MODULATED LYSINE VARIANT SPECIES COMPOSITIONS AND METHODS FOR PRODUCING AND USING THE SAME

RELATED APPLICATIONS

This application claims priority to International Patent Application Serial No. PCT/US2013/031389, filed on March 14, 2013, the contents of which is hereby incorporated herein by reference in its entirety.

BACKGROUND OF THE INVENTION

Large-scale production of antibodies for biopharmaceutical applications involves the use of cell cultures that are known to produce antibodies, and antigen-binding portions thereof, exhibiting varying levels of heterogeneity, which may lead to either decreased product efficacy and stability or just the opposite depending upon the nature of the heterogeneity. One source of antibody heterogeneity involves C-terminal lysine residues, such as those found on the heavy chains of antibody molecules. For example, C-terminal lysines can potentially be present on both the heavy chains of an antibody (Lys 2), on either one of the heavy chains (Lys 1), or neither of them (Lys 0). Since lysine can carry a positive charge, antibodies lacking the basic C-terminal lysine(s) differ in their charge state from ones that contain the lysine, so that the distribution of lysine variants (%Lys 0, %Lys 1, %Lys 2 of the total lysine sum) can be detected using ion-exchange chromatographic methods, for example, using a ProPac WCX-10 Weak Cation-Exchange column for high-resolution separation of protein isoforms (Dionex, CA), or other methods known in the art, and subsequently quantified.

C-terminal lysine heterogeneity is commonly observed in biopharmaceutical antibody and protein compositions. However, the development of compositions comprising antibodies, or antigen-binding portions thereof, with lower or higher levels of certain lysine variants is an important, need in the biopharmaceutical industry.

SUMMARY

In one aspect, there is provided a method for producing a modulated lysine variant species composition comprising an antibody, or antigen-binding portion thereof, comprising implementing a change to a cell culture condition used to produce said modulated lysine variant species composition, wherein the change in the cell culture condition results in a decrease in the amount of a lysine variant species that lacks a C-terminal lysine (Lys 0) as compared to the amount of Lys 0 in a control composition comprising an antibody, or antigen-binding portion thereof, produced without the change to the cell culture condition.

In one aspect, there is provided a composition comprising human anti-TNFα antibodies, wherein said human anti-TNFα antibodies comprise C-terminal lysine variant species, wherein less than 65% of said lysine variant species in said composition have zero C-terminal lysines (Lys 0), and wherein said human anti-TNFα antibodies comprise a light chain variable region (LCVR) having a CDR1 domain comprising the amino acid sequence of SEQ ID NO:7, a CDR2 domain comprising the amino acid sequence of SEQ ID NO:5, and a CDR3 domain comprising the amino acid sequence of SEQ ID NO:3; and a heavy chain variable region (HCVR) having a CDR1 domain comprising the amino acid sequence of SEQ ID NO:8, a CDR2 domain comprising the amino acid sequence of SEQ ID NO:6, and a CDR3 domain comprising the amino acid sequence of SEQ ID NO:4.

In one aspect, there is provided a composition comprising human anti-TNFα antibodies, wherein said human anti-TNFα antibodies comprise C-terminal lysine variant species, wherein greater than 35% of said lysine variant species in said composition have one C-terminal lysine (Lys 1) or two C terminal lysines (Lys 2), and wherein said human anti-TNFα antibodies comprise a light chain variable region (LCVR) having a CDR1 domain comprising the amino acid sequence of SEQ ID NO:7, a CDR2 domain comprising the amino acid sequence of SEQ ID NO:5, and a CDR3 domain comprising the amino acid sequence of SEQ ID NO:3; and a heavy chain variable region (HCVR) having a CDR1 domain comprising the amino acid sequence of SEQ ID NO:8, a CDR2 domain comprising the amino acid sequence of SEQ ID NO:6, and a CDR3 domain comprising the amino acid sequence of SEQ ID NO:4.

In one aspect, there is provided a pharmaceutical formulation comprising the composition as disclosed herein and a pharmaceutically acceptable carrier.

In one aspect, there is provided the use of the formulation as disclosed herein in the manufacture of a medicament for treating a subject having a disease or disorder in which TNFα activity is detrimental, wherein a therapeutically effective amount of the formulation is to be administered to the subject, thereby treating the TNFα-associated disease or disorder.

In one aspect, there is provided a method for producing the composition as disclosed herein, comprising culturing cells expressing said human anti-TNFα antibodies in a culture media.

The present disclosure is based on the identification and optimization of processes for the production of antibodies or antigen-binding portions thereof (*e.g.,* cell culture processes), which result in the production of compositions comprising antibodies, or antigen-binding portions thereof, that comprise modified distributions of C-terminal lysine variants. C-

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C-terminal lysine heterogeneity is commonly observed in biopharmaceutical antibody and protein compositions. However, the development of compositions comprising antibodies, or antigen-binding portions thereof, with lower or higher levels of certain lysine variants is an important, need in the biopharmaceutical industry.

