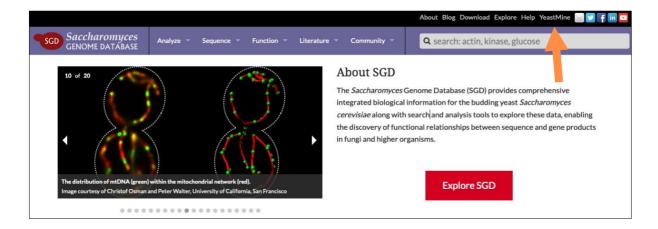
## **Search Strategies in SGD**

In addition to searching for data using our faceted search tool, SGD provides **YeastMine** (<a href="https://yeastmine.yeastgenome.org/">https://yeastmine.yeastgenome.org/</a>), a multifaceted search and retrieval environment that provides access to diverse datatypes. YeastMine enables rapid retrieval and manipulation of curated biological data on *S. cerevisiae* genes and genomic features. By creating gene lists, users can retrieve data on multiple genes at once. Gene lists can then be sequentially modified, analyzed, and refined, enabling you to answer more complex biological questions such as, "How many plasma membrane proteins are required for viability?" or "Which kinases, if knocked out, increase chronological lifespan?"

YeastMine can be accessed from the SGD home page (<a href="http://www.yeastgenome.org">http://www.yeastgenome.org</a>).

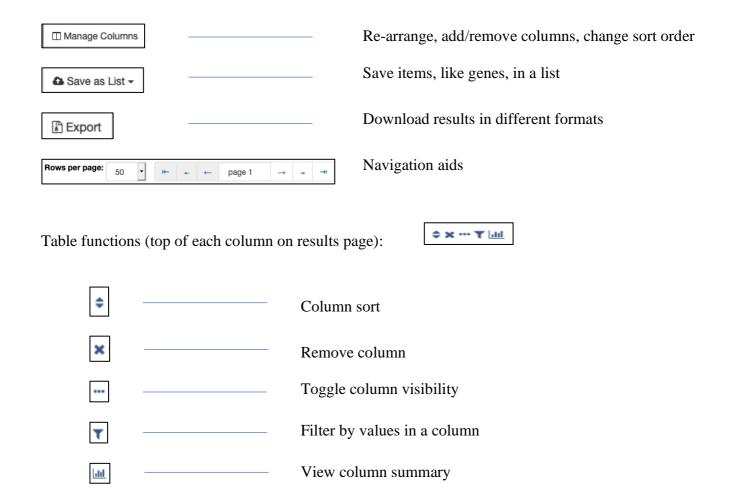


YeastMine contains several basic functionalities:

- Predefined queries (templates) (access via tab at the top (1) or tabbed bar middle (2)
  - Filter by category
  - o Filter by keyword(s)
- List creation
  - o Create and save list (name and add description), rename, share (MyMine
  - Add to list
- List operations (access via Lists tab at top)
  - Union all genes in two lists
  - o Intersect overlap of genes in two lists
  - o Subtract total unique non-overlapping genes
  - o Asymmetric Difference unique to one list of non-overlapping genes



Template results page options (top of page):





In the following exercise, we will use YeastMine to search for as yet under- and/or uncharacterized mitochondrial ribosomal proteins in yeast.

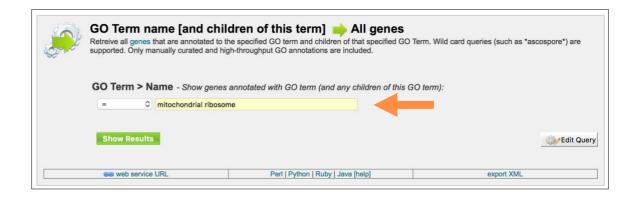
• Access YeastMine from SGD home page (<a href="http://www.yeastgenome.org">http://www.yeastgenome.org</a>); click on YeastMine in the upper right corner above the search box.

