We claim:

1. A genetically modified mouse embryonic stem (ES) cell whose genome comprises at least two low affinity human FcγR α-chain genes that replace the endogenous mouse low affinity FcγR α-chain genes, wherein the mouse ES cell comprises a functional endogenous FcR γ-chain gene.

2. The genetically modified mouse ES cell of claim 1, wherein the at least two low affinity human FcγR α-chain genes are selected from the group consisting of a human FcγRIIA α-chain gene, a human FcγRIIB α-chain gene, a human FcγRIIC α-chain gene, a human FcγRIIIA α-chain gene and a human FcγRIIIB α-chain gene.

3. The genetically modified mouse ES cell of claim 1, wherein the at least two low affinity human FcγR α-chain genes are a human FcγRIIA α-chain gene and a human FcγRIIIA α-chain gene.

4. The genetically modified mouse ES cell of claim 1, wherein the genome of the mouse ES cell comprises a human FcγRIIB α-chain gene, a human FcγRIIC α-chain gene, and a human FcγRIIIB α-chain gene.

5. A method of making a genetically modified mouse comprising:
obtaining the genetically modified mouse ES cell of claim 1;
transplanting the genetically modified ES cell into a recipient mouse embryo; and
obtaining a genetically modified mouse whose genome comprises at least two low affinity human FcγR α-chain genes that replace the endogenous low affinity FcγR α-chain genes and a functional endogenous FcR γ-chain gene.

6. The method of claim 5, wherein the endogenous low affinity FcγR α-chain genes are replaced with a human FcγRIIA α-chain gene and a human FcγRIIIA α-chain gene.

7. The method of claim 5, wherein the endogenous low affinity FcγR α-chain genes are replaced with a human FcγRIIB α-chain gene, a human FcγRIIC α-chain gene, and a human FcγRIIIB α-chain gene.

8. The method of claim 5, wherein the endogenous low affinity FcγR α-chain genes are replaced with a human FcγRIIA α-chain gene, a human FcγRIIB α-chain gene, a human FcγRIIC α-chain gene, a human FcγRIIIA α-chain gene and a human FcγRIIIB α-chain gene.

9. A genetically modified mouse embryonic stem (ES) cell whose genome comprises a human FcγRIIIA α-chain gene that replaces the endogenous FcγRIIB, FcγRIII, and FcγRIV α-chain genes, wherein the mouse ES cell comprises a functional endogenous FcR γ-chain gene.

10. A mouse embryonic stem (ES) cell having a genome that comprises at least one human low affinity FcγR α-chain gene encoding a human low affinity FcγR α-chain with a polymorphism, wherein the human low affinity FcγR α-chain gene replaces an endogenous low affinity FcγR α-chain gene, and wherein the mouse ES cell comprises a functional endogenous FcR γ-chain gene.

11. The mouse ES cell of claim 10, wherein the human low affinity FcγR α-chain is a low affinity FcγRIIA α-chain.

12. The mouse ES cell of claim 11, wherein the polymorphism is a 131His polymorphism or a 131Arg polymorphism.

13. The mouse ES cell of claim 10, wherein the human low affinity FcγR α-chain is a low affinity FcγRIIB α-chain.

14. The mouse ES cell of claim 13, wherein the polymorphism is a 232Ile polymorphism or a 232Thr polymorphism.

15. The mouse ES cell of claim 10, wherein the human low affinity FcγR α-chain is a low affinity FcγRIIIA α-chain.

16. The mouse ES cell of claim 15, wherein the polymorphism is a 158Val polymorphism or a 158Phe polymorphism.

17. A mouse embryo comprising the mouse ES cell of any one of claims 1, 9 or 10.

18. A method of making a genetically modified mouse comprising:
obtaining the genetically modified mouse ES cell of claim 9;
transplanting the genetically modified ES cell into a recipient mouse embryo; and
obtaining a genetically modified mouse whose genome comprises a human FcγRIIIA α-chain gene that replaces the endogenous FcγRIIB, FcγRIII, and FcγRIV α-chain genes and a functional endogenous FcR γ-chain gene.

19. A method for making a genetically modified mouse embryonic stem (ES) cell whose genome comprises at least two low affinity human FcγR α-chain genes and a functional endogenous FcR γ-chain gene, the method comprising
replacing an endogenous low affinity FcγR α-chain genes in the genome of a mouse ES cell with at least two low affinity human FcγR α-chain genes such that a genetically modified mouse ES cell whose genome comprises at least two low affinity human FcγR α-chain genes and a functional endogenous FcR γ-chain is obtained.

