National Human Genome Research Institute

Multi-omics in Health and Disease
Current Applications, Challenges and Future Directions

Executive Summary

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June 17-18, 2021
Executive Summary

The NHGRI virtually hosted "Multi-omics in Health and Disease: Current Applications, Challenges and Future Directions". The meeting's goal was to understand the state of the field of multi-omics and to gather recommendations on a research strategy using multi-omics that is in line with the objectives in the NHGRI 2020 Strategic Vision. The meeting had the following objectives:

- To gain insight on how multi-omics data can improve our understanding of health and disease
- To identify study design, data integration and technological gaps and challenges to the use of multi-omics technology and its application to observational studies
- To consider steps required for future clinical implementation
- To define opportunities to overcome these challenges that are relevant to NHGRI's mission

Experts from government agencies and academia in multi-omics technologies and observational studies moderated four presentation sessions, three guided discussions and a concluding recommendation gathering session to examine two major themes:

- **Day 1: Technology, data integration and study design**
    - Experimental and computational technology/big data
    - Study design and sample collection
    - Data integration
- **Day 2: Application of multi-omics to study health and disease**
    - Application of multi-omics to observational studies
    - Future clinical implementation and roadblocks

The meeting concluded with a brainstorming session focused on generating a list of recommendations. A consolidated list representing discussions from throughout the meeting and from the brainstorming session was compiled by NHGRI staff and reviewed by the workshop planning committee for completeness. A narrative accounting of the workshop can be found in the Workshop Summary.

Ensure Diversity and Inclusion

- Ensure that multi-omics studies include individuals from all racial and ethnic groups or underrepresented minorities.
- Ensure that members of the population that are understudied in biomedical research, such as children, pregnant women, and elderly individuals, are included. This is especially important to understand development and aging.
- Ensure inclusion of diverse samples in establishing references and reference ranges for accurate interpretation and clinical decisions.
- Assess factors that prevent implementation in the clinic and consider steps to overcome them.

Develop High-throughput Technologies, Methods, and Analytical Tools

- Support development of technologies that allow the collection of multiple data points on the same sample such that individual trajectories can be assessed.
- Develop methods to capture multi-omics data from both accessible (e.g. blood, skin, saliva, and urine) and less accessible tissues (e.g. biopsy samples). Determine correlation and whether one could be used as a proxy for the other.
- Develop methods and tools that integrate: 1) different 'omes assayed in the same sample and at the same time point as well as 2) different 'omes in different samples.
- Support development of analytic tools that allow assessment of multiple modalities (e.g. multiple cells and cell types, multiple individuals, multiple 'omes)
- Determine stability of multi-omics measurements over time.
- Develop methods and tools for multi-omics studies in the context of single cells.
- Develop methods that integrate CRISPR-based experimental approaches (e.g. CROPseq/Perturb-Seq) with multi-omics data.
- Encourage efforts to integrate multi-omics studies that use model organisms with those involving human cohorts.
- Develop methods that integrate exposures and environmental factors with multi-omics data.
- Develop approaches to increase integration of wearable outputs with multi-omics data.
- Improve computational algorithms to better capture unstructured EHR data and integrate it with multi-omics data from observational studies.

Enhance Cohort Studies

- Support multi-omics studies among healthy individuals to understand natural variation, including cyclic patterns.
- Improve understanding of the genetic and non-genetic components of multi-omics biomarkers.

- Prioritize disease areas of focus where multi-omics technologies could have significant impact.
- Increase efforts to use multi-omics technologies to define endo-phenotypes of disease.
- Ensure that key disease-related timepoints within longitudinal studies (e.g. periods of asthma exacerbations) are the focus of analysis.
- Design data collection strategies that either reduce or anticipate, and account for, missing data (e.g. imputation methods), thereby increasing the validity of studies.
- Design approaches that focus on data re-use and facilitate collaborative and multidisciplinary networks of groups with existing data.
- Leverage cohorts, such as the *All of Us Research Program*, that already have sample diversity, to capture clinical data in EHR and encourage the use of wearables to capture exposures and environmental data.

Establish Consensus and Best Practices

- Evaluate optimal study design strategies to maximize output and reduce redundancy, especially given the cost.
- Consider different strategies to determine when a study has been properly validated.
- Perform benchmarking studies to understand best practices with respect to different kinds of technologies and methods, particularly for combined single cell multi-omics and for double, triple or more data types from single cells.
- Develop approaches to harmonize and standardize multi-omics data that are generalizable and can be applied to both existing as well as newly obtained data.
- Create consensus analysis pipelines and a data repository for multi-omics data.
- Establish a catalog to register multi-omics studies for easy searchability and comparison across studies.