Yeast ORFan Gene Project: Module 7 Guide

Gene Deletion Phenotypes

Your ORFan gene was most likely included in the yeast deletion collection and after creation of this collection some basic questions were asked of all of these strains. We will now mine this data to determine if there is any information that might aid in our determination of the function of your protein.

Yeast Fitness Database

This site provides a graphical interface to the supplementary data presented in two publications: "The Chemical Genomic Portrait of Yeast: Uncovering a phenotype for all genes" (Hillenmeyer et al., Science 2008) and "Chemical genomic profiles predict gene function and mechanism of drug action" (Hillenmeyer et al., Genome Biol. 2010). This data should therefore provide us with information about the phenotype of cells with your gene mutated when exposed to various drugs and then based on these data the program will report what other gene mutations show similar sensitivities to the same drugs to which your mutated strains is sensitive.

Navigate to the Yeast Fitness Database at http://chemogenomics.med.utoronto.ca/fitdb/fitdb2.cgi and enter your standard gene name in the Search box and submit the Search.

Sensitivity data can be informative based on how and what the drug is known to target. Scroll down to the Homozygous knockout section, which shows the most impactful drug effects on cellular fitness when the cell lacks all copies of your gene of interest. Identify the top 3 drugs with significant p-values (<0.05) and perform an Internet search to determine how these drug work in a cell. (You need to separately look up the mechanism of action for the drugs showing significant fitness defects because the list of tested drugs is too long to provide this information in this document). In your **Module 7 Worksheet** record the drug, the Fitness Defect (z-score), the p-value and the mechanism of action of the drug (include the citation of where you found this information).

In Section 2: Co-fitness interactions of the Yeast Fitness Database an algorithm is used to identify if cells with other mutated genes show similar sensitivities to the drugs that cells mutated for your gene of interest do, as this can imply a similarity in function. Look up the functions of up to all of the 10 given genes and record that information in your **Module 7 Worksheet**, including taking the time to correlate the information and generate a hypothesis. [To look up the genes and their known functions navigate to SGD and type the gene names into the search box, when the gene page loads copy the Description portion into your worksheet.]

Not only are the names of these genes provided for you to investigate their known functions through SGD – but they have also been classified by Gene Ontology groupings (to the right of the homozygous co-fitness interaction diagram). [The Gene Ontology (GO) project is a major bioinformatics initiative with the aim of standardizing the representation of gene and gene product attributes across species and databases. The project provides **a controlled vocabulary of terms** for describing gene product characteristics and gene product annotation data from GO Consortium members, as well as tools to access and process this data.*] All proteins with known functions are grouped into all of the categories for which their function applies with respect to Molecular Function, Biological Process and Cellular Component. (For instance, if you wanted to classify information about a Strawberry you could put it into groups of Color: Red, Type: Berry, Seeds: Outside – etc. and then look for other types of fruit that are red, or berries or have seeds on the outside as an indicator of potential relatedness.) Once again this data can be useful because it may indicate that your gene/protein will have a similar function and could be assigned to the groups/ontologies that are identified. Record any Enriched GO terms of interactors that are indicated on your Yeast Fitness Database page in your **Module 7 Worksheet.** If you do not know what any of the terms in the GO annotation mean look them up individually and also together in their full GO term to decipher their functional implication.

* Information regarding the functionality of each software/algorithm and operational information was taken directly from the websites and included here for instructional purposes only. [rev 6.6.2022 remove prophecy; no longer available]