WHAT IS CLAIMED IS:

1. A genetically-modified, non-human animal comprising at the endogenous light chain immunoglobulin locus, an exogenous light chain variable region gene sequence, wherein the exogenous light chain variable region gene sequence comprises no more than three human IGKV genes and no more than two human IGKJ genes, wherein the no more than three human IGKV genes and the no more than two human IGKJ genes are operably linked to an endogenous light chain constant domain gene.

~~2. The animal of claim 1, wherein the no more than three human IGKV genes are selected from Table 1, and the no more than two human IGKJ genes are selected from Table 2.~~

~~3.~~2. The animal of claim 1 ~~or 2~~, wherein the exogenous light chain variable region gene sequence comprises one human IGKV gene and one human IGKJ gene.

~~4.~~3. The animal of any one of claims 1-~~3~~2, wherein the exogenous light chain variable region gene sequence further comprises a human IGKJ 3'-UTR sequence.

~~5.~~4. The animal of any one of claims 1-~~4~~3, wherein the exogenous light chain variable region gene in one or more cells of the animal can subject to somatic hypermutations.

~~6. The animal of claim 5, wherein the somatic hypermutations can result in up to one, two, or three amino acid changes in light chain variable regions in the one or more cells of the animal.~~

~~7.~~5. The animal of any one of claims 1-~~6~~4, wherein exogenous light chain variable region gene sequence comprises one human IGKV gene and one human IGKJ gene, wherein the human IGKV gene is selected from the group consisting of IGKV3-20, IGKV3-11, and IGKV1-39, wherein the human IGKJ gene is selected from the group consisting of IGKJ1 and IGKJ4, and wherein the human IGKV gene and the human IGKJ gene are operably linked.

~~8. The animal of claim 7, wherein the human IGKV gene is IGVK3-11.~~

~~9. The animal of any one of claims 7-8, wherein the human IGKJ gene is selected from the group consisting of IGKJ1 and IGKJ4.~~

~~10.~~6. The animal of any one of claims 1-~~9~~5, wherein the human IGKV gene is IGKV1-39 and the human IGKJ gene is IGKJ4.

~~11.~~7. The animal of any one of claims 1-~~9~~5, wherein the human IGKV gene is IGKV3-11 and the human IGKJ gene is IGKJ1.

~~12.~~8. The animal of any one of claims 1-~~9~~5, wherein the human IGKV gene is IGKV3-20 and the human IGKJ gene is IGKJ1.

~~13.~~9. The animal any one of claims 1-~~12~~8, wherein the animal further comprises a promoter sequence that is operably linked to the human IGKV gene, wherein the promoter sequence is within 2500 or 3000 bp of the human IGKV gene.

~~14. The animal of claim 13, wherein the promoter is an IGKV3-20 promoter, an IGKV3-11 promoter, or an IGKV1-39 promoter.~~

~~15.~~10. The animal of any one of claims 1-~~14~~9, wherein the animal comprises a disruption in the animal's endogenous light chain immunoglobulin gene locus.

~~16. The animal of claim 15, wherein the animal is a mouse and the disruption in the animal's endogenous light chain immunoglobulin gene locus comprises a deletion of one or more mouse IGKV genes in Table 3 and one or more mouse IGKJ genes in Table 4.~~

~~17. The animal of claim 16, wherein the animal is a mouse and the disruption in the animal's endogenous light chain immunoglobulin gene locus comprises a deletion of a sequence starting from mouse IGKV2-137 to mouse IGKJ5.~~

~~18.~~11. The animal of any one of claims 1-~~17~~10, wherein the animal comprises an endogenous IGKC.

~~19. The animal of any one of claims 1-18, wherein the animal further comprises a kappa intronic enhancer 5' with respect to the endogenous IGKC and/or a kappa 3' enhancer.~~

~~20.~~12. The animal of any one of claims 1-~~19~~11, wherein the human light chain variable region is a rearranged sequence.

~~21.~~13. The animal of any one of claims 1-~~20~~12, wherein the animal is homozygous or heterozygous with respect to the light chain immunoglobulin gene locus.

~~22. The animal of any one of claims 1-20, wherein the animal is heterozygous with respect to the light chain immunoglobulin gene locus.~~

~~23. The animal of any one of claims 1-22, wherein the animal comprises a disruption in the animal's endogenous lambda light chain immunoglobulin gene locus.~~

~~24.~~14. The animal of any one of claims 1-~~23~~13, wherein the animal is a rodent (e.g., a mouse).

~~25.~~15. The animal of any one of claims 1-~~24~~14, wherein the animal further comprises at an endogenous heavy chain immunoglobulin gene locus, one or more human IGHV genes, one or more human IGHD genes, and one or more human ~~IGHKJ~~ IGHJ genes, wherein the human IGHV genes, the human IGHD genes, and the human IGHJ genes are operably linked and can undergo VDJ rearrangement.