## 1. Create a list of proteins that are known subunits of the mitochondrial ribosome (MTR):

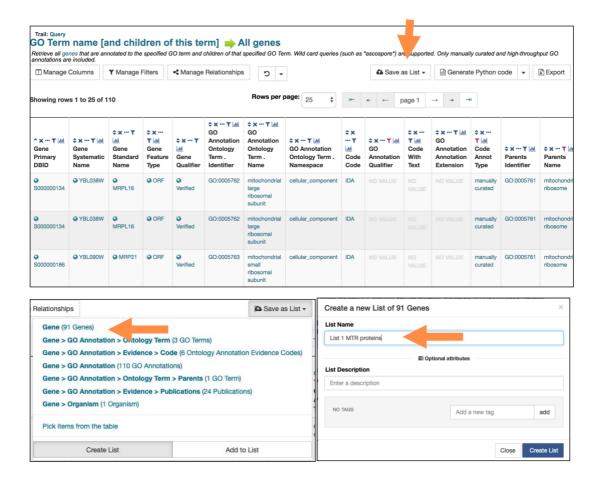
Open the FUNCTION tab & select GO Term name [and children of this term] ->
 All genes



• Enter mitochondrial ribosome into the query box; hit Show Results

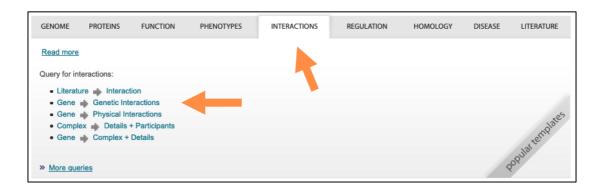


On the Results page, you should see a table with 110 rows. Click on Save as List and select the option Gene (91 Genes). Give your list a name, such as "List 1 MTR proteins" and hit Create List (you should see a green Success banner on top)

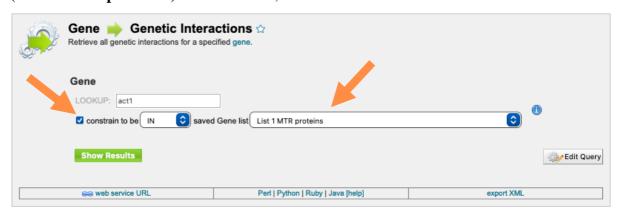


## 2. Find genes/proteins that genetically/physically interact with MTR proteins:

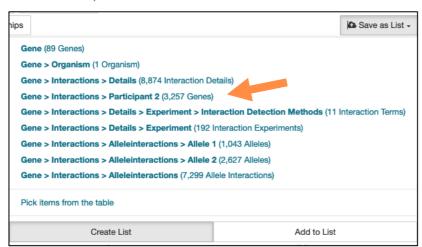
 Go back to YeastMine home page (click on Home in the purple banner on top). Open the INTERACTIONS tab and select Gene -> Genetic Interaction



• Check the box next to **constrain to be IN** and select your previously created list ("List 1 MTR proteins") from the menu; hit Show Results



The result shows all genes that interact genetically with MTR genes from List 1. Save the MTR genetic interactors by clicking on Save as List and selecting Gene > Interactions > Participant 2. Give your list a name ("List 2 MTR genetic interactors") and hit Create List.



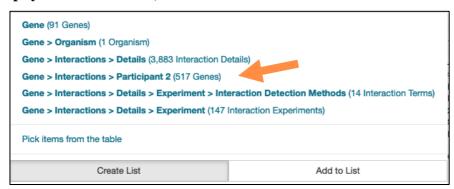
 Now go back to the YeastMine home page, open the INTERACTIONS tab again but this time select Gene -> Physical Interactions



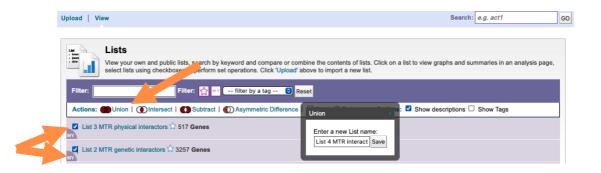
• Check the box next to **constrain to be IN** and select your previously created list ("List 1 MTR proteins") from the menu; hit Show Results



This results page shows all proteins that interact physically with the MTR proteins from List 1. Save the MTR physical interactors by clicking on Save as List and selecting Gene > Interactions > Participant 2. Give your list a name ("List 3 MTR physical interactors") and hit Create List.



