WHAT IS CLAIMED IS:

1. A process for producing a polypeptide in a mammalian host cell expressing said polypeptide, comprising culturing the mammalian host cell in a production phase of the culture in a glutamine-free production culture medium containing asparagine.

2. The process of claim 1 wherein the asparagine is added at a concentration in the range of 2.5 mM to 15 mM.

3. The process of claim 1 wherein the asparagine is added at a concentration in the range of 7.5 mM to 10 mM.

4. The process of claim 1 wherein the asparagine is added at a concentration of 10 mM.

5. The process of claim 1 wherein the asparagine is added at a concentration of 10 mM.

6. The method of claim 1 wherein said recombinant host cell is an eukaryotic host cell.

7. The method of claim 6 wherein said eukaryotic host cell is a mammalian host cell.

8. The method of claim 7 wherein said mammalian host cell is a Chinese Hamster Ovary (CHO) cell.

9. The process of claim 86 wherein the mammalian host cell is a dhfr$^-$ CHO cell.

10. The process of claim 1 wherein the production medium is serum-free.

11. The process of claim 1 wherein the production culture medium comprises one or more ingredients selected from the group consisting of

1) an energy source;

2) essential amino acids;

3) vitamins;

4) free fatty acids; and

5) trace elements.

12. The process of claim 11 wherein the production culture medium additionally

comprises one or more ingredients selected from the group consisting of:

1) hormones and other growth factors;

2) salts and buffers; and

3) nucleosides.

13. The process of claim 1 wherein the production phase is a batch or fed batch culture phase.

14. The process of claim 1 further comprising the step of isolating said polypeptide.

15. The process of claim 14 further comprising determining one or more of cell viability, culture longevity, specific productivity and final recombinant protein titer following isolation.

16. The process of claim 15 wherein at least one of the cell viability, culture longevity, specific productivity and final recombinant protein titer is increased relative to the same polypeptide produced in a glutamine-containing production medium of the same composition.

17. The process of claim 1 wherein the polypeptide is a mammalian glycoprotein.

18. The process of claim 1 wherein the polypeptide is selected from the group consisting of antibodies, antibody fragments, and immunoadhesins.

19. The process of claim 18 wherein said antibody fragment is selected from the group consisting of Fab, Fab', F(ab')2, scFv, (scFv)2, dAb, complementarity determining region (CDR) fragments, linear antibodies, single-chain antibody molecules, minibodies, diabodies, and multispecific antibodies formed from antibody fragments.

20. The process of claim 18 wherein the antibody or antibody fragment is chimeric, humanized or human.

21. The method of claim 18 wherein said antibody or antibody fragment is a therapeutic antibody or a biologically functional fragment thereof.

22. The method of claim 21 wherein said therapeutic antibody is selected from the group consisting of anti-HER2 antibodies anti-CD20 antibodies; anti-IL-8 antibodies; anti-VEGF antibodies; anti-CD40 antibodies, anti-CD11a antibodies; anti-CD18 antibodies; anti-IgE antibodies; anti-Apo-2 receptor antibodies; anti-Tissue Factor (TF) antibodies; anti-human $\alpha 4\beta 7$

integrin antibodies; anti-EGFR antibodies; anti-CD3 antibodies; anti-CD25 antibodies; anti-CD4 antibodies; anti-CD52 antibodies; anti-Fc receptor antibodies; anti-carcinoembryonic antigen (CEA) antibodies; antibodies directed against breast epithelial cells; antibodies that bind to colon carcinoma cells; anti-CD38 antibodies; anti-CD33 antibodies; anti-CD22 antibodies; anti-EpCAM antibodies; anti-GpIIb/IIIa antibodies; anti-RSV antibodies; anti-CMV antibodies; anti-HIV antibodies; anti-hepatitis antibodies; anti-CA 125 antibodies; anti-αvβ3 antibodies; anti-human renal cell carcinoma antibodies; anti-human 17-1A antibodies; anti-human colorectal tumor antibodies; anti-human melanoma antibody R24 directed against GD3 ganglioside; anti-human squamous-cell carcinoma; and anti-human leukocyte antigen (HLA) antibodies, and anti-HLA DR antibodies.

23. The method of claim 21 wherein said therapeutic antibody is an antibody binding to a HER receptor, VEGF, IgE, CD20, CD11a, CD40, BR3 or DR5.

