CLAIMS

1. A method for producing a protein molecule composition, comprising

   (a) introducing in a host cell which is an immortalized human blood cell at least one nucleic acid encoding at least a part of said protein; and
   (b) culturing said host cell under conditions which permit the production of said protein molecule composition; and
   (c) isolating said protein molecule composition.

2. A method according to claim 1 for producing a protein molecule composition, preferably an antibody molecule composition, comprising the following steps:

   (a) introducing in a host cell which is an immortalized human blood cell at least one nucleic acid encoding a protein or at least one part thereof; wherein said host cell is selected to produce a protein composition having at least one of the following glycosylation characteristics:

      (i) it comprises no detectable NeuGc; and/or

      (ii) it has a galactosylation degree on the total carbohydrate structures or on the carbohydrate structures at one particular glycosylation site of the protein molecule of the protein molecules in said protein molecule composition, that is increased compared to the same amount of protein molecules in at least one protein molecule composition of the same protein molecule isolated from CHOdhfr- [ATCC No. CRL-9096] when expressed therein; and/or

      (iii) it has an amount of G2 structures on the total carbohydrate structures or on the carbohydrate structures at one particular glycosylation site of the protein molecule of said protein molecules in said protein molecule composition which is at least 5% higher compared to the same amount of protein molecules in at least one protein molecule composition of the same protein molecule isolated from CHOdhfr- [ATCC No. CRL-9096] when expressed therein; and/or

      (iv) it has an amount of G0 structures on the total carbohydrate structures or on the carbohydrate structures at one particular glycosylation site of the protein molecule of said protein molecules in said protein molecule composition which is at least 5% lower compared to the same amount of protein molecules in at least one protein molecule composition of the same protein molecule isolated from CHOdhfr- [ATCC No. CRL-9096] when expressed therein; and/or

(v) it comprises no detectable terminal Galalpha1-3Gal; and/or

(vi) it comprises an amount of fucose on the total carbohydrate structures or on the carbohydrate structures at one particular glycosylation site of the protein molecule of said protein molecules in said protein molecule composition which is at least 5% less compared to the same amount of protein molecules in at least one protein molecule composition of the same protein molecule isolated from CHOdhfr- [ATCC No. CRL-9096] when expressed therein; and/or

(vii) it comprises at least one carbohydrate structure containing bisecting GlcNAc; and/or

(viii) it has a sialylation pattern which is altered compared to the sialylation pattern of at least one protein molecule composition of the same protein molecule isolated from CHOdhfr- [ATCC No. CRL-9096] when expressed therein,

(b) culturing said host cell under conditions which permits the production of said protein molecule composition; and

(c) isolating said protein molecule composition, wherein the protein molecules have at least one of the glycosylation characteristics (i) to (viii).

3. Method according to claim 1 or 2, wherein said sialylation pattern is characterised by at least one of the following characteristics:

- it comprises alpha2-6 linked NeuNAc; and/or

- it has an increased sialylation degree with an amount of NeuNAc on the total carbohydrate structures or on the carbohydrate structures at one particular glycosylation site of the protein molecule of the protein molecules in said protein molecule composition which is at least 15% higher compared to the same amount of protein molecules in at least one protein molecule composition of the same protein molecule isolated from CHOdhfr- [ATCC No. CRL-9096] when expressed therein, and/or

- it has a decreased sialylation degree with at least a 15% lower amount of NeuNAc on the total carbohydrate structures or on the carbohydrate structures at one particular glycosylation site of the protein molecule of the protein molecules in said protein molecule composition than the same amount of protein molecules of at least one protein molecule composition of the same

protein molecule isolated from CHOdhfr- [ATCC No. CRL-9096] when expressed therein, and/or

- it comprises at least 20% more charged N-glycosidically linked carbohydrate chains of the total carbohydrate units or of at least one particular carbohydrate chain at a particular glycosylation site of the protein molecule of the protein molecules in said protein molecule composition compared to the same amount of protein molecules in at least one protein molecule composition of the same protein molecule isolated from CHOdhfr- [ATCC No. CRL-9096] when expressed therein, and/or

- it comprises at least 20% less charged N-glycosidically linked carbohydrate chains of the total carbohydrate units or of at least one particular carbohydrate chain at a particular glycosylation site of the protein molecule of the protein molecules in said protein molecule composition compared to the same amount of protein molecules in at least one protein molecule composition of the same protein molecule isolated from CHOdhfr- [ATCC No. CRL-9096] when expressed therein.

4. Method according to at least one of the claims 1 to 3, wherein said host cell is selected to produce a glycoprotein, comprising at least 10% carbohydrate structures of the total carbohydrate units or of at least one particular carbohydrate chain at a particular glycosylation site of the protein molecule of the protein molecules in said protein molecule composition, lacking fucose.

5. Method according to at least one of the claims 1 to 4, wherein said host cell is selected to produce a glycoprotein, comprising at least 2% carbohydrate structures of the total carbohydrate units or of at least one particular carbohydrate chain at a particular glycosylation site of the protein molecule of the protein molecules in said protein molecule composition which contains bisecting GlcNAc.

6. Method according ti at least one of the claims 1 to 5, wherein said host cell is selected to produce a glycoprotein, comprising

- more than 35% G2 structures on the total carbohydrate structures or on the carbohydrate structures at one particular glycosylation site of the protein molecule in said protein molecule composition; and/or

- it comprises less than 22% G0 structures on the total carbohydrate structures or on the carbohydrate structures at one particular glycosylation site of the protein molecule in said protein molecule composition.

7. Method according to at least one of the claims 1 to 6, wherein said protein molecule composition produced has at least one of the following characteristics:

   - it has an increased activity and/or increased yield in particular compared to at least one protein molecule composition of the same protein molecule when expressed in the cell line CHOdhfr- [ATCC No. CRL-9096];

   - it has an improved homogeneity in particular compared to at least one protein molecule composition of the same protein molecule when expressed in the cell line CHOdhfr- [ATCC No. CRL-9096];

   - it has an increased average or maximum yield which is at least 10% higher than the yield of at least one protein molecule composition from the same protein molecule when expressed in the cell line CHOdhfr- [ATCC No. CRL-9096];

   - it has an improved homogeneity, which is an improved glycosylation homogeneity compared to at least one protein molecule composition of the same protein molecule when expressed in the cell line CHOdhfr- [ATCC No. CRL-9096];

   - it has an increased activity compared to at least one protein molecule composition of the same protein molecule when expressed in the cell line CHOdhfr- [ATCC No. CRL-9096];

   - in case said protein molecule is an antibody molecule, it has an increased Fc-mediated cellular cytotoxicity which is at least 2 times higher than the Fc-mediated cellular cytotoxicity of at least one antibody molecule composition from the same antibody molecule when expressed in the cell line CHOdhfr- [ATCC No. CRL-9096];

   - in case said protein molecule is an antibody molecule, it has an increased antigen mediated or Fc-mediated binding which is at least 15%, preferably 20%, 25%, 30%, 35%, 40%, 45% and preferably 50% higher than the binding of at least one antibody molecule composition from the same antibody molecule when expressed in the cell line CHOdhfr- [ATCC No. CRL-9096].

8. The method of at least one of the claims 1 to 7, wherein the host cell grows and produces the protein molecule composition under serum-free conditions.

9. The method according to at least one of the claims 1 to 8, wherein the host cell is selected to produce a protein composition comprising protein molecules having the following characteristic glycosylation combinations:

(a)
- it comprises no detectable NeuGc
- it comprises no detectable Galalpha1-3Gal
- it comprises a galactosylation pattern as defined in claim 2
- it has a fucose content as defined in claim 2
- it comprises bisecGlcNAc
- it comprises an increased amount of sialic acid compared to a protein composition of the same protein molecule when expressed in the cell line CHOdhfr-[ATCC No. CRL-9096] or compared to a sialylation deficient cell line such as NM-F9 and NM-D4;

(b)
- it comprises no detectable NeuGc
- it comprises no detectable Galalpha1-3Gal
- it comprises a galactosylation pattern as defined in claim 2
- it has a fucose content as defined in claim 2
- it comprises bisecGlcNAc
- it comprises an decreased amount of sialic acid compared to a protein composition of the same protein molecule when expressed in the cell line CHOdhfr-[ATCC No. CRL-9096];

(c)
- it comprises no detectable NeuGc
- it comprises no detectable Galalpha1-3Gal
- it comprises a galactosylation pattern as defined in claim 2
- it has a fucose content as defined in claim 2
- it comprises bisecGlcNAc
- it comprises 2-6 NeuNAc

10. The method of at least one of the claims 1 to 9, wherein a host cell is used, which is selected from the following groups 1 to 4:

(a) group 1, comprising host cells having a high sialylation activity such as K562 or cell lines derived therefrom;
(b) group 2, comprising host cells having due to a genetic deficiency or an expression suppression system a low or no sialylation activity, comparable to and including NM-F9 [DSM ACC2606], NM-D4 [DSM ACC2605] and GT-2X or cell lines derived therefrom;

(c) group 3, comprising host cells having a higher sialylation degree than K562 such as NM-H9 and NM-H9D8 or cell lines derived therefrom;
(d) group 4, comprising host cells having a low or no fucosylation activity such as NM-H9D8-E6 and NM-H9D8-E6Q12 or cell lines derived therefrom.

