Post-biosynthetic labeling strategies can be applied to any set of samples, including primary cell culture and human, because they are performed post-lysis.The peptide amino-termini and lysine side-chains are targeted by the amine-specific reactive group.Chemical labeling targets reactive groups on the side-chains of amino acids or peptide termini.Improving on the use of isotope-coded affinity tags (ICAT) [51], isobaric mass tags are all the same mass and it is only upon fragmentation that the different mass tags are observed [52].Accurately distinguishing the small mass difference produced by enzymatic labeling requires an instrument with high mass accuracy and high mass resolution.Consequently, comprehensive stable isotope incorporation is difficult to achieve because labeling is sequence-dependent.A popular version of isobaric mass tags is the iTRAQ reagent [53], which has recently expanded to incorporate up to eight reporter mass ions.This is of particular relevance to biological experiments in which multiple conditions or multiple time-points are being evaluated such as signaling networks [54].Enzymatic labeling is performed using H2 18O during the peptide bond hydrolysis step of the digestion [50].The isobaric mass tag consists of an amine-specific reactive group, a balancer group and a reporter mass group.