AMENDED CLAIMS
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What is claimed is:

1. A genetically modified mouse comprising a B cell population that expresses a limited repertoire of human light chain variable (V_L) domains, or a single human V_L domain, derived from a single human light chain sequence present in the germline of the mouse, wherein the mouse lacks an unrearranged endogenous immunoglobulin Vκ gene segment, an unrearranged endogenous immunoglobulin κ light chain joining (Jκ) gene segment, or a combination thereof; and wherein the mouse exhibits a κ:λ light chain ratio that is about the same as a mouse that comprises a wild type complement of immunoglobulin light chain Vκ and Jκ gene segments.

2. The mouse of claim 1, wherein the single human light chain sequence is a rearranged human immunoglobulin light chain sequence.

3. The mouse of claim 1 or 2, wherein the mouse exhibits a κ:λ ratio that is about from 55:1 to 75:1.

4. The mouse of claim 1 or 2, wherein the mouse exhibits a κ:λ ratio that is about from 18:1 to 23:1.

5. The mouse of any one of claims 1-4, wherein the human light chain sequence is operably linked to an immunoglobulin light chain constant region sequence selected from a mouse, rat and human sequence.

6. The mouse of claim 2, wherein the rearranged human immunoglobulin light chain sequence includes human Vκ and Jκ gene segments.

7. The mouse of claim 6, wherein the human Vκ segment is selected from human Vκ1-39 and human Vκ3-20, and human Jκ gene segment is selected from human Jκ1 and human Jκ5.

8. A genetically modified mouse that expresses a human κ light chain derived from a single rearranged human κ light chain sequence, wherein the mouse lacks an unrearranged endogenous immunoglobulin Vκ gene segment, an unrearranged endogenous immunoglobulin Jκ gene segment, or a combination thereof; and

wherein the mouse exhibits a κ light chain usage that is about 100-fold or more, at least about 200-fold or more, at least about 300-fold or more, at least about 400-fold or more, at least about 500-fold or more, at least about 600-fold or more, at least about 700-fold or more, at least about 800-fold or more, at least about 900-fold or more, at least about 1000-fold or more greater than the same κ light chain usage exhibited by a mouse bearing a complete or substantially complete human κ light chain locus.

9. The mouse of claim 8, wherein the rearranged human κ light chain sequence comprises a human Vκ1-39 sequence.

10. The mouse of claim 8 or 7, wherein the rearranged human κ light chain sequence is a human Vκ1-39Jκ5 sequence.

11. The mouse of claim 8 or 7, wherein the rearranged human κ light chain sequence is a human Vκ3-20Jκ1 sequence.

12. The mouse of claim 8, 9, 10, or 11, wherein the rearranged human κ light chain sequence is operably linked to a mouse immunoglobulin κ constant (Cκ) region.

13. A genetically modified mouse comprising a B cell that expresses a human V_L domain derived from a rearranged human Vκ1-39/Jκ5 sequence, wherein the mouse lacks an unrearranged endogenous immunoglobulin Vκ gene segment and an unrearranged endogenous immunoglobulin Jκ gene segment; and wherein the human V_L domain(s) is associated with a human heavy chain variable (V_H) domain derived from a rearranged human $V_H/D_H/J_H$ region selected from 2-5/3-22/1, 3-13/6-6/5, 3-23/2-8/4, 3-23/6-6/4, 3-23/7-27/4, 3-30/1-1/4, 3-30/3-3/4, 3-30/5-5/2, 3-30/7-27/6, 1-69/6-6/5 and 1-69/6-13/4.

14. The mouse of claim 13, wherein the human Vκ1-39/Jκ5 sequence is operably linked to a mouse Cκ region.

15. The mouse of claim 13, wherein the human V_H domain is operably linked to a mouse heavy chain constant (C_H) region sequence selected from a C_H1, a hinge, a C_H2, a C_H3, and a combination thereof.

