

What is claimed is:

1. A method of identifying host cell protein (HCP) impurities in a sample, comprising:
contacting the sample to solid support,
wherein said sample includes at least one high-abundance peptide or protein,
wherein interacting peptide ligands have been attached to said solid support, and
wherein said HCP impurities can bind to the interacting peptide ligands;
washing said solid support using a solution comprising a surfactant providing an eluent;
subjecting said eluent with an enzymatic digestion condition to generate components of
isolated HCP impurities; and
identifying components of the isolated HCP impurities using a mass spectrometer.
2. The method of claim 1, wherein the surfactant is a phase transfer surfactant, an ionic surfactant, an anionic surfactant, a cationic surfactant, or combinations thereof.
3. The method of claim 1, wherein the surfactant is sodium deoxycholate, sodium lauryl sulfate, or sodium dodecylbenzene sulphonate.
4. The method of claim 1, wherein a concentration of the at least one high-abundance peptide or protein is about at least 1000 times, 10,000 times, 100,000 times or 1,000,000 times higher than a concentration of the each HCP impurity.
5. The method of claim 1, wherein the interacting peptide ligands are a library of combinatorial hexapeptide ligands.
6. The method of claim 1, wherein the HCP impurities are quantified using the mass spectrometer, wherein a detection limit of the each HCP impurity is about 0.05-0.1 ppm.
7. The method of claim 1, wherein the at least one high-abundance peptide or protein is an antibody, a bispecific antibody, an antibody fragment, a Fab region of an antibody, an antibody-drug conjugate, a fusion protein, a protein pharmaceutical product, or a drug.
8. The method of claim 1, wherein an enzyme of the enzymatic digestion reaction is trypsin.

9. The method of claim 1, wherein the mass spectrometer is an electrospray ionization mass spectrometer, nano-electrospray ionization mass spectrometer, or a triple quadrupole mass spectrometer, wherein the mass spectrometer is coupled to a liquid chromatography system.
10. The method of claim 1, wherein the mass spectrometer is capable of performing LC-MS (liquid chromatography-mass spectrometry) or a LC-MRM-MS (liquid chromatography-multiple reaction monitoring-mass spectrometry) analyses.
11. A system for identifying host cell protein (HCP) impurities in a sample, comprising:
a solid support;
interacting peptide ligands,
wherein said interacting peptide ligands are attached to said solid support, and
wherein said HCP impurities can bind to the interacting peptide ligands;
a solution comprising a surfactant;
an enzymatic digestion solution capable of generating components from said HCP impurities; and
a mass spectrometer capable of identifying or quantifying said components.
12. The system of claim 11, wherein the surfactant is a phase transfer surfactant, an ionic surfactant, an anionic surfactant, a cationic surfactant, or combinations thereof.
13. The system of claim 11, wherein the surfactant is sodium deoxycholate, sodium lauryl sulfate, or sodium dodecylbenzene sulphonate.
14. The system of claim 11, wherein a concentration of the at least one high-abundance peptide or protein is about at least 1000 times, 10,000 times, 100,000 times or 1,000,000 times higher than a concentration of the each HCP impurity.
15. The system of claim 11, wherein the interacting peptide ligands are a library of combinatorial hexapeptide ligands.
16. The system of claim 11, wherein a detection limit of the each HCP impurity is about 0.05-0.1 ppm.

17. The system of claim 11, wherein the at least one high-abundance peptide or protein is an antibody, a bispecific antibody, an antibody fragment, a Fab region of an antibody, an antibody-drug conjugate, a fusion protein, a protein pharmaceutical product, or a drug.
18. The system of claim 11, wherein an enzyme of the enzymatic digestion solution is trypsin.
19. The system of claim 11, wherein the mass spectrometer is an electrospray ionization mass spectrometer, nano-electrospray ionization mass spectrometer, or a triple quadrupole mass spectrometer, wherein the mass spectrometer is coupled to a liquid chromatography system.
20. The system of claim 11, wherein the mass spectrometer is capable of performing LC-MS (liquid chromatography-mass spectrometry) or a LC-MRM-MS (liquid chromatography-multiple reaction monitoring-mass spectrometry) analyses.