11. The method according to at least one of the claims 1 to 10, wherein the host cell is of human myeloid leukaemia origin and is preferably selected from the group consisting of K562, NM-F9 [DSM ACC2606], NM-D4 [DSM ACC2605], GT – 2X [DSM ACC 2858], NM-H9, NM-E-2F9, NM-C-2F5, NM-H9D8 [DSM ACC 2806], NM-H9D8-E6, NM-H9D8-E6Q12 or a cell or cell line derived therefrom.

12. Method according to at least one of the claims 1 to 11, wherein a nucleic acid is introduced in the host cell, encoding an antifolate resistant DHFR- variant.

13. Method according to claim 12, wherein the nucleic acid encoding said antifolate resistant DHFR variant is introduced via a separate vector in addition to a vector comprising the nucleic acid encoding at least a part of said protein to be expressed or wherein a vector is used, comprising at least the nucleic acid encoding at least part of said protein to be expressed and the nucleic acid encoding the antifolate resistant DHFR variant.

14. Method according to claims 12 or 13, wherein the host cell is cultured with said antifolate.

15. Method according to at least one of the claims 12 to 14, wherein the nucleic acid sequence encoding at least part of said protein molecule to be expressed is amplified by stepwise increasing the antifolate concentration in the culture.

16. Method according to at least one of the claims 12 to 15, wherein at least one of the following characteristics is fulfilled

(a) the antifolate is methotrexate
(b) the nucleic acid encoding said antifolate resistant DHFR variant encodes a polypeptide of the group of sequence ID No. 1 to 9, preferably ID. No 1.

17. Method according to at least one of the claims 1 to 16, wherein said protein is an antibody.

18. A method according to at least one of the claims 1 to 17, for producing an antibody molecule composition, comprising:

(a) introducing in a host cell of human myeloid leukaemia origin at least one nucleic acid encoding an antibody molecule or at least one part thereof, and at least one nucleic

acid comprising at least one nucleic acid sequence encoding at least one polypeptide of the group of sequence #1 to sequence #9; and

(b) amplifying the nucleic acid sequence encoding said antibody molecule or at least one part thereof by culturing said host cell with methotrexate; and

(c) culturing said host cell under conditions which permits the production of said antibody molecule composition, and

(d) isolating said antibody molecule composition.

19. A method according to at least one of the claims 1 to 18 for producing an antibody molecule composition having increased activity and/or increased yield and/or improved homogeneity, comprising:

(a) introducing in a host cell of human myeloid leukaemia origin at least one nucleic acid encoding an antibody molecule or at least one part thereof; and

(b) culturing said host cell under conditions which permits the production of said antibody molecule compositions; and

(c) isolating said antibody molecule composition having increased activity and/ or increased yield and/ or improved homogeneity.

20. A method according to at least one of the claims 1 to 19 for producing an antibody molecule composition having increased activity and/ or increased yield and/ or improved homogeneity, comprising:

(a) introducing in a host cell of human myeloid leukaemia origin at least one nucleic acid encoding an antibody molecule or at least one part thereof, and at least one nucleic acid comprising at least one nucleic acid sequence encoding at least one polypeptide of the group of sequence #1 to sequence #9; and

(b) amplifying the nucleic acid sequence encoding said antibody molecule or at least one part thereof by culturing said host cell with methotrexate; and

(c) culturing said host cell under conditions which permits the production of said antibody molecule composition, and

(d) isolating said antibody molecule composition having increased activity and/ or increased yield and/ or improved homogeneity.

21. A method for selecting a host cell for producing a protein composition having at least one of the following glycosylation characteristics:

(i) it comprises no detectable NeuGc; and/or

(ii) it has a galactosylation degree of galactose, which is linked to GlcNAc, on the total carbohydrate structures or on the carbohydrate structures at one particular glycosylation site of the protein molecule of the protein molecules in said protein molecule composition, that is increased compared to the same

amount of protein molecules in at least one protein molecule composition of the same protein molecule isolated from CHOdhfr- [ATCC No. CRL-9096] when expressed therein; and/or

(iii) it has an amount of G2 structures on the total carbohydrate structures or on the carbohydrate structures at one particular glycosylation site of the protein molecule of said protein molecules in said protein molecule composition which is at least 5% higher compared to the same amount of protein molecules in at least one protein molecule composition of the same protein molecule isolated from CHOdhfr- [ATCC No. CRL-9096] when expressed therein; and/or

(iv) it has an amount of G0 structures on the total carbohydrate structures or on the carbohydrate structures at one particular glycosylation site of the protein molecule of said protein molecules in said protein molecule composition which is at least 5% lower compared to the same amount of protein molecules in at least one protein molecule composition of the same protein molecule isolated from CHOdhfr- [ATCC No. CRL-9096] when expressed therein; and/or

(v) it comprises no detectable terminal Gal*alpha*1-3Gal; and/or

(vi) it comprises an amount of fucose on the total carbohydrate structures or on the carbohydrate structures at one particular glycosylation site of the protein molecule of said protein molecules in said protein molecule composition which is at least 5% less compared to the same amount of protein molecules in at least one protein molecule composition of the same protein molecule isolated from CHOdhfr- [ATCC No. CRL-9096] when expressed therein; and/or

(vii) it comprises at least one carbohydrate structure containing bisecting GlcNAc; and/or

(viii) it has a sialylation pattern which is altered compared to the sialylation pattern of at least one protein molecule composition of the same protein molecule isolated from CHOdhfr- [ATCC No. CRL-9096] when expressed therein;

by the following steps

(a) introducing in at least two different host cells providing a diverging glycosylation pattern at least one nucleic acid encoding a protein or at least one part thereof; wherein at least one of said host cells is an immortalized human blood cell and

(b) culturing said at least two different host cells, wherein each different host cell produces a protein composition having a glycosylation pattern diverging from the glycosylation pattern produced by the other host cell;
(c) isolating said expressed protein compositions carrying a different glycosylation pattern from the at least two different host cells; and
(d) selecting said host cell producing a protein composition which has at least one of the glycosylation characteristics defined in (i) to (viii).

22. The method according to claim 21, wherein said protein composition depicts at least one of the following characteristics:

- in case it is an antibody molecule composition it has an increased Fc-mediated cellular cytotoxicity which is at least 2 times higher than the Fc-mediated cellular cytotoxicity of at least one antibody molecule composition from the same antibody molecule when expressed in the cell line CHOdhfr- [ATCC No. CRL-9096];

and/or

- in case it is an antibody molecule composition it has an increased antigen mediated or Fc-mediated binding which is at least 50% higher than the binding of at least one antibody molecule composition from the same antibody molecule when expressed in the cell line CHOdhfr- [ATCC No. CRL-9096];

and/or

- it has an increased average or maximum yield of said protein molecule composition which is at least 10% higher than the yield of at least one protein molecule composition from the same protein molecule when expressed in the cell line CHOdhfr- [ATCC No. CRL-9096].

23. The method of claim 21 or 22, wherein at least one of said at least two different host cells of human myeloid leukaemia origin is K562, NM-F9 [DSM ACC2606], NM-D4 [DSM ACC2605], GT – 2X [DSM ACC 2858], NM-H9, NM-E-2F9, NM-C-2F5, NM-H9D8 [DSM ACC 2806], NM-H9D8-E6, NM-H9D8-E6Q12 or a cell or cell line derived therefrom.

24. The method of claim 21 or 22, wherein the at least two different host cells are selected from the following groups 1 to 4:

(a) group 1, comprising host cells having a high sialylation activity such as K562 or cell lines derived therefrom;

(b) group 2, comprising host cells due to a genetic deficiency a low or no sialylation such as NM-F9 [DSM ACC2606], NM-D4 [DSM ACC2605] and GT-2X or cell lines derived therefrom;
(c) group 3, comprising host cells having a higher sialylation degree than K562 such as NM-H9 and NM-H9D8 or cell lines derived therefrom;
(d) group 4, comprising host cells having a low or no fucosylation activity such as NM-H9D8-E6 or NM-H9D8-E6Q12 or cell lines derived therefrom.

25. The method according to at least one of the claims 21 to 24, wherein at least one host cell is selected, which produces a protein composition, preferably an antibody composition, depicting a glycosylation pattern as defined in claims 2 to 9.

26. A protein or protein molecule composition obtainable by the production method according to at least one of the claims 1 to 20.