SUMMARY

In one aspect, there is provided a composition comprising a human anti-TNFα antibody, wherein less than 65% of the lysine variant species in said composition have zero C-terminal lysines (Lys 0),

and wherein the human anti-TNFα antibody comprises a light chain variable region (LCVR) having a CDR1 domain comprising the amino acid sequence of SEQ ID NO:7, a CDR2 domain comprising the amino acid sequence of SEQ ID NO:5, and a CDR3 domain comprising the amino acid sequence of SEQ ID NO:3; and a heavy chain variable region (HCVR) having a CDR1

domain comprising the amino acid sequence of SEQ ID NO:8, a CDR2 domain comprising the amino acid sequence of SEQ ID NO:6, and a CDR3 domain comprising the amino acid sequence of SEQ ID NO:4.

In one aspect, there is provided a composition comprising a human anti-TNFα antibody, wherein the sum of the lysine variant species having one C-terminal lysine (Lys 1) and the lysine variant species having two C-terminal lysines (Lys 2) in said composition is greater than 35%,

and wherein the human anti-TNFα antibody comprises a light chain variable region (LCVR) having a CDR1 domain comprising the amino acid sequence of SEQ ID NO:7, a CDR2 domain comprising the amino acid sequence of SEQ ID NO:5, and a CDR3 domain comprising the amino acid sequence of SEQ ID NO:3; and a heavy chain variable region (HCVR) having a CDR1 domain comprising the amino acid sequence of SEQ ID NO:8, a CDR2 domain comprising the amino acid sequence of SEQ ID NO:6, and a CDR3 domain comprising the amino acid sequence of SEQ ID NO:4.

In one aspect, there is provided a pharmaceutical formulation comprising the composition as described herein and a pharmaceutically acceptable carrier.

In one aspect, there is provided the use of the composition as described herein in the manufacture of a medicament for treating a subject having a disease or disorder selected from the group consisting of rheumatoid arthritis, juvenile idiopathic arthritic, psoriatic arthritis, ankylosing spondylitis, Crohn's Disease, and plaque psoriasis, ulcerative colitis, hidradenitis suppurativa (HS), uveitis, active axial spondyloarthritis (active axSpA) or non-radiographic axial spondyloarthritis (nr-axSpA), wherein a therapeutically effective amount of the composition is administered to the subject, thereby treating the disease or disorder.

In one aspect, there is provided a pharmaceutical formulation comprising

a composition comprising a human anti-TNFα antibody, wherein less than 65% of the lysine variant species in said composition have zero C-terminal lysines (Lys 0), and

wherein the human anti-TNFα antibody comprises a light chain variable region (LCVR) having a CDR1 domain comprising the amino acid sequence of SEQ ID NO:7, a CDR2 domain comprising the amino acid sequence of SEQ ID NO:5, and a CDR3 domain comprising the amino acid sequence of SEQ ID NO:3; and a heavy chain variable region (HCVR) having a CDR1 domain comprising the amino acid sequence of SEQ ID NO:8, a CDR2 domain comprising the amino acid sequence of SEQ ID NO:6, and a CDR3 domain comprising the amino acid sequence of SEQ ID NO:4; and

a pharmaceutically acceptable carrier.

In one aspect, there is provided a pharmaceutical formulation comprising a composition comprising a human anti-TNFα antibody, wherein the sum of the lysine variant species having one C-terminal lysine (Lys 1) and the lysine variant species having two C-terminal lysines (Lys 2) in said composition is greater than 35%,

and wherein the human anti-TNFα antibody comprises a light chain variable region (LCVR) having a CDR1 domain comprising the amino acid sequence of SEQ ID NO:7, a CDR2 domain comprising the amino acid sequence of SEQ ID NO:5, and a CDR3 domain comprising the amino acid sequence of SEQ ID NO:3; and a heavy chain variable region (HCVR) having a CDR1 domain comprising the amino acid sequence of SEQ ID NO:8, a CDR2 domain comprising the amino acid sequence of SEQ ID NO:6, and a CDR3 domain comprising the amino acid sequence of SEQ ID NO:4; and

a pharmaceutically acceptable carrier.

In one aspect, there is provided the use of the pharmaceutical formulation as described herein in the manufacture of a medicament for treating a subject having a disease or disorder selected from the group consisting of rheumatoid arthritis, juvenile idiopathic arthritic, psoriatic arthritis, ankylosing spondylitis, Crohn's Disease, and plaque psoriasis, ulcerative colitis, hidradenitis suppurativa (HS), uveitis, active axial spondyloarthritis (active axSpA) or non-radiographic axial spondyloarthritis (nr-axSpA), wherein a therapeutically effective amount of the pharmaceutical formulation is administered to the subject, thereby treating the disease or disorder.