16. The mouse of claim 13, wherein the human V_H domain is expressed from an endogenous immunoglobulin heavy chain locus.

17. A genetically modified mouse comprising a B cell that expresses a human V_L domain derived from a rearranged human Vκ3-20/Jκ1 sequence, wherein the mouse lacks an unrearranged endogenous immunoglobulin Vκ gene segment and an unrearranged endogenous immunoglobulin Jκ gene segment; and wherein the human V_L domain(s) is associated with a human V_H domain derived from a rearranged human $V_H/D_H/J_H$ region selected from 3-30/3-3/3, 3-33/1-7/4, 3-33/2-15/4 and 3-53/1-1/4.

18. The mouse of claim 16, wherein the human Vκ3-20/Jκ1 sequence is operably linked to a mouse Cκ region.

19. The mouse of claim 16, wherein the human V_H domain is operably linked to a mouse C_H region sequence selected from a C_H1, a hinge, a C_H2, a C_H3, and a combination thereof.

20. The mouse of claim 16, wherein the human V_H domain is expressed from an endogenous immunoglobulin heavy chain locus.

What is claimed is:

1. A genetically modified mouse comprising a B cell that expresses a human light chain variable (V_L) domain derived from a rearranged human Vκ1-39/J_K5 sequence that is present in the germline of the mouse, wherein the mouse lacks an unrearranged endogenous immunoglobulin Vκ gene segment and an unrearranged endogenous immunoglobulin Jκ gene segment; and wherein the human V_L domain(s) is associated with a human heavy chain variable (V_H) domain derived from a rearranged human $V_H/D_H/J_H$ region selected from 2-5/3-22/1, 3-13/6-6/5, 3-23/2-8/4, 3-23/6-6/4, 3-23/7-27/4, 3-30/1-1/4, 3-30/3-3/4, 3-30/5-5/2, 3-30/7-27/6, 1-69/6-6/5 or 1-69/6-13/4.

2. The mouse of claim 1, wherein:

(a) the human Vκ1-39/J_K5 sequence is operably linked to a mouse Cκ region sequence;

(b) a sequence encoding the human V_H domain is operably linked to a sequence encoding a mouse heavy chain constant (C_H) region sequence selected from a C_H1, a hinge, a C_H2, a C_H3, or a combination thereof; or

(c) the human V_H domain is expressed from an endogenous immunoglobulin heavy chain locus.

3. The mouse of claim 1, wherein all or substantially all of the mouse V_K and J_K gene segments are replaced by the rearranged human V_K1-39/J_K5 sequence.

4. The mouse of claim 1, wherein the rearranged human V_K1-39/J_K5 is operably linked to an immunoglobulin light chain constant region sequence selected from a mouse, rat or human sequence.

5. A genetically modified mouse comprising a B cell that expresses a human light chain variable (V_L) domain derived from a rearranged human Vκ3-20/J_K1 sequence that is present in the germline of the mouse, wherein the mouse lacks an unrearranged endogenous immunoglobulin Vκ gene segment and an unrearranged endogenous

immunoglobulin Jκ gene segment; and wherein the human V_L domain(s) is associated with a human heavy chain variable (V_H) domain derived from a rearranged human $V_H/D_H/J_H$ region selected from 3-30/3-3/3, 3-33/1-7/4, 3-33/2-15/4 or 3-53/1-1/4.

6. The mouse of claim 5, wherein:

(a) the human Vκ3-20/J_K1 sequence is operably linked to a mouse Cκ region sequence;

(b) a sequence encoding the human V_H domain is operably linked to a sequence encoding a mouse C_H region sequence selected from a C_H1, a hinge, a C_H2, a C_H3, or a combination thereof; or

(c) the human V_H domain is expressed from an endogenous immunoglobulin heavy chain locus.

7. The mouse of claim 5, wherein all or substantially all of the mouse V_K and J_K gene segments are replaced by the rearranged human Vκ3-20/J_K1 sequence.

