WHAT IS CLAIMED IS:

1. A composition comprising a human immunoglobulin having an affinity constant (K_a) of at least 2 x 10^9 M^{-1} for binding to a predetermined human antigen, wherein said immunoglobulin consists of:

a human sequence light chain composed of (1) a light chain variable region encoded by a human V_L gene segment and a human J_L gene segment, and (2) a light chain constant region encoded by a human C_L gene segment; and

a human sequence heavy chain composed of a (1) a heavy chain variable region encoded by a human V_H gene segment, optionally a D region, and a human J_H gene segment, and (2) a constant region encoded by a human C_H gene segment;

wherein the immunoglobulin is from at least one nonhuman animal B cell.

2. The composition of claim 1, wherein the human sequence heavy chain and human sequence light chain are separately encoded by a human heavy chain transgene and a human light chain transgene, respectively, which are integrated into a mouse cell genome.

3. The composition of claim 1, wherein the composition comprises a monoclonal antibody of a single idiotype.

4. The composition of claim 1, wherein the predetermined human antigen is a human protein which naturally occurs as a surface or transmembrane protein in at least one cell type of somatic cells of a human.

5. The composition of claim 1, wherein the human sequence light chain has a κ constant region.

6. The composition of claim 1, wherein the human sequence heavy chain has a γ constant region.

7. The composition of claim 1, wherein the immunoglobulin comprises a human sequence light chain having a κ constant region and a human sequence heavy chain having a γ constant region.

8. The composition of claim 4, wherein the predetermined human antigen is a human CD4 protein or antigenic fragment thereof.

9. The composition of claim 7, wherein the predetermined human antigen is a human CD4 protein or antigenic fragment thereof.

10. An isolated human immunoglobulin having an affinity constant (K_a) of at least 1 x 10^{10} M^{-1} for binding to a predetermined human antigen, wherein said immunoglobulin consists of:

a human sequence light chain composed of (1) a light chain variable encoded by a human V_L gene segment and a human J_L gene segment, and (2) a light chain constant region encoded by a human C_L gene segment; and

a human sequence heavy chain composed of (1) a heavy chain variable region encoded by a human V_H gene segment, optionally a D region, and a human J_H gene segment, and (2) a constant region encoded by a human C_H gene segment;

wherein the immunoglobulin is from at least one nonhuman animal B cell.

~~11. The immunoglobulin of claim 10, wherein the predetermined human antigen is a human protein which naturally occurs as a surface or a transmembrane protein in at least one cell type of somatic cells of a human.~~

~~12. The immunoglobulin of claim 11, wherein the human protein is human CD4 or an antigenic fragment thereof.~~

~~13. The immunoglobulin of claim 10, wherein the human sequence light chain is a κ chain and the human sequence heavy chain is a γ chain.~~

~~14~~1. A hybridoma composed of B cell obtained from a transgenic mouse having a genome comprising a human heavy chain transgene and a human light chain transgene, said B cell fused to an immortalized cell suitable to generate a hybridoma, wherein said hybridoma produces into culture supernatant a detectable amount of ~~the immunoglobulin of claim 10~~an isolated human immunoglobulin having an affinity constant (Ka) of at least 1 x 10^{10} M^{-1} for binding to a predetermined human antigen, wherein said immunoglobulin consists of:

a human sequence light chain composed of (1) a light chain variable encoded by a human VL gene segment and a human JL gene segment, and (2) a light chain constant region encoded by a human CL gene segment; and

a human sequence heavy chain composed of (1) a heavy chain variable region encoded by a human VH gene segment, optionally a D region, and a human JH gene segment, and (2) a constant region encoded by a human CH gene segment;

wherein the immunoglobulin is from at least one nonhuman animal B cell ~~into culture supernatant~~.

~~15~~2. A hybridoma of claim ~~14~~1, wherein said immunoglobulin consists of a human sequence κ chain and the human sequence γ chain.

~~16~~3. A hybridoma of claim ~~14~~1, wherein the immunoglobulin binds to human CD4 with an affinity of at least 1.1 x 10^{10} M^{-1}.

~~17~~4. A hybridoma of claim ~~15~~2, wherein the immunoglobulin binds to human CD4 with an affinity of at least 1.1 x 10^{10} M^{-1}.

