

multiSLIDE User Manual

Version 2.0

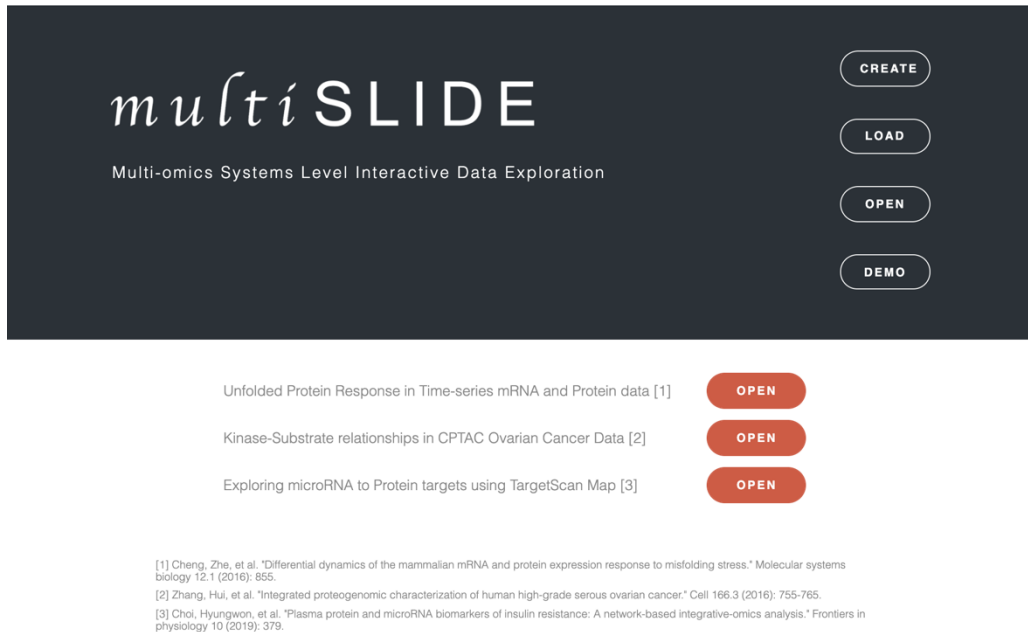
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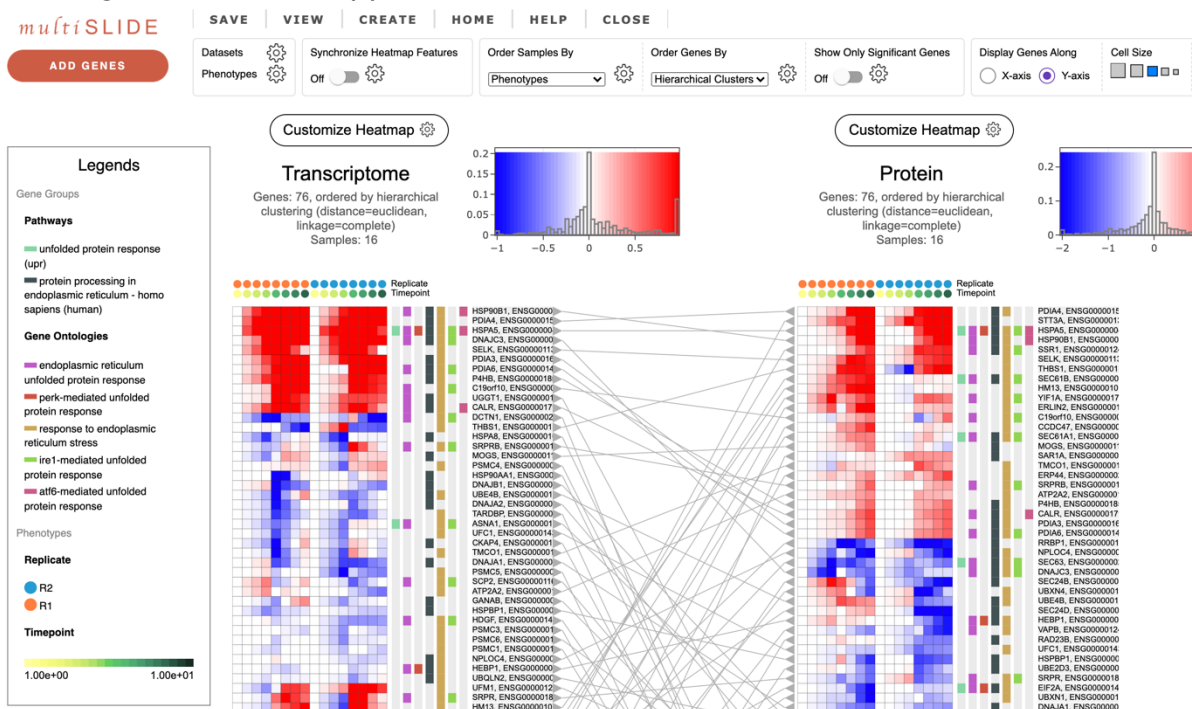
1. Run pre-existing demos

