115. The isolated B cell of claim 113 or 114, wherein the single rearranged human Vκ1-39/Jκ sequence comprises a human Jκ5 gene segment.

116. The isolated B cell of claim 115, wherein the single rearranged human Vκ1-39/Jκ5 sequence comprises the sequence as set forth in nucleotides 2362 through 2686 of SEQ ID NO:1.

117. The isolated B cell of any one of claims 109-112, wherein the single rearranged human Vκ/Jκ sequence is a single rearranged human Vκ3-20/Jκ sequence.

118. The isolated B cell of any one of claims 109-112 and 117, wherein the single rearranged human Vκ/Jκ sequence is a single rearranged human Vκ3-20/Jκ sequence comprising a single human germline Vκ3-20 segment and a single human germline Jκ segment.

119. The isolated B cell of claim 117 or 118, wherein the single rearranged human Vκ3-20/Jκ sequence comprises a human Jκ1 gene segment.

120. The isolated cell of claim 119, wherein the single rearranged human Vκ3-20/Jκ1 sequence comprises the sequence as set forth in nucleotides 2373 through 2697 of SEQ ID NO:11.

121. The isolated B cell of claim 109, wherein the isolated B cell comprises a rearranged human immunoglobulin heavy chain variable region sequence that encodes a human immunoglobulin heavy chain variable domain derived from a human V_H2-5, V_H3-23, V_H3-30, V_H4-39, V_H4-59, or V_H5-51 gene segment, and a human D1-7, D1-26, D3-3, D3-16, D3-10, D3-22, D5-5, D5-12, D6-6, D6-13, or D7-27 gene segment.

122. The isolated B cell of claim 121, wherein the rearranged human immunoglobulin heavy chain variable region sequence is derived from a human J_H1, J_H3, J_H4, J_H5 or J_H6 gene segment.

123. A hybridoma made from the B cell of any one of claims 109-122.

124. A mouse embryonic stem (ES) cell that has been genetically modified so that it comprises in its genome:

(a) a single rearranged human Vκ/Jκ sequence operably linked to a mouse κ constant region, wherein the single rearranged human Vκ/Jκ sequence replaces all endogenous mouse immunoglobulin κ light chain variable gene segments at the endogenous immunoglobulin κ light chain locus, wherein the single rearranged human Vκ/Jκ sequence is a single rearranged human Vκ1-39/Jκ sequence or a single rearranged human Vκ3-20/Jκ sequence, and wherein the genome of the mouse ES cell lacks an endogenous mouse κ immunoglobulin light chain variable region that is capable of rearranging in a mouse to form a sequence that encodes a mouse immunoglobulin κ light chain variable domain; and

(b) a plurality of human immunoglobulin heavy chain variable region gene segments operably linked to the endogenous mouse immunoglobulin heavy chain constant region, wherein the plurality of human immunoglobulin heavy chain variable region gene segments replaces endogenous mouse immunoglobulin heavy chain variable region gene segments at the endogenous mouse immunoglobulin heavy chain locus; and wherein the human immunoglobulin heavy chain variable region gene segments are capable of rearranging in a mouse to form a sequence that encodes a human immunoglobulin heavy chain variable domain.

125. The ES cell of claim 124, wherein the genome of the ES cell comprises a mouse κ intronic enhancer positioned upstream of the mouse κ constant region.

126. The ES cell of claim 124 or 125, wherein the genome of the ES cell comprises a mouse κ 3' enhancer positioned downstream of the mouse κ constant region.

127. The ES cell of any one of claims 124-126, wherein the plurality of human immunoglobulin heavy chain variable region gene segments comprises a human V_H1-2, V_H1-8, V_H1-18, V_H1-24, V_H2-5, V_H3-7, V_H3-9, V_H3-11, V_H3-13, V_H3-15, V_H3-20, V_H3-23, V_H3-30, V_H3-33, V_H3-43, V_H3-48, V_H4-31, V_H4-34, V_H4-59, or V_H6-1 gene segment, or a combination thereof.

128. The ES cell of any one of claims 124-127, wherein the plurality of human immunoglobulin heavy chain variable region gene segments comprises a human D1-7, D1-26, D3-3, D3-10, D3-16, D3-22, D5-5, D5-12, D6-6, D6-13, or D7-27 gene segment, or a combination thereof.

129. The ES cell of any one of claims 124-128, wherein the plurality of human immunoglobulin heavy chain variable region gene segments comprises a human J_H1, J_H3, J_H4, J_H5, or J_H6 gene segment, or a combination thereof.

130. The ES cell of any one of claims 124-129, wherein the mouse κ constant region is the endogenous mouse κ constant region.

131. The ES cell of any one of claims 124-130, wherein the single rearranged human Vκ/Jκ sequence is a single rearranged human Vκ1-39/Jκ sequence.

132. The ES cell of any one of claims 124-131, wherein the single rearranged human Vκ/Jκ sequence is a single rearranged human Vκ1-39/Jκ sequence comprising a single human germline Vκ1-39 segment and a single human germline Jκ segment.

133. The ES cell of claim 131 or 132, wherein the single rearranged human Vκ1-39/Jκ sequence comprises a human Jκ5 gene segment.

134. The ES cell of claim 133, wherein the single rearranged human Vκ1-39/Jκ5 sequence comprises the sequence as set forth in nucleotides 2362 through 2686 of SEQ ID NO:1.

135. The ES cell of claim 133 or 134, wherein the plurality of human immunoglobulin heavy chain variable region gene segments comprises a V_H2-5, V_H3-23, V_H3-30, V_H4-59, and V_H5-51 gene segment.