24. The method of claim 23 wherein said HER receptor is HER1 and/or HER2.

25. The method of claim 24 wherein the HER receptor is HER2.

26. The method of claim 25 wherein said therapeutic antibody comprises a heavy and/or light chain variable domain sequence selected from the group consisting of SEQ ID NOS: 16, 17, 18, and 19.

27. The method of claim 23 wherein said therapeutic antibody is an antibody that binds to CD20.

28. The method of claim 27 wherein said therapeutic antibody comprises a heavy and/or light chain variable domain sequence selected from the group consisting of SEQ ID NOS: 1 through 15.

29. The method of claim 23 wherein said therapeutic antibody is an antibody that binds to VEGF.

30. The method of claim 29 wherein said therapeutic antibody comprises a heavy and/or light chain variable domain sequence selected from the group consisting of SEQ ID NOS: 20 through 25.

31. The method of claim 23 wherein said therapeutic antibody is an antibody that binds CD11a.

32. The method of claim 31 wherein said therapeutic antibody comprises a heavy and/or light chain variable domain sequence selected from the group consisting of SEQ ID NOS: 26 through 29.

33. The method of claim 23 wherein said therapeutic antibody binds to a DR5 receptor.

34. The method of claim 33 wherein said therapeutic antibody is selected from the group consisting of Apomabs 1.1, 2.1, 3.1, 4.1, 5.1, 5.2, 5.3 , 6.1, 6.2, 6.3, 7.1, 7.2, 7.3,8.1, 8.3, 9.1, 1.2, 2.2, 3.2, 4.2, 5.2, 6.2, 7.2, 8.2, 9.2, 1.3, 2.2, 3.3, 4.3, 5.3, 6.3, 7.3, 8.3, 9.3, and 25.3.

35. The method of claim 33 wherein said therapeutic antibody is Apomab 8.3 or Apomab 7.3.

36. The method of claim 35 wherein said therapeutic antibody is Apomab 7.3.

37. The method of claim 23 wherein said therapeutic antibody is an anti-BR3 antibody or BR3-Fc immunoadhesin..

38. The method of claim 1 wherein said polypeptide is a therapeutic polypeptide.

39. The method of claim 38 wherein said therapeutic polypeptide is selected from the group consisting of a growth hormone, including human growth hormone and bovine growth hormone; growth hormone releasing factor; parathyroid hormone; thyroid stimulating hormone; lipoproteins; alpha-1-antitrypsin; insulin A-chain; insulin B-chain; proinsulin; follicle stimulating hormone; calcitonin; luteinizing hormone; glucagon; clotting factors such as factor VIIIC, factor IX, tissue factor, and von Willebrands factor; anti-clotting factors such as Protein C; atrial natriuretic factor; lung surfactant; a plasminogen activator, such as urokinase or human urine or tissue-type plasminogen activator (t-PA); bombesin; thrombin; hemopoietic growth factor; tumor necrosis factor-alpha and -beta; enkephalinase; RANTES (regulated on activation normally T-cell expressed and secreted); human macrophage inflammatory protein (MIP-1-alpha); a serum albumin such as human serum albumin; Muellerian-inhibiting substance; relaxin A-chain; relaxin B-chain; prorelaxin; mouse gonadotropin-associated peptide; a microbial protein, such as beta-lactamase; DNase; IgE; a cytotoxic T-lymphocyte associated antigen (CTLA), such as CTLA-4; inhibin; activin; vascular endothelial growth factor (VEGF); receptors for hormones or growth factors; Protein A or D; rheumatoid factors; a neurotrophic factor such as bone-derived neurotrophic factor (BDNF), neurotrophin-3, -4, -5, or -6 (NT-3, NT-4, NT-5, or NT-6), or a nerve growth factor such as NGF-β; platelet-derived growth factor