In one aspect, there is provided a method for producing a composition comprising a human anti-TNFα antibody, comprising culturing a cell producing the antibody in a cell culture media comprising an amount of one or more basic amino acids sufficient to produce a composition comprising the antibody in which less than 65% of the lysine variant species of the antibody have zero C-terminal lysines (Lys 0), and

wherein the antibody comprises a light chain variable region (LCVR) having a CDR1 domain comprising the amino acid sequence of SEQ ID NO:7, a CDR2 domain comprising the amino acid sequence of SEQ ID NO:5, and a CDR3 domain comprising the amino acid sequence of SEQ ID NO:3; and a heavy chain variable region (HCVR) having a CDR1 domain comprising the amino acid sequence of SEQ ID NO:8, a CDR2 domain comprising the amino acid sequence of SEQ ID NO:6, and a CDR3 domain comprising the amino acid sequence of SEQ ID NO:4.

In one aspect, there is provided a method for producing a composition comprising a human anti-TNFα antibody, comprising culturing a cell producing the antibody in a cell culture media comprising an amount of lysine sufficient to produce a composition comprising the

antibody in which less than 65% of the lysine variant species of the antibody have zero C-terminal lysines (Lys 0), and

wherein the human anti-TNFα antibody comprises a light chain variable region (LCVR) having a CDR1 domain comprising the amino acid sequence of SEQ ID NO:7, a CDR2 domain comprising the amino acid sequence of SEQ ID NO:5, and a CDR3 domain comprising the amino acid sequence of SEQ ID NO:3; and a heavy chain variable region (HCVR) having a CDR1 domain comprising the amino acid sequence of SEQ ID NO:8, a CDR2 domain comprising the amino acid sequence of SEQ ID NO:6, and a CDR3 domain comprising the amino acid sequence of SEQ ID NO:4.

In one aspect, there is provided a method for producing a modulated lysine variant species composition comprising an antibody, or antigen-binding portion thereof, comprising implementing a change to a cell culture condition used to produce said modulated lysine variant species composition, wherein the change in the cell culture condition results in a decrease in the amount of a lysine variant species that lacks a C-terminal lysine (Lys 0) as compared to the amount of Lys 0 in a control composition comprising an antibody, or antigen-binding portion thereof, produced without the change to the cell culture condition.

In one aspect, there is provided a composition comprising human anti-TNFα antibodies, wherein said human anti-TNFα antibodies comprise C-terminal lysine variant species, wherein less than 65% of said lysine variant species in said composition have zero C-terminal lysines (Lys 0), and wherein said human anti-TNFα antibodies comprise a light chain variable region (LCVR) having a CDR1 domain comprising the amino acid sequence of SEQ ID NO:7, a CDR2 domain comprising the amino acid sequence of SEQ ID NO:5, and a CDR3 domain comprising the amino acid sequence of SEQ ID NO:3; and a heavy chain variable region (HCVR) having a CDR1 domain comprising the amino acid sequence of SEQ ID NO:8, a CDR2 domain comprising the amino acid sequence of SEQ ID NO:6, and a CDR3 domain comprising the amino acid sequence of SEQ ID NO:4.

In one aspect, there is provided a composition comprising human anti-TNFα antibodies, wherein said human anti-TNFα antibodies comprise C-terminal lysine variant species, wherein greater than 35% of said lysine variant species in said composition have one C-terminal lysine (Lys 1) or two C terminal lysines (Lys 2), and wherein said human anti-TNFα antibodies comprise a light chain variable region (LCVR) having a CDR1 domain comprising the amino acid sequence of SEQ ID NO:7, a CDR2 domain comprising the amino acid sequence of SEQ ID NO:5, and a CDR3 domain comprising the amino acid sequence of SEQ ID NO:3; and a heavy chain variable region (HCVR) having a CDR1 domain comprising the amino acid sequence of SEQ ID NO:8, a CDR2 domain comprising the amino acid sequence of SEQ ID NO:6, and a CDR3 domain comprising the amino acid sequence of SEQ ID NO:4.

In one aspect, there is provided a pharmaceutical formulation comprising the composition as disclosed herein and a pharmaceutically acceptable carrier.

In one aspect, there is provided the use of the formulation as disclosed herein in the manufacture of a medicament for treating a subject having a disease or disorder in which TNFα activity is detrimental, wherein a therapeutically effective amount of the formulation is to be administered to the subject, thereby treating the TNFα-associated disease or disorder.

