Claims:

1. A mammalian host cell engineered to express at least one nucleic acid encoding a fusion glycosyltransferase having β(1,4)-N-acetylglucosaminyltransferase III activity and the Golgi localization domain of mannosidase II, in an amount sufficient to modify the oligosaccharides in the Fc region of a polypeptide produced by said host cell, wherein said polypeptide is selected from the group consisting of a whole antibody molecule, an antibody fragment, and a fusion protein that includes a region equivalent to the Fc region of an immunoglobulin.

2. A mammalian host cell engineered to express at least one nucleic acid encoding a fusion glycosyltransferase having β(1,4)-N-acetylglucosaminyltransferase III activity and the Golgi localization domain of a Golgi resident glycosyltransferase selected from the group consisting of: mannosidase I, β(1,2)-N-acetylglucosaminyltransferase I, β(1,2)-N-acetylglucosaminyltransferase II, and α1-6 core fucosyltransferase, in an amount sufficient to modify the oligosaccharides in the Fc region of a polypeptide produced by said host cell, wherein said polypeptide is selected from the group consisting of a whole antibody molecule, an antibody fragment, and a fusion protein that includes a region equivalent to the Fc region of an immunoglobulin.

3. A mammalian host cell engineered to express at least one nucleic acid encoding a fusion glycosyltransferase having β(1,4)-galactosyltransferase activity and the Golgi localization domain of a Golgi resident glycosyltransferase selected from the group consisting of: mannosidase I, mannosidase II, β(1,2)-N-acetylglucosaminyltransferase I, β(1,2)-N-acetylglucosaminyltransferase II, and α1-6 core fucosyltransferase, in an amount sufficient to modify the oligosaccharides in the Fc region of a polypeptide produced by said host cell, wherein said polypeptide is selected from the group consisting of a whole antibody molecule, an antibody fragment, and a fusion protein that includes a region equivalent to the Fc region of an immunoglobulin.

4. The host cell according to any one of claims 1-3, wherein said polypeptide produced by said host cell is IgG or a fragment thereof.

5. The host cell according to any one of claims 1-3, wherein said polypeptide produced by said host cell is IgG1 or a fragment thereof.

6. The host cell according to any one of claims 1-3, wherein said polypeptide produced by said host cell is a fusion protein that includes a region equivalent to the Fc region of a human IgG.

7. The host cell according to any one of claims 1-3, wherein said polypeptide produced by said host cell exhibits increased Fc receptor binding affinity as a result of said modification.

8. The host cell according to any one of claims 1-3, wherein said polypeptide produced by said host cell exhibits increased effector function as a result of said modification.

9. A host cell according to claim 1, wherein said fusion glycosyltransferase comprises the catalytic domain of β(1,4)-N-acetylglucosaminyltransferase III.

10. A host cell according to claim 2, wherein said fusion glycosyltransferase comprises the catalytic domain of β(1,4)-N-acetylglucosaminyltransferase III.

11. A host cell according to claim 10, wherein said Golgi localization domain is from a heterologous Golgi resident polypeptide.

12. A host cell according to claim 3, wherein said fusion glycosyltransferase comprises the catalytic domain of β(1,4)-galactosyltransferase.

13. A host cell according to claim 12, wherein said Golgi localization domain is from a heterologous Golgi resident glycosyltransferase.

14. A host cell according to claim 13, wherein said Golgi localization domain is the localization domain of mannosidase II.

15. A host cell according to claim 11 or claim 13, wherein said Golgi localization domain is the localization domain of β(1,2)-N-acetylglucosaminyltransferase I.

16. A host cell according to claim 11 or claim 13, wherein said Golgi localization domain is the localization domain of β(1,2)-N-acetylglucosaminyltransferase II.

17. A host cell according to claim 11 or claim 13, wherein said Golgi localization domain is the localization domain of mannosidase I.

18. A host cell according to claim 11 or claim 13, wherein said Golgi localization domain is the localization domain of α1-6 core fucosyltransferase.

19. A host cell according to claim 8, wherein said increased effector function is increased Fc-mediated cellular cytotoxicity.