27. A protein or protein molecule composition according to claim 26, wherein said composition has at least one of the following characteristics:

(i) it comprises no detectable NeuGc; and/or

(ii) it has a galactosylation degree of galactose on the total carbohydrate structures or on the carbohydrate structures at one particular glycosylation site of the protein molecule of the protein molecules in said protein molecule composition, that is increased compared to the same amount of protein molecules in at least one protein molecule composition of the same protein molecule isolated from CHOdhfr- [ATCC No. CRL-9096] when expressed therein; and/or

(iii) it has an amount of G2 structures on the total carbohydrate structures or on the carbohydrate structures at one particular glycosylation site of the protein molecule of said protein molecules in said protein molecule composition which is at least 5% higher compared to the same amount of protein molecules in at least one protein molecule composition of the same protein molecule isolated from CHOdhfr- [ATCC No. CRL-9096] when expressed therein; and/or

(iv) it has an amount of G0 structures on the total carbohydrate structures or on the carbohydrate structures at one particular glycosylation site of the protein molecule of said protein molecules in said protein molecule composition which is at least 5% lower compared to the same amount of protein molecules in at least one protein molecule composition of the same protein molecule isolated from CHOdhfr- [ATCC No. CRL-9096] when expressed therein; and/or

(v) it comprises no detectable terminal Galalpha1-3Gal; and/or

(vi) it comprises an amount of fucose on the total carbohydrate structures or on the carbohydrate structures at one particular glycosylation site of the protein molecule of said protein molecules in said protein molecule composition which is at least 5% less compared to the same amount of protein molecules in at least one protein molecule composition of the same protein molecule isolated from CHOdhfr- [ATCC No. CRL-9096] when expressed therein; and/or

(vii) it comprises at least one carbohydrate structure containing bisecting GlcNAc; and/or

(viii) it has a sialylation pattern which is altered compared to the sialylation pattern of at least one protein molecule composition of the same protein molecule isolated from CHOdhfr- [ATCC No. CRL-9096] when expressed therein.

28. A protein or protein molecule composition according to claim 27, wherein the protein molecule composition has at least one of the following characteristics:

- it comprises alpha2-6 linked NeuNAc, and/or

- it has an increased sialylation degree with an amount of NeuNAc on the total carbohydrate structures or on the carbohydrate structures at one particular glycosylation site of the protein molecule of the protein molecules in said protein molecule composition which is at least 15% higher compared to the same amount of protein molecules in at least one protein molecule composition of the same protein molecule isolated from CHOdhfr- [ATCC No. CRL-9096] when expressed therein, and/or

- it has a decreased sialylation degree with at least a 15% lower amount of NeuNAc on the total carbohydrate structures or on the carbohydrate structures at one particular glycosylation site of the protein molecule of the protein molecules in said protein molecule composition than the same amount of protein molecules of at least one protein molecule composition of the same protein molecule isolated from CHOdhfr- [ATCC No. CRL-9096] when expressed therein, and/or

- it comprises at least 20% more charged N-glycosidically linked carbohydrate chains of the total carbohydrate units or of at least one particular carbohydrate chain at a particular glycosylation site of the protein molecule of the protein

molecules in said protein molecule composition compared to the same amount of protein molecules in at least one protein molecule composition of the same protein molecule isolated from CHOdhfr- [ATCC No. CRL-9096] when expressed therein, and/or

- it comprises at least 20% less charged N-glycosidically linked carbohydrate chains of the total carbohydrate units or of at least one particular carbohydrate chain at a particular glycosylation site of the protein molecule of the protein molecules in said protein molecule composition compared to the same amount of protein molecules in at least one protein molecule composition of the same protein molecule isolated from CHOdhfr- [ATCC No. CRL-9096] when expressed therein; and/or

- it comprises at least 10% carbohydrate structures of the total carbohydrate units or of at least one particular carbohydrate chain at a particular glycosylation site of a protein molecule of the protein molecules in said protein molecule composition, lacking fucose; and/or

- it comprises at least 2% carbohydrate structures of the total carbohydrate units or of at least one particular carbohydrate chain at a particular glycosylation site of a protein molecule of the protein molecules in said protein molecule composition which contains bisecting GlcNAc; and/or

- it comprises more than 35% G2 structures on the total carbohydrate structures or on the carbohydrate structures at one particular glycosylation site of a protein molecule of the protein molecules in said protein composition; and/or

- it comprises less than 22% G0 structures on the total carbohydrate structures or on the carbohydrate structures at one particular glycosylation site of a protein molecule of the protein molecules in said protein composition; and/or

- it has an increased activity and/or increased yield compared to at least one protein molecule composition of the same protein molecule when expressed in the cell line CHOdhfr- [ATCC No. CRL-9096]; and/or

- it has an improved homogeneity compared to at least one protein molecule composition of the same protein molecule when expressed in the cell line CHOdhfr- [ATCC No. CRL-9096]; and/or

- it has an increased average or maximum yield which is at least 10% higher than the yield of at least one protein molecule composition from the same

protein molecule when expressed in the cell line CHOdhfr- [ATCC No. CRL-9096]; and/or

- it has an increased activity which is at least 10% higher than the activity of at least one protein molecule composition from the same protein molecule when expressed in the cell line CHOdhfr- [ATCC No. CRL-9096]; and/or

- it has an improved homogeneity, which is an improved glycosylation homogeneity wherein said antibody molecule composition has a lower sialylation degree than the sialylation degree of at least one antibody molecule composition from the same antibody molecule when expressed in the cell line CHOdhfr-[ATCC No. CRL-9096]; and/or

- in case said protein molecule is an antibody molecule, it has an increased Fc-mediated cellular cytotoxicity which is at least 2 times higher than the Fc-mediated cellular cytotoxicity of at least one antibody molecule composition from the same antibody molecule when expressed in the cell line CHOdhfr-[ATCC No. CRL-9096]; and/or

- in case said protein molecule is an antibody molecule, it has an increased antigen mediated or Fc-mediated binding which is at least 20%, prerfarbly 30 or 50% higher than the binding of at least one antibody molecule composition from the same antibody molecule when expressed in the cell line CHOdhfr-[ATCC No. CRL-9096].

29. A protein or protein molecule composition according to at least one of the claims 26 to 28, wherein said composition comprises at least one antibody molecule, binding a MUC1 epitope, comprising the amino acid sequence DTR of the extracellular tandem repeat region.

30. A protein or protein molecule composition according to claim 29, wherein said antibody binds the TA- MUC1 epitope, comprising the amino acid sequence DTR, wherein the T is glycosylated.

31. Antibody or antibody molecule composition according to claim 30, wherein said antibody binds the glycosylated epitope with a higher affinity than the non-glycosylated epitope or does not bind the non-glycosylated epitope.

32. Antibody or antibody molecule composition according to claim 30 or 31, wherein said antibody is selected from

- the antibody PankoMab or a variant thereof, competitively binding the same TA – MUC 1 epitope as PankoMab;

- the antibody Panko 1 or a variant thereof, competitively binding the same TA – MUC 1 epitope as Panko 1;

- the antibody Panko 2 or a variant thereof, competitively binding the same TA – MUC 1 epitope as Panko 2.

33. Antibody or antibody molecule composition according to one of the claims 26 to 32 in particular claim 32, wherein said antibody has at least one of the following glycosylation characteristics:

(a) it has an increased sialylation degree with at least a 15% higher amount of N-acetylneuraminic acid on the total carbohydrate structures or on the carbohydrate structures at one particular glycosylation site of the antibody molecule of the antibody molecules in said antibody molecule composition than the same amount of antibody molecules of at least one antibody molecule composition of the same antibody molecule isolated from CHOdhfr- [ATCC No. CRL-9096] when expressed therein;

(b) it has a higher galactosylation degree with at least a 5% higher amount of G2 structures on the total carbohydrate structures or on the carbohydrate structures at one particular glycosylation site of the antibody molecule of the antibody molecules in said antibody molecule composition than the same amount of antibody molecules of at least one antibody molecule composition of the same antibody molecule isolated from CHOdhfr- [ATCC No. CRL-9096] when expressed therein;

(c) it comprises bisecGlcNAc.

34. Antibody or antibody molecule composition according to one of the claims 26 to 33 in particular claim 33, wherein the glycosylation pattern results in the following activity pattern:

(a) a CDC activity which is more than 15% higher than the activity of the same antibody expressed in CHO cells;

(b) a serum half life which is elongated by factor 2 compared to an antibody which carries no or a low degree of detectable sialylation;

(c) it has an increased Fc-mediated cellular cytotoxicity which is at least 2 times higher than the Fc-mediated cellular cytotoxicity of at least one antibody molecule composition from the same antibody molecule when expressed in the cell line CHOdhfr- [ATCC No. CRL-9096].

