

comprises no more than about 15 ppm DsbA. In some embodiments, the composition comprises no more than about 5 ppm DsbA. In some embodiments, the composition comprises no more than about 15 ppm DsbC. In some embodiments, the composition comprises no more than about 5 ppm DsbC. In some embodiments, the DsbA is determined by immunoassay. In some embodiments, the DsbC is measured by immunoassay.

[0029] The disclosure provides methods for purifying a polypeptide from a composition comprising the multispecific antibody and one or more impurities, the method comprising the sequential steps of a) subjecting the composition to affinity chromatography to produce an affinity eluate, b) subjecting the affinity eluate to mixed-mode chromatography to generate a mixed-mode eluate, and c) subjecting the mixed-mode eluate to hydrophobic interaction chromatography and collecting a fraction comprising the polypeptide, wherein the method reduces the amount of product-specific impurities from the composition. Disclosed is a method for purifying a polypeptide from a composition comprising the polypeptide and one or more impurities, a) subjecting the composition to affinity chromatography to produce an affinity eluate, b) subjecting the affinity eluate to mixed-mode chromatography to generate a mixed-mode eluate, and c) subjecting the mixed-mode eluate to hydrophobic interaction chromatography and collecting a fraction comprising the polypeptide, wherein the method reduces the amount of product-specific impurities from the composition. In some embodiments, the mixed-mode chromatography is a mixed-mode anion exchange chromatography. In some embodiments, the affinity chromatography is carried out in bind and elute mode. In some embodiments, the mixed-mode chromatography is carried out in bind and elute mode. In some embodiments, the HIC is carried out in flow-through mode.

[0030] Disclosed is a method for purifying a multispecific antibody from a composition comprising the multispecific antibody and one or more impurities, wherein the multispecific antibody comprises multiple arms, each arm comprising a VH/VL unit, the method comprising the sequential steps of a) subjecting the composition to protein A chromatography to produce a protein A eluate, b) subjecting the protein A eluate to mixed-mode chromatography to generate a mixed-mode eluate, and c) subjecting the mixed-mode eluate to hydrophobic interaction chromatography and collecting a fraction comprising the multispecific antibody, wherein the method reduces the amount of product-specific impurities from the composition. In some embodiments, the mixed-mode chromatography is a mixed-mode anion exchange chromatography. In some embodiments, the affinity chromatography is carried out in bind and elute mode. In some embodiments, the mixed-mode chromatography is carried out in bind and elute mode. In some embodiments, the HIC is carried out in flow-through mode.

[0031] Disclosed are methods for purifying a multispecific antibody from a composition comprising the multispecific antibody and one or more impurities, wherein the multispecific antibody comprises multiple arms, each arm comprising a VH/VL unit, wherein each arm of the multispecific antibody is produced separately, the method comprising the sequential steps of a) subjecting each arm of the multispecific antibody to protein A chromatography to produce protein A eluates for each arm of the multispecific antibody, b) forming a mixture comprising protein A eluates of each arm of the multispecific antibody under conditions sufficient to produce a composition comprising the multispecific antibody, c) subjecting the composition comprising the multispecific antibody to mixed-mode chromatography to generate a mixed-mode eluate, and d) subjecting the mixed-mode eluate to hydrophobic interaction chromatography (HIC) and collecting a fraction comprising the multispecific antibody wherein the method reduces the amount of product-specific impurities from the composition. In

some embodiments, the mixed-mode chromatography is a mixed-mode anion exchange chromatography. In some embodiments, the affinity chromatography is carried out in bind and elute mode. In some embodiments, the mixed-mode chromatography is carried out in bind and elute mode. In some embodiments, the hydrophobic interaction chromatography is carried out in flow-through mode. In some embodiments, the mixed-mode eluate is subjected to anion exchange chromatography prior to hydrophobic interaction chromatography. In some embodiments, the anion exchange chromatography is carried out in bind and elute mode.

[0032] In some embodiments, the methods further comprising the step of subjecting the hydrophobic interaction chromatography fraction comprising the multispecific antibody to cation exchange chromatography and collecting a fraction comprising the multispecific antibody. In some embodiments, the cation exchange chromatography is carried out in bind and elute mode.