20. A host cell according to claim 8, wherein said increased effector function is increased binding to NK cells.

21. A host cell according to claim 8, wherein said increased effector function is increased binding to macrophages.

22. A host cell according to claim 8, wherein said increased effector function is increased binding to polymorphonuclear cells.

23. A host cell according to claim 8, wherein said increased effector function is increased binding to monocytes.

24. A host cell according to claim 8, wherein said increased effector function is increased direct signaling inducing apoptosis.

25. A host cell according to claim 8, wherein said increased effector function is increased dendritic cell maturation.

26. A host cell according to claim 8, wherein said increased effector function is increased T cell priming.

27. A host cell according to claim 7, wherein said Fc receptor is Fcγ activating receptor.

28. A host cell according to claim 7, wherein said Fc receptor is FcγRIIIA receptor.

29. A host cell according to any one of claims 1-3, wherein said host cell is a CHO cell, a BHK cell, a NSO cell, a SP2/0 cell, a YO myeloma cell, a P3X63 mouse myeloma cell, a PER cell, a PER.C6 cell or a hybridoma cell.

30. The host cell of any one of claims 1-3, wherein said polypeptide produced by said host cell is an anti-CD20 antibody.

31. The host cell of claim 30, wherein said anti-CD20 antibody is IDEC-C2B8.

32. The host cell of any one of claims 1-3, wherein said polypeptide produced by said host cell is the chimeric anti-human renal cell carcinoma monoclonal antibody chG250.

33. The host cell of any one of claims 1-3, further comprising at least one transfected nucleic acid encoding an antibody molecule, an antibody fragment, or a fusion protein that includes a region equivalent to the Fc region of an immunoglobulin.

34. The host cell of any one of claims 1-3, wherein said at least one nucleic acid encoding a fusion glycosyltransferase is operably linked to a constitutive promoter element.

35. The host cell of claim 33, wherein said at least one transfected nucleic acid encodes an anti-CD20 antibody, the chimeric anti-human neuroblastoma monoclonal antibody chCE7, the chimeric anti-human renal cell carcinoma monoclonal antibody chG250, the chimeric anti-human colon, lung, and breast carcinoma monoclonal antibody ING-1, the humanized anti-human 17-1A antigen monoclonal antibody 3622W94, the humanized anti-human colorectal tumor antibody A33, the anti-human melanoma antibody directed against GD3 ganglioside R24, the chimeric anti-human squamous-cell carcinoma monoclonal antibody SF-25, an anti-human EGFR antibody, an anti-human EGFRvIII antibody, an anti-human PSMA antibody, an anti-human PSCA antibody, an anti-human CD22 antibody, an anti-human CD30 antibody, an anti-

human CD33 antibody, an anti-human CD38 antibody, an anti-human CD40 antibody, an anti-human CD45 antibody, an anti-human CD52 antibody, an anti-human CD138 antibody, an anti-human HLA-DR variant antibody, an anti-human EpCAM antibody, an anti-human CEA antibody, an anti-human MUC1 antibody, an anti-human MUC1 core protein antibody, an anti-human aberrantly glycosylated MUC1 antibody, an antibody against human fibronectin variants containing the ED-B domain, or an anti-human HER2/neu antibody.

36. A method for producing a polypeptide in a mammalian host cell, comprising:

a. culturing a mammalian host cell engineered to express at least one nucleic acid encoding a fusion glycosyltransferase having β(1,4)-N-acetylglucosaminyltransferase III activity and the Golgi localization domain of mannosidase II, under conditions which permit the production of a polypeptide selected from the group consisting of a whole antibody molecule, an antibody fragment, and a fusion protein that includes a region equivalent to the Fc region of an immunoglobulin, wherein said fusion glycosyltransferase is expressed in an amount sufficient to modify the oligosaccharides in the Fc region of said polypeptide produced by said host cell; and

b. isolating said polypeptide.

37. A method for producing a polypeptide in a mammalian host cell, comprising:

a. culturing a mammalian host cell engineered to express at least one nucleic acid encoding a fusion glycosyltransferase having β(1,4)-N-acetylglucosaminyltransferase III activity and the Golgi localization domain of a Golgi resident glycosyltransferase selected from the group consisting of: mannosidase I, β(1,2)-N-acetylglucosaminyltransferase I, β(1,2)-N-acetylglucosaminyltransferase II, and α1-6 core fucosyltransferase, under conditions which permit the production of a polypeptide selected from the group consisting of a whole antibody molecule, an antibody fragment, and a fusion protein that includes a region equivalent to the Fc region of an immunoglobulin, wherein said fusion glycosyltransferase is expressed in an amount sufficient to modify the oligosaccharides in the Fc region of said polypeptide produced by said host cell; and

b. isolating said polypeptide.