35. Antibody or antibody molecule composition according to at least one of the claims 29 to 34, wherein said antibody is selected from the following group consisting of:

(a) the PankoMab antibody or a variant thereof, having

(i) an increased ADCC activity which is at least 2 or at least 4 fold higher than the activity of the antibody molecule composition from the same antibody molecule expressed in the cell line CHOdhfr- [ATCC No. CRL-9096]; and/or

(ii) an increased CDC activity which is at least 2 fold higher than the activity of the antibody molecule composition from the same antibody molecule expressed in the cell line CHOdhfr- [ATCC No. CRL-9096]; and/or

(iii) a higher antigen binding activity that is at least 20%, preferably 30% or 40% higher than the activity of the antibody molecule composition from the same antibody molecule expressed in the cell line CHOdhfr- [ATCC No. CRL-9096]; and/or

(iv) an amount of G2 structures on the total carbohydrate structures or on the carbohydrate structures at one particular glycosylation site of the antibody molecule of said antibody molecules in said antibody molecule composition which is at least 50% higher compared to the same amount of antibody molecules in at least one antibody molecule composition of the same antibody molecule isolated from CHOdhfr- [ATCC No. CRL-9096] when expressed therein; and/or

(v) an amount of bisectingGlcNAc structures on the total carbohydrate structures or on the carbohydrate structures at one particular glycosylation site of the protein molecule of said antibody molecules in said antibody molecule composition which is at least 20% higher compared to the same amount of antibody molecules in at least one antibody molecule composition of the same antibody molecule isolated from CHOdhfr- [ATCC No. CRL-9096] when expressed therein

wherein said PankoMab molecule composition is obtainable at a higher yield by producing it in the host cell NM-F9 compared to a PankoMab molecule composition isolated from CHOdhfr- [ATCC No. CRL-9096] when expressed therein;

(b) the PankoMab antibody or a variant thereof, having

(i) an increased ADCC activity which is at least 3 fold higher than the activity of the antibody molecule composition from the same antibody molecule expressed in the cell line CHOdhfr- [ATCC No. CRL-9096]; and/or

(ii) an increased CDC activity which is at least 20%, preferably 30% or 40% higher than the activity of the antibody molecule composition from the same antibody molecule expressed in the cell line CHOdhfr- [ATCC No. CRL-9096]; and/or

(iii) detectable 2-6 NeuNAc and/or

(iv) a serum half-life which is preferably more than at least 1,5 times prolonged compared to an antibody molecule composition of the same antibody molecule isolated from NM-F9 when expressed therein; and/or

(v) an amount of G2 structures on the total carbohydrate structures or on the carbohydrate structures at one particular glycosylation site of the antibody molecule of said antibody molecules in said antibody molecule composition which is at least 50% higher compared to the same amount of antibody molecules in at least one antibody molecule composition of the same antibody molecule isolated from CHOdhfr- [ATCC No. CRL-9096] when expressed therein; and/or

(vi) an amount of bisectingGlcNAc structures on the total carbohydrate structures or on the carbohydrate structures at one particular glycosylation site of the protein molecule of said antibody molecules in said antibody molecule composition which is at least 20% higher compared to the same amount of antibody molecules in at least one antibody molecule composition of the same antibody molecule isolated from CHOdhfr- [ATCC No. CRL-9096] when expressed therein;

wherein said PankoMab molecule composition is obtainable at a higher yield by producing it in the host cell NM-H9D8 compared to a PankoMab molecule composition isolated from CHOdhfr- [ATCC No. CRL-9096] when expressed therein;

(c) the Panko 2 antibody or a variant thereof, having

(i) an increased ADCC activity which is at least 4 fold higher than the activity of the antibody molecule composition from the same antibody molecule expressed in the cell line CHOdhfr- [ATCC No. CRL-9096]; and/or

(ii) detectable 2-6 NeuNAc and/or

(iii) a higher antigen binding activity that is at least 30%, preferably 40% or 50% higher than the activity of the antibody molecule composition from the same antibody molecule expressed in the cell line CHOdhfr- [ATCC No. CRL-9096];

wherein said Panko 2 molecule composition is obtainable by producing it in the host cell NM-H9D8;

(d) the Panko 2 antibody or a variant thereof, having

(i) an increased ADCC activity which is at least 4 fold higher than the activity of the antibody molecule composition from the same antibody molecule expressed in the cell line CHOdhfr- [ATCC No. CRL-9096], and/or

(ii) a higher antigen binding activity that is at least 30%, preferably 40% or 50% higher than the activity of the antibody molecule composition from the same antibody molecule expressed in the cell line CHOdhfr- [ATCC No. CRL-9096];

wherein said Panko 2 molecule composition is obtainable by producing it in the host cell GT-2x;

(e) the Panko 1 antibody or a variant thereof, having

(i) an increased ADCC activity which is at least 8 fold higher than the activity of the antibody molecule composition from the same antibody molecule expressed in the cell line CHOdhfr- [ATCC No. CRL-9096]; and/or

(ii) an amount of G2 structures on the total carbohydrate structures or on the carbohydrate structures at one particular glycosylation site of the antibody molecule of said antibody molecules in said antibody molecule composition which is at least 50% higher compared to the same amount of antibody molecules in at least one antibody molecule composition of the same antibody molecule isolated from CHOdhfr- [ATCC No. CRL-9096] when expressed therein; and/or

(iii) a higher amount of non-fucosylated structures on the total carbohydrate structures or on the carbohydrate structures at one particular glycosylation site of the antibody molecule of said antibody molecules in said antibody molecule composition which is at least 70% higher compared to the same amount of antibody molecules in at least one antibody molecule composition of the same antibody molecule isolated from CHOdhfr- [ATCC No. CRL-9096] when expressed therein;

wherein said Panko 1 molecule composition is obtainable by producing it in the host cell NM-H9D8-E6;

(f) the Panko 1 antibody or a variant thereof, having

(i) an increased ADCC activity which is at least 50% higher than the activity of the antibody molecule composition from the same antibody molecule expressed in the cell line CHOdhfr- [ATCC No. CRL-9096]; and/or

(ii) an amount of G2 structures on the total carbohydrate structures or on the carbohydrate structures at one particular glycosylation site of the antibody molecule of said antibody molecules in said antibody molecule composition which is at least 50% higher compared to the same amount of antibody molecules in at least one antibody molecule composition of the same antibody molecule isolated from CHOdhfr- [ATCC No. CRL-9096] when expressed therein; and/or

(iii) a higher amount of non-fucosylated structures on the total carbohydrate structures or on the carbohydrate structures at one particular glycosylation site of the antibody molecule of said antibody molecules in said antibody molecule composition which is at least 50% higher compared to the same amount of antibody molecules in at least one antibody molecule composition of the same antibody molecule isolated from CHOdhfr- [ATCC No. CRL-9096] when expressed therein;

wherein said Panko 1 molecule composition is obtainable by producing it in the host cell NM-H9D8.

36. An antibody according to at least one of the claims 26 to 34, which is the antibody cetuximab or a variant thereof, binding the same epitope as cetuximab.

37. A protein according to at least one of the claims 26 to 30, wherein said protein is FSH.

38. Protein according to claim 37, wherein said FSH comprises detectable 2-6 linked NeuNAc.

39. An immortalized human blood cell, which is preferably a host cell of human myeloid leukaemia origin for producing a protein and particularly an antibody composition according to at least one of the claims 26 to 38, comprising at least one nucleic acid encoding a protein molecule or at least one part thereof in an appropriate expression vector.

40. A host cell according to claim 39, comprising at least one nucleic acid encoding a protein molecule or at least one part thereof, and at least one nucleic acid comprising at least one nucleic acid sequence encoding at least one polypeptide of the group of sequence #1 to sequence #9.

41. A host cell according to claim 39 or 36, wherein the host cell is K562, NM-F9 [DSM ACC2606], NM-D4 [DSM ACC2605], NM-H9, H9, NM-H10, NM-E-2F9, NM-C-2F5, NM-H9D8, or NM-H9D8-E6, or a cell or cell line derived from anyone of said host cells, comprising at least one nucleic acid encoding a protein molecule or at least one part thereof, and at least one nucleic acid comprising at least one nucleic acid sequence encoding at least one polypeptide of the group of sequence #1 to sequence #9.

42. A host cell according to at least one of the claims 39 to 41 comprising at least one nucleic acid nucleic acid of claim 41 or 42.

43. A host cell of any of the claims 39 to 42, wherein the antibody molecule encoded is an antibody defined in claims 31 to 36.

44. A host cell of any of the claim 39 to 43, wherein the antibody molecule encoded is a chimearic or humanized antibody, in particular PankoMab, Panko 1, Panko 2 or Cetuximab, or a variant thereof, binding the same epitope.

45. A host cell of any of the claims 39 to 44, which grows and produces the antibody molecule composition under serum-free conditions.

46. A nucleic acid comprising
    (a) a sequence encoding an protein molecule or at least one part thereof, and
    (b) at least one sequence encoding a sequence from the group of sequence #1 to sequence #9.

47. A nucleic acid comprising
    (a) a sequence encoding an protein molecule or at least one part thereof, and
    (b) at least one sequence encoding a sequence from the group of sequence #1.