[0033] In some embodiments, the disclosure provides methods for purifying a polypeptide from a composition comprising the polypeptide and one or more impurities, the method comprising the sequential steps of a) subjecting the composition to affinity chromatography to produce an affinity eluate, b) subjecting the affinity eluate to mixed-mode chromatography to generate a mixed-mode eluate, and c) subjecting the mixed-mode eluate to anion exchange chromatography to generate an anion exchange eluate, d) subjecting the anion exchange eluate to hydrophobic interaction chromatography and collecting a fraction comprising the polypeptide, wherein the method reduces the amount of product-specific impurities from the composition. In one aspect, there is provided a method for purifying a polypeptide from a composition comprising the polypeptide and one or more impurities, a) subjecting the composition to affinity chromatography to produce a affinity eluate, b) subjecting the affinity eluate to mixed-mode chromatography to generate a mixed-mode eluate, and c) subjecting the mixed-mode eluate to anion exchange chromatography to generate an anion exchange eluate, d) subjecting the anion exchange eluate to hydrophobic interaction chromatography and collecting a fraction comprising the polypeptide, wherein the method reduces the amount of product-specific impurities from the composition.

[0034] In some aspects, there is provided methods for purifying a multispecific antibody from a composition comprising the multispecific antibody and one or more impurities, wherein the multispecific antibody comprises multiple arms, each arm comprising a VH/VL unit, the method comprising the sequential steps of a) subjecting the composition to protein A chromatography to produce a protein A eluate, b) subjecting the protein A eluate to mixed-mode chromatography to generate a mixed-mode eluate, and c) subjecting the mixed-mode eluate to anion exchange chromatography to generate an anion exchange eluate, d) subjecting the anion exchange eluate to hydrophobic interaction chromatography and collecting a fraction comprising the multispecific antibody, wherein the method reduces the amount of product-specific impurities from the composition.

[0035] In some aspects, there is provided methods for purifying a multispecific antibody from a composition comprising the multispecific antibody and one or more impurities, wherein the multispecific antibody comprises multiple arms, each arm comprising a VH/VL unit, wherein each arm of the multispecific antibody is produced separately, the method comprising the sequential steps of a) subjecting each arm of the multispecific antibody to protein A chromatography to produce protein A eluates for each arm of the multispecific antibody, b) forming a mixture comprising protein A eluates of each arm of the multispecific antibody under conditions sufficient to produce a composition comprising the multispecific antibody c) subjecting the composition comprising the multispecific antibody to mixed-mode chromatography to generate a mixed-mode eluate, and d) subjecting the mixed-mode eluate to anion

[0036c] In one aspect, there is provided a method for purifying a multispecific antibody from a composition comprising the multispecific antibody and one or more impurities, wherein the multispecific antibody comprises multiple arms, each arm comprising a VH/VL unit, wherein each arm of the multispecific antibody is produced separately, the method comprising the sequential steps of a) subjecting each arm of the multispecific antibody to protein A chromatography to produce protein A eluates for each arm of the multispecific antibody, b) forming a mixture comprising protein A eluates of each arm of the multispecific antibody under conditions sufficient to produce a composition comprising the multispecific antibody c) subjecting the composition comprising the multispecific antibody to mixed-mode chromatography to generate a mixed-mode eluate, and d) subjecting the mixed-mode eluate to anion exchange chromatography to generate an anion exchange eluate, e) subjecting the anion exchange eluate to hydrophobic interaction chromatography in and collecting a fraction comprising the multispecific antibody and collecting a fraction comprising the multispecific antibody, f) subjecting the hydrophobic interaction eluate to cation exchange chromatography and collecting a fraction comprising the polypeptide, wherein the method reduces the amount of product-specific impurities from the composition.