1. On the multiSLIDE homepage, clicking the “Demo” button displays three pre-loaded analyses. Click the “Open” to open the corresponding analysis. The details of the demos are available in the Case Studies section of our paper:

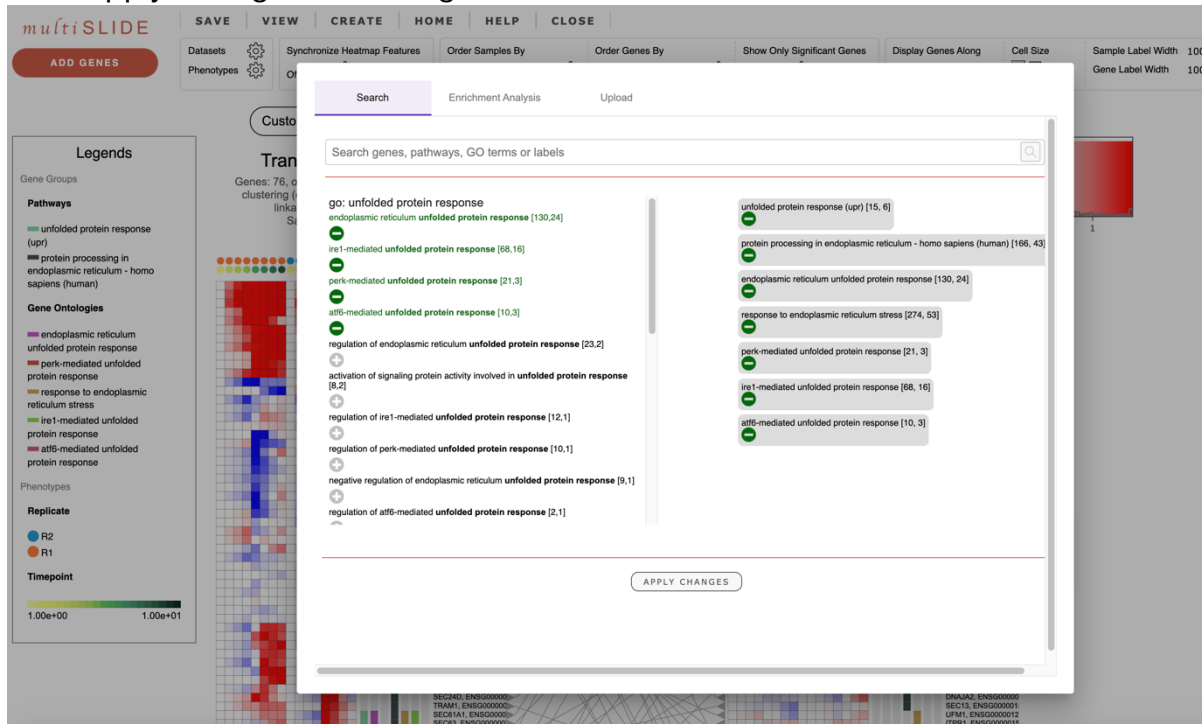
<https://www.biorxiv.org/content/10.1101/812271v2>.



2. Clicking ‘Open’ on multiSLIDE homepage leads to the visualization page. Here pathways, GO terms have been pre-selected and the clustering and feature ordering has also been applied.



3. Clicking 'Add Genes' on the top-left corner of the visualization page opens a panel showing the pre-selected pathways and GO terms. The '+' and '-' buttons can be used to add or remove pathways for visualization, respectively. Selected (added for visualization) search results are added to the right-side panel. Finally click 'Apply Changes' for changes to take effect.



4. To customize visualizations, set global clustering and statistical filtering parameters and customize individual heatmaps techniques see Section 4.

