

We claim:

1. A mouse, comprising in its germline an unrearranged light chain V segment and an unrearranged J segment operably linked with a heavy chain constant region nucleic acid sequence.
2. The mouse of claim 1, wherein the unrearranged light chain V segment is selected from a human κ segment, a human λ segment, and a combination thereof.
3. The mouse of claim 1, wherein the heavy chain constant region nucleic acid sequence is selected from the group consisting of a C_{H1} sequence, a hinge sequence, a C_{H2} sequence, a C_{H3} sequence, and a combination thereof.
4. The mouse of claim 1, wherein the unrearranged light chain V segment and the unrearranged J segment replace an endogenous mouse heavy chain V segment and an endogenous mouse heavy chain J segment at the endogenous mouse heavy chain locus.
5. The mouse of claim 4, wherein the unrearranged light chain V segment replaces all or substantially all functional mouse heavy chain V segments of the endogenous mouse heavy chain locus.
6. The mouse of claim 4, wherein the unrearranged J segment comprises a light chain J segment, and the light chain J segment replaces all or substantially all functional mouse heavy chain J segments of the endogenous mouse heavy chain locus.
7. The mouse of claim 6, wherein the unrearranged light chain V segment and the unrearranged light chain J segment are operably linked and the mouse lacks a functional D segment between the unrearranged light chain V segment and the unrearranged light chain J segment.
8. The mouse of claim 7, wherein the unrearranged light chain V segment is a human κ segment and the unrearranged light chain J segment is a human κ segment.
9. The mouse of claim 1, comprising a B cell that comprises in its genome a rearranged immunoglobulin gene that comprises a human κ variable region operably linked to a mouse constant region gene.
10. The mouse of claim 1, wherein the rearranged immunoglobulin gene is at an endogenous mouse immunoglobulin heavy chain locus.
11. The mouse of claim 1, further comprising in its germline a human light chain V segment and a human light chain J segment operably linked to a light chain constant gene.
12. The mouse of claim 11, wherein the light chain constant gene is a mouse light chain constant gene.
13. The mouse of claim 12, wherein the human light chain V segment is a human κ V segment.

14. The mouse of claim 13, wherein the mouse light chain constant gene is a mouse κ light chain constant gene.
15. A mouse that expresses from its germline an immunoglobulin comprising a first polypeptide comprising a first human light chain variable region sequence fused with an immunoglobulin heavy chain constant region, and a second polypeptide comprising a second human light chain variable region fused with an immunoglobulin light chain constant region.
16. The mouse of claim 15, wherein the first human light chain variable region sequence comprises a human κ variable region sequence, and the second human light chain variable region is selected from a human κ variable region and a human λ variable region.
17. The mouse of claim 16, wherein the immunoglobulin heavy chain constant region is selected from a human heavy chain constant region and a mouse heavy chain constant region.
18. The mouse of claim 16, wherein the immunoglobulin light chain constant region is selected from a human light chain constant region and a mouse light chain constant region.
19. The mouse of claim 16, wherein the first polypeptide is expressed from a modified endogenous mouse immunoglobulin heavy chain locus that lacks a functional endogenous heavy chain V gene segment.
20. The mouse of claim 19, wherein the second polypeptide is expressed from a modified endogenous mouse immunoglobulin light chain locus that lacks a functional endogenous light chain V gene segment.
21. A mouse, comprising a replacement in the germline of the mouse at an endogenous mouse immunoglobulin heavy chain locus of all or substantially all functional endogenous mouse heavy chain variable gene segments with at least six or more unrearranged light chain V gene segments and one or more unrearranged J gene segments, wherein the unrearranged light chain V gene segments and the J gene segments are operably linked, wherein the mouse is incapable of expressing an immunoglobulin heavy chain derived from a heavy chain V gene segment, and wherein the mouse comprises a splenic B cell population (B220⁺/IgM⁺) that is at least about 75% the size of a splenic B cell population (B220⁺/IgM⁺) of a wild-type mouse.
22. Use of a mouse according to any of the preceding claims to produce a binding protein that comprises a human light chain variable domain.
23. Use of a mouse according to any of claims 1-21 to produce an antibody.
24. The use according to claim 23, wherein the antibody is a human antibody.

25. Use of a mouse according to any one of claims 1-21 to produce a bispecific antibody.
26. A cell or tissue derived from a mouse according to any one of claims 1-21.
27. A cell according to claim 26, wherein the cell is selected from an ES cell, a B cell, and a hybridoma.

The claims defining the invention are as follows:

1. A mouse, comprising in its germline an immunoglobulin hybrid chain locus comprising at least one unrearranged light chain variable region (V_L) gene segment, at least one unrearranged light chain joining (J_L) gene segment, and an immunoglobulin heavy chain constant region nucleic acid sequence capable of associating with a light chain constant region,

wherein each of the unrearranged V_L and J_L gene segments comprise recombination signal sequences that allow the unrearranged V_L and J_L gene segments to recombine such that the mouse further comprises a rearranged immunoglobulin hybrid gene comprising light chain variable region (V_L/J_L) nucleotide sequence operably linked with the immunoglobulin heavy chain constant region nucleic acid sequence.

2. The mouse of claim 1, wherein the at least one unrearranged light chain V_L gene segment is selected from an unrearranged human κ gene segment, an unrearranged human λ gene segment, and a combination thereof.