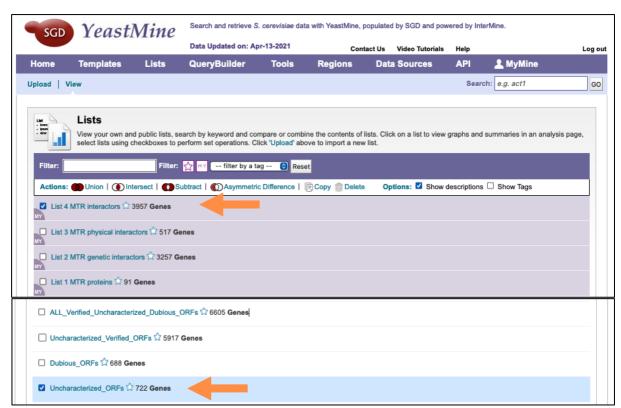
Now combine the genetic and physical interactors by performing a "Union" to get a
combined list of both genetic AND physical interactors. Go to the Lists tab, select the
check boxes next to List 2 MTR genetic interactors and List 3 MTR physical
interactors and select Union, and enter the name "List 4 MTR interactors"



## 3. Find MTR interactors that are uncharacterized:

Use a pre-made list of uncharacterized yeast genes: select Lists from the purple banner on top and click on View in the upper left corner. Scroll down the page to check the box next to Uncharacterized\_ORFs. Also check your previously saved list (List 4 MTR interactors) that should be on top, highlighted in purple.

•



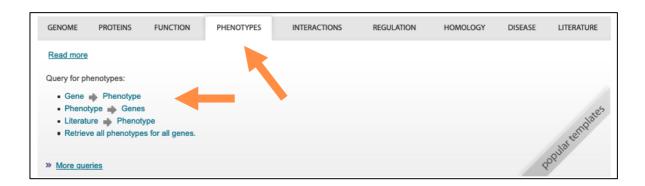
From the Actions, click on Intersect, give your list a name ("List 5 uncharacterized MTR interactors") and select Save; a green confirmation banner should appear.



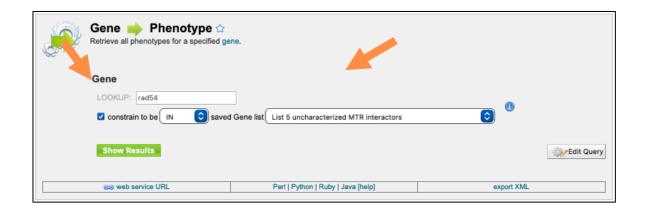
- Click on your list to see the results.
- Because we have over 200 genes in our results, it would be a good idea to narrow down our candidates further. For example, because the MTR is a mitochondrial

complex, we would expect that deleting bona fide subunits of the MTR would disrupt aerobic respiration. Let's refine our list of predicted MTR subunits by seeing which genes disrupt respiratory growth when deleted.