In one aspect, there is provided a method for producing the composition as disclosed herein, comprising culturing cells expressing said human anti-TNFα antibodies in a culture media.

The present disclosure is based on the identification and optimization of processes for the production of antibodies or antigen-binding portions thereof (*e.g.,* cell culture processes), which result in the production of compositions comprising antibodies, or antigen-binding portions thereof, that comprise modified distributions of C-terminal lysine variants. C-

CLAIMS

1. A method for producing a modulated lysine variant species composition comprising an antibody, or antigen-binding portion thereof, comprising implementing a change to a cell culture condition used to produce said modulated lysine variant species composition, wherein the change in the cell culture condition results in a decrease in the amount of a lysine variant species that lacks a C-terminal lysine (Lys 0) as compared to the amount of Lys 0 in a control composition comprising an antibody, or antigen-binding portion thereof, produced without the change to the cell culture condition.

2. The method of claim 1, wherein the change to a cell culture condition is a change to the cell culture media.

3. The method of claim 1, wherein the change to the cell culture media is an increase in the amount of an amino acid selected from the group consisting of arginine, lysine, histidine, and combinations thereof, in the cell culture media.

4. The method of claim 3, wherein the change to the cell culture media further comprises an increase in the amount of ornithine.

5. The method of claim 3, wherein the amino acid concentration is increased to a concentration of between about 0.025 and 20 g/L.

6. The method of claim 3, wherein the amino acid concentration is increased to a total concentration of about: arginine 9g/L, lysine 11 g/L, and histidine 10 g/L.

7. The method of claim 1, wherein the change to a cell culture condition is modulation of the amount of zinc in the cell culture media.

8. The method of claim 7, wherein the zinc concentration in the cell culture media is below 60 μM.

9. The method of claim 8, wherein the change to a cell culture condition further comprises an increase in the amount of arginine, lysine, and histidine.

10. The method of claim 1, wherein the change to a cell culture condition is a change to the cell culture pH.

11. The method of claim 1, wherein the change to a cell culture condition is a change to the concentration of dissolved oxygen (DO) in the cell culture media.

12. The method of claim 1, wherein the change to a cell culture condition is a change to the concentration of phosphate in the cell culture media.

13. The method of claim 12, wherein the phosphate concentration is increased to a total concentration of about 30mM.

14. The method of claim 1, wherein the change to a cell culture condition is a change to the cell culture temperature.

15. The method of claim 12, wherein the temperature is changed to a temperature of between about 30 and 50 °C.

16. The method of claim 12, wherein the temperature is changed to a temperature of between about 30 and 37 °C.

17. The method of claim 12, wherein the temperature is changed to a temperature of about 31 °C.

18. A composition comprising human anti-TNFα antibodies, wherein said human anti-TNFα antibodies comprise C-terminal lysine variant species, wherein less than 65% of said lysine variant species in said composition have zero C-terminal lysines (Lys 0), and wherein said human anti-TNFα antibodies comprise a light chain variable region (LCVR) having a CDR1 domain comprising the amino acid sequence of SEQ ID NO:7, a CDR2 domain comprising the amino acid sequence of SEQ ID NO:5, and a CDR3 domain comprising the amino acid sequence of SEQ ID NO:3; and a heavy chain variable region (HCVR) having a CDR1 domain comprising the amino acid sequence of SEQ ID NO:8, a CDR2 domain comprising the amino acid sequence of SEQ ID NO:6, and a CDR3 domain comprising the amino acid sequence of SEQ ID NO:4.

19. The composition of claim 18, wherein less than 60%, less than 55%, less than 50%, less than 45%, less than 40%, less than 30%, less than 25%, less than 20%, less than 15%, less than 10%, less than 5%, less than 4%, less than 3%, less than 2%, or less than 1% of said lysine variant species in said composition have zero C-terminal lysines (Lys 0).

20. A composition comprising human anti-TNFα antibodies, wherein said human anti-TNFα antibodies comprise C-terminal lysine variant species, wherein greater than 35% of said lysine variant species in said composition have one C-terminal lysine (Lys 1) or two C terminal lysines (Lys 2), and wherein said human anti-TNFα antibodies comprise a light chain variable region (LCVR) having a CDR1 domain comprising the amino acid sequence of SEQ ID NO:7, a CDR2 domain comprising the amino acid sequence of SEQ ID NO:5, and a CDR3 domain comprising the amino acid sequence of SEQ ID NO:3; and a heavy chain variable region (HCVR) having a CDR1 domain comprising the amino acid sequence of SEQ ID NO:8, a CDR2 domain comprising the amino acid sequence of SEQ ID NO:6, and a CDR3 domain comprising the amino acid sequence of SEQ ID NO:4.