~~18~~5. A transgenic mouse comprising: a homozygous pair of functionally disrupted endogenous heavy chain alleles, a homozygous pair of functionally disrupted endogenous light chain alleles, at least one copy of a heterologous immunoglobulin light chain transgene, and at least one copy of a heterologous immunoglobulin heavy chain transgene, and wherein said animal makes an antibody response following immunization with a human antigen wherein the antibody response comprises an

isolated human immunoglobulin having an affinity constant (K_a) of at least 1 x 10^{10} M^{-1} for binding to a predetermined human antigen, wherein said immunoglobulin consists of:

a human sequence light chain composed of (1) a light chain variable encoded by a human V_L gene segment and a human J_L gene segment, and (2) a light chain constant region encoded by a human C_L gene segment; and

a human sequence heavy chain composed of (1) a heavy chain variable region encoded by a human V_H gene segment, optionally a D region, and a human J_H gene segment, and (2) a constant region encoded by a human C_H gene segment;

wherein the immunoglobulin is from at least one nonhuman animal B cell.

~~immunoglobulin of claim 10.~~

~~1~~96. A transgenic mouse of claim ~~1~~85, ~~wherein~~ said immunoglobulin ~~of claim 10~~ comprises a human sequence κ chain and a human sequence γ chain.

~~2~~07. A transgenic mouse of claim ~~1~~85, wherein said immunoglobulin binds to a human surface or transmembrane protein present on at least one somatic cell type of a human, wherein the immunoglobulin binds said human surface or transmembrane protein with an affinity constant (K_a) of between 1.5 x 10^9 M^{-1} and 1.8 x 10^{10} M^{-1}.

~~2~~18. A transgenic mouse of claim ~~2~~07, wherein the human surface or transmembrane protein is human CD4.

~~2~~29. A hybridoma of claim ~~1~~41, wherein said transgenic mouse is a transgenic mouse of claim ~~1~~85.

~~2~~310. A method for producing a transgenic mouse of claim ~~1~~85, comprising breeding a transgenic mouse comprising a germline copy of a human heavy chain transgene capable of undergoing intratransgene isotype switching with a suitable transgenic mouse of the opposite sex, such that offspring will comprise a transgenic mouse of claim 5~~1~~8.

~~2~~411. The method of claim ~~2~~310, wherein the suitable transgenic mouse of the opposite sex comprises a germline copy of a human light chain transgene and a knockout background comprising germline copies of a functionally disrupted mouse heavy chain allele and a functionally disrupted light chain allele.

~~2~~512. A transgenic mouse of claim ~~1~~85, wherein B cells of said mouse undergo B cell maturation, expression of human sequence immunoglobulin, class switching, and somatic mutation in the absence of expression of a functional mouse sequence heavy or light chain.

~~2~~613. A method for producing a transgenic mouse having an expanded repertoire of human variable region gene segments said method comprising co-introducing into the mouse genome a human immunoglobulin transgene and a human V gene polynucleotide containing human V gene segments which are not present in said human immunoglobulin transgene.

~~2~~714. The method of claim ~~2~~613, wherein the V gene polynucleotide is a yeast artificial chromosome comprising a portion of a human κ immunoglobulin locus.

~~2~~815. A transgenic mouse produced by the method of claim ~~2~~613, wherein the mouse expresses an immunoglobulin chain comprising a variable region sequence encoded by a V region gene segment present on the V region polynucleotide.

~~2~~916. A transgenic mouse comprising at least 5 distinct Vκ genes.

~~3~~017. A method of propagating the trait of human sequence immunoglobulin expression, comprising breeding a transgenic mouse of claim ~~2~~815.

~~31. The immunoglobulin of claim 10 produced by the transgenic mouse of claim 29.~~

~~32~~18. A method for producing a human sequence immunoglobulin polypeptide comprising the steps:

(A) obtaining a transgenic mouse, wherein said transgenic mouse comprises a homozygous pair of functionally disrupted endogenous heavy chain alleles, a homozygous pair of functionally disrupted endogenous light chain alleles, at least one copy of a human immunoglobulin light chain transgene, and at least one copy of a human immunoglobulin heavy chain transgene;

(B) immunizing the transgenic mouse with a predetermined antigen, wherein an immune response is induced and whereby a transgene of the mouse undergoes V-D-J rearrangement, whereby a rearranged transgene is produced;

(C) isolating and sequencing a nucleic acid encoding at least a portion of a variable region of the rearranged transgene, and determining the amino acid sequence of an immunoglobulin polypeptide encoded by the sequenced portion of the rearranged transgene;

(D) making an artificial gene that encodes a second immunoglobulin polypeptide, wherein the second immunoglobulin polypeptide comprises an amino acid sequence that is substantially similar to the amino acid sequence of the immunoglobulin polypeptide encoded by the sequenced portion of the rearranged transgene;

(E) linking the artificial gene to a transcription promoter sequence; and

(F) introducing the artificial gene into a cell;

whereby a human sequence immunoglobulin polypeptide is produced.

