What is claimed is:

1. A method of identifying host cell protein (HCP) impurities in a sample containing at least one high-abundance protein, the method comprising:

contacting the sample with at least one probe capable of attaching to a HCP impurity, wherein the probe includes a warhead and a tag, and wherein the warhead is capable of binding to an active site of the probe-attached HCP impurity;

contacting the sample with a solid support, wherein the solid support comprises a ligand, and wherein the ligand is capable of binding to the tag; and

washing the solid support using a solution to isolate the probe-attached HCP impurity and to provide an eluent.

2. The method of claim 1, wherein the warhead is capable of binding covalently to a residue in the active site of the probe-attached HCP impurity.

3. The method of claim 1, wherein the tag is a conjugation tag, an affinity tag, or a reporter tag.

4. The method of claim 1 further comprising:

treating the eluent with an enzymatic digestion reaction to generate components of the isolated probe-attached HCP impurity; and

subsequently identifying the components of the isolated probe-attached HCP impurity using a mass spectrometer.

5. The method of claim 1, wherein the warhead comprises an enzymatic inhibitor, an enzymatic substrate-based scaffold or a protein-reactive molecule.

6. The method of claim 1, wherein the at least one probe further comprises a linker.

7. The method of claim 1, wherein the at least one high-abundance 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 4, wherein an enzyme of the enzymatic digestion reaction is trypsin.

9. The method of claim 4, wherein the mass spectrometer is an electrospray ionization mass spectrometer, nano-electrospray ionization mass spectrometer, such as an Orbitrap mass

spectrometer, a Q-TOF mass spectrometer or a triple quadrupole mass spectrometer, wherein the mass spectrometer is coupled to a liquid chromatography system.

10. The method of claim 4, wherein the mass spectrometer is capable of performing LC-MS (liquid chromatography-mass spectrometry), nano-LC-MS, LC-MS/MS, nano-LC-MS/MS or a LC-MRM-MS (liquid chromatography-multiple reaction monitoring-mass spectrometry) analyses.

11. The method of claim 1, wherein the tag is detected using Western blot, capillary electrophoresis, SDS-PAGE, fluorescent visualization, or fluorescent gel imaging.

12. The method of claim 1, wherein the active site of the probe-attached HCP impurity is a cysteine protease active site, a serine protease active site, a serine hydrolase active site, a cathepsin active site, a metalloprotease active site, a cholinesterase active site, an active site of a lipid-binding protein, an active site of a sphingolipid-binding protein, an active site of a ceramide-binding protein, a lipase active site, a protease active site, a hydrolase active site, an oxidoreductase active site, or an isomerase active site.

13. The method of claim 1, wherein the tag comprises a fluorophore or a fluorophore conjugation site, such as rhodamine, biotin, phosphine, alkyne, azide, acetylene, cyclooctyne, phenyl azide, or omega-terminal azide.

14. The method of claim 1, wherein the warhead comprises fluorophosphonate, epoxysuccinate, photo-activatable lipid, photo-activatable sphingosine, N-acetylated amino acid, quinolimine methide coupled amino acid, or p-aminomandelic acid coupled amino acid.

15. The method of claim 1, wherein the probe comprises azido-fluorophosphonate; desthiobiotin-fluorophosphonate; tetramethylrhodamine-fluorophosphonate; ethyl (2S, 3S)-epoxysuccinate-Leu-Tyr-Acp-Lys(Biotin)-NH_2; 1-palmitoyl-2-(9-(3-pent-4-ynyl-3-H-diazirin-3-yl)-nonanoyl)-*sn*-glycero-3-phosphocholine; (2S,3R,E)-2-amino-13-(3-(pent-4-yn-1-yl)-3H-diazirin-3-yl)tridec-4-ene-1,3-diol; N-(9-(3-pent-4-ynyl-3-H-diazirin-3-yl)-nonanoyl)-D-erythro-sphingosine; 1,2-dipalmitoyl-sn-glycero-3-phosphoethanolamine-N-(5-hexynoyl); or D-galactosyl-ß-1,1' N-(6"-azidohexanoyl)-D-erythro-sphingosine.