2. Open a “.mslide” file

The analysis workspace can be saved as a ‘.mslide’ file. To reopen a “.mslide” file click ‘Load’ button in the multiSLIDE homepage. This opens a panel below where the file can be selected using ‘Choose file’. Clicking ‘Upload’ re-opens the saved workspace. Pre-generated example .mslide files for the demo visualizations are available in https://github.com/soumitag/multiSLIDE/tree/master/demo_data.



Upload File

Choose file No file chosen

UPLOAD

3. Upload your own data

1. To start uploading your data click 'Create' in multiSLIDE homepage. In the panel that opens up, provide an Analysis Name in the textbox and click 'Create'.



Analysis Name

CREATE

2. In the data upload page, first select the Species type from the dropdown list

The screenshot shows the data upload interface. It is divided into three main sections. The first section, '1. Provide Species for Analysis 'test'', contains a 'Species Type' dropdown menu with options: 'Homo sapiens', 'Mus musculus', and 'Other'. The second section, '2. Please Upload a Single Clinical Information File for the Experiment', includes a 'Choose file' button, a 'Clinical Information File Delimiter' dropdown, and an 'UPLOAD' button. The third section, '3. Please Upload -omics Data File(s) using this module', includes a 'Data Type' dropdown, a 'Data File Upload' section with a 'Choose file' button, and a 'Data File Delimiter' dropdown. On the right side, there is a table header with columns: 'Display Name', 'Filename', 'Data Type', 'Delimiter', and 'Metadata Column'. Below the header, it says 'No files added yet'. A 'RESET' button is also visible.

3. In the data upload page, select a sample/clinical information file using the 'Choose file' button, select the appropriate file delimiter from the dropdown list, and click 'Upload' button. Successful completion of file upload will prompt a success message. Example sample information files are available in https://github.com/soumitag/multiSLIDE/tree/master/demo_data.

1. Provide Species for Analysis 'test'

Species Type

2. Please Upload a Single Clinical Information File for the Experiment

Upload Clinical Information File

Choose file ER_Stress_sa...ing_info.txt

Clinical Information File Delimiter

Tab

UPLOAD

File ER_Stress_sample_groupin g_info.txt uploaded successfully

3. Please Upload -omics Data File(s) using this module

Data Type

4. Using the panel on the bottom left of the data upload page, upload each omics data file one at a time. To upload an omics file, select the Data Type from the dropdown list to indicate the type of 'omics' data. Then use 'Choose file' button to select the omics file, select the file delimiter from the dropdown list, and click the 'Submit' button. On successful file upload the file will be listed in the table on the right. Examples of omics quantitative expression files are available here: https://github.com/soumitag/multiSLIDE/tree/master/demo_data.

Analysis 'test'

Species Type

2. Please Upload a Single Clinical Information File for the Experiment

Upload Clinical Information File

Choose file ER_Stress_sa...ing_info.txt

Clinical Information File Delimiter

Tab

UPLOAD

File ER_Stress_sample_groupin g_info.txt uploaded successfully

3. Please Upload -omics Data File(s) using this module

Data Type

Protein

Data File Upload

Choose file protein_ER_st...malized.txt

Data File Delimiter

Tab

RESET SUBMIT

Display Name	Filename	Data Type	Delimiter	Metadata Column Information	Edit	Preview	Delete
Transcriptome	mRNA_ER_stress_baseline_normalized.txt	Gene Expression (mRNA)	Tab	Metadata Columns: Linker(Gene) Column Mapping: Molecular-level Specific Identifier(s):			

RESET CREATE

5. The table shows the details of uploaded omics files. Clicking 'Edit' will open the Metadata Column Selection and Identifier Mapping panel. All information requested in this panel has to be completed for each omics file before clicking 'Create' to create the analysis.

Display Name	Filename	Data Type	Delimiter	Metadata Column Information	Edit	Preview	Delete
Transcriptome	mRNA_ER_stress_baseline_normalized.txt	Gene Expression (mRNA)	Tab	Metadata Columns: Linker(Gene) Column Mapping: Molecular-level Specific Identifier(s):			
Protein	protein_ER_stress_baseline_normalized.txt	Protein	Tab	Metadata Columns: Linker(Gene) Column Mapping: Molecular-level Specific Identifier(s):			

RESET
CREATE

6. Identify all metadata columns (non-quantitative expression data) in the data file, by selecting from the dropdown list. To align omics data, specify any linker columns, if available. Linker columns can be mappable to one of the standard identifiers, such as Gene Symbol, Entrez etc. Next, if molecular level specific identifiers such as genomic coordinates, phosphosites are also available, identify these columns from the dropdown list. Click 'Save Changes' and return to the main page. Once the details for all datasets have been filled click 'Create' to create the analysis.

