MOBN: an interactive database of multi-omics biological networks

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Abstract

Summary: The associations among different omics are essential to understand human wellness and disease. However, very few studies have focused on collecting and exhibiting multi-omics associations in a single database. Here, we present an interactive database of multi-omics biological networks (MOBN) and describe associations between clinical chemistry, anthropometrics, plasma proteome, plasma metabolome and gut microbiome obtained from the same individuals. MOBN allows the user to interactively explore the association of a single feature with other omics data and customize its specific context (e.g. male/female specific). MOBN is designed for users who may not have a formal bioinformatics background to facilitate research in human wellness and diseases.

Availability: The database is accessible at http://multiomics.inetmodels.com without any limitation.

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1 Introduction

During the past decade, the development of high-throughput technologies has dramatically decreased the cost of generating large-scale multi-omics datasets (Goodwin, et al., 2016), and has opened up the possibilities to comprehensively and systematically study human wellness and disease (Karczewski and Snyder, 2018). Although analysis of individual omics methodologies has been proven to be useful in different clinical applications, integration of multiple omics data may offer novel insights and provide a more comprehensive understanding of biological functions in the human body (Hasin, et al., 2017). For instance, a recent study integrated time series phenomics, fluxomics and metabolomics data from subjects with various degrees of liver fat and revealed a novel glycine and serine deficiency phenotype in the patients with non-alcoholic fatty liver disease (Mardinoglu, et al., 2017). In another study, longitudinal phenomics, transcriptomics, metagenomics, and metabolomics data has been obtained from 10 subjects over a two-week period to illustrate the benefit of an isocaloric low-carbon diet for non-alcoholic fatty liver disease patients (Mardinoglu, et al., 2018). Moreover, several other studies have also demonstrated the use of longer-period longitudinal multi-omics data in capturing the dynamics of human diseases systematically (Chen, et al., 2012; David, et al., 2014; Smarr, 2012).

In order to provide a better framework to facilitate these types of investigations, we created an interactive database of multi-omics biological networks (MOBN), a user-friendly database which provides exploratory capabilities and interactive visualization of clinical chemistry, anthropometrics, plasma proteins, metabolites, and gut microbiomes associated with user-queried features (Figure 1). The data in MOBN are obtained from recent studies with large-scale multi-omics data collected on a series of individuals (Supplementary Info). To our knowledge, MOBN is the first database that provide association between multi-omics data obtained from the same subjects in physiological context rather than from text mining.

Fig. 1. Concept of MOBN.

2 Datasources and analysis

The data included in the MOBN are obtained from three independent studies with large-scale personalized longitudinal multi-omics data: (1) the Swedish SciLifeLab SCAPIS Wellness Profiling project which collected multi-omics data from 98 different subjects during 6 visits in 2 years (Bergstrom, et al., 2015), (2) the P100 Wellness study (Price, et al., 2017) where 108 subjects are followed for 9 month and profiled with different omics data (accessible phs001363.v1.p1 from dbGaP) and (3) the iPOP diet perturbation study which employed multi-omics data to describe the systematic dynamics in human with weight gain and weight loss during 3 visits within 1 year (Piening, et al., 2018). All of these studies provided information of the anthropometrics, clinical

chemistry, plasma proteome, plasma metabolome and gut microbiome for each individual involved in the study, and thus, the consensus of these multi-omics data is included in MOBN.

Data from the different studies were first standardized to apply the same omics feature names across all datasets, and normalized to remove bias. Different omics d+ata were subsequently corrected based on the age (for all networks) and sex (for non-gender specific networks) using trimmed mean robust regression (Price, et al., 2017). The corrected data were consequently utilized to determine the inter- and intra-omics associations based on Spearman's correlation, and the final association networks were constructed by collecting associations with significant correlation (FDR < 5%). All networks can be downloaded from the database under the 'Downloads' section.

3 Features

MOBN provides a free, flexible and simple-to-use visualization of multi-omics association networks that are freely-accessible. Users can customize their specific network based on their individual interests as shown in Figure 2.