20. A mouse lymphocyte comprising in its genome at least two low affinity human FcγR α-chain genes that replace the endogenous mouse low affinity FcγR α-chain genes, wherein the cell comprises a functional FcR γ-chain and functionally expresses the at least two low affinity human FcγR α-chain genes.

21. The lymphocyte of claim 20, wherein the at least two low affinity human FcγR α-chain genes are selected from the group consisting of a human FcγRIIA α-chain gene, a human FcγRIIB α-chain gene, a human FcγRIIC α-chain gene, a human FcγRIIIA α-chain gene and a human FcγRIIIB α-chain gene.

22. The lymphocyte of claim 20, wherein the at least two low affinity human FcγR genes are a human FcγRIIA α-chain gene and a human FcγRIIIA α-chain gene.

23. The lymphocyte of claim 22, wherein the human FcγRIIIA α-chain comprises a phenylalanine or a valine at amino acid position 158.

24. The lymphocyte of claim 20, wherein the lymphocyte is a NK cell or a B cell.

25. The lymphocyte of claim 20, wherein the lymphocyte is a B cell comprising a human nucleotide sequence that encodes a human CD20 protein, and wherein the lymphocyte does not express an endogenous mouse CD20 protein.

26. The lymphocyte of claim 20, wherein the lymphocyte is an NK cell that expresses a human FcγRIIIA α-chain.

27. The lymphocyte of claim 20, wherein the lymphocyte is an NK cell that expresses an α-chain of human FcγRIIC.

28. The lymphocyte of claim 20, wherein the lymphocyte is a monocyte, a macrophage, a polymorphonuclear (PMN) cell, a basophil, an eosinophil, or a T cell, and wherein the lymphocyte expresses a human FcγRIIA α-chain.

29. The lymphocyte of claim 20, wherein the genome of the lymphocyte comprises a human FcγRIIB α-chain gene, a human FcγRIIC α-chain gene, and a human FcγRIIIB α-chain gene.

30. The lymphocyte of claim 20, wherein the functional FcR γ-chain is an endogenous FcR γ-chain.

31. A mouse NK cell comprising in its genome a human FcγRIIIA α-chain gene that replaces the endogenous mouse FcγRIIB, FcγRIII, and FcγRIV α-chain genes, wherein the NK cell functionally expresses the human FcγRIIIA α-chain gene on its surface with a mouse FcR γ-chain.

32. An isolated mouse lymphocyte whose genome comprises a human FcγRIIIA α-chain gene that replaces the endogenous mouse FcγRIIB, FcγRIII, and FcγRIV α-chain genes, wherein the lymphocyte functionally expresses a human FcγRIIIA α-chain on its surface with a mouse FcR γ-chain.

33. A mouse lymphocyte having a genome that comprises at least one human low affinity FcγR α-chain gene encoding a human low affinity FcγR α-chain with a polymorphism, wherein the human low affinity FcγR α-chain gene replaces an endogenous low affinity FcγR α-chain gene, and wherein the mouse lymphocyte comprises a functional endogenous FcR γ-chain and functionally expresses the human low affinity FcγR α-chain gene.

34. The mouse lymphocyte of claim 33, wherein the human low affinity FcγR α-chain is a low affinity FcγRIIA α-chain.

35. The mouse lymphocyte of claim 34, wherein the polymorphism is a 131His polymorphism or a 131Arg polymorphism.

36. The mouse lymphocyte of claim 33, wherein the human low affinity FcγR α-chain is a low affinity FcγRIIB α-chain.

37. The mouse lymphocyte of claim 36, wherein the polymorphism is a 232Ile polymorphism or a 232Thr polymorphism.

38. The mouse lymphocyte of claim 33, wherein the human low affinity FcγR α-chain is a low affinity FcγRIIIA α-chain.

39. The mouse lymphocyte of claim 38, wherein the polymorphism is a 158Val polymorphism or a 158Phe polymorphism.

40. The mouse lymphocyte of claim 33, wherein the mouse lymphocyte is a mouse natural killer (NK) cell, a mouse B cell, or a mouse T cell.