~~26. The animal of claim 25, wherein the animal comprises at least 150 human IGHV genes selected from Table 5, at least 20 human IGHD genes selected from Table 6, and at least 5 human IGHJ genes selected from Table 7.~~

27. The animal of claim 25, wherein the animal comprises all human IGHV genes, all human IGHD genes, and all human IGHJ genes at the endogenous heavy chain immunoglobulin gene locus of human chromosome 14 of a human subject.

28. The animal of claim 25, wherein the animal comprises all human IGHV genes, all human IGHD genes, and all human IGHJ genes at the endogenous heavy chain immunoglobulin gene locus of human chromosome 14 of a human cell.

29. The animal of any one of claims 25-28, wherein the animal comprises an unmodified human sequence derived from a human heavy chain immunoglobulin gene locus, wherein the unmodified human sequence is at least 800 kb.

30. The animal of any one of claims 25-29, wherein the animal comprises an unmodified human sequence derived from a human heavy chain immunoglobulin gene locus starting from human IGHV(III)-82 to human IGHV1-2.

31. The animal of any one of claims 25-29, wherein the animal comprises an unmodified human sequence derived from a human heavy chain immunoglobulin gene locus starting from human IGHV(III)-82 to human IGHV6-1.

32. The animal of any one of claims 25-31, wherein the animal comprises an unmodified human sequence derived from a human heavy chain immunoglobulin gene locus starting from human IGHD1-1 to human IGHJ6.

33. The animal of any one of claims 25-29, wherein the animal comprises an unmodified human sequence derived from a human heavy chain immunoglobulin gene locus starting from human IGHV(III)-82 to human IGHJ6.

34. The animal of any one of claims 1-24, further comprising at an endogenous heavy chain immunoglobulin gene locus,

a first sequence comprising one or more human IGHV genes;

~~a second sequence comprising an endogenous sequence; and~~

~~a third sequence comprising one or more human IGHD genes, and one or more human IGHJ genes,~~

~~wherein the first sequence, the second sequence, and the third sequence are operably linked.~~

~~35. The animal of claim 34, wherein the first sequence comprises at least 150 human IGHV genes selected from Table 5.~~

~~36. The animal of claim 34 or 35, wherein the first sequence comprises at least 20 human IGHD genes selected from Table 6.~~

~~37. The animal of any one of claims 34-36, wherein the first sequence is an unmodified sequence derived from a human heavy chain immunoglobulin gene locus.~~

~~38. The animal of any one of claims 34-37, wherein the first sequence is at least 800 kb.~~

~~39. The animal of any one of claims 34-38, wherein the second sequence comprises an endogenous sequence that is at least 3 kb.~~

~~40. The animal of any one of claims 34-39, wherein the third sequence comprises at least 20 human IGHD genes selected from Table 6, and at least 5 human IGHJ genes selected from Table 7.~~

~~41. The animal of any one of claims 34-39, wherein the third sequence comprises all human IGHD genes in Table 6, and all human IGHJ genes in Table 7.~~

~~42. The animal of any one of claims 34-41, wherein the third sequence is an unmodified sequence derived from a human heavy chain immunoglobulin gene locus.~~

~~43. The animal of any one of claims 34-42, wherein the third sequence is at least 50 kb.~~

~~44. The animal of any one of claims 25-43, wherein the animal comprises a disruption in the animal's endogenous heavy chain immunoglobulin gene locus.~~

~~45. The animal of claim 44, wherein the animal is a mouse and the disruption in the animal's endogenous heavy chain immunoglobulin gene locus comprises a deletion of one or more mouse IGHV genes in Table 8, one or more mouse IGHD genes in Table 9, and one or more mouse IGHJ genes in Table 10.~~

~~46. The animal of claim 44, wherein the animal is a mouse and the disruption in the animal's endogenous heavy chain immunoglobulin gene locus comprises a deletion of a sequence starting from mouse IGHV1-85 to mouse IGHJ4.~~

~~47. The animal of any one of claims 1-46, wherein the animal comprises one or more endogenous IGHM, IGHδ, IGHG3, IGHG1, IGHG2b, IGHG2a, IGHE, and IGHA genes.~~

~~48. The animal of any one of claims 1-47, wherein the animal is homozygous with respect to the heavy chain immunoglobulin gene locus.~~

~~49. The animal of any one of claims 1-47, wherein the animal is heterozygous with respect to the heavy chain immunoglobulin gene locus.~~

~~50.~~16. A genetically-modified, non-human animal whose genome comprises an endogenous light chain immunoglobulin locus comprising:

a replacement of one or more endogenous IGKV with one or more human IGKV genes selected from Table 1; and

a replacement of one or more endogenous IGKJ genes with one or more human IGKJ genes selected from Table 2,

wherein the human IGKV gene and the human IGKJ gene are operably linked to an endogenous IGKC gene.

