# Mass Spectrometry-based Multi-Omics: Combinations of Proteomics, Metabolomics, and/or Lipidomics

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## Abstract

Studies that integrate unbiased measurements across at least two omics layers are often referred to as “multiomics”. Measurable “omes” include the genome, transcriptome, proteome, and metabolome. Any combination of omic measures can be referred to as multiomics; for the scope of this review we focus on research combining proteomics and metabolomics. Mass spectrometry is the leading technique for analysis of the proteome and the metabolome. Due to improvements in sample preparation and data collection, more studies are incorporating both mass spectrometry-based proteomics and metabolomics. In this review, we discuss the perceived value of multiomics, advances in sample preparation and data collection, the current state of multiomic data integration, and clinical examples of multiomic analysis. Finally, we explore major barriers preventing democratization of mass spectrometry based multiomics to the same level as nucleic acid analysis, and we suggest solutions to break these barriers.

# Introduction

Topics:

[Importance of omic measurement]: A major goal of biomedical research is understanding how changes in biomolecule compositions of cells and tissues lead to disease phenotypes. The genome serves as a library of possible transcripts, some of which are instructions for proteins, and proteins act on metabolites. The genome thus indirectly determines the set of possible cellular states, and the exact cellular state depends on the endogenous and exogenous environmental cues. To understand how the genome connects to phenotype, measurement of there genome must be accompanied by measurement of downstream layers of the central dogma of biochemistry. Measurement of multiple omic layers is know as multiomics.

2. concept of multiomics

3. What is proteomics

4. what is metabolomics

    - polar metabolomics
    - lipidomics

5. what does multi-omic integration mean?

6. Other reviews

    Multiomic studies in mitochondria [1]

    - discussion of how to prepare samples, QC, and methods to analyze the samples by MS
    - includes mention of linking to functional (phenotype) readout

    Multi-omics approaches to disease [2]

    - overview of each omic technology
    - first section is discusses considerations for before multiomic studies: consider the exact disease, sample size, human samples versus model organisms, plan for analysis strategy before collecting data
    - second section is focus on methods for omic integration:
    - third is future directions:

List of Planned Figures: 1. overview of how omic layers are related showing different ‘flavors’ of each omic analysis * genomics * transcriptomics * proteomics * metabolomics * microbiomics

3.

# Sample Preparation for Multi-Omic Analysis

Integrative multi-omics analysis is a powerful approach to study complex biological responses and has gained popularity in recent years. To avoid the potential

1, Sample preparation for proteomics

2, Sample preparation for metabolomics

2.1 non-targeted metabolomics

[3]

2.2 targeted metabolomics

2.3 lipidomics

[4]

3, Integrative sample prepatation for multi-omics

In the context of multi-omics analyses, being able to perform multiple measurements on the same sample can also decrease experimental variation.

[5]

[6]

[7]

## New developments of mass spectrometry-based methods for multi-omics

4.1 proteomics

4.1.1 Traditional standard methods for proteomics

(Remember to mention here)

4.1.2 Direct infusion methods for proteome analysis (high-throughput methods)

For current proteomic analysis methods, time-consuming chromatographic separation (typically requiring 30–60 min per sample or even longer) is required to protect the coverage, repeatiability, robustness and quantification ability. However, with the rapid application of multiomics results in drug development, biomarker discovery studies and clinical diagnosis. High-throughput methods is highly desirable to boost these fields forward.[8]

(as a high-throughput method, MALDI based proteome analysis should be mentioned here, for example, the application of MALDI for identification of species of bacteria and fungas through their specific peptides)

4.2 metabolomics

To accurately and reliably interpret data derived from metabolomics and lipidomics studies, enormous mass spectrometry based methods were developed during the past decades. (remember

to mention the application of MALDI for metabolites analysis, although the drawback of MALDI-tof is obvious.(

Drawbacks: 1,the background of organic matrix in the low molecular weight region 2,the obtained information of MALDI is still very limited, no more than 300 identified metabolites, and also quantification is difficult.
3,as a non-consistent ion source, currently TOF is the typical mass analyser for MALDI, which still suffers from relative low resolution. FTICR can connect MALDI )

4.2.2 Direct infusion mass spectrometry methods for high-throughput analysis of metabolites.()

(direct infusion and so called flow injection MS. do not know the differences, seems saying the same thing.)

[4]

[4]

4.4 integrated methods

Mass spectrometry (MS) serves as the centerpiece technology for proteome and metabolome analysis. To gain a better understanding of the multifaceted networks of myriad actions in complex organisms, integration of different multiomic layers is increasingly explored such as joint methods of different omics.

[9]

[10, =pdf]

[11, =pdf]

# Examples of Mass spectrometry-based multi-omics applied to model organisms

1. “Multiomics Method Enabled by Sequential Metabolomics and Proteomics for Human Pluripotent Stem-Cell-Derived Cardiomyocytes” [12]:
2. Multi-omics Reveal Specific Targets of the RNA-Binding Protein Puf3p and Its Orchestration of Mitochondrial Biogenesis [13]
3. Mitochondrial protein functions elucidated by multiomic mass spectrometry [14]
4. Multi-omic mitoprotease profiling reveals role for oct1p [15]

For the data integration section:

Argonaut data integration manuscript - [16] “Integration strategies of multi-omics data for machine learning analysis” [17]

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