What is claimed is:

1. A method for determining an amino acid sequence of a polypeptide of interest, comprising:

contacting a first sample containing the polypeptide of interest with a first protease that cleaves peptide bonds after a basic amino acid, under conditions that permit the first protease to digest the polypeptide of interest to produce a first set of digested peptide fragments;

fragmenting the first set of digested peptide fragments to produce a first set of fragmented peptide ions corresponding to peptides in the first set of digested peptide fragments;

determining masses of the first set of fragmented peptide ions;

contacting a second sample containing the polypeptide of interest with a second protease that cleaves peptide bonds before a basic amino acid, under conditions that permit the second protease to digest the polypeptide of interest to produce a second set of digested peptide fragments;

fragmenting the second set of digested peptide fragments to produce a second set of fragmented peptide ions corresponding to peptides in the second set of digested peptide fragments;

determining masses of the second set of fragmented peptide ions;

selecting pairs of peptide ions from the first set of fragmented peptide ions and the second set of fragmented peptide ions that differ in mass by a mass of an arginine amino acid residue or a mass of a lysine amino acid residue;

assigning ion type for the pairs of peptide ions to generate a list of the same-type peptide ions;

selecting a mass ladder of peptide ions with incremental mass by the mass of amino acid residue(s) to identify individual amino acid residues and assembling the identified amino acid residues to determine the amino acid sequence of the polypeptide of interest.

2. The method of claim 1, wherein the first protease is a Trypsin protease.

3. The method of claim 1 or 2, wherein the second protease is a Tryp-N protease.

4. The method of any one of claims 1-3, further comprising,

selecting a first digested peptide fragment from the first set of digested peptide fragments; and selecting a second digested peptide fragment from the second set of digested

peptide fragments with a mass identical to the first digested peptide fragment.

5. The method of any one of claims 1-4, further comprising,

selecting a first digested peptide fragment from the first set of digested peptide fragments; and

selecting a second digested peptide fragment from the second set of digested peptide fragment with a mass that has a mass difference equal to the mass difference between a lysine amino acid residue and a arginine amino acid residue to the first digested peptide fragment.

6. The method of any one of claims 1-5, wherein a first digested peptide fragment from the first set of digested peptide fragments is fragmented to produce a first series of fragmented peptide ions corresponding to the first digested peptide fragment and a second digested peptide fragment from the second set of digested peptide fragments corresponding to the first digested peptide fragment is fragmented to produce a second series of fragmented peptide ions corresponding to the second digested peptide fragment; and wherein assigning the pairs of peptide ions to derive amino acid sequences comprises:

assigning ion type for the pairs of peptide ions to generate a list of the same-type peptide ions;

selecting a mass ladder of peptide ions with incremental mass by the mass of amino acid residue(s) to identify individual amino acid residues for the list; and

and assembling the identified amino acid residues to determine the amino acid sequence of the polypeptide of interest.

7. The method of any one of claims 1-6, wherein the pairs of peptide ions from the first set of fragmented peptide ions and the second set of fragmented peptide ions are selected that differ in mass by the mass of an arginine amino acid residue.

8. The method of claim 7, where a negative difference in mass of an arginine amino acid residue between pairs of peptide ions from the first set of fragmented peptide ions and the second set of fragmented peptide ions indicates that the peptide has an N-terminal arginine residue.

9. The method of claim 7, where a positive difference in mass of an arginine amino acid residue between pairs of peptide ions from the first set of fragmented peptide ions and the second set of fragmented peptide ions indicates that the peptide has a C-terminal

arginine residue.

10. The method of any one of claims 1-6, wherein the pairs of peptide ions from the first set of fragmented peptide ions and the second set of fragmented peptide ions are selected that differ in mass by the mass of a lysine amino acid residue.

11. The method of claim 10, where a negative difference in mass of a lysine amino acid residue between pairs of peptide ions from the first set of fragmented peptide ions and the second set of fragmented peptide ions indicates that the peptide has an N-terminal lysine residue.

12. The method of claim 10, where a positive difference in mass of a lysine amino acid residue between pairs of peptide ions from the first set of fragmented peptide ions and the second set of fragmented peptide ions indicates that the peptide has a C-terminal lysine residue.

13. The method of any one of claims 1-12, wherein the selected fragmented peptide ions from the first set of fragmented peptide ions correspond with the selected fragmented peptide ions from the second set of fragmented peptide ions.

14. The method of any one of claims 1-13, wherein the selected fragmented peptide ions from the first set of fragmented peptide ions are b ions and the selected fragmented peptide ions from the second set of fragmented peptide ions are b ions having a difference in mass of an arginine amino acid residue or a mass of a lysine amino acid residue.

15. The method of any one of claims 1-13, wherein the selected fragmented peptide ions from the first set of fragmented peptide ions are y ions and the selected fragmented peptide ions from the second set of fragmented peptide ions are y ions having a difference in mass of an arginine amino acid residue or a mass of a lysine amino acid residue.

16. The method of any one of claim 1-15, wherein mass is determined using mass spectrometry.

17. The method of any one of claim 1-16, wherein the fragment ions are produced using tandem mass spectrometry.

18. The method of any one of claim 1-17, wherein the polypeptide of interest comprises a protein.

19. The method of any one of claims 1-18, wherein the polypeptide of interest comprises a monoclonal antibody.

20. The method of any one of claims 1-19, wherein the polypeptide of interest comprises a monospecific antibody or a bispecific antibody.