Claims

1. A method for producing a protein molecule composition, comprising

(a) introducing in a host cell which is an immortalized human blood cell at least one nucleic acid encoding at least a part of said protein; and
(b) culturing said host cell under conditions which permit the production of said protein molecule composition; and
(c) isolating said protein molecule composition;

wherein the host cell is selected from the group consisting of DSM ACC2858 (GT-2X), DSM ACC 2806 (NM-H9D8), DSM ACC 2807 (NM-H9D8-E6), DSM ACC 2856 (NM-H9D8-E6Q12) or a cell or cell line derived therefrom.

2. The method according to claim 1 for producing a protein molecule composition, preferably an antibody molecule composition, wherein said host cell is selected to produce a protein composition having at least one of the following glycosylation characteristics:

(i) it comprises no detectable NeuGc; and/or
(ii) it has a galactosylation degree on the total carbohydrate structures or on the carbohydrate structures at one particular glycosylation site of the protein molecule of the protein molecules in said protein molecule composition, that is increased compared to the same amount of protein molecules in at least one protein molecule composition of the same protein molecule isolated from ATCC No. CRL-9096 (CHOdhfr-) when expressed therein; and/or
(iii) it has an amount of G2 structures on the total carbohydrate structures or on the carbohydrate structures at one particular glycosylation site of the protein molecule of said protein molecules in said protein molecule composition which is at least 5% higher compared to the same amount of protein molecules in at least one protein molecule composition of the same protein molecule isolated from ATCC No. CRL-9096 (CHOdhfr-) when expressed therein; and/or
(iv) it has an amount of G0 structures on the total carbohydrate structures or on the carbohydrate structures at one particular glycosylation site of the protein molecule of said protein molecules in said protein molecule composition which is at least 5% lower compared to the same amount of protein molecules in at least one protein molecule composition of the same protein molecule isolated from ATCC No. CRL-9096 (CHOdhfr-) when expressed therein; and/or
(v) it comprises no detectable terminal Gal*alpha*1-3Gal; and/or
(vi) it comprises an amount of fucose on the total carbohydrate structures or on the carbohydrate structures at one particular glycosylation site of the protein molecule of said protein molecules in said protein molecule composition which is at least 5% less compared to the same amount of protein molecules in at least one protein molecule composition of the same protein molecule isolated from ATCC No. CRL-9096 (CHOdhfr-) when expressed therein; and/or
(vii) it comprises at least one carbohydrate structure containing bisecting GlcNAc; and/or
(viii) it has a sialylation pattern which is altered compared to the sialylation pattern of at least one protein molecule composition of the same protein molecule isolated from ATCC No. CRL-9096 (CHOdhfr-) when expressed therein,

and wherein the protein molecules have at least one of the glycosylation characteristics (i) to (viii).

3. The method according to claim 1 or 2, wherein said sialylation pattern is characterised by at least one of the following characteristics:

- it comprises alpha2-6 linked NeuNAc; and/or
- it has an increased sialylation degree with an amount of NeuNAc on the total carbohydrate structures or on the carbohydrate structures at one particular glycosylation site of the protein molecule of the protein molecules in said protein molecule composition which is at least 15% higher compared to the same amount of protein molecules in at least one protein molecule composition of the same protein molecule isolated from ATCC No. CRL-9096 (CHOdhfr-) when expressed therein, and/or
- it comprises at least 20% more charged N-glycosidically linked carbohydrate chains of the total carbohydrate units or of at least one particular carbohydrate chain at a particular glycosylation site of the protein molecule of the protein molecules in said protein molecule composition compared to the same amount of protein molecules in at least one protein molecule composition of the same protein molecule isolated from ATCC No. CRL-9096 (CHOdhfr-) when expressed therein.

4. The method according to at least one of the claims 1 to 3, wherein said host cell is selected to produce a glycoprotein, comprising

a) at least 10% carbohydrate structures of the total carbohydrate units or of at least one particular carbohydrate chain at a particular glycosylation site of the protein molecule of the protein molecules in said protein molecule composition, lacking fucose; and/or
b) at least 2% carbohydrate structures of the total carbohydrate units or of at least one particular carbohydrate chain at a particular glycosylation site of the protein molecule of the protein molecules in said protein molecule composition which contains bisecting GlcNAc; and/or
c) more than 35% G2 structures on the total carbohydrate structures or on the carbohydrate structures at one particular glycosylation site of the protein molecule in said protein molecule composition; and/or
d) it comprises less than 22% G0 structures on the total carbohydrate structures or on the carbohydrate structures at one particular glycosylation site of the protein molecule in said protein molecule composition.

5. The method according to at least one of the claims 1 to 4, wherein said protein molecule composition produced has at least one of the following characteristics:

- it has an increased activity and/or increased yield in particular compared to at least one protein molecule composition of the same protein molecule when expressed in the cell line ATCC No. CRL-9096 (CHOdhfr-);
- it has an improved homogeneity in particular compared to at least one protein molecule composition of the same protein molecule when expressed in the cell line ATCC No. CRL-9096 (CHOdhfr-);
- it has an increased average or maximum yield which is at least 10% higher than the yield of at least one protein molecule composition from the same protein molecule when expressed in the cell line ATCC No. CRL-9096 (CHOdhfr-); and/or
- it has an improved homogeneity, which is an improved glycosylation homogeneity compared to at least one protein molecule composition of the same protein molecule when expressed in the cell line ATCC No. CRL-9096 (CHOdhfr-);
- it has an increased activity compared to at least one protein molecule composition of the same protein molecule when expressed in the cell line ATCC No. CRL-9096 (CHOdhfr-);
- in case said protein molecule is an antibody molecule, it has an increased Fc-mediated cellular cytotoxicity which is at least 2 times higher than the Fc-mediated cellular cytotoxicity of at least one antibody molecule composition from the same antibody molecule when expressed in the cell line ATCC No. CRL-9096 (CHOdhfr-); and/or
- in case said protein molecule is an antibody molecule, it has an increased antigen mediated or Fc-mediated binding which is at least 15%, preferably 20%, 25%, 30%, 35%, 40%, 45% and preferably 50% higher than the binding of at least one antibody molecule composition from the same antibody molecule when expressed in the cell line ATCC No. CRL-9096 (CHOdhfr-).

6. The method according to at least one of the claims 1 to 5, wherein the host cell is selected to produce a protein composition comprising protein molecules having the following characteristic glycosylation combinations:

(a)

- it comprises no detectable NeuGc
- it comprises no detectable Galalpha1-3Gal
- it comprises a galactosylation pattern as defined in claim 2
- it has a fucose content as defined in claim 2
- it comprises bisecGlcNAc
- it comprises an increased amount of sialic acid compared to a protein composition of the same protein molecule when expressed in the cell line ATCC No. CRL-9096 (CHOdhfr-) or compared to a sialylation deficient cell line such as DSM ACC2606 (NM-F9) and DSM ACC2605 (NM-D4); or

(b)

- it comprises no detectable NeuGc
- it comprises no detectable Galalpha1-3Gal
- it comprises a galactosylation pattern as defined in claim 2
- it has a fucose content as defined in claim 2
- it comprises bisecGlcNAc
- it comprises 2-6 NeuNAc

7. The method according to any one of claims 1 to 6, wherein the protein is selected from the group consisting of the group of cytokines and their receptors, such as the tumor necrosis factors TNF-alpha and TNF-beta; renin; human growth hormone and bovine growth hormone; growth hormone releasing factor; parathyroid hormone; thyroid stimulating hormone; lipoproteins; alpha-1-antitrypsin; insulin A-chain and B-chain; gonadotrophins, such as follicle stimulating hormone (FSH), luteinizing hormone (LH), thyrotrophin, and human chorionic gonadotrophin (hCG); calcitonin; glucagon; clotting factors such as factor VIIIC, factor IX, factor VII, tissue factor and von Willebrands factor; anti-clotting factors such as protein C; atrial natriuretic factor; lung surfactant; plasminogen activators, such as urokinase, human urine and tissue-type plasminogen activator; bombesin; thrombin; hemopoietic growth factor; enkephalinase; human macrophage inflammatory protein; a serum albumin such as human serum albumin; mullerian-inhibiting substance; relaxin A-chain and B-chain; prorelaxin; mouse gonadotropin-associated peptide; vascular endothelial growth factor; receptors for hormones or growth factors; integrin; protein A and D; rheumatoid factors; neurotrophic factors such as bone-derived neurotrophic factor, neurotrophin-3, neurotrophin-4, neurotrophin-5, neurotrophin-6 and nerve growth factor-beta; platelet-derived growth factor; fibroblast growth factors; epidermal growth factor; transforming growth factor such as TGF-alpha and TGF-beta; insulin-like growth factor-I and -II; insulin-like growth factor binding proteins; CD proteins such as CD-3, CD-4, CD-8 and CD-19; erythropoietin (EPO); osteoinductive factors; immunotoxins; bone morphogenetic proteins; interferons such as interferon-alpha, interferon-beta, and interferon-gamma; colony stimulating factors (CSF's), such as M-CSF, GM-CSF and G-CSF; interleukins (IL's), such as IL-1 to IL-12; superoxide dismutase; T-cell receptors; surface membrane proteins; decay accelerating factor; antibodies and immunoadhesins; glycophorin A; MUC1.