38. A method for producing a polypeptide in a mammalian host cell, comprising:

a. culturing a mammalian host cell engineered to express at least one nucleic acid encoding a fusion glycosyltransferase having β(1,4)-galactosyltransferase activity and the Golgi localization domain of a Golgi resident glycosyltransferase selected from the group consisting of: mannosidase I, mannosidase II, β(1,2)-N-acetylglucosaminyltransferase I, β(1,2)-N-acetylglucosaminyltransferase II, and α1-6 core fucosyltransferase, under conditions which permit the production of a polypeptide selected from the group consisting of a whole antibody molecule, an antibody fragment, and a fusion protein that includes a region equivalent to the Fc region of an immunoglobulin, wherein said fusion glycosyltransferase is expressed in an amount

sufficient to modify the oligosaccharides in the Fc region of said polypeptide produced by said host cell, and

b. isolating said polypeptide.

39. A method according to claim 36, wherein said fusion glycosyltransferase comprises the catalytic domain of β(1,4)-N-acetylglucosaminyltransferase III.

40. A method according to claim 37, wherein said fusion glycosyltransferase comprises the catalytic domain of β(1,4)-N-acetylglucosaminyltransferase III.

41. A method according to claim 40, wherein said Golgi localization domain is from a heterologous Golgi resident polypeptide.

42. A method according to claim 38, wherein said fusion glycosyltransferase comprises the catalytic domain of β(1,4)-galactosyltransferase.

43. A method according to claim 42, wherein said Golgi localization domain is from a heterologous Golgi resident polypeptide.

44. A method according to claim 43, wherein said Golgi localization domain is the localization domain of mannosidase II.

45. A method according to claim 41 or claim 43, wherein said Golgi localization domain is the localization domain of β(1,2)-N-acetylglucosaminyltransferase I.

46. A method according to claim 41 or claim 43, wherein said Golgi localization domain is the localization domain of mannosidase I.

47. A method according to claim 41 or claim 43, wherein said Golgi localization domain is the localization domain of β(1,2)-N-acetylglucosaminyltransferase II.

48. A method according to claim 41 or claim 43, wherein said Golgi localization domain is the localization domain of α1-6 core fucosyltransferase.

49. A method according to any one of claims 36-38, wherein said polypeptide has increased effector function as a result of said modification.

50. A method according to claim 49, wherein said increased effector function is increased Fc-mediated cellular cytotoxicity.

51. A method according to claim 49, wherein said increased effector function is increased binding to NK cells.

52. A method according to claim 49, wherein said increased effector function is increased binding to macrophages.

53. A method according to claim 49, wherein said increased effector function is increased binding to monocytes.

54. A method according to claim 49, wherein said increased effector function is increased binding to polymorphonuclear cells.

55. A method according to claim 49, wherein said increased effector function is direct signaling inducing apoptosis.

56. A method according to claim 49, wherein said increased effector function is increased dendritic cell maturation.

57. A method according to claim 49, wherein said increased effector function is increased T cell priming.

58. A method according to any one of claims 36-38, wherein said polypeptide produced by said host cell exhibits increased Fc receptor binding affinity as a result of said modification.

59. A method according to claim 58, wherein said Fc receptor is Fc activating receptor.

60. A method according to claim 58, wherein said Fc receptor is FcγRIIIA receptor.

61. A method according to any one of claims 36-38, wherein said polypeptide produced by said host cell has an increased proportion of bisected oligosaccharides in the Fc region of said polypeptide.

62. A method according to any one of claims 36-38, wherein said polypeptide produced by said host cell has an increased proportion of nonfucosylated oligosaccharides in the Fc region of said polypeptide.