41. A method of testing an agent comprising an Fc region of a human antibody, the method comprising:

(a) administering an agent comprising an Fc region of a human antibody to a genetically modified mouse whose genome comprises at least one human low affinity FcγR α-chain gene encoding a human low affinity FcγR α-chain with a polymorphism, wherein the human low affinity FcγR α-chain gene replaces an endogenous low affinity FcγR α-chain gene, wherein the mouse comprises a functional endogenous FcR γ-chain and functionally expresses the human low affinity FcγR α-chain gene, wherein the agent comprising an Fc region of a human antibody binds to a target cell in the mouse; and

(b) measuring the cell-mediated immunity elicited by the agent comprising an Fc region of a human antibody in the mouse.

42. The method of claim 41, wherein the cell-mediated immunity elicited by the agent comprising an Fc region of a human antibody is measured in a blood sample of the mouse.

43. The method of claim 41, wherein the human low affinity FcγR α-chain is a low affinity FcγRIIA α-chain.

44. The method of claim 43, wherein the polymorphism is a 131His polymorphism or a 131Arg polymorphism.

45. The method of claim 41, wherein the human low affinity FcγR α-chain is a low affinity FcγRIIB α-chain.

46. The method of claim 45, wherein the polymorphism is a 232Ile polymorphism or a 232Thr polymorphism.

47. The method of claim 41, wherein the human low affinity FcγR α-chain is a low affinity FcγRIIIA α-chain.

48. The method of claim 47, wherein the polymorphism is a 158Val polymorphism or a 158Phe polymorphism.

49. A genetically modified mouse whose genome comprises at least one human low affinity FcγR α-chain gene encoding a human low affinity FcγR α-chain with a polymorphism, wherein the human low affinity FcγR α-chain gene replaces an endogenous low affinity FcγR α-chain gene, and wherein the mouse comprises a functional endogenous FcR γ-chain and functionally expresses the human low affinity FcγR α-chain gene.

50. The genetically modified mouse of claim 49, wherein the human low affinity FcγR α-chain is a low affinity FcγRIIA α-chain.

51. The genetically modified mouse of claim 50, wherein the polymorphism is a 131His polymorphism or a 131Arg polymorphism.

52. The genetically modified mouse of claim 49, wherein the human low affinity FcγR α-chain is a low affinity FcγRIIB α-chain.

53. The genetically modified mouse of claim 52, wherein the polymorphism is a 232Ile polymorphism or a 232Thr polymorphism.

54. The genetically modified mouse of claim 49, wherein the human low affinity FcγR α-chain is a low affinity FcγRIIIA α-chain.

55. The genetically modified mouse of claim 54, wherein the polymorphism is a 158Val polymorphism or a 158Phe polymorphism.

56. A method of making a genetically modified mouse whose genome comprises a replacement of the endogenous low affinity FcγR α-chain genes with at least two human low affinity FcγR α-chain genes encoding human low affinity FcγR α-chains, the method comprising:

replacing the endogenous low affinity FcγR α-chain genes with at least two human low affinity FcγR α-chain genes encoding human low affinity FcγR α-chains,

such that the mouse comprises a functional FcR γ-chain and functionally expresses the at least two human FcγR α-chain genes.

57. The method of claim 56, wherein the functional FcR γ-chain is an endogenous FcR γ-chain.

58. The method of claim 56, wherein the at least two human low affinity FcγR α chain genes are selected from a human low affinity FcγRIIA, FcγRIIB, FcγRIIC, FcγRIIIA, or FcγRIIIB α chain gene.

59. The method of claim 56, wherein the at least two human low affinity FcγR α chain genes are human low affinity FcγRIIA and FcγRIIIA α chain genes.

60. A method of making a mouse whose genome comprises a replacement of an endogenous low affinity FcγR α-chain gene with a human low affinity FcγR α-chain gene encoding a human low affinity FcγR α-chain comprising a polymorphism, the method

comprising replacing an endogenous low affinity FcγR α-chain gene with a human low affinity FcγR α-chain gene encoding a human low affinity FcγR α-chain gene comprising a polymorphism, wherein the mouse further comprises a functional endogenous FcR γ-chain.

61. The method of claim 60, wherein the human low affinity FcγR α-chain comprising a polymorphism is selected from the group consisting of a low affinity FcγRIIA α-chain comprising a 131His polymorphism, a low affinity FcγRIIA α-chain comprising a 131Arg polymorphism, a low affinity FcγRIIB α-chain comprising a 232Ile polymorphism, a low affinity FcγRIIB α-chain comprising a 232Thr polymorphism, a low affinity FcγRIIIA α-chain comprising a 158Val polymorphism, and a low affinity FcγRIIB α-chain comprising a 158Phe polymorphism.