Information File

Stress_saining_info.txt

File Delimiter

LOAD

Metadata Column Selection and Identifier Mapping

Metadata Columns

GeneSymbol

ADD

Ensembl

GeneSymbol

Does this dataset contain a 'Gene' column or a 'Linker' variable?

Linker variable are used to align omics identifiers across molecular levels. [Learn more.](#)

☒ Yes
☐ No

Map Linker Column -> Standard Identifier

Linker Column

GeneSymbol

Standard Identifiers

Gene Symbol

ADD

GeneSymbol

→

Gene Symbol

Does this dataset have molecular-level specific identifiers?

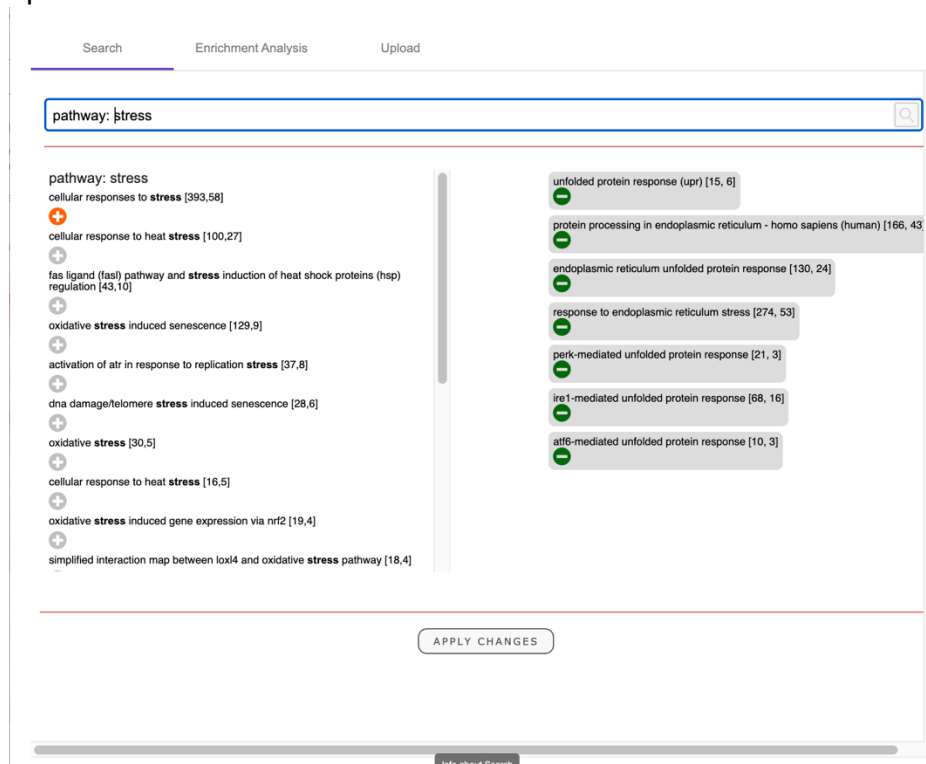
(for e.g. genomic coordinates, transcript identifiers etc.)

☐ Yes
☒ No

SAVE CHANGES

3.1 Query using keyword search

Clicking 'Add Genes' on the top-left corner of the visualization page opens a panel with three tabs: 'Search', 'Enrichment Analysis', and 'Upload'. Use the 'Search' tab for keyword search-based selection. Specify the search query in the search text box and click the search icon. The search results are indicated in the panel below. Scroll through the results and use the "+" and "-" icons to add or remove selections from visualization. Selected (added for visualization) search results are added to the right-side panel.



The table below shows three example queries that can be used in multiSLIDE. In the three examples, multiple searches are combined into a single query by specifying a semi-colon separated list of individual search queries. The individual queries can either take the form keyword=terms, for exact search, or keyword:terms, for inexact search. Here terms indicate the search terms, which can be a single search term or a comma separated list of search terms. Given that the user has to explicitly specify the keyword to search, multiSLIDE uses extensive name mapping, to support multiple syntaxes. For instance, in the examples in the table, "go", "go-term", and "Term" all imply the keyword GO term. Similarly, in the first and third examples, "path" and "PATHNAME" are equivalent and imply the keyword pathway name. To ensure composite searches containing multiple queries are not any slower than the individual searches these are performed parallelly.

