SEQUENCE LISTING

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Correia, Ivan R.

<120> VIRAL INACTIVATION DURING PURIFICATION OF ANTIBODIES

<130> 003168.0846

<140> US 12/582,556
<141> 2009-10-20

<150> US 61/196,754
<151> 2008-10-20

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<170> PatentIn version 3.5

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35 40 45

Ala Phe Ile Arg Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val
50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr
65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
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Ile Tyr Tyr Gly Asn Asp Gln Arg Pro Ser Gly Val Pro Asp Arg Phe
    50                  55                  60

Ser Gly Ser Lys Gly Thr Ser Ala Ser Leu Ala Ile Thr Gly Val Gln
65                  70                  75                  80

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Gly Phe Ile Tyr Pro Gly Asp Ser Glu Thr Arg Tyr Ser Pro Thr Phe
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Gln Gly Gln Val Thr Ile Ser Ala Asp Lys Ser Phe Asn Thr Ala Phe
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65 70 75 80

Leu Gln Trp Ser Ser Leu Lys Ala Ser Asp Thr Ala Met Tyr Tyr Cys
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Ala Arg Val Gly Ser Gly Trp Tyr Pro Tyr Thr Phe Asp Ile Trp Gly
100 105 110

Gln Gly Thr Met Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser
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Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala
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Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val
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Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
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35 40 45

Tyr Thr Ala Ser Thr Arg Ala Thr Asp Ile Pro Ala Arg Phe Ser Gly
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Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Asn Asn Trp Pro Ser
                85                  90                  95

Ile Thr Phe Gly Gln Gly Thr Arg Leu Glu Ile Lys Arg Thr Val Ala
            100                 105                 110

Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser
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Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu
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Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser
145                 150                 155                 160

Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu
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Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val
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Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
        35                  40                  45
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Ser Ala Ile Thr Trp Asn Ser Gly His Ile Asp Tyr Ala Asp Ser Val
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Glu Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu Tyr
65                  70                  75                  80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
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Gln Gly Thr Leu Val Thr Val Ser Ser
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Leu Ala Trp Tyr Gln Gln Lys Pro Gly Lys Ala Pro Lys Leu Leu Ile
        35                  40                  45

Tyr Ala Ala Ser Thr Leu Gln Ser Gly Val Pro Ser Arg Phe Ser Gly
    50                  55                  60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro
65                  70                  75                  80

Glu Asp Val Ala Thr Tyr Tyr Cys Gln Arg Tyr Asn Arg Ala Pro Tyr
                85                  90                  95

Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
            100                 105
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CLAIMS

What is claimed is:

1. A method for producing a host cell-protein (HCP) reduced antibody, or antigen binding portion thereof, preparation from a sample mixture comprising an antibody, or antigen binding portion thereof, an HCP and a viral particle, wherein said sample mixture has not been exposed to Protein A, and wherein the preparation comprises a decreased number of viral particles or decreased viral activity in comparison to the sample mixture, said method comprising:

(a) subjecting said sample mixture to a reduction in pH thus forming a primary recovery sample, wherein said reduction in pH is to a pH of 3.8 and said reduction is achieved by the addition of citric or phosphoric acid;

(b) adjusting said primary recovery sample to a pH of about 5.0 followed by;

(c) applying said primary recovery sample to an ion exchange resin and collecting an ion exchange sample;

(d) applying said ion exchange sample to a hydrophobic interactive chromatography (HIC) resin and collecting an HIC sample, wherein said HIC sample comprises said HCP-reduced antibody, or antigen binding portion thereof, preparation.

2. The method of claim 1, wherein said ion exchange resin is a cation exchange resin.

3. The method of claim 2, wherein said cation exchange resin comprises a substituted matrix wherein the substituents are selected from the group consisting of carboxymethyl, sulfoethyl, sulfopropyl, SO_3^-, phosphate and sulfonate.

4. The method of claim 3, wherein said substituent is SO_3^-.

5. The method of claim 1, wherein said ion exchange resin is an anion exchange resin.

6. The method of claim 5, wherein said anion exchange resin comprises a substituted matrix wherein the substituents are selected from the group consisting of diethylaminoethyl, quaternary aminoethyl, and quaternary amine groups.

