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Utilizing ^{13}C-labeled Biological Materials for Targeted and Untargeted Metabolomics

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Isotopically labelled standards are invaluable for quantitative mass spectrometry. Additionally, they have been utilized in untargeted mass spectrometry for improving the confidence in data processing and annotation. In this two-part presentation, we describe our use of a ^{13}C-labelled yeast sample for both quantitative assay development and untargeted metabolomics software benchmarking. (1) NAD^+ is a critical coenzyme for reduction-oxidation reactions in all living cells. Aging and age-associated diseases are linked to the decline in NAD^+ levels and alterations of NAD^+ metabolic pathway activity. The major metabolites that are involved in NAD metabolism, (referred to as NADome), include NAD^+, NADH, $NADP^+$, NADPH, ADPR, cADPR, NMN, NAMN, NAAD, NR, NAR, NAM, NA, Me2PY, Me4PY. Determination of the concentration levels of the NADome has been challenging because of chemical instability of NAD metabolites, their chemical structural diversity and similarity, and a lack of availability of internal standards. We present the use of ^{13}C-labelled yeast as an internal standard in developing a targeted 'NADome' assay. (2) Informatics tools are critical to fully utilizing the rich depth of untargeted metabolomics datasets. However, there are few resources available for determining how well software is performing. We describe efforts to develop a benchmark dataset which utilizes commercially available complex reference materials, including paired ^{12}C/^{13}C yeast, and authentic standards and internal standards to enable objective metrics of software performance.