~~33~~19. The method of claim ~~32~~ 18 wherein the second immunoglobulin polypeptide comprises an amino acid sequence that is the same as the amino acid sequence of the immunoglobulin polypeptide encoded by the sequenced portion of the rearranged transgene.

~~34~~20. The method of claim ~~32~~ 18 wherein the nucleic acid of step (c) is isolated from a hybridoma secreting a human sequence immunoglobulin.

~~35~~21. The method of claim ~~32~~ 18 wherein the rearranged transgene is a human immunoglobulin heavy chain transgene.

~~36~~22. The method of claim ~~35~~ 21 wherein the artificial gene encodes a gamma isotype constant region.

~~37~~23. The method of claim ~~35~~21, further comprising introducing a second artificial gene into the cell of step (F), wherein the second artificial gene is made according to steps A-E of claim 4 except that the rearranged transgene is a human immunoglobulin light chain transgene, and wherein the cell produces an immunoglobulin.

~~38~~24. The method of claim ~~37~~ 23 wherein the human immunoglobulin heavy chain transgene and the human immunoglobulin light chain transgene are expressed in a hybridoma produced by fusing a single B cell from a transgenic mouse to an immortal cell.

~~39~~25. The method of claim ~~37~~ 23 wherein the cell produces an immunoglobulin that binds the predetermined antigen with an affinity constant (K_a) of at least about 10^8 M^{-1}.

~~40~~26. An immunoglobulin produced by the method of claim ~~32~~18.

~~41~~27. A cell comprising at least one artificial gene encoding at least a portion of an immunoglobulin polypeptide, wherein the cell produces a detectable amount of an immunoglobulin that binds a predetermined human antigen, and wherein the immunoglobulin polypeptide has substantially the same sequence as an immunoglobulin polypeptide secreted by a hybridoma obtained from a transgenic mouse, said mouse comprising a homozygous pair of functionally disrupted endogenous heavy chain alleles, a homozygous pair of functionally disrupted endogenous light chain alleles, at least one copy of a human immunoglobulin light chain transgene, and at least one copy of a human immunoglobulin heavy chain transgene.

~~42~~28. A eukaryotic cell of claim ~~41~~27.

~~43~~29. The cell of claim ~~42~~ 28 wherein the immunoglobulin binds human CD4 or an antigenic fragment thereof.

~~44~~30. An immunoglobulin that specifically binds human CD4, wherein said immunoglobulin comprises a human sequence light chain variable region comprising an amino acid sequence substantially identical to an amino acid sequence encoded by Seq. I.D. No. 1, Seq. I.D. No. 2, Seq. I.D.No. 3, Seq. I.D. No. 4, Seq. I.D. No. 5, Seq. I.D. No. 6, Seq. I.D. No. 7, Seq. I.D. No. 8, Seq. I.D. No. 9, or Seq. I.D., No. 10.

~~45~~31. The immunoglobulin of claim ~~44~~ 30 wherein the immunoglobulin comprises the sequence of Seq. I.D. No. 61 or Seq. I.D. No. 62.

~~46~~32. A method for selecting a hybridoma secreting a human sequence immunoglobulin that specifically bind a preselected antigen comprising the steps:

a) obtaining B cells from a trangenic mouse, wherein the transgenic mouse comprises a homozygous pair of functionally disrupted endogenous heavy chain alleles, a homozygous pair of functionally disrupted endogenous light chain alleles, at least one copy of a human immunoglobulin light chain transgene, and at least one copy of a human immunoglobulin heavy chain transgene comprising sequences encoding : and non-: segments, and wherein the mouse has been immunized with the predetermined antigen;

b) fusing the B cells to immortal cells wherein hybridomas are produced;

c) identifying a first group of hybridomas that secrete non-: non-6 isotype immunoglobulins;

d) identifying a second group of hybridomas, wherein the second group is a subset of the first group of hybridomas, and wherein hybridomas in the second secrete immunoglobulins that specifically bind the predetermined antigen;

e) selecting from the second group of hybridomas a hybridoma secreting a human sequence immunoglobulin that specifically binds to the preselected antigen.