63. A method according to claim 62, wherein said nonfucosylated oligosaccharides are hybrid.

64. A method according to claim 62, wherein said nonfucosylated oligosaccharides are complex.

65. A method according to any one of claims 36-38, wherein said polypeptide produced by said host cell has an increased proportion of bisected, nonfucosylated oligosaccharides in the Fc region of said polypeptide.

66. A method according to claim 65, wherein said bisected, nonfucosylated oligosaccharides are hybrid.

67. A method according to claim 65, wherein said bisected, nonfucosylated oligosaccharides are complex.

68. A method according to claim 65, wherein at least 20% of the oligosaccharides in the Fc region of said polypeptide are bisected, nonfucosylated.

69. A method according to claim 65, wherein at least 25% of the oligosaccharides in the Fc region of said polypeptide are bisected, nonfucosylated.

70. A method according to claim 65, wherein at least 30% of the oligosaccharides in the Fc region of said polypeptide are bisected, nonfucosylated.

71. A method according to claim 65, wherein at least 35% of the oligosaccharides in the Fc region of said polypeptide are bisected, nonfucosylated.

Claims:

1. A mammalian host cell engineered to express at least one nucleic acid encoding a fusion glycosyltransferase having β(1,4)-N-acetylglucosaminyltransferase III activity in an amount sufficient to modify the oligosaccharides in the Fc region of a polypeptide produced by said host cell, wherein said fusion glycosyltransferase comprises the catalytic domain of β(1,4)-N-acetylglucosaminyltransferase III and the Golgi localization domain of mannosidase II, wherein said polypeptide produced by said host cell is selected from the group consisting of a whole antibody molecule, an antibody fragment, and a fusion protein that includes a region equivalent to the Fc region of an immunoglobulin, and wherein said polypeptide produced by said host cell exhibits increased Fc receptor binding affinity or increased effector function as a result of said modification.

2. A mammalian host cell engineered to express at least one nucleic acid encoding a fusion glycosyltransferase having β(1,4)-N-acetylglucosaminyltransferase III activity in an amount sufficient to modify the oligosaccharides in the Fc region of a polypeptide produced by said host cell, wherein said fusion glycosyltransferase comprises the catalytic domain of β(1,4)-N-acetylglucosaminyltransferase III and the Golgi localization domain of a Golgi resident glycosyltransferase selected from the group consisting of: mannosidase I, β(1,2)-N-acetylglucosaminyltransferase I, β(1,2)-N-acetylglucosaminyltransferase II, and α1-6 core fucosyltransferase, wherein said polypeptide produced by said host cell is selected from the group consisting of a whole antibody molecule, an antibody fragment, and a fusion protein that includes a region equivalent to the Fc region of an immunoglobulin, and wherein said polypeptide produced by said host cell exhibits increased Fc receptor binding affinity or increased effector function as a result of said modification.

3. The host cell according to claim 1 or claim 2, wherein said polypeptide produced by said host cell is IgG or a fragment thereof.

4. The host cell according to claim 1 or claim 2, wherein said polypeptide produced by said host cell is IgG1 or a fragment thereof.

5. The host cell according to claim 1 or claim 2, wherein said polypeptide produced by said host cell is a fusion protein that includes a region equivalent to the Fc region of a human IgG.

6. The host cell according to claim 1 or claim 2, wherein said polypeptide produced by said host cell exhibits increased Fc receptor binding affinity as a result of said modification.

7. The host cell according to claim 1 or claim 2, wherein said polypeptide produced by said host cell exhibits increased effector function as a result of said modification.

8. A host cell according to claim 2, wherein said Golgi localization domain is from a heterologous Golgi resident polypeptide.

9. A host cell according to claim 2, wherein said Golgi localization domain is the localization domain of β(1,2)-N-acetylglucosaminyltransferase I.

10. A host cell according to claim 2, wherein said Golgi localization domain is the localization domain of β(1,2)-N-acetylglucosaminyltransferase II.

11. A host cell according to claim 2, wherein said Golgi localization domain is the localization domain of mannosidase I.

12. A host cell according to claim 2, wherein said Golgi localization domain is the localization domain of α1-6 core fucosyltransferase.

13. A host cell according to claim 7, wherein said increased effector function is increased Fc-mediated cellular cytotoxicity.

