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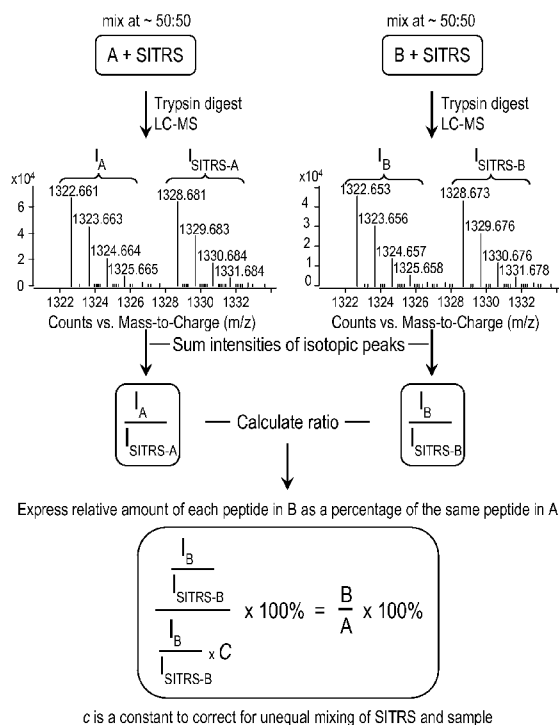
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(54) Title: COMPARISON OF PROTEIN SAMPLES

**Fig. 1**

(57) Abstract: Methods of qualitatively and/or quantitatively detecting the presence of mutations, modifications or impurities in a protein sample are provided. The methods utilize isotopically labeled variants of amino acids incorporated into proteins prior to protein digest to enable comparisons of two protein samples in bottom-up liquid chromatography. The measurements achieved by the present invention take into account not only the masses of peptides generated during proteolytic digest, but also the abundance of each resulting peptide. Measuring of the abundance of peptides by MS is enabled by utilizing a SITSR sample that is mixed with an unlabeled protein prior to protein digest. As used herein, the term "SITSR sample" or "SITSR standard" means a protein (e.g., an antibody) of known sequence, labeled with a stable isotopically labeled variant of at least one amino acid present in the protein.



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