8. The method according to claim 7, wherein the protein is follicle stimulating hormone (FSH).

9. The method according to claim 8, wherein the protein is follicle stimulating hormone (FSH) and wherein the host cell is DSM ACC 2806 (NM-H9D8).

10. The method according to at least one of the claims 1 to 6, wherein said protein is an antibody or a fragment thereof.

11. The method according to claim 10, wherein the antibody is selected from the group consisting of antibodies against ganglioside GD3, antibodies against human interleukin-5 receptor alpha-chain, antibodies against HER2, antibodies against CC chemokine receptor 4, antibodies against CD20, antibodies against CD22, antibodies against neuroblastoma, antibodies against MUC1, antibodies against epidermal growth factor receptor; in particular an antibody selected from the group consisting of Pankomab, Muromomab, Daclizumab, Basiliximab, Abciximab, Rituximab, Herceptin, Gemtuzumab, Alemtuzumab, Ibritumomab, Cetuximab, Bevacizumab, Tositumomab, Pavlizumab, Infliximab, Eculizumab, Epratuzumab, Omalizumab, Efalizumab, Adalimumab, OKT3, anti-CC chemokine receptor 4 antibody KM2160, and anti-neuroblastoma antibody chCE7.

12. The method according to claim 11, wherein the antibody is selected from the group consisting of an antibody against MUC1; an antibody against HER2; and an antibody against EGFR.

13. The method according to claim 11, wherein the antibody is Cetuximab or a variant thereof, binding the same epitope as Cetuximab.

14. The method according to claim 13, wherein the antibody is Cetuximab and wherein the host cell is DSM ACC 2856 (NM-H9D8-E6Q12).

15. The method according to claim 11, wherein the antibody is Pankomab or a variant thereof, competitively binding the same TA-MUC1 epitope as PankoMab.

16. The method according to claim 15, wherein the antibody is Pankomab and wherein the host cell is DSM ACC 2806 (NM-H9D8).

17. The method according to claim 11, wherein the antibody is Herceptin.

18. The method according to any one of claims 1 to 17, wherein said protein

(i) is fused to another peptide or polypeptide sequence such as a linker, an activating molecule or a toxin; or
(ii) is an antibody fragment fused to another protein sequence, in particular a protein sequence selected from the group consisting of cytokines, co-stimulatory factors, toxins, antibody fragments from other antibodies, multimerisation sequences, and sequences for detection, purification, secretion or stabilization such as tags,

localization signals or linkers; or
(iii) is an antibody or antibody fragment coupled to an effector molecule which mediates a therapeutic effect, such as an immune effector molecule, a toxin or a radioisotope.

19. An antibody molecule composition obtainable by a production method comprising the steps of

(a) introducing in a host cell of human myeloid leukeamia origin at least one nucleic acid encoding at least a part of said antibody; and
(b)culturing said host cell under conditions which permit the production of said antibody molecule composition; and
(c) isolating said antibody molecule composition;

wherein the host cell is selected from the group consisting of DSM ACC 2806 (NM-H9D8), DSM ACC 2807 (NM-H9D8-E6) and DSM ACC 2856 (NM-H9D8-E6Q12); and
wherein the antibody molecule composition

- comprises no detectable NeuGc;
- comprises α2,6-linked NeuNAc; and
- has an increased sialylation degree with an amount of NeuNAc on the total carbohydrate structures or on the carbohydrate structures at one particular glycosylation site of the antibody molecule of said antibody molecules in said antibody molecule composition which is at least 15% higher compared to the same amount of antibody molecules in at least one antibody molecule composition of the same antibody molecule isolated from ATCC No. CRL-9096 (CHOdhfr-) when expressed therein; and

wherein the antibody is a therapeutic whole antibody.

20. The antibody molecule composition according to claim 19, wherein the antibody molecule composition comprises at least 2%, preferably at least 5%, more preferably at least 10% and most preferably at least 15% carbohydrate structures of the total carbohydrate units or of at least one particular carbohydrate chain at a particular glycosylation site of an antibody molecule of the antibody molecules in said antibody molecule composition which contains bisecting GlcNAc.

21. The antibody molecule composition according to claim 19 or 20, wherein the antibody molecule composition has an increased sialylation degree with an amount of NeuNAc on the total carbohydrate structures or on the carbohydrate structures at one particular glycosylation site of the antibody molecule of said antibody molecules in said antibody molecule composition which is at least 20%, preferably at least 30% higher compared to the same amount of antibody molecules in at least one antibody molecule composition of the same antibody molecule isolated from ATCC No. CRL-9096 (CHOdhfr-) when expressed therein.

22. The antibody molecule composition according to any one of claims 19 to 21, wherein the antibody molecule composition comprises at least 50%, preferably at least 60% and more preferably at least 70% carbohydrate structures of the total carbohydrate units or of at least one particular carbohydrate chain at a particular glycosylation site of an antibody molecule of the antibody molecules in said antibody molecule composition, lacking fucose.

23. The antibody molecule composition according to any one of claims 19 to 22, wherein the antibody molecule composition has a higher degree of sialylation than is reached in DSM ACC2606 (NM-F9) or DSM ACC2605 (NM-D4) cells; wherein the DSM ACC2606 (NM-F9) and DSM ACC2605 (NM-D4) cells only reach about 50 to 60% of the sialylation degree that is obtained with the host cell used in step (a) of the production method.

24. The antibody molecule composition according to any one of claims 19 to 23, wherein the antibody molecule composition comprises no detectable terminal Gal*alpha*1-3Gal.

25. The antibody molecule composition according to any one of claims 19 to 24 wherein the antibody is selected from the group consisting of antibodies against ganglioside GD3, antibodies against human interleukin-5 receptor alpha-chain, antibodies against HER2, antibodies against CC chemokine receptor 4, antibodies against CD20, antibodies against CD22, antibodies against neuroblastoma, antibodies against MUC1, antibodies against epidermal growth factor receptor; in particular an antibody selected from the group consisting of Pankomab, Muromomab, Daclizumab, Basiliximab, Abciximab, Rituximab, Herceptin, Gemtuzumab, Alemtuzumab, Ibritumomab, Cetuximab, Bevacizum-

ab, Tositumomab, Pavlizumab, Infliximab, Eculizumab, Epratuzumab, Omalizumab, Efalizumab, Adalimumab, OKT3, anti-CC chemokine receptor 4 antibody KM2160, and anti-neuroblastoma antibody chCE7.

26. The antibody molecule composition according to any one of claims 19 to 25, wherein the antibody is of the IgG class, preferably a human, humanized or chimeric IgG which comprises a human Fc region.

27. The antibody molecule composition according to any one of claims 19 to 26, comprising at least one glycoform of an antibody molecule with at least one carbohydrate chain attached to another glycosylation site of the antibody molecule than the amino acid Asn-297 in the second domain of the Fc region.

28. The antibody molecule composition according to any one of claims 19 to 27, wherein the antibody has at least one N-glycosylation site having the amino acid sequence Asn-Xaa-Ser/Thr, wherein Xaa can be any amino acid except Pro, and/or at least one O-glycosylation site in the sequence of the Fab region.

29. The antibody molecule composition according to any one of claims 15 to 28, comprising

(i) an antibody molecule which comprises at least one carbohydrate chain attached to another glycosylation site of the antibody molecule than the amino acid Asn-297 in the second domain of the Fc part, wherein the antibody composition has an extended serum-half life and/or bioavailability, when measured in at least one mammal such as mice, rats, or humans, than the antibody molecule composition of the same antibody molecule isolated from at least one of the cell lines CHO, CHOdhfr-, BHK, NSO, SP2/0, DSM ACC2606 (NM-F9), DSM ACC2605 (NM-D4), PerC.6 or mouse hybridoma when expressed therein; or
(ii) an antibody molecule which comprises at least one carbohydrate chain attached to at least one N-glycosylation site and/or at least one O-glycosylation site in a sequence of the Fab region of the antibody molecule, wherein the antibody composition has an extended serum-half life and/or bioavailability, when measured in at least one mammal such as mice, rats, or humans, than the antibody molecule composition of the same antibody molecule isolated from at least one of the cell lines CHO, CHOdhfr-, BHK, NSO, SP2/0, PerC.6 or mouse hybridoma when expressed therein.