14. A host cell according to claim 7, wherein said increased effector function is increased binding to NK cells.

15. A host cell according to claim 7, wherein said increased effector function is increased binding to macrophages.

16. A host cell according to claim 7, wherein said increased effector function is increased binding to polymorphonuclear cells.

17. A host cell according to claim 7, wherein said increased effector function is increased binding to monocytes.

18. A host cell according to claim 7, wherein said increased effector function is increased direct signaling inducing apoptosis.

19. A host cell according to claim 7, wherein said increased effector function is increased dendritic cell maturation.

20. A host cell according to claim 7, wherein said increased effector function is increased T cell priming.

21. A host cell according to claim 6, wherein said Fc receptor is Fcγ activating receptor.

22. A host cell according to claim 6, wherein said Fc receptor is FcγRIIIA receptor.

23. A host cell according to claim 1 or claim 2, wherein said host cell is a CHO cell, a BHK cell, a NSO cell, a SP2/0 cell, a YO myeloma cell, a P3X63 mouse myeloma cell, a PER cell, a PER.C6 cell or a hybridoma cell.

24. The host cell of claim 1 or claim 2, wherein said polypeptide produced by said host cell is an anti-CD20 antibody.

25. The host cell of claim 24, wherein said anti-CD20 antibody is IDEC-C2B8.

26. The host cell of claim 1 or claim 2, wherein said polypeptide produced by said host cell is the chimeric anti-human renal cell carcinoma monoclonal antibody chG250.

27. The host cell of claim 1 or claim 2, further comprising at least one transfected nucleic acid encoding an antibody molecule, an antibody fragment, or a fusion protein that includes a region equivalent to the Fc region of an immunoglobulin.

28. The host cell of claim 1 or claim 2, wherein said at least one nucleic acid encoding a fusion glycosyltransferase is operably linked to a constitutive promoter element.

29. The host cell of claim 27, wherein said at least one transfected nucleic acid encodes an anti-CD20 antibody, the chimeric anti-human neuroblastoma monoclonal antibody chCE7, the chimeric anti-human renal cell carcinoma monoclonal antibody chG250, the chimeric anti-human colon, lung, and breast carcinoma monoclonal antibody ING-1, the humanized anti-human 17-1A antigen monoclonal antibody 3622W94, the humanized anti-human colorectal tumor antibody A33, the anti-human melanoma antibody directed against GD3 ganglioside R24, the chimeric anti-human squamous-cell carcinoma monoclonal antibody SF-25, an anti-human EGFR antibody, an anti-human EGFRvIII antibody, an anti-human PSMA antibody, an anti-human PSCA antibody, an anti-human CD22 antibody, an anti-human CD30 antibody, an anti-human CD33 antibody, an anti-human CD38 antibody, an anti-human CD40 antibody, an anti-human CD45 antibody, an anti-human CD52 antibody, an anti-human CD138 antibody, an anti-human HLA-DR variant antibody, an anti-human EpCAM antibody, an anti-human CEA antibody, an anti-human MUC1 antibody, an anti-human MUC1 core protein antibody, an anti-human aberrantly glycosylated MUC1 antibody, an antibody against human fibronectin variants containing the ED-B domain, or an anti-human HER2/neu antibody.

30. A method for producing a polypeptide in a mammalian host cell, comprising:

a. culturing a mammalian host cell engineered to express at least one nucleic acid encoding a fusion glycosyltransferase having β(1,4)-N-acetylglucosaminyltransferase III activity under conditions which permit the production of a polypeptide selected from the group consisting of a whole antibody molecule, an antibody fragment, and a fusion protein that includes a region equivalent to the Fc region of an immunoglobulin, wherein said fusion glycosyltransferase comprises the catalytic domain of β(1,4)-N-acetylglucosaminyltransferase III and the Golgi localization domain of mannosidase II, wherein said fusion glycosyltransferase is expressed in an amount sufficient to modify the oligosaccharides in the Fc region of said polypeptide produced by said host cell, wherein said polypeptide produced by said host cell exhibits increased Fc receptor binding affinity or increased effector function as a result of said modification; and

b. isolating said polypeptide.