Return to YeastMine home page, open up PHENOTYPES tab and select the Gene ->
 Phenotype query

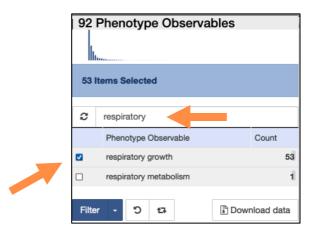


• Check the **constrain to be IN** checkbox and select your saved list ("**List 5** uncharacterized MTR interactors"); click on **Show Results** 

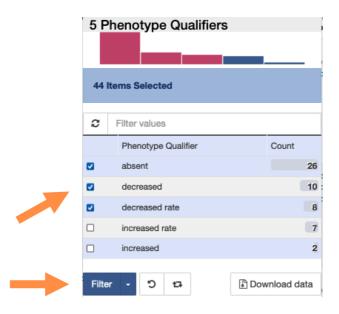


In the Results table, find a column labelled **Phenotypes Observable**. Hover your mouse over the small icons above the column name and click on **View Column Summary** (the bar graph icon on the right).

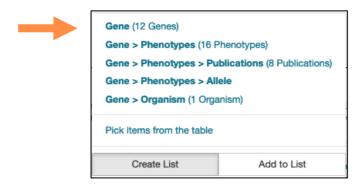
In the **Filter values** box, enter **respiratory** and scroll down the list to check the box next to **Respiratory growth**; hit **Filter**.



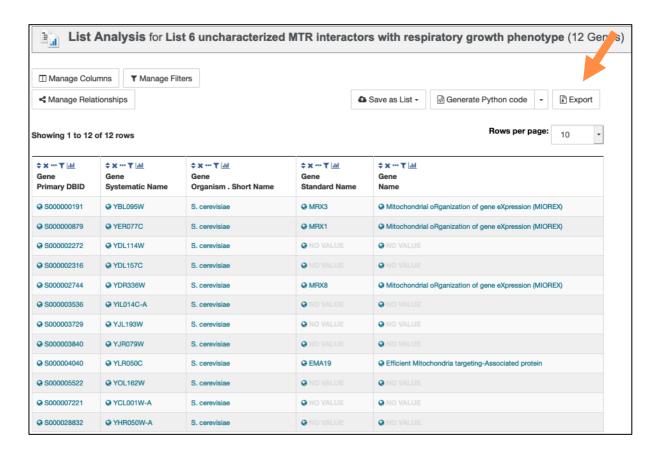
To filter the phenotypes for those where respiratory growth is impeded, find the
 Phenotype Qualifiers column and open the View Column Summary menu. Select
 all items that refer to hindering respiratory growth: "decreased", "decreased rate",
 "absent", etc. Then, hit Filter.



You should now have a list of uncharacterized yeast genes whose products interact
with mitochondrial ribosomes and mutations lead to respiratory growth defects. Use
the Save as List function to save the list of genes and enter the name "List 6
uncharacterized MTR interactors with respiratory growth phenotype"



• View the list and save the results into a .tsv file by clicking on the **Export** button, and then on the "**Download file**" button in the resulting pop-up window.

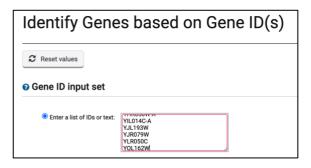


- The results of the above YeastMine analysis suggest 12 genes that potentially encode
  undiscovered subunits of the mitochondrial ribosome. Although these genes are
  uncharacterized, more data may exist on their orthologs in other organisms. Use
  FungiDB to survey the function of orthologs in Fungi and Oomycetes.
- Open the FungiDB homepage (<a href="https://fungidb.org/">https://fungidb.org/</a>). In the "Search for Genes" box, open the "Annotation, curation and identifiers" section and click on "Gene ID(s)".

 Using your exported .tsv file from YeastMine, copy and paste the systematic names of your results into the box. Click on "Get Answer".



Click on the red "Add Step" button. In the resulting pop-up window, click on Transform into related records > Orthology. Select Fungi and Oomycetes, then click on Run Step.



Orthologs from multiple species will be shown in the results table. Peruse the "Product Description" column. Click on the columns button. Do the descriptions of these orthologs support the prediction that the 12 yeast genes encode subunits of the mitochondrial ribosome? Click on the bar graph icon by the Product Description column to see a word cloud of entries in this column.