30. The antibody molecule composition according to any one of claims 19 to 29, wherein the antibody

(i) is fused to another peptide or polypeptide sequence such as a linker, an activating molecule or a toxin; or
(ii) is coupled to an effector molecule which mediates a therapeutic effect, such as an immune effector molecule, a toxin or a radioisotope.

31. The antibody molecule composition according to any one of claims 19 to 30, wherein said composition has at least one of the following characteristics:

- it has a galactosylation degree of galactose, which is linked to GlcNAc, on the total carbohydrate structures or on the carbohydrate structures at one particular glycosylation site of the antibody molecule of the antibody molecules in said antibody molecule composition, that is increased compared to the same amount of antibody molecules in at least one antibody molecule composition of the same antibody molecule isolated from ATCC No. CRL-9096 (CHOdhfr-) when expressed therein; and/or
- it has an amount of G2 structures on the total carbohydrate structures or on the carbohydrate structures at one particular glycosylation site of the antibody molecule of said antibody molecules in said antibody molecule composition which is at least 5% higher compared to the same amount of antibody molecules in at least one antibody molecule composition of the same antibody molecule isolated from ATCC No. CRL-9096 (CHOdhfr-) when expressed therein; and/or
- it has an amount of G0 structures on the total carbohydrate structures or on the carbohydrate structures at one particular glycosylation site of the antibody molecule of said antibody molecules in said antibody molecule composition which is at least 5% lower compared to the same amount of antibody molecules in at least one antibody molecule composition of the same antibody molecule isolated from ATCC No. CRL-9096 (CHOdhfr-) when expressed therein; and/or
- it comprises an amount of fucose on the total carbohydrate structures or on the carbohydrate structures at one particular glycosylation site of the antibody molecule of said antibody molecules in said antibody molecule composition which is at least 5% less compared to the same amount of antibody molecules in at least one antibody molecule composition of the same antibody molecule isolated from ATCC No. CRL-9096 (CHOdhfr-) when expressed therein.

- it comprises at least 20% more charged N-glycosidically linked carbohydrate chains of the total carbohydrate units or of at least one particular carbohydrate chain at a particular glycosylation site of the antibody molecule of the antibody molecules in said antibody molecule composition compared to the same amount of antibody molecules in at least one antibody molecule composition of the same antibody molecule isolated from ATCC No. CRL-9096 (CHOdhfr-) when expressed therein, and/or
- it comprises more than 35% G2 structures on the total carbohydrate structures or on the carbohydrate structures at one particular glycosylation site of an antibody molecule of the antibody molecules in said antibody composition; and/or
- it comprises less than 22% GO structures on the total carbohydrate structures or on the carbohydrate structures at one particular glycosylation site of an antibody molecule of the antibody molecules in said antibody composition; and/or
- it has an increased activity and/or increased yield compared to at least one antibody molecule composition of the same antibody molecule when expressed in the cell line ATCC No. CRL-9096 (CHOdhfr-); and/or
- it has an improved homogeneity compared to at least one antibody molecule composition of the same antibody molecule when expressed in the cell line ATCC No. CRL-9096 (CHOdhfr-); and/or
- it has an increased activity which is at least 10% higher than the activity of at least one antibody molecule composition from the same antibody molecule when expressed in the cell line ATCC No. CRL-9096 (CHOdhfr-); and/or
- it has an increased Fc-mediated cellular cytotoxicity which is at least 2 times higher than the Fc-mediated cellular cytotoxicity of at least one antibody molecule composition from the same antibody molecule when expressed in the cell line ATCC No. CRL-9096 (CHOdhfr-); and/or
- it has an increased antigen mediated or Fc-mediated binding which is at least 50% higher than the binding of at least one antibody molecule composition from the same antibody molecule when expressed in the cell line ATCC No. CRL-9096 (CHOdhfr-); and/or
- it has ADCC and/or CDC activity.

32. The antibody molecule composition according to any one of claims 19 to 31, wherein said antibody molecule recognizes cancer, tumor or metastasis, or at least one cancer cell or tumor cell in at least one human.

33. The antibody molecule composition according to at least one of the claims 19 to 32, wherein said composition comprises at least one antibody molecule, having one or more of the following characteristics:

a) it binds a MUC1 epitope, comprising the amino acid sequence DTR of the extracellular tandem repeat region; and/or
b) the antibody according to (a) which binds the TA-MUC1 epitope, comprising the amino acid sequence DTR, wherein the T is glycosylated; and/or
c) the antibody according to (b) which binds the glycosylated epitope with a higher affinity than the non-glycosylated epitope; and/or
d) the antibody according to (b) or (c) which is selected from

- the antibody PankoMab or a variant thereof, competitively binding the same TA-MUC1 epitope as PankoMab;
- the antibody Panko 1 or a variant thereof, competitively binding the same TA-MUC1 epitope as Panko 1;
- the antibody Panko 2 or a variant thereof, competitively binding the same TA-MUC1 epitope as Panko 2.

34. The antibody molecule composition according to one of the claims 19 to 33, wherein said antibody has a higher galactosylation degree with at least a 5% higher amount of G2 structures on the total carbohydrate structures or on the carbohydrate structures at one particular glycosylation site of the antibody molecule of the antibody molecules in said antibody molecule composition than the same amount of antibody molecules of at least one antibody molecule composition of the same antibody molecule isolated from ATCC No. CRL-9096 (CHOdhfr-) when expressed therein.

35. The antibody molecule composition according to one of the claims 19 to 34, wherein the glycosylation pattern results in the following activity pattern:

(a) a CDC activity which is more than 15% higher than the activity of the same antibody expressed in CHO cells;
(b) a serum half life which is elongated by factor 2 compared to an antibody which carries no or a low degree of detectable sialylation;
(c) it has an increased Fc-mediated cellular cytotoxicity which is at least 2 times higher than the Fc-mediated

cellular cytotoxicity of at least one antibody molecule composition from the same antibody molecule when expressed in the cell line ATCC No. CRL-9096 (CHOdhfr-).

36. The antibody molecule composition according to at least one of the claims 19 to 35, wherein said antibody is selected from the following group consisting of:

(a) the PankoMab antibody or a variant thereof, having

(i) an increased ADCC activity which is at least 3 fold higher than the activity of the antibody molecule composition from the same antibody molecule expressed in the cell line ATCC No. CRL-9096 (CHOdhfr-); and/or
(ii) an increased CDC activity which is at least 20%, preferably 30% or 40% higher than the activity of the antibody molecule composition from the same antibody molecule expressed in the cell line ATCC No. CRL-9096 (CHOdhfr-); and/or
(iii) detectable 2-6 NeuNAc and/or
(iv) a prolonged serum half-life compared to an antibody molecule composition of the same antibody molecule isolated from NM-Fwhen expressed therein; and/or
(v) an amount of G2 structures on the total carbohydrate structures or on the carbohydrate structures at one particular glycosylation site of the antibody molecule of said antibody molecules in said antibody molecule composition which is at least 50% higher compared to the same amount of antibody molecules in at least one antibody molecule composition of the same antibody molecule isolated from ATCC No. CRL-9096 (CHOdhfr-) when expressed therein; and/or
(vi) an amount of bisectingGlcNAc structures on the total carbohydrate structures or on the carbohydrate structures at one particular glycosylation site of the antibody molecule of said antibody molecules in said antibody molecule composition which is at least 20% higher compared to the same amount of antibody molecules in at least one antibody molecule composition of the same antibody molecule isolated from ATCC No. CRL-9096 (CHOdhfr-) when expressed therein;

wherein said PankoMab molecule composition is obtainable at a higher yield by producing it in the host cell DSM ACC 2806 (NM-H9D8) compared to a PankoMab molecule composition isolated from ATCC No. CRL-9096 (CHOdhfr-) when expressed therein;
(b) the Panko 2 antibody or a variant thereof, having

(i) an increased ADCC activity which is at least 4 fold higher than the activity of the antibody molecule composition from the same antibody molecule expressed in the cell line ATCC No. CRL-9096 (CHOdhfr-); and/or
(ii) detectable 2-6 NeuNAc and/or
(iii) a higher antigen binding activity that is at least 30%, preferably 40% or 50% higher than the activity of the antibody molecule composition from the same antibody molecule expressed in the cell line ATCC No. CRL-9096 (CHOdhfr-);

wherein said Panko 2 molecule composition is obtainable by producing it in the host cell DSM ACC 2806 (NM-H9D8);
(c) the Panko 1 antibody or a variant thereof, having

(i) an increased ADCC activity which is at least 8 fold higher than the activity of the antibody molecule composition from the same antibody molecule expressed in the cell line ATCC No. CRL-9096 (CHOdhfr-); and/or
(ii) an amount of G2 structures on the total carbohydrate structures or on the carbohydrate structures at one particular glycosylation site of the antibody molecule of said antibody molecules in said antibody molecule composition which is at least 50% higher compared to the same amount of antibody molecules in at least one antibody molecule composition of the same antibody molecule isolated from ATCC No. CRL-9096 (CHOdhfr-) when expressed therein; and/or
(iii) a higher amount of non-fucosylated structures on the total carbohydrate structures or on the carbohydrate structures at one particular glycosylation site of the antibody molecule of said antibody molecules in said antibody molecule composition which is at least 70% higher compared to the same amount of antibody molecules in at least one antibody molecule composition of the same antibody molecule isolated from ATCC No. CRL-9096 (CHOdhfr-) when expressed therein;

wherein said Panko 1 molecule composition is obtainable by producing it in the host cell DSM ACC 2807 (NM-H9D8-E6);