~~51. The animal of claim 50, wherein the one or more human IGKV genes are selected from the group consisting of IGKV3-20, IGKV3-11, and IGKV1-39.~~

~~52. The animal of claim 51, wherein the human IGKV gene is IGKV3-11.~~

~~53. The animal of any one of claims 50-52, wherein the one or more human IGKJ genes are selected from the group consisting of IGKJ1 and IGKJ4.~~

~~54. The animal of any one of claims 50-53, wherein the animal further comprises an insertion of a human IGKJ 3'-UTR sequence.~~

~~55. The animal of any one of claims 50-54, wherein the human IGKV gene is IGKV1-39 and the human IGKJ gene is IGKJ4.~~

~~56. The animal of any one of claims 50-54, wherein the human IGKV gene is IGKV3-11 and the human IGKJ gene is IGKJ1.~~

~~57. The animal of any one of claims 50-54, wherein the human IGKV gene is IGKV3-20 and the human IGKJ gene is IGKJ1.~~

~~58. The animal of any one of claims 50-57, wherein all endogenous IGKV genes are replaced by the one or more human IGKV genes.~~

~~59. The animal of any one of claims 50-58, wherein all endogenous IGKJ genes are replaced by the one or more human IGKJ genes.~~

~~60. The animal of any one of claims 50-59, wherein the animal further comprises a promoter sequence before the human IGKV gene, wherein the promoter sequence is within 3000 bp of the human IGKV gene.~~

~~61. The animal of any one of claims 50-60, wherein the animal further comprises a kappa intronic enhancer at the 5' of the endogenous IGKC.~~

~~62. The animal of any one of claims 50-61, wherein the animal further comprises a kappa 3' enhancer.~~

~~63.~~17. The animal of ~~any one of claims 50-62~~claim 16, whose genome further comprises an endogenous heavy chain immunoglobulin locus comprising: a replacement of one or more endogenous IGHV, endogenous IGHD, and endogenous IGHJ genes with one or more human IGHV, human IGHD, and human IGHJ genes, wherein the one or more human IGHV, human IGHD, and human IGHJ genes are operably linked to one or more of endogenous IGHM, IGHδ, IGHG, IGHE, and IGHA genes.

~~64. The animal of claim 63, wherein the one or more endogenous IGHV, endogenous IGHD, and endogenous IGHJ genes are replaced by at least 150 human IGHV genes in Table 5, at least 20 human IGHD genes in Table 6, and at least 5 human IGHJ genes in Table 7.~~

~~65. The animal of claim 63 or 64, wherein the animal is a mouse, and at least 180 mouse IGHV genes in Table 8, all mouse IGHD genes in Table 9, and all mouse IGHJ genes in Table 10 are replaced.~~

~~66. The animal of any one of claims 1-65, wherein the animal lacks an endogenous immunoglobulin heavy chain variable region locus that is capable of rearranging and forming a nucleic acid sequence that encodes an endogenous heavy chain variable domain (e.g., a mouse heavy chain variable domain).~~

~~67. The animal of any one of claims 1-66, wherein the animal lacks an endogenous immunoglobulin light chain variable region locus that is capable of rearranging and forming a nucleic acid sequence that encodes an endogenous light chain variable domain (e.g., a mouse light chain variable domain).~~

~~68.~~18. The animal of any one of claims 1-~~67~~17, wherein the animal can produce a humanized antibody.

~~69. The animal of claim 68, wherein the antibody comprises a light chain variable region encoded by the IGKV gene and IGKJ gene.~~

~~70.~~19. A cell obtained from the animal of any one of claims 1-~~69~~18.

~~71. The cell of claim 70, wherein the cell is a B cell that expresses a chimeric immunoglobulin light chain comprising an immunoglobulin light chain variable domain that is encoded by a human IGKV gene selected from the group consisting of IGKV3-20, IGKV3-11, and IGKV1-39, and a human IGKJ gene selected from the group consisting of IGKJ1 and IGKJ4; and wherein the immunoglobulin light chain variable domain is operably linked to a non-human light chain constant region.~~

~~72. The cell of claim 70 or 71, wherein the B cell that expresses a chimeric immunoglobulin heavy chain comprising an immunoglobulin heavy chain variable domain that is derived from a rearrangement of one or more human IGHV genes, one or more human IGHD genes, and one or more human IGHJ genes, wherein the immunoglobulin heavy chain variable domain is operably linked to a non-human heavy chain constant region.~~

~~73. The cell of any one of claims 70-72, wherein the cell is an embryonic stem (ES) cell.~~