~~47~~33. The method of claim ~~46~~ 32 wherein the first group of hybridomas secrete IgG immunoglobulins.

~~48~~34. The method of claim ~~46~~ 32 wherein the human sequence immunoglobulin of step (e) binds the predetermined antigen with an affinity constant (K_a) of at least about 10^9 M^{-1}.

~~49~~35. A human anti-CD4 immunoglobulin that specifically binds CD4 from humans and specifically binds CD4 from at least one non-human primate.

~~50~~36. The immunoglobulin of claim ~~18~~ 5 wherein the non-human primate is Rhesus monkey, cynomolgus monkey, or chimpanzee.

~~51~~37. The immunoglobulin of claim ~~50~~ 36 wherein the human anti-CD4 immunoglobulin specifically binds CD4 from both rhesus monkey and cynomolgus monkey.

~~52~~38. The immunoglobulin of claim ~~50~~ 36 wherein the human anti-CD4 immunoglobulin specifically binds CD4 from rhesus monkey, cynomolgus monkey and chimpanzee.

~~53~~39. A human sequence immunoglobulin comprising a VH4-34 segment, a DXP'1 segment, a JH4 segment, and a heavy chain CDR3 region comprising the sequence DITMVRGPH [Seq. I.D. No. 63].

~~54~~40. A human sequence immunoglobulin comprising a VH5-51 segment, a DHQ52 segment, a JH2 segment, and a heavy chain CDR3 region comprising the sequence PANWNWYFVL [Seq. I.D. No. 64].

~~55~~41. A human sequence immunoglobulin comprising a VH4-34 segment, a JH5 segment, and a heavy chain CDR3 region comprising the sequence VINWFDP [Seq. I.D. No. 65].

~~56~~42. A human sequence immunoglobulin comprising a VH5-51 segment, a DHQ52 segment, a JH4 segment , and a heavy chain CDR3 region comprising the sequence DQLGLFDY [Seq. I.D. No. 66].

~~57~~43. A human sequence immunoglobulin comprising a VkA27/A11 segment, a Jk4 segment, and a light chain CDR3 region comprising the sequence QQYGSSPLT [Seq. I.D. No. 67].

~~58~~44. A human sequence immunoglobulin comprising a VkL18 segment, a Jk4 segment, and a light chain CDR3 region comprising the sequence QQFISYPQLT [Seq. I.D. No. 68).

~~59~~45. A human sequence immunoglobulin comprising a VkL19 segment, a Jk2 segment, and a light chain CDR3 region comprising the sequence QQANSFPYT [Seq. I.D. No. 69].

~~60~~46. A human sequence immunoglobulin comprising a VkL15 segment, a Jk2 segment, and a light chain CDR3 region comprising the sequence QQYDSYPYT [Seq. I.D. No. 70].

~~61~~47. A hybridoma secreting an immunoglobulin, wherein the immunoglobulin is selected from the group consisting of: a human sequence immunoglobulin comprising a VH4-34 segment, a DXP'1 segment, a JH4 segment, and a heavy chain CDR3 region comprising the sequence DITMVRGPH [SEQ. I.D. No. 63], a human sequence immunoglobulin comprising a VH5-51 segment, a DHQ52 segment, a JH2 segment, and a heavy chain CDR3 region comprising the sequence PANWNWYFVL [SEQ. I.D. No. 64], a human sequence immunoglobulin comprising a VH4-34 segment, a JH5 segment, and a heavy chain CDR3 region comprising the sequence VINWFDP [SEQ. I.D. No. 65], a human sequence immunoglobulin comprising a VH5-51 segment, a DHQ52 segment, a JH4 segment , and a heavy chain CDR3 region comprising the sequence DQLGLFDY [SEQ. I.D. No. 66], a human sequence immunoglobulin comprising a VkA27/A11 segment, a Jk4 segment, and a light chain CDR3 region comprising the sequence QQYGSSPLT

[SEQ. I.D. No. 67], a human sequence immunoglobulin comprising a VkL18 segment, a Jk4 segment, and a light chain CDR3 region comprising the sequence QQFISYPQLT [SEQ. I.D. No. 68], a human sequence immunoglobulin comprising a VkL19 segment, a Jk2 segment, and a light chain CDR3 region comprising the sequence QQANSFPYT [SEQ. I.D. No. 69], and a human sequence immunoglobulin comprising a VkL15 segment, a Jk2 segment, and a light chain CDR3 region comprising the sequence QQYDSYPYT [SEQ. I.D. No. 70].