8. The mouse of claim 5, wherein the rearranged human Vκ3-20/J_K1 sequence is operably linked to an immunoglobulin light chain constant region sequence selected form a mouse, rat or human sequence.

9. The mouse of any of the preceding claims, wherein the mouse comprises a non-functional immunoglobulin lambda (λ) light chain locus.

10. Use of the mouse of any one of claims 1-4 or 9 in making an antibody comprising a human heavy chain variable (V_H) domain derived from a rearranged human $V_H/D_H/J_H$ region selected from 2-5/3-22/1, 3-13/6-6/5, 3-23/2-8/4, 3-23/6-6/4, 3-23/7-27/4, 3-30/1-1/4, 3-30/3-3/4, 3-30/5-5/2, 3-30/7-27/6, 1-69/6-6/5 or 1-69/6-13/4.

11. The use of claim 10, wherein the antibody is a bispecific antibody.

12. Use of the mouse of any one of claims 5-9 in making an antibody comprising a human heavy chain variable (V_H) domain derived from a rearranged $V_H/D_H/J_H$ region selected from 3-30/3-3/3, 3-33/1-7/4, 3-33/2-15/4 or 3-53/1-1/4.

13. The use of claim 12, wherein the antibody is a bispecific antibody.

14. The use of either one of claims 11 and 13, wherein the production is by a method comprising steps of expressing the human heavy chain variable domains in a single cell.

15. The use of any one of claims 10-14, wherein the heavy chains of the antibody are fully human.

16. The use of any one of claims 10, 11, 14, or 15, wherein heavy chains comprising the human heavy chain variable domains pair with a light chain comprising the human V_L domain derived from a rearranged V_K1-39/J_K sequence.

17. The use of any one of claims 12-15, wherein heavy chains comprising the human heavy chain variable domains pair with a light chain comprising the human V_L domain derived from a rearranged human V_K3-20/J_K sequence.

18. The use of any one of claims 10-17, wherein the human heavy chain variable domain(s) are selected by immunizing the mouse with an antigen of interest, determining the sequences of human heavy chain variable domains expressed by the mouse, and expressing the sequences in the cell.

19. A method of producing an antibody to an antigen of interest comprising a human heavy chain variable domain derived from a rearranged human $V_H/D_H/J_H$ region selected from 2-5/3-22/1, 3-13/6-6/5, 3-23/2-8/4, 3-23/6-6/4, 3-23/7-27/4, 3-30/1-1/4, 3-30/3-3/4, 3-30/5-5/2, 3-30/7-27/6, 1-69/6-6/5 or 1-69/6-13/4 comprising:

(a) immunizing the mouse of any one of claims 1-4 with an antigen of interest;

(b) obtaining from the mouse a human heavy chain variable domain derived from a rearranged human $V_H/D_H/J_H$ region selected from 2-5/3-22/1, 3-13/6-6/5, 3-23/2-8/4, 3-23/6-6/4, 3-23/7-27/4, 3-30/1-1/4, 3-30/3-3/4, 3-30/5-5/2, 3-30/7-27/6, 1-69/6-6/5 or 1-69/6-13/4; and

(c) employing the immunoglobulin variable region sequence obtained in (b) in an antibody that specifically binds the antigen of interest.

20. A method of producing an antibody to an antigen of interest comprising a human heavy chain variable domain derived from a rearranged human $V_H/D_H/J_H$ region selected from 3-30/3-3/3, 3-33/1-7/4, 3-33/2-15/4 or 3-53/1-1/4 comprising:

(a) immunizing the mouse of any one of claims 5-8 with an antigen of interest;

(b) obtaining from the mouse a human heavy chain variable domain derived from a rearranged human $V_H/D_H/J_H$ region selected from 3-30/3-3/3, 3-33/1-7/4, 3-33/2-15/4 or 3-53/1-1/4; and

(c) employing the immunoglobulin variable region sequence obtained in (b) in an antibody that specifically binds the antigen of interest.