[0037] Disclosed is a method for purifying a polypeptide from a composition comprising the polypeptide and one or more impurities, the method comprising the sequential steps of: a) subjecting the composition to affinity chromatography to produce a affinity eluate, b) subjecting the affinity eluate to mixed-mode chromatography to generate a mixed-mode eluate, and c) subjecting the mixed-mode eluate to anion exchange chromatography to generate an anion exchange eluate, d) subjecting the anion exchange eluate to hydroxyapatite chromatography and collecting a fraction comprising the polypeptide, wherein the method reduces the amount of product-specific impurities from the composition. The disclosure also provides a method for purifying a multispecific antibody from a composition comprising the multispecific antibody and one or more impurities, wherein the multispecific antibody comprises multiple arms, each arm comprising a VH/VL unit, the method comprising the sequential steps of a) subjecting the composition to protein A chromatography to produce a protein A eluate, b) subjecting the protein A eluate to mixed-mode chromatography to generate a mixed-mode eluate, and c) subjecting the mixed-mode eluate to anion exchange chromatography to generate an anion exchange eluate, d) subjecting the anion exchange eluate to hydroxyapatite chromatography and collecting a fraction comprising the multispecific antibody, wherein the method reduces the amount of product-specific impurities from the composition. The disclosure further provides a method for purifying a multispecific antibody from a composition comprising the multispecific antibody and one or more impurities, wherein the multispecific antibody comprises multiple arms, each arm comprising a VH/VL unit, wherein each arm of the multispecific antibody is produced separately, the method comprising the sequential steps of a) subjecting each arm of the

species (HMW), low molecular weight species (LMW), acidic variants, or basic variants. In some embodiments, the methods reduce the amount of any one of *E. coli* protein (ECP), FkpA, DsbA, DsbC, leached protein A, nucleic acid, cell culture media components, or viral impurities in the composition.

[0048] In some embodiments, the multispecific antibody is a bispecific antibody. In some embodiments, a first arm of the multispecific antibody binds IL13. In some embodiments, the IL13 is human IL13. In some embodiments, the IL13 comprises the amino acid sequence of SEQ ID NO:1 or SEQ ID NO:2. In some embodiments, the first arm of the multispecific antibody comprises HVR-H1 comprising the amino acid sequence of SEQ ID NO:7, HVR-H2 comprising the amino acid sequence of SEQ ID NO:8, HVR-H3 comprising the amino acid sequence of SEQ ID NO:9, HVR-L1 comprising the amino acid sequence of SEQ ID NO:10, HVR-L2 comprising the amino acid sequence of SEQ ID NO:11, and HVR-L3 comprising the amino acid sequence of SEQ ID NO:12. In some embodiments, the first arm of the multispecific antibody comprises a VH sequence comprising the amino acid sequence of SEQ ID NO:13 and a VL sequence comprising the amino acid sequence of SEQ ID NO:14. In some embodiments, the first arm of the multispecific antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO:15. In some embodiments, the first arm of the multispecific antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO:16. In some embodiments, the first arm of the multispecific antibody comprises a light chain comprising the amino acid sequence of SEQ ID NO:17. In some embodiments, a second arm of the antibody binds IL17. In some embodiments, the IL17 is human IL17. In some embodiments, the IL17 comprises the amino acid sequence of SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5 or SEQ ID NO:6. In some embodiments, a second arm of the multispecific antibody comprises HVR-H1 comprising the amino acid sequence of SEQ ID NO:18, HVR-H2 comprising the amino acid sequence of SEQ ID NO:19, HVR-H3 comprising the amino acid sequence of SEQ ID NO:20, HVR-L1 comprising the amino acid sequence of SEQ ID NO:21, HVR-L2 comprising the amino acid sequence of SEQ ID NO:22, and HVR-L3 comprising the amino acid sequence of SEQ ID NO:23. In some embodiments, the second arm of the multispecific antibody comprises a VH sequence comprising the amino acid sequence of SEQ ID NO:25 and a VL sequence comprising the amino acid sequence of SEQ ID NO:26. In some embodiments, the second arm of the multispecific antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO:27. In some embodiments, the second arm of the multispecific antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO:28. In some embodiments, the second arm of the multispecific antibody comprises a light chain comprising the amino acid sequence of SEQ ID NO:29.