21. The composition of claim 20, wherein greater than 40%, greater than 45%, greater than 50%, greater than 55%, greater than 60%, greater than 65%, greater than 70%, greater than 75%, greater than 80%, greater than 85%, greater than 90%, greater than 95%, greater than 96%, greater than 97%, greater than 98%, greater than 99%, or 100% of said lysine variant species in said composition have one C terminal lysine (Lys 1) or two Cterminal lysines (Lys 2).

22. The composition of claim 20 or 21, wherein greater than 20%, greater than 25%, greater than 30%, greater than 35%, greater than 40%, greater than 45%, greater than 50%, greater than 55%, greater than 60%, greater than 65%, greater than 70%, greater than 75%, greater than 80%, greater than 85%, greater than 90%, greater than 95%, greater than 96%, greater than 97%, greater than 98%, greater than 99%, or 100% of said lysine variant species in said composition have one C-terminal lysine (Lys 1).

23. The composition of claim 20 or 21, wherein greater than 20%, greater than 25%, greater than 30%, greater than 35%, greater than 40%, greater than 45%, greater than 50%, greater than 55%, greater than 60%, greater than 65%, greater than 70%, greater than 75%, greater than 80%, greater than 85%, greater than 90%, greater than 95%, greater than 96%, greater than 97%, greater than 98%, greater than 99%, or 100% of said lysine variant species in said composition have two C-terminal lysines (Lys 2).

24. The composition of any one of claims 18 to 23, wherein said human anti-TNFα antibodies are adalimumab.

25. A pharmaceutical formulation comprising the composition of any one of claims 18 to 24 and a pharmaceutically acceptable carrier.

26. The formulation of claim 25, wherein the formulation is selected from the group consisting of a liquid formulation, a lyophilized formulation, and a reconstituted lyophilized formulation.

27. The formulation of claim 25 or 26, wherein the antibodies are present in said formulation at a concentration of between 1 mg/ml and 25 mg/ml, between 1 mg/ml and 200 mg/ml, between 25 mg/ml and 200 mg/ml, between 50 mg/ml and 200 mg/ml, between 75 mg/ml and 200 mg/ml, between 100 mg/ml and 200 mg/ml, between 125 mg/ml and 200 mg/ml, between 150 mg/ml and 200 mg/ml, between 25 mg/ml and 150 mg/ml, between 50 mg/ml and 150 mg/ml, between 75 mg/ml and 150 mg/ml, between 100 mg/ml and 150 mg/ml, between 125 mg/ml and 150 mg/ml, between 25 mg/ml and 125 mg/ml, between 50 mg/ml and 125 mg/ml, between 75 mg/ml and 125 mg/ml, between 100 mg/ml and 125 mg/ml, between 25 mg/ml and 100 mg/ml, between 50 mg/ml and 100 mg/ml, between 75 mg/ml and 100 mg/ml, between 25 mg/ml and 75 mg/ml, between 50 mg/ml and 75 mg/ml, or between 25 mg/ml and 50 mg/ml.

28. The formulation of any one of claims 25 to 27, further comprising an excipient selected from the group consisting of buffering agent, sugar, salt, surfactant, amino acid, polyol, chelating agent, emulsifier, and preservative.

29. The formulation of claim 28, wherein:
(a) the buffering agent is selected from the group consisting of histidine, citrate, phosphate, glycine, and acetate;
(b) the sugar is selected from the group consisting of trehalose, sucrose, mannitol, maltose, raffinose, and sorbitol; and/or
(c) the surfactant is selected from the group consisting of polysorbate 20, polysorbate 40, polysorbate 80, and polysorbate 80.

30. Use of the formulation of any one of claims 25 to 29 in the manufacture of a medicament for treating a subject having a disease or disorder in which TNFα activity is detrimental, wherein a therapeutically effective amount of the formulation is to be administered to the subject, thereby treating the TNFα-associated disease or disorder.

31. The use according to claim 30, wherein the disease or disorder in which TNFα activity is detrimental is selected from the group consisting of rheumatoid arthritis, juvenile idiopathic arthritic, psoriatic arthritis, ankylosing spondylitis, Crohn's Disease, and plaque psoriasis.

32. A method for producing the composition of any one of claims 18 to 24, comprising culturing cells expressing said human anti-TNFα antibodies in a culture media.

33. The method of claim 32, further comprising supplementing the media with one or more amino acids during cell culture, optionally wherein the one or more amino acids is selected from the group consisting of arginine, lysine, histidine, ornithine, and combinations thereof.