(PDGF); fibroblast growth factor such as aFGF and bFGF; epidermal growth factor (EGF); transforming growth factor (TGF) such as TGF-alpha and TGF-beta, including TGF-β1, TGF-β2, TGF-β3, TGF-β4, or TGF-β5; insulin-like growth factor-I and -II (IGF-I and IGF-II); des(1-3)-IGF-I (brain IGF-I), insulin-like growth factor binding proteins; CD proteins such as CD3, CD4, CD8, CD19, CD20, CD34, and CD40; erythropoietin; osteoinductive factors; immunotoxins; a bone morphogenetic protein (BMP); an interferon such as interferon-alpha, -beta, and -gamma; colony stimulating factors (CSFs), e.g., M-CSF, GM-CSF, and G-CSF; interleukins (ILs), e.g., IL-1 to IL-10; superoxide dismutase; T-cell receptors; surface membrane proteins; decay accelerating factor; viral antigen such as, for example, a portion of the AIDS envelope; transport proteins; homing receptors; addressins; regulatory proteins; integrins such as CD11a, CD11b, CD11c, CD18, an ICAM, VLA-4 and VCAM; a tumor associated antigen such as HER2, HER3 or HER4 receptor; and fragments of said polypeptides.

40. A ready-to-use glutamine-free cell culture medium for the production of a polypeptide in a production phase.

CLAIMS

1. A process for producing a polypeptide in a mammalian host cell expressing said polypeptide, comprising culturing the mammalian host cell in a production phase of the culture in a glutamine-free production culture medium containing asparagine, wherein the asparagine is added at a concentration in the range of 7.5 mM to 15 mM.

2. The process of claim 1 wherein the asparagine is added at a concentration in the range of 7.5 mM to 10 mM.

3. The process of claim 1 wherein said recombinant host cell is an eukaryotic host cell.

4. The process of claim 3 wherein said eukaryotic host cell is a Chinese Hamster Ovary (CHO) cell.

5. The process of claim 4 wherein the mammalian host cell is a dhfr−CHO cell.

6. The process of claim 1 wherein the production medium is serum-free.

7. The process of claim 1 wherein the production culture medium comprises one or more ingredients selected from the group consisting of

1) an energy source;
2) essential amino acids;
3) vitamins;
4) free fatty acids; and
5) trace elements.

8. The process of claim 7 wherein the production culture medium additionally comprises one or more ingredients selected from the group consisting of:

1) hormones and other growth factors;
2) salts and buffers; and
3) nucleosides.

9. The process of claim 1 wherein the production phase is a batch or fed batch culture phase.

10. The process of claim 1 further comprising the step of isolating said polypeptide.

11. The process of claim 10 further comprising determining one or more of cell viability, culture longevity, specific productivity and final recombinant protein titer following isolation.

12. The process of claim 11 wherein at least one of the cell viability, culture longevity, specific productivity and final recombinant protein titer is increased relative to the same polypeptide produced in a glutamine-containing production medium of the same composition.

13. The process of claim 1 wherein the polypeptide is a mammalian glycoprotein.

14. The process of claim 1 wherein the polypeptide is selected from the group consisting of antibodies, antibody fragments, and immunoadhesins.

15. The process of claim 14 wherein said antibody fragment is selected from the group consisting of Fab, Fab', F(ab')2, scFv, (scFv)2, dAb, complementarity determining region (CDR) fragments, linear antibodies, single-chain antibody molecules, minibodies, diabodies, and multispecific antibodies formed from antibody fragments.

16. The process of claim 14 wherein the antibody or antibody fragment is chimeric, humanized or human.

17. The process of claim 14 wherein said antibody or antibody fragment is a therapeutic antibody or a biologically functional fragment thereof.

18. The process of claim 17 wherein said therapeutic antibody is selected from the group consisting of anti-HER2 antibodies anti-CD20 antibodies; anti-IL-8 antibodies; anti-VEGF antibodies; anti-CD40 antibodies, anti-CD11a antibodies; anti-CD18 antibodies; anti-IgE antibodies; anti-Apo-2 receptor antibodies; anti-Tissue Factor (TF) antibodies; anti-human $\alpha 4\beta 7$ integrin antibodies; anti-EGFR antibodies; anti-CD3 antibodies; anti-CD25 antibodies; anti-CD4 antibodies; anti-CD52 antibodies; anti-Fc receptor antibodies; anti-carcinoembryonic antigen (CEA) antibodies; antibodies directed against breast epithelial cells; antibodies that bind to colon carcinoma cells; anti-CD38 antibodies; anti-CD33 antibodies; anti-CD22 antibodies; anti-EpCAM antibodies; anti-GpIIb/IIIa antibodies; anti-RSV antibodies; anti-CMV antibodies; anti-HIV antibodies; anti-hepatitis antibodies; anti-CA 125 antibodies; anti-$\alpha v\beta 3$ antibodies; anti-human renal cell carcinoma antibodies; anti-human 17-1A antibodies; anti-human colorectal tumor antibodies; anti-human melanoma antibody R24 directed against GD3 ganglioside; anti-human squamous-cell carcinoma; and anti-human leukocyte antigen (HLA) antibodies, and anti-HLA DR antibodies.