[0049] Disclosed is a composition comprising a polypeptide or a multispecific antibody purified by any of the method described herein, wherein the composition comprises no more than about 5%, 4%, 3%, 2% or 1% product specific impurities. In some embodiments, the product specific impurity is one or more of non-paired antibody arms, antibody homodimers, aggregates, high molecular weight species (HMW), low molecular weight species (LMW), acidic variants, or basic variants. In some embodiments, the composition comprises less than about composition comprises no more than about 5%,

CLAIMS

WHAT IS CLAIMED IS:

1. A method for purifying a polypeptide from a composition comprising the polypeptide and one or more impurities,
 - a) subjecting the composition to affinity chromatography to produce a affinity eluate,
 - b) subjecting the affinity eluate to mixed-mode chromatography to generate a mixed-mode eluate, and
 - c) subjecting the mixed-mode eluate to anion exchange chromatography to generate an anion exchange eluate,
 - d) subjecting the anion exchange eluate to hydrophobic interaction chromatography and collecting a fraction comprising the polypeptide,wherein the method reduces the amount of product-specific impurities from the composition.
2. A method for purifying a multispecific antibody from a composition comprising the multispecific antibody and one or more impurities, wherein the multispecific antibody comprises multiple arms, each arm comprising a VH/VL unit, the method comprising the sequential steps of
 - a) subjecting the composition to protein A chromatography to produce a protein A eluate,
 - b) subjecting the protein A eluate to mixed-mode chromatography to generate a mixed-mode eluate, and
 - c) subjecting the mixed-mode eluate to anion exchange chromatography to generate an anion exchange eluate,
 - d) subjecting the anion exchange eluate to hydrophobic interaction chromatography and collecting a fraction comprising the multispecific antibody,wherein the method reduces the amount of product-specific impurities from the composition.
3. A method for purifying a multispecific antibody from a composition comprising the multispecific antibody and one or more impurities, wherein the multispecific antibody comprises multiple arms, each

arm comprising a VH/VL unit, wherein each arm of the multispecific antibody is produced separately, the method comprising the sequential steps of

- a) subjecting each arm of the multispecific antibody to protein A chromatography to produce protein A eluates for each arm of the multispecific antibody,
 - b) forming a mixture comprising protein A eluates of each arm of the multispecific antibody under conditions sufficient to produce a composition comprising the multispecific antibody
 - c) subjecting the composition comprising the multispecific antibody to mixed-mode chromatography to generate a mixed-mode eluate, and
 - d) subjecting the mixed-mode eluate to anion exchange chromatography to generate an anion exchange eluate,
 - e) subjecting the anion exchange eluate to hydrophobic interaction chromatography in and collecting a fraction comprising the multispecific antibody and collecting a fraction comprising the multispecific antibody,
- wherein the method reduces the amount of product-specific impurities from the composition.

4. The method of any one of claims 1-3, wherein the mixed-mode chromatography is a mixed-mode anion exchange chromatography.

5. The method of any one of claims 1-4, further comprising the step of subjecting the hydrophobic interaction chromatography fraction comprising the polypeptide or multispecific antibody to cation exchange chromatography.

6. A method for purifying a polypeptide from a composition comprising the polypeptide and one or more impurities,

- a) subjecting the composition to affinity chromatography to produce a affinity eluate,
 - b) subjecting the affinity eluate to mixed-mode chromatography to generate a mixed-mode eluate, and
 - c) subjecting the mixed-mode eluate to anion exchange chromatography to generate an anion exchange eluate,
 - d) subjecting the anion exchange eluate to hydrophobic interaction chromatography and collecting a fraction comprising the polypeptide,
 - e) subjecting the hydrophobic interaction eluate to cation exchange chromatography and collecting a fraction comprising the polypeptide,
- wherein the method reduces the amount of product-specific impurities from the composition.