Firstly, MOBN provides a broad selection of networks. Users may select networks constructed based on a specific study with a specific context, such as gender-specific networks or insulin resistance/sensitive networks. In addition, both cross-sectional and delta networks are constructed using the methodology presented in the P100 wellness study (Price, et al., 2017) for each network. Cross-sectional networks present multi-omics correlations in the context of individualized variation, while delta networks allow users to investigate features that co-vary within the same time intervals.

To search within a specific network, users need to input the commonly known name (gene symbol, metabolite name etc.) of (up to 3) analytes of interests to search and/or select from the drop-down list. Once the search is executed, the network will be generated and visualized in the graphic area. Next, users can filter the types of omics data shown in the graphic area based on their interests by checking/unchecking the corresponding box, showing only first neighbor edges and tailoring the network based on the number of edges and/or a specified statistical property, e.g. FDR.

All information about each analyte (network nodes) and related associations (network edges) is shown in the table area: the analyte name, short description, unit, correlation and P value of the association etc. In addition, wherever possible, analytes are linked with external databases such as KEGG (Kanehisa, et al., 2017), Human Protein Atlas (Thul, et al., 2017; Uhlen, et al., 2015; Uhlen, et al., 2017), Uniprot (UniProt, 2019) and HMDB (Wishart, et al., 2018) to facilitate further biological interpretation and investigation. Moreover, users can easily retrieve information provided in their network, export as a tab-separated file and analyze the networks with other tools following the 'Tutorial' section on the website.

4 Conclusion

MOBN is the first database that shows multi-omics associations based on personalized data. It's designed in a simple and user-friendly way, and accessible to a wide range of users including bench scientists with limited to no formal bioinformatics background. In this context, we expect MOBN to help catalyze deeper multi-omic investigations that may reveal novel biological mechanisms underlying human wellness and disease.

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Conflict of Interest: none declared.

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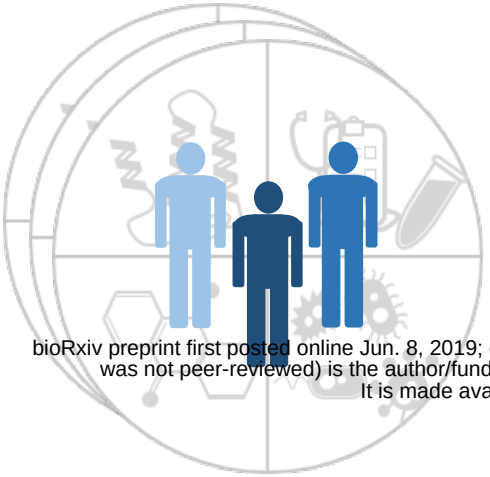
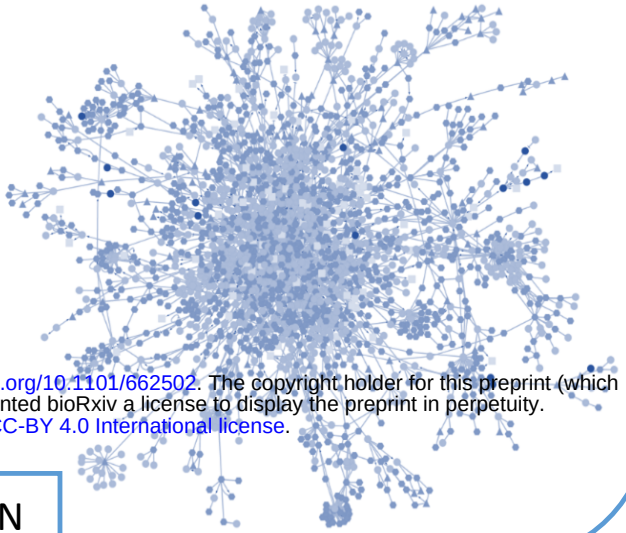
Multi-omics datasets