136. The ES cell of any one of claims 124-130, wherein the single rearranged human Vκ/Jκ sequence is a single rearranged human Vκ3-20/Jκ sequence.

137. The ES cell of any one of claims 124-130, and 136, wherein the single rearranged human Vκ/Jκ sequence is a single rearranged human Vκ3-20/Jκ sequence comprising a single human germline Vκ3-20 segment and a single human germline Jκ segment.

138. The ES cell of claim 136 or 137, wherein the single rearranged human Vκ3-20/Jκ sequence comprises a human Jκ1 gene segment.

139. The ES cell of claim 138, wherein the single rearranged human Vκ3-20/Jκ1 sequence comprises the sequence as set forth in nucleotides 2373 through 2697 of SEQ ID NO:11.

140. The ES cell of claim 138 or 139, wherein the plurality of human immunoglobulin heavy chain variable region gene segments comprises a V_H4-39 and V_H5-51 gene segment.

141. A method of making a mouse comprising gestating a mouse embryo derived from the ES cell of claim 124 in a surrogate mother, and allowing the surrogate mother to give birth to progeny derived in whole or in part from the embryonic stem cell.

142. A method of making a genetically modified mouse embryonic stem (ES) cell, the method comprising genetically modifying a mouse ES cell so that it comprises in its genome:

(a) a single rearranged human Vκ/Jκ sequence operably linked to a mouse κ constant region, wherein the single rearranged human Vκ/Jκ sequence replaces all endogenous mouse immunoglobulin κ light chain variable region gene segments at the endogenous immunoglobulin κ light chain locus, and wherein the single rearranged human Vκ/Jκ sequence is a single rearranged human Vκ1-39/Jκ sequence or a single rearranged human Vκ3-20/Jκ sequence, and wherein the genome of the mouse ES cell lacks an endogenous mouse κ immunoglobulin light chain variable region that is capable of rearranging in a mouse to form a sequence that encodes a mouse immunoglobulin κ light chain variable domain; and

(b) a plurality of human immunoglobulin heavy chain variable region gene segments operably linked to the endogenous mouse immunoglobulin heavy chain constant region, wherein the plurality of human immunoglobulin heavy chain variable region gene segments replaces endogenous mouse immunoglobulin heavy chain variable region gene segments at the endogenous mouse immunoglobulin heavy chain locus; and wherein the human immunoglobulin heavy chain variable region gene segments are capable of rearranging in a mouse to form a sequence that encodes a human immunoglobulin heavy chain variable domain.

143. The method of claim 142, wherein the genome of the mouse ES cell comprises a mouse κ intronic enhancer positioned upstream of the mouse κ constant region.

144. The method of claim 142 or 143, wherein the genome of the mouse ES cell comprises a mouse κ 3' enhancer positioned downstream of the mouse κ constant region.

145. The method of any one of claims 142-144, wherein the plurality of human immunoglobulin heavy chain variable region gene segments comprises a human V_H1-2, V_H1-8, V_H1-18, V_H1-24, V_H2-5, V_H3-7, V_H3-9, V_H3-11, V_H3-13, V_H3-15, V_H3-20, V_H3-23, V_H3-30, V_H3-33, V_H3-43, V_H3-48, V_H4-31, V_H4-34, V_H4-59, or V_H6-1 gene segment, or a combination thereof.

146. The method of any one of claims 142-145, wherein the plurality of human immunoglobulin heavy chain variable region gene segments comprises a human D1-7, D1-26, D3-3, D3-10, D3-16, D3-22, D5-5, D5-12, D6-6, D6-13, or D7-27 gene segment, or a combination thereof.

147. The method of any one of claims 142-146, wherein the plurality of human immunoglobulin heavy chain variable region gene segments comprises a human J_H1, J_H3, J_H4, J_H5, or J_H6 gene segment, or a combination thereof.

148. The method of any one of claims 142-147, wherein the mouse κ constant region is the endogenous mouse κ constant region.

149. The method of any one of claims 142-148, wherein the single rearranged human Vκ/Jκ sequence is a single rearranged human Vκ1-39/Jκ sequence.

150. The method of any one of claims 142-149, wherein the single rearranged human Vκ/Jκ sequence is a single rearranged human Vκ1-39/Jκ sequence comprising a single human germline Vκ1-39 segment and a single human germline Jκ segment.

151. The method of claim 149 or 150, wherein the single rearranged human Vκ1-39/Jκ sequence comprises a human Jκ5 gene segment.

152. The method of claim 151, wherein the single rearranged human Vκ1-39/Jκ5 sequence comprises the sequence as set forth in nucleotides 2362 through 2686 of SEQ ID NO:1.

153. The method of claim 151 or 152, wherein the plurality of human immunoglobulin heavy chain variable region gene segments comprises a V_H2-5, V_H3-23, V_H3-30, V_H4-59, and V_H5-51 gene segment.

154. The method of any one of claims 142-148, wherein the single rearranged human Vκ/Jκ sequence is a single rearranged human Vκ3-20/Jκ sequence.

155. The method of any one of claims 142-148, and 154, wherein the single rearranged human Vκ/Jκ sequence is a single rearranged human Vκ3-20/Jκ sequence comprising a single human germline Vκ3-20 segment and a single human germline Jκ segment.

156. The method of claim 154 or 155, wherein the single rearranged human Vκ3-20/Jκ sequence comprises a human Jκ1 gene segment.

157. The method of claim 156, wherein the single rearranged human Vκ3-20/Jκ1 sequence comprises the sequence as set forth in nucleotides 2373 through 2697 of SEQ ID NO:11.

158. The method of claim 156 or 157, wherein the plurality of human immunoglobulin heavy chain variable region gene segments comprises a V_H4-39 and V_H5-51 gene segment.