We claim:

1. A mouse comprising a germline genetic modification that comprises a deletion of a nucleotide sequence encoding a CH1 of an IgG, wherein the mouse expresses an IgM that comprises a CH1 domain and the mouse expresses in its serum an IgG antibody that lacks a CH1 domain and that lacks a light chain, and wherein the mouse is incapable of expressing an IgG mRNA that comprises a sequence encoding a CH1 domain.

2. The mouse of claim 1, wherein the deletion of the nucleotide sequence encoding the CH1 is in an IgG1 gene.

3. The mouse of claim 1, comprising a functional immunoglobulin light chain gene locus.

4. The genetically modified mouse of claim 1, wherein the IgG antibody that lacks a light chain comprises a human variable domain and a mouse constant domain that lacks a CH1 domain.

5. The genetically modified mouse of claim 1, wherein the IgG antibody that lacks a light chain comprises a mouse variable domain and a mouse constant domain that lacks a CH1 domain.

6. The genetically modified mouse of claim 1, comprising a deletion of an IgG2a gene.

7. The genetically modified mouse of claim 1, comprising a deletion of an IgG2b gene.

8. The genetically modified mouse of claim 1, comprising a deletion of an IgG2a gene and a deletion of an IgG2b gene.

9. The genetically modified mouse of claim 1, comprising a deletion of an IgG2a gene and a deletion of an IgG2b gene.

10. The genetically modified mouse of claim 1, comprising a replacement of one or more endogenous mouse heavy chain variable region gene segments with one or more human heavy chain variable region gene segments.

11. The genetically modified mouse of claim 10, wherein the one or more human heavy chain variable region gene segments are human VH1 family gene segments.

12. The genetically modified mouse of claim 11, wherein the VH1 family gene segments comprise FR1, FR2, and FR3 regions that are at least 90% identical to FR1, FR2, and FR3 gene segments of human VH gene segments 1-8, 1-18, and 1-69.

13. The genetically modified mouse of claim 11, further comprising a human D gene segment and a human J gene segment.

14. The genetically modified mouse of claim 11, wherein the mouse comprises a rearranged immunoglobulin gene that encodes and FR4 that is at least 90% identical to an FR4 encoded by a human D1-7/J4, D3-16/J6, D4-4/J4, D6-6/J4, D6-6/J2, D6-7/J4, or D6-19/J6.

15. The genetically modified mouse of claim 1, comprising a replacement of one or more endogenous mouse heavy chain variable region gene segments with one or more camelized human heavy chain variable region gene segments.

16. A method for making a somatically mutated heavy chain antibody in a mouse, comprising the step of

a. immunizing a mouse with an antigen, wherein the mouse comprises an unrearranged human or mouse heavy chain immunoglobulin variable region gene segment, and wherein the mouse lacks a nucleotide sequence of at least one allele that encodes a functional IgG CH1 domain, and wherein the mouse expresses an IgM that comprises a CH1 domain;

b. maintaining the mouse under conditions sufficient to initiate an immune response to the antigen; and,

c. isolating from the mouse a somatically mutated heavy chain antibody comprising a variable domain that is derived from the human or mouse heavy chain immunoglobulin variable region gene segment, and wherein the somatically mutated heavy chain antibody specifically binds the antigen.

17. A genetically modified mouse, comprising a replacement of all or substantially all V, D, and J gene segments with one or more human V, human D, and human J gene segments, wherein the one or more human V, D, and J gene segments are operably linked at the endogenous mouse locus to a mouse heavy chain constant region gene locus, wherein the mouse heavy chain constant region gene locus comprises a full-length IgM gene, an IgG gene comprising a deletion in a nucleotide

sequence encoding a CH1 domain in an IgG gene selected from an IgG1, IgG2a, IgG2b, IgG3, and a combination thereof; wherein the mouse expresses a B cell receptor that comprises an IgM with a CH1 region, wherein the IgM comprises a heavy chain associated with a cognate lambda or kappa light chain.

18. The genetically modified mouse of claim 17, wherein the one or more human V, D, and J gene segments comprise a human gene segment from a variable region family selected from VH1, VH3, VH4, and a combination thereof.

19. The genetically modified mouse of claim 18, wherein the one or more human gene segments are selected from 1-2, 1-8, 1-18, 1-46, 1-69, 3-21, 3-72, 4-59, and a combination thereof.

20. The genetically modified mouse of claim 18, wherein the one or more human V, D, and J gene segments comprise a D1-7, D3-16, D4-4, D6-6, D6-7, D6-19, J2, J3, J4, and a combination thereof.

We claim:

1. A transgenic mouse comprising a germline modification, which modification comprises:
(a) a deletion of a nucleic acid sequence encoding a CH1 domain of an endogenous IgG constant region gene; and

(b) an inclusion of one or more human heavy chain variable region gene segments, wherein the one or more human heavy chain variable region gene segments is operably linked to the endogenous IgG constant region of (a);

wherein the mouse comprises an intact IgM constant region gene and wherein the mouse expresses an IgG heavy chain antibody comprising a human variable domain, lacking a CH1 domain, in whole or in part, and lacking a cognate light chain and secretes said IgG heavy chain antibody into its serum.

2. The mouse of claim 1, wherein the IgG constant region gene is selected from the group consisting of an IgG1 constant region gene, an IgG2b constant region gene, a IgG2a constant region gene, and combinations thereof.

3. The mouse of claim 2, wherein the IgG constant region gene is an IgG1 constant region gene.

4. The mouse of claim 3, characterized in that the mouse additionally expresses:
a) wild-type IgG3 protein;

b) wild-type IgG2a protein; and

c) wild-type IgG2b protein.

5. The mouse of claim 4, further characterized in that the mouse expresses:
e) wild-type IgM protein;

f) wild-type IgD protein;

g) wild-type IgA protein; and

h) wild-type IgE protein.

6. The mouse of claim 1, characterized in that the IgG heavy chain antibody lacks the CH1 domain in whole.

7. The mouse of claim 1, wherein the IgG heavy chain antibody comprises the human variable domain, an IgG1 hinge, a CH2 domain, and a CH3 domain.

8. The mouse of claim 1, wherein the mouse comprises a functional immunoglobulin light chain gene locus.

9. The mouse of claim 8, wherein the immunoglobulin light chain gene locus is a κ light chain gene locus.

10. The mouse of claim 8, wherein the immunoglobulin light chain gene locus is a λ light chain gene locus.

11. The mouse of claim 1, wherein the mouse is from a strain selected from the group consisting of a 129 strain, a C57BL/6 strain, and a mixed 129×C57BL/6 strain.

12. The mouse of claim 11, wherein the mouse is 50% 129 and 50% C57BL/6.

13. An isolated cell of the mouse of claim 1.

14. The isolated cell of claim 13, wherein the cell is an embryonic stem (ES) cell.