7. The method of claim 6, wherein said substituent is a quaternary amine.

8. The method of claim 1, wherein said ion exchange sample is applied to a second ion exchange resin and a second ion exchange sample is collected prior to application to the hydrophobic interaction chromatography resin.

9. The method of claim 8, wherein said primary recovery sample is applied to a cation exchange resin and said ion exchange sample is applied to an anion exchange resin.

10. The method of claim 8, further comprising an intermediate step, wherein said intermediate step is a filtration step occurring after said ion exchange sample is collected and before said ion exchange sample is applied to said second ion exchange resin.

11. The method of claim 10, wherein said filtration step is accomplished by capture ultrafiltration/diafiltration.

12. The method of claim 1, wherein said HIC resin comprises a substituted matrix wherein the substituents consist of one or more hydrophobic groups.

13. The method of claim 12, wherein said substituents are selected from the group consisting of alkyl-groups, aryl-groups, and combinations thereof.

14. The method of claim 12, wherein said substituents are selected from the group consisting of: phenyl, 3-octoxypropane-1,2-diol, ether, propyl, methyl, and butyl groups.

15. The method of claim 14, wherein said resin comprises an agarose matrix comprising phenyl substituents.

16. The method of claim 1, further comprising a filtration step, wherein said HIC sample is subjected to filtration to remove viral particles and to facilitate buffer exchange.

17. The method of claim 1, wherein said HCP-reduced antibody, or antigen binding portion thereof, is adalimumab.

18. The method of claim 1, wherein said HCP-reduced antibody, or antigen binding portion thereof, preparation comprises an anti-IL-12 antibody or an anti-IL-18 antibody or antigen-binding portions thereof.

19. The method of claim 18, wherein said anti-IL-18 antibody or antigen-binding portion thereof neutralizes IL-18 both in vivo and in vitro.

20. The method of claim 1, wherein said preparation is substantially free of HCPs.

21. The method of claim 18, wherein said anti-IL-18 antibody or antigen-binding portion thereof is a humanized antibody, a chimeric antibody, or a multivalent antibody.

22. The method of claim 21, wherein said anti-IL-18 antibody or antigen-binding portion thereof is a humanized antibody.

23. A method for producing a host cell-protein (HCP) reduced antibody, or antigen binding portion thereof, preparation from a sample mixture comprising an antibody, or antigen binding portion thereof, and at least one HCP, and wherein said sample mixture has not been exposed to Protein A, said method comprising:

(a) subjecting said sample mixture to a reduction in pH thus forming a primary recovery sample, wherein said reduction in pH is to 3.8 and said reduction is achieved by the addition of citric or phosphoric acid;

(b) adjusting said primary recovery sample to a pH of about 5.0 followed by;

(c) applying said primary recovery sample to a cation exchange resin and collecting a cation exchange sample;

(d) applying said cation exchange sample to an anion exchange resin and collecting a anion exchange sample; and

(e) applying said anion exchange sample to a hydrophobic interactive chromatography (HIC) resin and collecting an HIC sample, wherein said HIC sample comprises said HCP-reduced antibody, or antigen binding portion thereof, preparation.

24. The method of claim 23, wherein said HCP-reduced antibody, or antigen binding portion thereof, is adalimumab.

25. A method for producing a host cell-protein (HCP) reduced antibody, or antigen binding portion thereof, preparation from a sample mixture comprising an antibody, or antigen binding portion thereof, and at least one HCP, and wherein said sample mixture has not been exposed to Protein A, said method comprising:

(a) subjecting said sample mixture to a reduction in pH thus forming a primary recovery sample, wherein said reduction in pH is to 3.8 and said reduction is achieved by the addition of citric or phosphoric acid;

(b) adjusting said primary recovery sample to a pH of about 5.0 followed by;

(c) applying said primary recovery sample to a cation exchange resin and collecting a cation exchange sample;

(d) subjecting said cation exchange sample to filtration and collecting a filtrate;

(e) applying said filtrate from (d) to an anion exchange resin and collecting an anion exchange sample; and

(f) applying said anion exchange sample to a hydrophobic interactive chromatography (HIC) resin and collecting an HIC sample, wherein said HIC sample comprises said HCP-reduced antibody, or antigen binding portion thereof, preparation.

26. The method of claim 25, wherein said HCP-reduced antibody, or antigen binding portion thereof, is adalimumab.