~~74. A method of making a chimeric antibody that specifically binds to an antigen, the method comprising~~
~~exposing the animal of any one of claims 1-69 to the antigen;~~
~~producing a hybridoma from a cell collected from the animal; and~~
~~collecting the chimeric antibody produced by the hybridoma.~~

~~75. The method of claim 74, wherein the method further comprises sequencing the genome of the hybridoma.~~

~~76.~~20. A method of making an antibody that specifically binds to an antigen, the method comprising

exposing the animal of any one of claims 1-~~69~~ 18 to the antigen;

sequencing nucleic acids encoding human heavy and light chain immunoglobulin variable regions in a cell that expresses a hybrid antibody that specifically binds to the antigen; and

operably linking in a cell the nucleic acid encoding the human heavy chain immunoglobulin variable region with a nucleic acid encoding a human heavy chain immunoglobulin constant region and the nucleic acid encoding the human light chain immunoglobulin variable region with a nucleic acid encoding a human light chain immunoglobulin constant region.

~~77. A method of making an antibody that specifically binds to an antigen, the method comprising~~

~~obtaining a nucleic acid sequence encoding human heavy and light chain immunoglobulin variable regions in a cell that expresses a hybrid antibody that specifically binds to the antigen, wherein the cell is obtained by exposing the animal of any one of claims 1-69 to the antigen;~~

~~operably linking the nucleic acid encoding the human heavy chain immunoglobulin variable region with a nucleic acid encoding a human heavy chain immunoglobulin constant region and the nucleic acid encoding the human light chain immunoglobulin variable region with a nucleic acid encoding a human light chain immunoglobulin constant region; and~~

~~expressing the nucleic acid in a cell, thereby obtaining the antibody.~~

~~78. A method of obtaining a nucleic acid that encodes an antibody binding domain that specifically binds to an antigen, the method comprising~~

~~exposing the animal of any one of claims 1-69 to the antigen; and~~

~~sequencing nucleic acids encoding human heavy and light chain immunoglobulin variable regions in a cell that expresses a hybrid antibody that specifically binds to the antigen.~~

~~79. A method of obtaining a sample, the method comprising~~

~~exposing the animal of any one of claims 1-69 to the antigen; and~~

~~collecting the sample from the animal.~~

80. The method of claim 79, wherein the sample is a spleen tissue, a spleen cell, or a B cell.

81. A method of making a bispecific antibody, the method comprising

expressing in a cell a nucleic acid sequence encoding a light chain polypeptide comprising a human VL, a nucleic acid sequence encoding a first heavy chain polypeptide comprising a first human VH, and a nucleic acid sequence encoding a second heavy chain polypeptide comprising a second human VH,

wherein the sequence encoding the first VH is obtained from the animal of any one of claims 1-69 after being exposed to a first antigen, and the sequence encoding the second VH is obtained from the animal or a different animal after being exposed to a second antigen.

82. The method of claim 81, wherein the first VH and the VL forms a first antigen-binding site that specifically binds to the first antigen.

83. The method of claim 81 or 82, wherein the second VH and the VL forms a second antigen-binding site that specifically binds to the second antigen.

84. An antibody or antigen binding fragment thereof comprising a human light chain variable region that has a sequence that is at least 90%, 95%, or 98% identical to SEQ ID NO: 38, 39, or 40.

85. A plurality of antibodies or antigen binding fragments thereof, wherein each antibody or antigen binding fragment thereof comprises a human light chain variable region that has a sequence that is at least 90%, 95%, or 98% identical to SEQ ID NO: 38, 39, or 40.

86. A method of making an antibody that specifically binds to a protein of interest, the method comprising

exposing the animal of any one of claims 1-69 to the protein of interest, wherein the animal does not express an endogenous protein that is homologous to the protein of interest; and

~~sequencing nucleic acids encoding human heavy and light chain immunoglobulin variable regions in a cell that expresses an antibody that specifically binds to the protein of interest.~~

~~87. The method of claim 86, wherein a gene encoding the endogenous protein is disrupted in the animal.~~

~~88. The method of claim 87, wherein the gene encoding the endogenous protein is knocked out.~~

~~89. The method of any one of claims 86-88, wherein the endogenous protein is at least 80%, 90%, 95% homologous to the protein of interest.~~

~~90. The method of any one of claims 86-88, wherein the endogenous protein is at least 80%, 90%, or 95% identical to the protein of interest.~~

~~91. The method of any one of claims 86-90, wherein the protein of interest is a human protein.~~

~~92. The method of any one of claims 86-91, wherein the protein of interest is PD-1, CTLA-4, LAG-3, BTLA, PD-L1, CD27, CD28, CD47, CD137, CD154, TIGIT, TIM-3, GITR, SIRPa, or OX40.~~