Examples of composite search queries in multiSLIDE

- 1) path = estrogen signaling pathway; go:chemotaxis; gene: cdk1, ESR1,traf2
- 2) path-id = 04915; go-term:chemotaxis; genesymbol: cdk1, ESR1,traf2
- 3) PATHNAME=estrogen signaling pathway; Term:chemotaxis;entrez: 983, 2099, 7186

3.2 Query by uploading pathways

Clicking 'Add Genes' panel on the top-left corner of the visualization page opens a panel with three tabs. Click on the third tab 'Upload' to upload your own pathways or subsets of data to visualize.

The screenshot shows the 'Upload' tab of the 'Add Genes' panel. At the top, there are three tabs: 'Search', 'Enrichment Analysis', and 'Upload', with 'Upload' being the active tab. Below the tabs is the title 'Upload Functional Group Information'. Under this title, there is a section 'Functional Group Information Upload' containing a 'Choose file' button and the text 'Pathways_36...8082020.txt'. Below this is a 'SUBMIT' button. A message states 'File Pathways_36_kinases_corresponding_substrates_28082020.txt uploaded successfully'. Below the message is a 'Functional Groups' section with a dropdown menu showing 'phospho (123 members)'. Below the dropdown is an 'ADD' button. At the bottom of the panel, there are two buttons labeled 'proteome' and 'phospho', both with green minus signs. At the very bottom of the panel is an 'APPLY CHANGES' button.

3.3 Query by enrichment analysis

Clicking 'Add Genes' panel on the top-left corner of the visualization page opens a panel with three tabs. Click on the second tab 'Enrichment Analysis' and specify the dataset and parameters to run enrichment analysis and list the enriched pathways. These pathways can be added in the visualization

The screenshot shows the 'Enrichment Analysis' tab of the 'Add Genes' panel. At the top, there are three tabs: 'Search', 'Enrichment Analysis', and 'Upload', with 'Enrichment Analysis' being the active tab. Below the tabs is the title 'Differential Analysis'. Under this title, there are several dropdown menus: 'Dataset' (set to 'protein'), 'Phenotype' (set to 'Proteomic-subtype'), and 'Test Type' (set to 'Parametric'). Below these is a 'Significance Level' input field set to '0.05'. There is a checkbox for 'Multiple Testing Correction' which is unchecked. Below this is a 'False Discovery Rate' input field set to '1' with a note '% (Enter a number between 1-100)'. Below the 'Differential Analysis' section is the 'Enrichment Analysis' section. It has an 'Enrichment Type' section with two options: 'Pathway' (checked) and 'Gene Ontology Terms' (unchecked). Below this is a 'Significance Level' input field set to '0.05'.

4. Functionalities



The above image shows the global settings available in multiSLIDE. The numbered panels can be used to:

1. select the omics datasets and phenotypes to visualize
2. turn on/off synchronized and unsynchronized (independent) clustering
3. select the sample ordering scheme
4. select the molecule ordering scheme
5. turn on/off statistical filtering of the data.
6. change the orientation of the heatmaps
7. adjust heatmap cell sizes to one of the five preset sizes
8. adjust the size heatmap labels

The settings buttons besides panels 1-5 can be used to specify parameters specific to the selected customizations.

Individual omics heatmaps can be customized (by setting the number of histogram bins, the heatmap color scheme, range of the data etc.) by clicking the ‘Customize Heatmap’ settings button available beside each heatmap. This opens the panel shown below. Click ‘Apply Changes’ to close and apply the selected changes to the heatmap.

Aggregate by Linker ☒ On

Aggregator Function Mean

Feature Identifier(s) gene_symbol ADD

gene_symbol +

Number of Colors 51 (Valid Values: 0-255)

Binning Range

- ☐ Use Min and Max of Data (Min=-5.59, Max=6.25)
- ☐ Use Symmetric Bins (about 0)
- ☒ Use Range