34. The method of claim 33, wherein the one or more amino acids is increased to a concentration of between about 0.025 and 20 g/L, or between about 0.05 and 15 g/L, or between about 0.1 and 14 g/L, or between about 0.2 and 13 g/L, or between about 0.25 and 12 g/L, or between about 0.5 and 11 g/L, or between about 1 and 10 g/L, or between about 1.5 and 9.5 g/L, or between about 2 and 9 g/L, or between about 2.5 and 8.5 g/L, or between about 3 and 8 g/L, or between about 3.5 and 7.5 g/L, or between about 4 and 7 g/L, or between about 4.5 and 6.5 g/L, or between about 5 and 6 g/L.

35. The method of claim 32, further comprising supplementing the media with zinc during cell culture.

36. The method of any one of claims 32 to 35, wherein the cultured cells are mammalian cells, optionally wherein the mammalian cells are selected from the group consisting of CHO cells, NS0 myeloma cells, COS cells, and SP2 cells.

CLAIMS

1. A composition comprising a human anti-TNFα antibody, wherein less than 65% of the lysine variant species in said composition have zero C-terminal lysines (Lys 0), and wherein the human anti-TNFα antibody comprises a light chain variable region (LCVR) having a CDR1 domain comprising the amino acid sequence of SEQ ID NO:7, a CDR2 domain comprising the amino acid sequence of SEQ ID NO:5, and a CDR3 domain comprising the amino acid sequence of SEQ ID NO:3; and a heavy chain variable region (HCVR) having a CDR1 domain comprising the amino acid sequence of SEQ ID NO:8, a CDR2 domain comprising the amino acid sequence of SEQ ID NO:6, and a CDR3 domain comprising the amino acid sequence of SEQ ID NO:4.

2. The composition of claim 1, wherein said human anti-TNFα antibody is adalimumab.

3. The composition of claim 2, wherein less than 60% of the lysine variant species in said composition have zero C-terminal lysines (Lys 0).

4. The composition of claim 2, wherein 50-60% of the lysine variant species in said composition have zero C-terminal lysines (Lys 0).

5. The composition of claim 2, wherein less than 55% of the lysine variant species in said composition have zero C-terminal lysines (Lys 0).

6. The composition of claim 1, wherein said composition is lyophilized.

7. The composition of claim 2, wherein said adalimumab is produced in a mammalian host cell grown in cell culture.

8. The composition of claim 7, wherein the mammalian host cell is selected from the group consisting of a CHO cell, an NSO cell, a COS cell, and an SP2 cell.

9. A composition comprising a human anti-TNFα antibody, wherein the sum of the lysine variant species having one C-terminal lysine (Lys 1) and the lysine variant species having two C-terminal lysines (Lys 2) in said composition is greater than 35%, and wherein the human anti-TNFα antibody comprises a light chain variable region (LCVR) having a CDR1 domain comprising the amino acid sequence of SEQ ID NO:7, a CDR2 domain comprising the amino acid sequence of SEQ ID NO:5, and a CDR3 domain comprising the amino acid sequence of SEQ ID NO:3; and a heavy chain variable region (HCVR) having a CDR1 domain comprising the amino acid sequence of SEQ ID NO:8, a

CDR2 domain comprising the amino acid sequence of SEQ ID NO:6, and a CDR3 domain comprising the amino acid sequence of SEQ ID NO:4.

10. The composition of claim 9, wherein said human anti-TNFα antibody is adalimumab.

11. The composition of claim 10, wherein the sum of the lysine variant species having one C-terminal lysine (Lys 1) and the lysine variant species having two C-terminal lysines (Lys 2) in said composition is greater than 40%.

12. The composition of claim 10, wherein the sum of the lysine variant species having one C-terminal lysine (Lys 1) and the lysine variant species having two C-terminal lysines (Lys 2) in said composition is 40-50%.

13. The composition of claim 10, wherein the sum of the lysine variant species having one C-terminal lysine (Lys 1) and the lysine variant species having two C-terminal lysines (Lys 2) in said composition is greater than 50%.

14. The composition of claim 10, wherein greater than 25% of the lysine variant species in said composition have one C-terminal lysine (Lys 1).

15. The composition of claim 10, wherein greater than 30% of the lysine variant species in said composition have one C-terminal lysine (Lys 1).

16. The composition of claim 9, wherein said composition is lyophilized.

17. The composition of claims 1 or 9, wherein the lysine variant species include the main peak and peaks that elute at a relative residence time later than the main peak, as detected using weak cation-exchange chromatography.

18. The composition of claim 10, wherein said adalimumab is produced in a mammalian host cell grown in cell culture.

19. The composition of claim 18, wherein the mammalian host cell is selected from the group consisting of a CHO cell, an NSO cell, a COS cell, and an SP2 cell.

20. A pharmaceutical formulation comprising the composition of any one of claims 1-19 and a pharmaceutically acceptable carrier.