3. The mouse of claim 1, wherein the heavy chain constant region nucleic acid sequence is selected from the group consisting of a C_H1 sequence, a hinge sequence, a C_H2 sequence, a C_H3 sequence, and a combination thereof.

4. The mouse of claim 1, wherein the at least one unrearranged light chain V_L gene segment and the at least one unrearranged J_L gene segment respectively replace an endogenous mouse heavy chain V_H gene segment and an endogenous mouse heavy chain J_H gene segment at the endogenous mouse heavy chain locus.

5. The mouse of claim 4, wherein the at least one unrearranged light chain V_L gene segment replaces all or substantially all functional mouse heavy chain V_H gene segments of the endogenous mouse heavy chain locus.

6. The mouse of claim 4, wherein the at least one unrearranged J_L gene segment replaces all or substantially all functional mouse heavy chain J_H gene segments of the endogenous mouse heavy chain locus.

7. The mouse of claim 6, wherein the at least one unrearranged light chain V_L gene segment and the unrearranged light chain J_L gene segment are operably linked and the mouse lacks a functional heavy chain D_H gene segment between the at least one unrearranged light chain V_L gene segment and the at least one unrearranged light chain J_L gene segment.

8. The mouse of claim 7, wherein the at least one unrearranged light chain V_L gene segment is an unrearranged human κ gene segment and the unrearranged light chain J_L gene segment is an unrearranged human κ gene segment.

9. The mouse of claim 1, comprising a B cell that comprises in its genome the rearranged immunoglobulin hybrid gene, and wherein the rearranged hybrid gene comprises a rearranged human κ variable region operably linked to a mouse constant region gene.
10. The mouse of claim 1, wherein the rearranged immunoglobulin hybrid gene is at an endogenous mouse immunoglobulin heavy chain locus.
11. The mouse of claim 1, further comprising in its germline an unrearranged human light chain V_L gene segment and an unrearranged human light chain joining J_L gene segment operably linked to a light chain constant gene.
12. The mouse of claim 11, wherein the light chain constant gene is a mouse light chain constant gene.
13. The mouse of claim 12, wherein the unrearranged human light chain V_L gene segment is an unrearranged human κ V_L gene segment.
14. The mouse of claim 13, wherein the mouse light chain constant gene is a mouse κ light chain constant gene.
15. A mouse comprising a hybrid immunoglobulin comprising a first polypeptide comprising a first human light chain variable region sequence fused with an immunoglobulin heavy chain constant region, and a second polypeptide comprising a second human light chain variable region fused with an immunoglobulin light chain constant region.
16. The mouse of claim 15, wherein the first human light chain variable region sequence comprises a human κ variable region sequence, and the second human light chain variable region is selected from a human κ variable region and a human λ variable region.
17. The mouse of claim 16, wherein the immunoglobulin heavy chain constant region is selected from a human heavy chain constant region and a mouse heavy chain constant region.
18. The mouse of claim 16, wherein the immunoglobulin light chain constant region is selected from a human light chain constant region and a mouse light chain constant region.
19. The mouse of claim 16, wherein the first polypeptide is expressed from a modified endogenous mouse immunoglobulin heavy chain locus that lacks a functional endogenous heavy chain V gene segment.
20. The mouse of claim 19, wherein the second polypeptide is expressed from a modified endogenous mouse immunoglobulin light chain locus that lacks a functional endogenous light chain V gene segment.
21. A mouse, comprising a replacement in the germline of the mouse at an endogenous mouse immunoglobulin heavy chain locus of all or substantially all functional endogenous mouse heavy chain variable (V_H) gene segments with at least six or more unrearranged human light chain V_L gene segments and one or more unrearranged human light chain J_L gene segments, wherein each of the unrearranged human light chain V_L and J_L gene

segments comprise recombination signal sequences that allow the unrearranged V_L and J_L gene segments to recombine such that the mouse further comprises a rearranged immunoglobulin hybrid gene comprising light chain variable region (V_L/J_L) nucleotide sequence operably linked to an immunoglobulin heavy chain constant region, wherein the mouse is incapable of expressing an immunoglobulin heavy chain derived from a heavy chain V gene segment, and wherein the mouse comprises a splenic B cell population ($B220^+/IgM^+$) that is at least about 75% the size of a splenic B cell population ($B220^+/IgM^+$) of a wild-type mouse.

22. Use of a mouse according to any one of claims 1 to 21 to produce a hybrid immunoglobulin binding protein that comprises a human light chain variable domain operably linked to heavy chain constant region.

23. Use of a mouse according to any one of claims 1 to 21 to produce an antigen binding protein comprising a hybrid immunoglobulin chain and a light chain, wherein the hybrid immunoglobulin chain comprises a light chain variable domain fused with a heavy chain constant region, and wherein the light chain comprises a light chain variable domain fused with a light chain constant region.

24. The use according to claim 23, wherein the antigen binding protein comprises human light chain variable domains.

25. Use of a mouse according to any one of claims 1 to 21 to produce a bispecific antibody.

26. A cell or tissue derived from a mouse according to any one of claims 1 to 21.

27. A cell according to claim 26, wherein the cell is selected from an ES cell, a B cell, and a hybridoma.