7. A method for purifying a multispecific antibody from a composition comprising the multispecific antibody and one or more impurities, wherein the multispecific antibody comprises multiple arms, each arm comprising a VH/VL unit, the method comprising the sequential steps of
- a) subjecting the composition to protein A chromatography to produce a protein A eluate,
 - b) subjecting the protein A eluate to mixed-mode chromatography to generate a mixed-mode eluate, and
 - c) subjecting the mixed-mode eluate to anion exchange chromatography to generate an anion exchange eluate,
 - d) subjecting the anion exchange eluate to hydrophobic interaction chromatography and collecting a fraction comprising the multispecific antibody,
 - e) subjecting the hydrophobic interaction eluate to cation exchange chromatography and collecting a fraction comprising the polypeptide,
- wherein the method reduces the amount of product-specific impurities from the composition.
8. A method for purifying a multispecific antibody from a composition comprising the multispecific antibody and one or more impurities, wherein the multispecific antibody comprises multiple arms, each arm comprising a VH/VL unit, wherein each arm of the multispecific antibody is produced separately, the method comprising the sequential steps of
- a) subjecting each arm of the multispecific antibody to protein A chromatography to produce protein A eluates for each arm of the multispecific antibody,
 - b) forming a mixture comprising protein A eluates of each arm of the multispecific antibody under conditions sufficient to produce a composition comprising the multispecific antibody
 - c) subjecting the composition comprising the multispecific antibody to mixed-mode chromatography to generate a mixed-mode eluate, and
 - d) subjecting the mixed-mode eluate to anion exchange chromatography to generate an anion exchange eluate,
 - e) subjecting the anion exchange eluate to hydrophobic interaction chromatography in and collecting a fraction comprising the multispecific antibody and collecting a fraction comprising the multispecific antibody,
 - f) subjecting the hydrophobic interaction eluate to cation exchange chromatography and collecting a fraction comprising the polypeptide,
- wherein the method reduces the amount of product-specific impurities from the composition.
9. The method of any one of claims 6-8, wherein the mixed-mode chromatography is a mixed-mode anion exchange chromatography.

10. The method of any one of claims 1-4 further comprising the step of subjecting the hydrophobic interaction chromatography fraction comprising the polypeptide or multispecific antibody to ultrafiltration.
11. The method of claims 5-9, further comprising the step of subjecting the cation exchange fraction comprising the polypeptide or multispecific antibody to ultrafiltration.
12. The method of any one of claims 10-11 wherein the ultrafiltration comprises sequentially a first ultrafiltration, a diafiltration and a second ultrafiltration.
13. The method of any one of claims 1-12, wherein the mixed-mode chromatography uses one or more of a mixed-mode pre-equilibration buffer, a mixed-mode equilibration buffer, a mixed-mode loading buffer or a mixed-mode wash buffer wherein the mixed-mode pre-equilibration buffer, the mixed-mode equilibration buffer, and/or mixed-mode wash buffer is between about pH 6 and about pH 7.
14. The method of claim 13, wherein the mixed-mode pre-equilibration buffer, the mixed-mode equilibration buffer, and/or mixed-mode wash buffer is about pH 6.5.
15. The method of claim 13 or 14, wherein the mixed-mode pre-equilibration buffer comprises about 200 mM acetate or about 500 mM acetate.
16. The method of any one of claims 13-15, wherein the mixed-mode equilibration buffer comprises about 50 mM acetate.
17. The method of any one of claims 13-16, wherein the mixed-mode chromatography is washed with wash buffer following load.

18. The method of claim 17 wherein the wash buffer is about 50 mM acetate and about pH 6.5 or about 200 mM acetate and about pH 6.5
19. The method of any one of claims 1-18, wherein the polypeptide or multispecific antibody is eluted from the mixed-mode chromatography by pH gradient.
20. The method of any one of claims 1-19, wherein the polypeptide or multispecific antibody is eluted from the mixed-mode chromatography by applying a mixed-mode elution buffer with low pH to the mixed-mode anion exchange chromatography.
21. The method of claim 20, wherein the mixed-mode elution buffer comprises about 25 mM acetate and about pH 5.2 or about pH 5.0.
22. The method of any one of claims 1-21 wherein the mixed-mode eluate is pooled where the OD₂₈₀ of the eluate is greater than about 0.5 to about 1.0.
23. The method of any one of claims 1-9, wherein the hydrophobic interaction chromatography (HIC) comprises a hydrophobic moiety.
24. The method of claim 23, wherein the hydrophobic interaction chromatography comprises a phenyl moiety.
25. The method of claim 23 or 24, wherein the hydrophobic interaction chromatography comprises a hydrophobic moiety linked to crosslinked agarose.
26. The method of any one of claims 23-25, wherein the hydrophobic interaction chromatography comprises a phenyl moiety or a butyl moiety linked to crosslinked agarose.
27. The method of any one of claims 23-26, wherein the hydrophobic interaction chromatography comprises a hexyl moiety.
28. The method of claim 27, wherein the hydrophobic interaction exchange chromatography uses one or more of a HIC equilibration buffer, a HIC loading buffer or a HIC wash buffer wherein the HIC equilibration buffer, the HIC load buffer and/or the HIC wash buffer is between about pH 6 and about pH 8.