31. A method for producing a polypeptide in a mammalian host cell, comprising:

a. culturing a mammalian host cell engineered to express at least one nucleic acid encoding a fusion glycosyltransferase having β(1,4)-N-acetylglucosaminyltransferase III activity under conditions which permit the production of a polypeptide selected from the group consisting of a whole antibody molecule, an antibody fragment, and a fusion protein that includes a region equivalent to the Fc region of an immunoglobulin, wherein said fusion glycosyltransferase comprises the catalytic domain of β(1,4)-N-acetylglucosaminyltransferase III

and the Golgi localization domain of a Golgi resident glycosyltransferase selected from the group consisting of: mannosidase I, β(1,2)-N-acetylglucosaminyltransferase I, β(1,2)-N-acetylglucosaminyltransferase II, and α1-6 core fucosyltransferase, wherein said fusion glycosyltransferase is expressed in an amount sufficient to modify the oligosaccharides in the Fc region of said polypeptide produced by said host cell, wherein said polypeptide produced by said host cell exhibits increased Fc receptor binding affinity or increased effector function as a result of said modification; and

b. isolating said polypeptide.

32. A method according to claim 31, wherein said Golgi localization domain is from a heterologous Golgi resident polypeptide.

33. A method according to claim 31, wherein said Golgi localization domain is the localization domain of β(1,2)-N-acetylglucosaminyltransferase I.

34. A method according to claim 31, wherein said Golgi localization domain is the localization domain of mannosidase I.

35. A method according to claim 31, wherein said Golgi localization domain is the localization domain of β(1,2)-N-acetylglucosaminyltransferase II.

36. A method according to claim 31, wherein said Golgi localization domain is the localization domain of α1-6 core fucosyltransferase.

37. A method according to claim 30 or claim 31, wherein said polypeptide produced by said host cell has increased effector function as a result of said modification.

38. A method according to claim 37, wherein said increased effector function is increased Fc-mediated cellular cytotoxicity.

39. A method according to claim 37, wherein said increased effector function is increased binding to NK cells.

40. A method according to claim 37, wherein said increased effector function is increased binding to macrophages.

41. A method according to claim 37, wherein said increased effector function is increased binding to monocytes.

42. A method according to claim 37, wherein said increased effector function is increased binding to polymorphonuclear cells.

43. A method according to claim 37, wherein said increased effector function is direct signaling inducing apoptosis.

44. A method according to claim 37, wherein said increased effector function is increased dendritic cell maturation.

45. A method according to claim 37, wherein said increased effector function is increased T cell priming.

46. A method according to claim 30 or claim 31, wherein said polypeptide produced by said host cell exhibits increased Fc receptor binding affinity as a result of said modification.

47. A method according to claim 46, wherein said Fc receptor is Fc activating receptor.

48. A method according to claim 46 , wherein said Fc receptor is FcγRIIIA receptor.

49. A method according to claim 30 or claim 31, wherein said polypeptide produced by said host cell has an increased proportion of bisected oligosaccharides in the Fc region of said polypeptide.

50. A method according to claim 30 or claim 31, wherein said polypeptide produced by said host cell has an increased proportion of nonfucosylated oligosaccharides in the Fc region of said polypeptide.

51. A method according to claim 50, wherein said nonfucosylated oligosaccharides are hybrid.

52. A method according to claim 50, wherein said nonfucosylated oligosaccharides are complex.

53. A method according to claim 30 or claim 31, wherein said polypeptide produced by said host cell has an increased proportion of bisected, nonfucosylated oligosaccharides in the Fc region of said polypeptide.

54. A method according to claim 53, wherein said bisected, nonfucosylated oligosaccharides are hybrid.

55. A method according to claim 53, wherein said bisected, nonfucosylated oligosaccharides are complex.

56. A method according to claim 53, wherein at least 20% of the oligosaccharides in the Fc region of said polypeptide are bisected, nonfucosylated.

57. A method according to claim 53 , wherein at least 25% of the oligosaccharides in the Fc region of said polypeptide are bisected, nonfucosylated.

58. A method according to claim 53 , wherein at least 30% of the oligosaccharides in the Fc region of said polypeptide are bisected, nonfucosylated.

59. A method according to claim 53, wherein at least 35% of the oligosaccharides in the Fc region of said polypeptide are bisected, nonfucosylated.