Start -3 and End 3

Heatmap Color Scheme

Diverging colormaps

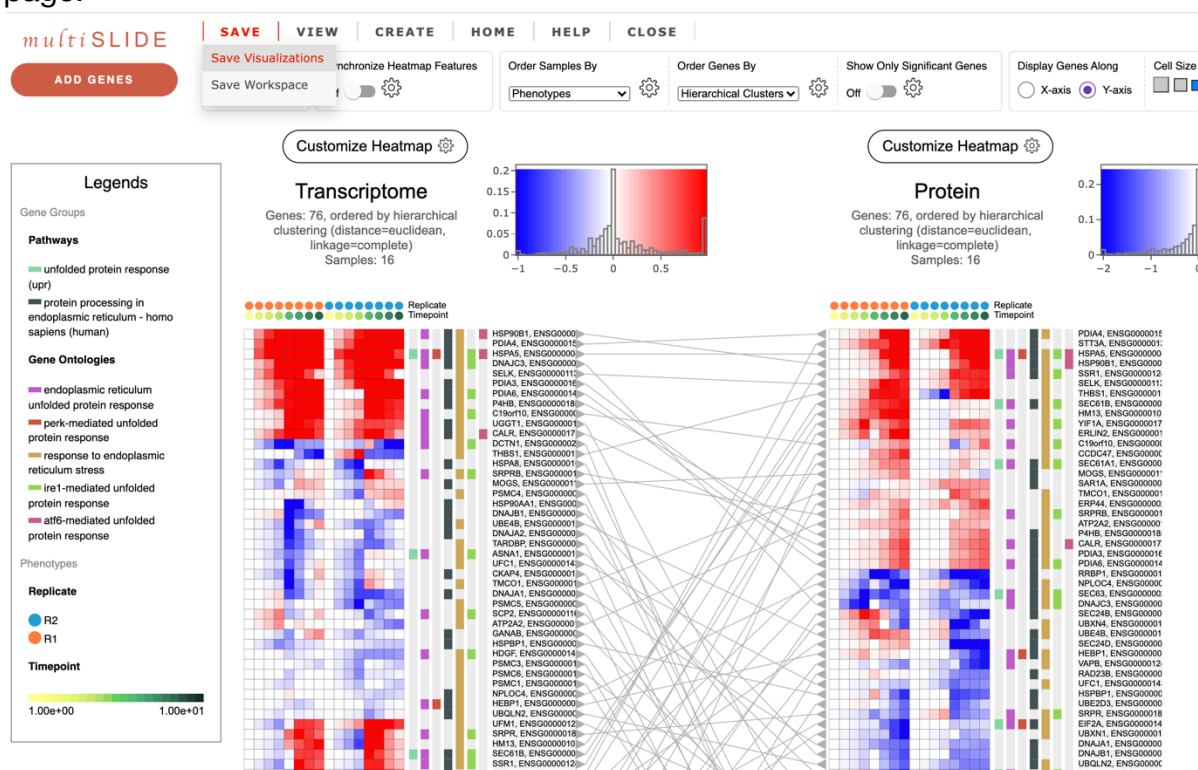
- ☐ BBKY
- ☒ BLWR
- ☐ BYR
- ☐ GBR
- ☐ SEISMIC
- ☐ COOLWARM
- ☐ BRBG
- ☐ PRGN
- ☐ PIYG
- ☐ RDYLG
- ☐ RDBU
- ☐ RDYLB
- ☐ SPECTRAL