(d) the Panko 1 antibody or a variant thereof, having

(i) an increased ADCC activity which is at least 50% higher than the activity of the antibody molecule composition from the same antibody molecule expressed in the cell line ATCC No. CRL-9096 (CHOdhfr-); and/or

(ii) an amount of G2 structures on the total carbohydrate structures or on the carbohydrate structures at one particular glycosylation site of the antibody molecule of said antibody molecules in said antibody molecule composition which is at least 50% higher compared to the same amount of antibody molecules in at least one antibody molecule composition of the same antibody molecule isolated from ATCC No. CRL-9096 (CHOdhfr-) when expressed therein; and/or

(iii) a higher amount of non-fucosylated structures on the total carbohydrate structures or on the carbohydrate structures at one particular glycosylation site of the antibody molecule of said antibody molecules in said antibody molecule composition which is at least 50% higher compared to the same amount of antibody molecules in at least one antibody molecule composition of the same antibody molecule isolated from ATCC No. CRL-9096 (CHOdhfr-) when expressed therein;

wherein said Panko 1 molecule composition is obtainable by producing it in the host cell DSM ACC 2806 (NM-H9D8).

37. The antibody molecule composition according to at least one of the claims 19 to 31, 34 and 35, wherein the antibody is an antibody against HER2, or against epidermal growth factor receptor (EGFR).

38. The antibody molecule composition according to claim 37, wherein the antibody is cetuximab or a variant thereof, binding the same epitope as cetuximab, or herceptin.

39. An immortalized human blood cell of myeloid leukaemia origin capable of producing an antibody molecule composition having the following glycosylation characteristics:

(i) it comprises no detectable NeuGc;

(ii) it comprises α2,6-linked NeuNAc;

(iii) it has an increased sialylation degree with an amount of NeuNAc on the total carbohydrate structures or on the carbohydrate structures at one particular glycosylation site of the antibody of said antibody molecules in said antibody molecule composition which is at least 15% higher compared to the same amount of antibody molecules in at least one antibody molecule composition of the same antibody molecule isolated from ATCC No. CRL-9096 (CHOdhfr-) when expressed therein; and

(iv) it comprises at least 50% carbohydrate structures of the total carbohydrate units or of at least one particular carbohydrate chain at a particular glycosylation site of an antibody molecule of the antibody molecules in said antibody molecule composition, lacking fucose;

wherein the antibody is a therapeutic whole antibody.

40. The immortalized human blood cell according to claim 39, capable of producing an antibody molecule composition having at least one of the following further glycosylation characteristics:

- it comprises at least 2%, preferably at least 5%, more preferably at least 10% and most preferably at least 15% carbohydrate structures of the total carbohydrate units or of at least one particular carbohydrate chain at a particular glycosylation site of an antibody molecule of the antibody molecules in said antibody molecule composition which contains bisecting GlcNAc;
- it has an increased sialylation degree with an amount of NeuNAc on the total carbohydrate structures or on the carbohydrate structures at one particular glycosylation site of the antibody molecule of said antibody molecules in said antibody molecule composition which is at least 20%, preferably at least 30% higher compared to the same amount of antibody molecules in at least one antibody molecule composition of the same antibody molecule isolated from ATCC No. CRL-9096 (CHOdhfr-) when expressed therein;
- it comprises at least 60%, preferably at least 70% carbohydrate structures of the total carbohydrate units or of at least one particular carbohydrate chain at a particular glycosylation site of an antibody molecule of the antibody molecules in said antibody molecule composition, lacking fucose; and/or

- it has a higher degree of sialylation than is reached in DSM ACC2606 (NM-F9) or DSM ACC2605 (NM-D4) cells; wherein the DSM ACC2606 (NM-F9) and DSM ACC2605 (NM-D4) cells only reach about 50 to 60% of the sialylation degree that is obtained with the immortalized human blood cell.

41. The immortalized human blood cell according to claim 39 or 40, being derived from the cell line ATCC CCL-243 (K652).

42. An immortalized human blood cell selected from the group consisting of DSM ACC2858 (GT-2X), DSM ACC 2806 (NM-H9D8), DSM ACC 2807 (NM-H9D8-E6), DSM ACC 2856 (NM-H9D8-E6Q12) or a cell or cell line derived therefrom.

43. Use of an immortalized human blood cell according to any one of claims 39 to 42, comprising at least one nucleic acid encoding a protein molecule or at least one part thereof in an appropriate expression vector for producing said protein or said part thereof.

44. A method for producing an antibody molecule composition, comprising

(a) introducing in a host cell which is an immortalized human blood cell of human myeloid leukeamia origin at least one nucleic acid encoding at least a part of said antibody; and
(b) culturing said host cell under conditions which permit the production of said antibody molecule composition; and
(c) isolating said antibody molecule composition;

wherein the host cell is selected to produce an antibody molecule composition having the following glycosylation characteristics:

- it comprises no detectable NeuGc;
- it comprises α2,6-linked NeuAc; and
- it has an increased sialylation degree with an amount of NeuNAc on the total carbohydrate structures or on the carbohydrate structures at one particular glycosylation site of the antibody of said antibody molecules in said antibody molecule composition which is at least 15% higher compared to the same amount of antibody molecules in at least one antibody molecule composition of the same antibody molecule isolated from ATCC No. CRL-9096 (CHOdhfr-) when expressed therein; and

wherein the antibody is a therapeutic whole antibody.

45. The method according to claim 44, wherein the host cell is selected from the group consisting of DSM ACC 2806 (NM-H9D8), DSM ACC 2807 (NM-H9D8-E6), DSM ACC 2856 (NM-H9D8-E6Q12) or a cell or cell line derived therefrom.

46. The method according to claim 44 or 45, wherein the host cell is selected to produce an antibody molecule composition having at least one of the following further glycosylation characteristics:

- it comprises at least 2%, preferably at least 5%, more preferably at least 10% and most preferably at least 15% carbohydrate structures of the total carbohydrate units or of at least one particular carbohydrate chain at a particular glycosylation site of an antibody molecule of the antibody molecules in said antibody molecule composition which contains bisecting GlcNAc;
- it has an increased sialylation degree with an amount of NeuNAc on the total carbohydrate structures or on the carbohydrate structures at one particular glycosylation site of the antibody molecule of said antibody molecules in said antibody molecule composition which is at least 20%, preferably at least 30% higher compared to the same amount of antibody molecules in at least one antibody molecule composition of the same antibody molecule isolated from ATCC No. CRL-9096 (CHOdhfr-) when expressed therein;
- it comprises at least 50%, preferably at least 60%, more preferably at least 70% carbohydrate structures of the total carbohydrate units or of at least one particular carbohydrate chain at a particular glycosylation site of an antibody molecule of the antibody molecules in said antibody molecule composition, lacking fucose; and/or
- it has a higher degree of sialylation than is reached in DSM ACC2606 (NM-F9) or DSM ACC2605 (NM-D4) cells; wherein the DSM ACC2606 (NM-F9) and DSM ACC2605 (NM-D4) cells only reach about 50 to 60% of the sialylation degree that is obtained with the host cell used in step (a) of the production method.

47. The method according to any one of claims 44 to 46, wherein the antibody is selected from the group consisting of

- an antibody against MUC1;
- an antibody against epidermal growth factor receptor;
- an antibody against HER2; and
- an antibody against CD20.

48. The method according to claim 47, wherein the antibody is selected from the group consisting of

(i) an antibody which binds the TA-MUC1 epitope comprising the amino acid sequence DTR, wherein the T is glycosylated, and which preferably binds the glycosylated epitope with a higher affinity than the non-glycosylated epitope, and/or preferably is selected from the group consisting of

- PankoMab or a variant thereof, competitively binding the same TA-MUC1 epitope as PankoMab;
- Panko 1 or a variant thereof, competitively binding the same TA-MUC1 epitope as Panko 1; and
- Panko 2 or a variant thereof, competitively binding the same TA-MUC1 epitope as Panko 2;

(ii) Cetuximab or a variant thereof, binding the same epitope as Cetuximab;
(iii) Herceptin; and
(iv) Rituximab.

49. The method according to any one of claims 44 to 48, wherein said host cell is selected to produce an antibody molecule composition having at least one of the characteristics according to any one of claims 2 to 6.

50. The method according to any one of claims 1 to 18 for producing an antibody molecule composition according to any one of claims 19 to 38.