21. Use of the composition of any one of claims 1-19 in the manufacture of a medicament for treating a subject having a disease or disorder selected from the group consisting of rheumatoid arthritis, juvenile idiopathic arthritic, psoriatic arthritis, ankylosing

spondylitis, Crohn's Disease, and plaque psoriasis, ulcerative colitis, hidradenitis suppurativa (HS), uveitis, active axial spondyloarthritis (active axSpA) or non-radiographic axial spondyloarthritis (nr-axSpA), wherein a therapeutically effective amount of the composition is administered to the subject, thereby treating the disease or disorder.

22. A pharmaceutical formulation comprising
a composition comprising a human anti-TNFα antibody, wherein less than 65% of the lysine variant species in said composition have zero C-terminal lysines (Lys 0), and
wherein the human anti-TNFα antibody comprises a light chain variable region (LCVR) having a CDR1 domain comprising the amino acid sequence of SEQ ID NO:7, a CDR2 domain comprising the amino acid sequence of SEQ ID NO:5, and a CDR3 domain comprising the amino acid sequence of SEQ ID NO:3; and a heavy chain variable region (HCVR) having a CDR1 domain comprising the amino acid sequence of SEQ ID NO:8, a CDR2 domain comprising the amino acid sequence of SEQ ID NO:6, and a CDR3 domain comprising the amino acid sequence of SEQ ID NO:4; and a pharmaceutically acceptable carrier.

23. A pharmaceutical formulation comprising a composition comprising a human anti-TNFα antibody, wherein the sum of the lysine variant species having one C-terminal lysine (Lys 1) and the lysine variant species having two C-terminal lysines (Lys 2) in said composition is greater than 35%,
and wherein the human anti-TNFα antibody comprises a light chain variable region (LCVR) having a CDR1 domain comprising the amino acid sequence of SEQ ID NO:7, a CDR2 domain comprising the amino acid sequence of SEQ ID NO:5, and a CDR3 domain comprising the amino acid sequence of SEQ ID NO:3; and a heavy chain variable region (HCVR) having a CDR1 domain comprising the amino acid sequence of SEQ ID NO:8, a CDR2 domain comprising the amino acid sequence of SEQ ID NO:6, and a CDR3 domain comprising the amino acid sequence of SEQ ID NO:4; and
a pharmaceutically acceptable carrier.

24. The pharmaceutical formulation of claims 22 or 23, wherein the lysine variant species include the main peak and peaks that elute at a relative residence time later than the main peak, as detected using weak cation-exchange chromatography.

25. The pharmaceutical formulation of claim 22, wherein said human anti-TNFα antibody is adalimumab.

26. The pharmaceutical formulation of claim 25, wherein less than 60% of the lysine variant species in said composition have zero C-terminal lysines (Lys 0).

27. The pharmaceutical formulation of claim 25, wherein adalimumab is present in said pharmaceutical composition at a concentration of 25-100 mg/ml.

28. The pharmaceutical formulation of claim 25, wherein said pharmaceutical composition comprises one or more excipient selected from the group consisting of a buffering agent, a surfactant and a polyol, or a combination thereof.

29. The pharmaceutical formulation of claim 23, wherein said human anti-TNFα antibody is adalimumab.

30. The pharmaceutical formulation of claim 29, wherein the sum of the lysine variant species having one C-terminal lysine (Lys 1) and the lysine variant species having two C-terminal lysines (Lys 2) in said composition is greater than 40%.

31. The pharmaceutical formulation of claim 29, wherein the sum of the lysine variant species having one C-terminal lysine (Lys 1) and the lysine variant species having two C-terminal lysines (Lys 2) in said composition is 40-50%.

32. The pharmaceutical formulation of claim 29, wherein the sum of the lysine variant species having one C-terminal lysine (Lys 1) and the lysine variant species having two C-terminal lysines (Lys 2) in said composition is greater than 50%.

33. Use of the pharmaceutical formulation of any one of claims 22-32 in the manufacture of a medicament for treating a subject having a disease or disorder selected from the group consisting of rheumatoid arthritis, juvenile idiopathic arthritic, psoriatic arthritis, ankylosing spondylitis, Crohn's Disease, and plaque psoriasis, ulcerative colitis, hidradenitis suppurativa (HS), uveitis, active axial spondyloarthritis (active axSpA) or non-radiographic axial spondyloarthritis (nr-axSpA), wherein a therapeutically effective amount of the pharmaceutical formulation is administered to the subject, thereby treating the disease or disorder.