Multi-omics association networks



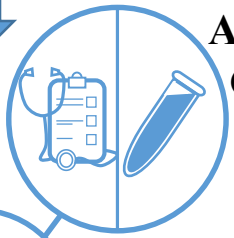
MOBN

Plasma Proteomics

Olink multiplexing
Immunoassay panels
Relative abundance

Anthropometrics & Clinical Chemistry

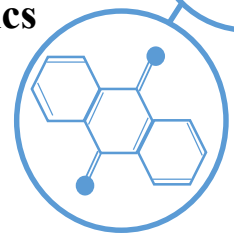
BMI, waist, height, etc
Blood and urine test



MOBN Query

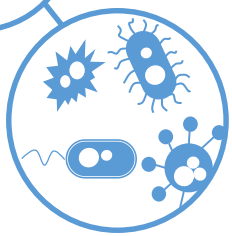
Plasma Metabolomics

LC-MS and/or GC-MS
Relative abundance



Gut Microbiome

16s profiling or
Shotgun metagenomes



MOBN
Multi-Omics Biological Network

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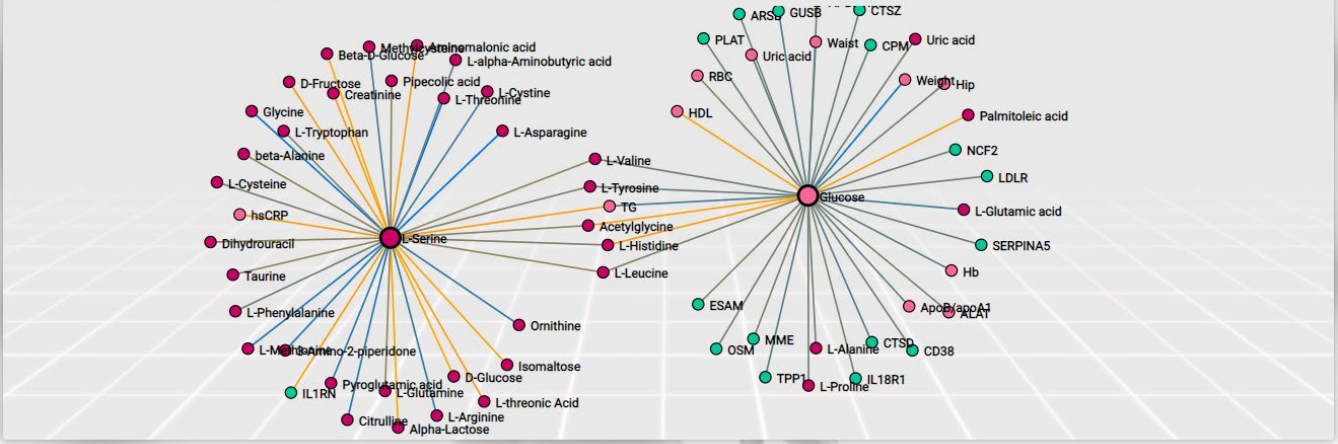
Cross-Sectional (Overall) ▾ | Glucose (CLINICAL) × L-Serine (METABOLITE) × | Search

Blue edge: postive corr. Orange edge: negative corr. Left click on edge Right click on node

Nodes Legend: Protein Metabolite Microbiome Anthropometric/Clinical Chemistry



Network filters | Save | Citation

Filter node by analyte type:

☑ Proteins ☑ Metabolites ☑ Microbiomes

☑ Anthropometrics/Clinical Chemistry

First Neighbor:

☐ Includes

NOTE:
Increasing the number of nodes will increase the loading time
Less than three genes to search
Less than 50 maximal nodes for multiple analytes

Maximum number of nodes (min-1 max-200): 36

Edge Pruning Parameter (-log10 P-Adjusted) (min-2 max-50): 2

Searched Nodes | All Nodes | Proteins | Metabolites | Microbiomes | Anthropometrics/Clinical Chemistry | Edges

Save Searched Genes as CSV file

#	Symbol	Location
1	Glucose	CLINICAL
2	L-Serine	METABOLITE