

What is claimed is:

1. A method for quantifying a post-translational modification of a protein of interest, comprising:
 - (a) contacting a sample including said protein of interest to a digestive enzyme to obtain a peptide digest;
 - (b) adding to said peptide digest a set of heavy peptide standards, wherein at least one heavy peptide standard includes said post-translational modification and at least one heavy peptide standard does not include said post-translational modification;
 - (c) subjecting said peptide digest with said added heavy peptide standards to analysis using liquid chromatography-mass spectrometry to acquire a signal corresponding to each peptide of the peptide digest and heavy peptide standards;
 - (d) generating a calibration curve using a relative signal of the at least one heavy peptide standard including said post-translational modification compared to the at least one heavy peptide standard not including said post-translational modification;
 - (e) quantifying a post-translational modification of said protein of interest using the relative signal of at least one peptide from said protein of interest including said post-translational modification compared to at least one peptide from said protein of interest not including said post-translational modification; and
 - (f) normalizing the result of (e) using the calibration curve of (d) to further quantify said post-translational modification of said protein of interest.
2. The method of claim 1, wherein the protein of interest is a therapeutic protein.
3. The method of claim 2, wherein said therapeutic protein is selected from a group consisting of an antibody, a soluble receptor, an antibody-drug conjugate, and an enzyme.
4. The method of claim 1, wherein said protein of interest is a monoclonal antibody.
5. The method of claim 1, wherein said protein of interest is a bispecific antibody.
6. The method of claim 1, wherein said post-translational modification is the presence of an unprocessed C-terminal lysine.

7. The method of claim 1, wherein said heavy peptide standards are present at molar ratios between about 1:1 and about 1:1000 relative to at least one other heavy peptide standard.
8. The method of claim 1, wherein said heavy peptide standards comprise between about 1 and about 16 heavy isotopes.
9. The method of claim 1, where said heavy peptide standards comprise C^{13} , N^{15} , or a combination thereof.
10. The method of claim 1, wherein said digestive enzyme is trypsin.
11. The method of claim 1, wherein said liquid chromatography method comprises reverse phase liquid chromatography, ion exchange chromatography, size exclusion chromatography, affinity chromatography, hydrophobic interaction chromatography, hydrophilic interaction chromatography, mixed-mode chromatography, or a combination thereof.
12. The method of claim 1, wherein said 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 said mass spectrometer is coupled to said liquid chromatography system, and wherein said mass spectrometer is capable of performing LC-MS, LC-MRM-MS, and/or LC-MS/MS analyses.
13. A kit for quantifying a post-translational modification of a protein of interest, comprising:
 - (a) a first composition including at least one heavy peptide standard including a post-translational modification; and
 - (b) a second composition including at least one heavy peptide standard not including said post-translational modification,wherein the first and second compositions are capable of being added to peptide digests, wherein a relative signal of the at least one heavy peptide standard including said post-translational modification compared to the at least one heavy peptide standard not including said post-translational modification can be used to generate a calibration curve when analyzed by mass spectrometry, and wherein said calibration curve can be used to quantify a post-translational modification of a protein of interest.
14. The kit of claim 13, wherein said post-translational modification is the presence of an unprocessed C-terminal lysine.

15. The kit of claim 13, wherein said heavy peptide standards are present at molar ratios between about 1:1 and about 1:1000 relative to at least one other heavy peptide standard.
16. The kit of claim 13, wherein said heavy peptide standards comprise between about 1 and about 16 heavy isotopes.
17. The kit of claim 13, where said heavy peptide standards comprise C^{13} , N^{15} , or a combination thereof.
18. The kit of claim 13, further comprising at least one light peptide standard.