34. A method for producing a composition comprising a human anti-TNFα antibody, comprising culturing a cell producing the antibody in a cell culture media comprising an amount of one or more basic amino acids sufficient to produce a composition comprising the antibody in which less than 65% of the lysine variant species of the antibody have zero C-terminal lysines (Lys 0), and

wherein the antibody comprises a light chain variable region (LCVR) having a CDR1 domain comprising the amino acid sequence of SEQ ID NO:7, a CDR2 domain comprising the amino acid sequence of SEQ ID NO:5, and a CDR3 domain comprising the amino acid sequence of SEQ ID NO:3; and a heavy chain variable region (HCVR) having a CDR1 domain comprising the amino acid sequence of SEQ ID NO:8, a CDR2 domain comprising the amino acid sequence of SEQ ID NO:6, and a CDR3 domain comprising the amino acid sequence of SEQ ID NO:4.

35. The method of claim 34, wherein the lysine variant species include the main peak and peaks that elute at a relative residence time later than the main peak, as detected using weak cation-exchange chromatography.

36. The method of claim 34, wherein the antibody is adalimumab.

37. The method of claim 36, wherein the one or more amino acids in the cell culture media is selected from the group consisting of arginine, lysine, histidine, ornithine, and combinations thereof.

38. The method of claim 36, wherein the one or more amino acids in the cell culture media is ornithine.

39. The method of claim 37, wherein the one or more amino acids in the cell culture media is arginine.

40. The method of claim 39, wherein the arginine concentration in the cell culture media is 6 to 9 g/L.

41. The method of claim 39, wherein the arginine concentration in the cell culture media is 6 g/L or more, 8 g/L or more, or 9 g/L or more.

42. The method of claim 37, wherein the one or more amino acids in the cell culture media is lysine.

43. The method of claim 42, wherein the lysine concentration in the cell culture media is 4 to 10 g/L.

44. The method of claim 42, wherein the lysine concentration in the cell culture media is 4 g/L or more, 8 g/L or more, or 10 g/L or more.

45. The method of claim 37, wherein the one or more amino acids in the cell culture media is histidine.

46. The method of claim 45, wherein the histidine concentration in the cell culture media is 8 g/L or more.

47. The method of claim 34, wherein 61% or less of the lysine variant species of said antibody have zero C-terminal lysines (Lys 0).

48. The method of claim 34, wherein 60% or less of the lysine variant species of said antibody have zero C-terminal lysines (Lys 0).

49. The method of claim 34, wherein 58% or less of the lysine variant species of said antibody have zero C-terminal lysines (Lys 0).

50. The method of claim 34, wherein 55% or less of the lysine variant species of said antibody have zero C-terminal lysines (Lys 0).

51. The method of claim 34, wherein 48% or less of the lysine variant species of said antibody have zero C-terminal lysines (Lys 0).

52. The method of claim 34, wherein the cell is a mammalian cell.

53. The method of claim 52, wherein the mammalian cell is selected from the group consisting of CHO cells, NS0 myeloma cells, COS cells, and SP2 cells.

54. A method for producing a composition comprising a human anti-TNFα antibody, comprising culturing a cell producing the antibody in a cell culture media comprising an amount of lysine sufficient to produce a composition comprising the antibody in which less than 65% of the lysine variant species of the antibody have zero C-terminal lysines (Lys 0), and

wherein the human anti-TNFα antibody comprises a light chain variable region (LCVR) having a CDR1 domain comprising the amino acid sequence of SEQ ID NO:7, a CDR2 domain comprising the amino acid sequence of SEQ ID NO:5, and a CDR3 domain

comprising the amino acid sequence of SEQ ID NO:3; and a heavy chain variable region (HCVR) having a CDR1 domain comprising the amino acid sequence of SEQ ID NO:8, a CDR2 domain comprising the amino acid sequence of SEQ ID NO:6, and a CDR3 domain comprising the amino acid sequence of SEQ ID NO:4.

55. The method of claim 54, wherein the lysine variant species include the main peak and peaks that elute at a relative residence time later than the main peak, as detected using weak cation-exchange chromatography.

56. The method of claim 54, wherein the antibody is adalimumab.

57. The method of claim 56, wherein the lysine concentration in the cell culture media is 4 to 10 g/L.

58. The method of claim 56, wherein the lysine concentration in the cell culture media is 4 g/L or more.

59. The method of claim 56, wherein the lysine concentration in the cell culture media is 8 g/L or more.

60. The method of claim 56, wherein the lysine concentration in the cell culture media is 10 g/L or more.

61. The method of claim 56, wherein 61% or less of the lysine variant species of said antibody have zero C-terminal lysines (Lys 0).

62. The method of claim 56, wherein 55% or less of the lysine variant species of said antibody have zero C-terminal lysines (Lys 0).

63. The method of claim 56, wherein 48% or less of the lysine variant species of said antibody have zero C-terminal lysines (Lys 0).

64. The method of claim 56, wherein the cell is a mammalian cell.

65. The method of claim 64, wherein the mammalian cell is selected from the group consisting of CHO cells, NS0 myeloma cells, COS cells, and SP2 cells.