Perceptually uniform colormaps

- ☐ VIRIDIS
- ☐ CIVIDIS
- ☐ INFERNO
- ☐ MAGMA
- ☐ PLASMA

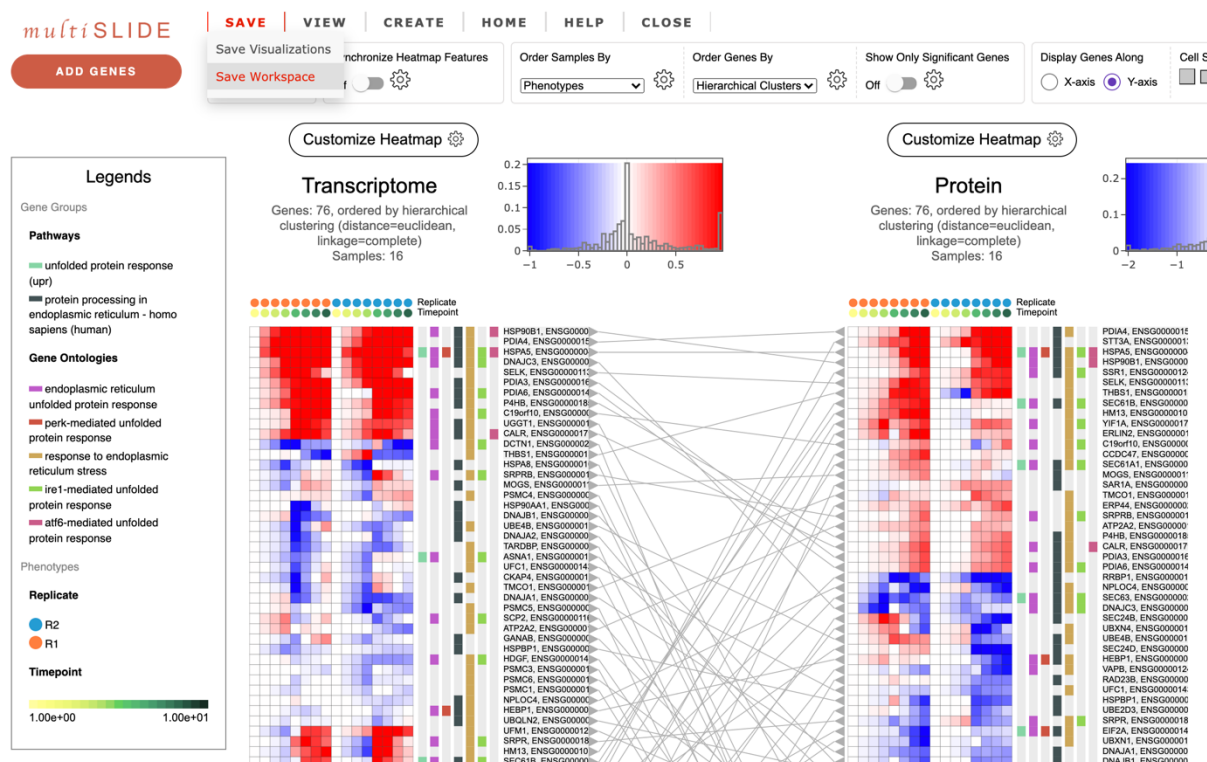
5. Save visualizations

In the top menu panel of the visualization page, mouse-over the 'Save' option opens a drop-down list. Clicking 'Save Visualizations' opens a new tab with the visualization. Right-click anywhere on the page and select 'Print' from the Context menu. In the Print dialog that opens select Destination 'Save as PDF' and using the 'Scale' option in the Print Settings Panel, scale the visualization to fit it in a single page.



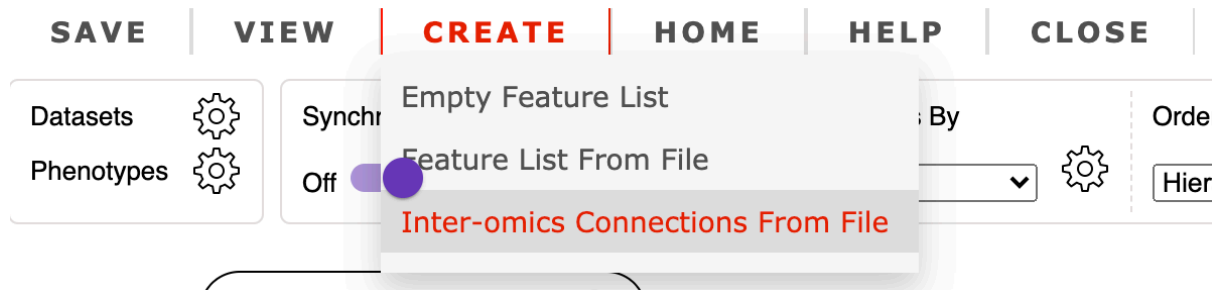
6. Save workspace

In the top menu panel of the visualization page, mouse-over the 'Save' option opens a drop-down list. Clicking 'Save Workspace' opens the Save Workspace panel. Click the 'Download' button to download the analysis workspace as .mslide file.



7. Upload externally curated network

In the top menu panel of the visualization page, mouse-over the 'Create' option opens a drop-down list. Clicking 'Inter-omics Connections From File' opens a panel where you can upload externally curated networks to the visualization. Provide a name to the network and select the file and its delimiter and click 'Upload'



Upload Inter-omics Connections

Give This Set of Connections a Name

Choose a File

 kinase_substr...28082020.txt

File Delimiter

Available Inter-omics Connections

kinase_substrate
(kinase_substrate_network_28082020.txt)