16. A system for identifying host cell protein (HCP) impurities in a sample, comprising:

at least one probe, wherein the at least one probe comprises a warhead and a tag, wherein the at least one probe is capable of binding to a HCP impurity to provide a probe-attached HCP impurity, wherein the warhead is capable of binding to an active site of the probe-attached HCP impurity, and wherein the sample comprises at least one high-abundance protein;

a solid support, wherein the solid support comprises a ligand which is capable of binding to the tag;

a solution for washing the solid support to isolate the probe-attached HCP impurities and to provide an eluent;

an enzymatic digestion solution capable of generating components of the isolated probe-attached HCP impurities; and

a mass spectrometer capable of identifying the components from the isolated probe-attached HCP impurity.

17. The system of claim 16, wherein the warhead is capable of binding covalently to a residue in the active site of the probe-attached HCP impurity.

18. The system of claim 16, wherein the tag is a conjugation tag, an affinity tag, or a reporter tag.

19. The system of claim 16, wherein the warhead comprises an enzymatic inhibitor, an enzymatic substrate-based scaffold or a protein-reactive molecule.

20. The system of claim 16, wherein the at least one probe further comprises a linker.

21. The system of claim 16, wherein the at least one high-abundance 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.

22. The system of claim 16, wherein an enzyme of the enzymatic digestion solution is trypsin.

23. The system of claim 16, wherein the mass spectrometer is an electrospray ionization mass spectrometer, nano-electrospray ionization mass spectrometer, such as an Orbitrap mass

spectrometer, a Q-TOF mass spectrometer or a triple quadrupole mass spectrometer, wherein the mass spectrometer is coupled to a liquid chromatography system.

24. The system of claim 16, wherein the mass spectrometer is capable of performing LC-MS (liquid chromatography-mass spectrometry), nano-LC-MS, LC-MS/MS, nano-LC-MS/MS or a LC-MRM-MS (liquid chromatography-multiple reaction monitoring-mass spectrometry) analyses.

25. The system of claim 16, wherein the tag is detected using Western blot, capillary electrophoresis, SDS-PAGE, fluorescent visualization, or fluorescent gel imaging.

26. The system of claim 16, wherein the active site of the probe-attached HCP impurity is a cysteine protease active site, a serine protease active site, a serine hydrolase active site, a cathepsin active site, a metalloprotease active site, a cholinesterase active site, an active site of a lipid-binding protein, an active site of a sphingolipid-binding protein, an active site of a ceramide-binding protein, a lipase active site, a protease active site, a hydrolase active site, an oxidoreductase active site, or an isomerase active site.

27. The system of claim 16, wherein the tag comprises a fluorophore or a fluorophore conjugation site, such as rhodamine, biotin, phosphine, alkyne, azide, acetylene, cyclooctyne, phenyl azide, or omega-terminal azide.

28. The system of claim 16, wherein the warhead comprises fluorophosphonate, epoxysuccinate, photo-activatable lipid, photo-activatable sphingosine, N-acetylated amino acid, quinolimine methide coupled amino acid, or p-aminomandelic acid coupled amino acid.

29. The system of claim 16, wherein the probe comprises azido-fluorophosphonate; desthiobiotin-fluorophosphonate; tetramethylrhodamine-fluorophosphonate; ethyl (2S, 3S)-epoxysuccinate-Leu-Tyr-Acp-Lys(Biotin)-NH_2; 1-palmitoyl-2-(9-(3-pent-4-ynyl-3-H-diazirin-3-yl)-nonanoyl)-*sn*-glycero-3-phosphocholine; (2S,3R,E)-2-amino-13-(3-(pent-4-yn-1-yl)-3H-diazirin-3-yl)tridec-4-ene-1,3-diol; N-(9-(3-pent-4-ynyl-3-H-diazirin-3-yl)-nonanoyl)-D-erythro-sphingosine; 1,2-dipalmitoyl-sn-glycero-3-phosphoethanolamine-N-(5-hexynoyl); or D-galactosyl-ß-1,1' N-(6"-azidohexanoyl)-D-erythro-sphingosine.