29. The method of claim 28, wherein the HIC equilibration buffer, the load buffer, and/or the wash buffer is about pH 7.0.
30. The method of claim 28 or 29, wherein the HIC equilibration buffer and the wash buffer comprises about 50 mM 3-(N-Morpholino)propanesulfonic acid (MOPS) and 125 mM acetate.
31. The method of any one of claims 27-30, wherein the hydrophobic interaction chromatography is washed with HIC wash buffer following load.
32. The method of any one of claims 23-31 wherein the hydrophobic interaction eluate is pooled where the OD₂₈₀ of the eluate is greater than about 0.5 to about 1.0.
33. The method of any one of claims 1-32, where anion exchange chromatography comprises a quaternary amine.
34. The method of claim 33, wherein the anion exchange chromatography comprises a quaternary amine linked to crosslinked agarose.
35. The method of claim 34, wherein the mixed-mode anion exchange chromatography is a QSFF chromatography.
36. The method of any one of claims 33-35, wherein the anion exchange chromatography uses one or more of an anion exchange pre-equilibration buffer, an anion exchange equilibration buffer or an anion exchange loading buffer wherein the anion exchange pre-equilibration buffer, the anion exchange equilibration buffer and/or anion exchange the load buffer is between about pH 8 and about pH 9.
37. The method of claim 36, wherein the anion exchange pre-equilibration buffer, the anion exchange equilibration buffer and/or the anion exchange load buffer is about pH 8.5.
38. The method of claim 36 or 37, wherein the anion exchange pre-equilibration buffer comprises about 50 mM Tris and about 500 mM sodium acetate or about 100 mM sodium acetate.
39. The method of any one of claims 36-38, wherein the anion exchange equilibration buffer comprises about 50 mM Tris.
40. The method of any one of claims 36-39, wherein the anion exchange chromatography is washed with anion exchange equilibration buffer following load.

41. The method of any one of claims 36-40, wherein the polypeptide or multispecific antibody is eluted from the anion exchange chromatography by salt gradient.
42. The method of any one of claims 36-41, wherein the polypeptide or multispecific antibody is eluted from the anion exchange chromatography by applying an anion exchange elution buffer with increased salt concentration to the anion exchange chromatography.
43. The method of claim 42, wherein the anion exchange elution buffer comprises about 50 mM Tris and about 100 mM sodium acetate at about pH 8.5.
44. The method of any one of claims 36-43 wherein the anion exchange eluate is pooled where the OD₂₈₀ of the eluate is greater than about 0.5 to about 1.0.
45. The method of claim 5-34, where cation exchange chromatography comprises a carboxylic acid moiety or a sulfonic acid moiety.

46. The method of claim 45, wherein the cation exchange chromatography uses one or more of a cation exchange pre-equilibration buffer, an cation exchange equilibration buffer, cation exchange loading buffer or cation exchange wash buffer wherein the cation exchange pre-equilibration buffer, the cation exchange equilibration buffer, the cation exchange load buffer and/or cation exchange wash buffer is between about pH 5.0 and about pH 6.0.

47. The method of claim 46, wherein the cation exchange cation exchange the equilibration buffer, the cation exchange load buffer and/or cation exchange wash buffer is about pH 5.5 or about pH 5.8.

48. The method of claim 46 or 47, wherein the cation exchange equilibration buffer and/or the cation exchange wash buffer comprises 50 mM sodium acetate.

49. The method of any one of claims 46-48, wherein the polypeptide or multispecific antibody is eluted from the cation exchange chromatography by applying a cation exchange elution buffer with increased salt concentration to the cation exchange chromatography.

50. The method of claim 49, wherein the cation exchange elution buffer comprises 500 mM sodium acetate, pH 5.8.

51. The method of claim 50, wherein the elution is a gradient elution of 10% to 100% cation exchange elution buffer.

52. The method of any one of claims 1-51, wherein the polypeptide or the multispecific antibody is produced in an *E. coli* cell engineered to express one or more chaperones.

53. The method of claim 52, wherein the chaperone is one or more of FkpA, DsbA or DsbC.

54. The method of any one of claims 52-53, wherein polyethlyeneimine (PEI) is added to the cell lysate prior to chromatography.

55. The method of any one of claims 1-5, or 7-54 wherein the multispecific antibody is a bispecific antibody.