19. The process of claim 17 wherein said therapeutic antibody is an antibody binding to a HER receptor, VEGF, IgE, CD20, CD11a, CD40, BR3 or DR5.

20. The process of claim 19 wherein said therapeutic antibody binding to DR5 is selected from the group consisting of Apomabs 1.1, 2.1, 3.1, 4.1, 5.1, 5.2, 5.3, 6.1, 6.2, 6.3, 7.1, 7.2, 7.3, 8.1, 8.3, 9.1, 1.2, 2.2, 3.2, 4.2, 5.2, 6.2, 7.2, 8.2, 9.2, 1.3, 2.2, 3.3, 4.3, 5.3, 6.3, 7.3, 8.3, 9.3, and 25.3.

21. The process of claim 19 wherein said therapeutic antibody is an anti-BR3 antibody.

22. The process of claim 14 wherein said immunadhesin is a BR3-Fc immunoadhesin.

23. The process of claim 1 wherein said polypeptide is a therapeutic polypeptide.

24. The process of claim 23 wherein said therapeutic polypeptide is selected from the group consisting of a growth hormone, including human growth hormone and bovine growth hormone;

growth hormone releasing factor; parathyroid hormone; thyroid stimulating hormone; lipoproteins; alpha-1-antitrypsin; insulin A-chain; insulin B-chain; proinsulin; follicle stimulating hormone; calcitonin; luteinizing hormone; glucagon; clotting factors such as factor VIIIC, factor IX, tissue factor, and von Willebrands factor; anti-clotting factors such as Protein C; atrial natriuretic factor; lung surfactant; a plasminogen activator, such as urokinase or human urine or tissue-type plasminogen activator (t-PA); bombesin; thrombin; hemopoietic growth factor; tumor necrosis factor-alpha and -beta; enkephalinase; RANTES (regulated on activation normally T-cell expressed and secreted); human macrophage inflammatory protein (MIP-1-alpha); a serum albumin such as human serum albumin; Muellerian-inhibiting substance; relaxin A-chain; relaxin B-chain; prorelaxin; mouse gonadotropin-associated peptide; a microbial protein, such as beta-lactamase; DNase; IgE; a cytotoxic T-lymphocyte associated antigen (CTLA), such as CTLA-4; inhibin; activin; vascular endothelial growth factor (VEGF); receptors for hormones or growth factors; Protein A or D; rheumatoid factors; a neurotrophic factor such as bone-derived neurotrophic factor (BDNF), neurotrophin-3, -4, -5, or -6 (NT-3, NT-4, NT-5, or NT-6), or a nerve growth factor such as NGF-β; platelet-derived growth factor (PDGF); fibroblast growth factor such as aFGF and bFGF; epidermal growth factor (EGF); transforming growth factor (TGF) such as TGF-alpha and TGF-beta, including TGF-β1, TGF-β2, TGF-β3, TGF-β4, or TGF-β5; insulin-like growth factor-I and -II (IGF-I and IGF-II); des(1-3)-IGF-I (brain IGF-I), insulin-like growth factor binding proteins; CD proteins such as CD3, CD4, CD8, CD19, CD20, CD34, and CD40; erythropoietin; osteoinductive factors; immunotoxins; a bone morphogenetic protein (BMP); an interferon such as interferon-alpha, -beta, and -gamma; colony stimulating factors (CSFs), e.g., M-CSF, GM-CSF, and G-CSF; interleukins (ILs), e.g., IL-1 to IL-10; superoxide dismutase; T-cell receptors; surface membrane proteins; decay accelerating factor; viral antigen such as, for example, a portion of the AIDS envelope; transport proteins; homing receptors; addressins; regulatory proteins; integrins such as CD11a, CD11b, CD11c, CD18, an ICAM, VLA-4 and VCAM; a tumor associated antigen such as HER2, HER3 or HER4 receptor; and fragments of said polypeptides.

25. A ready-to-use glutamine-free cell culture medium containing asparagine for the production of a polypeptide in a production phase, wherein the asparagine is at a concentration in the range of 7.5 mM to 15 mM.