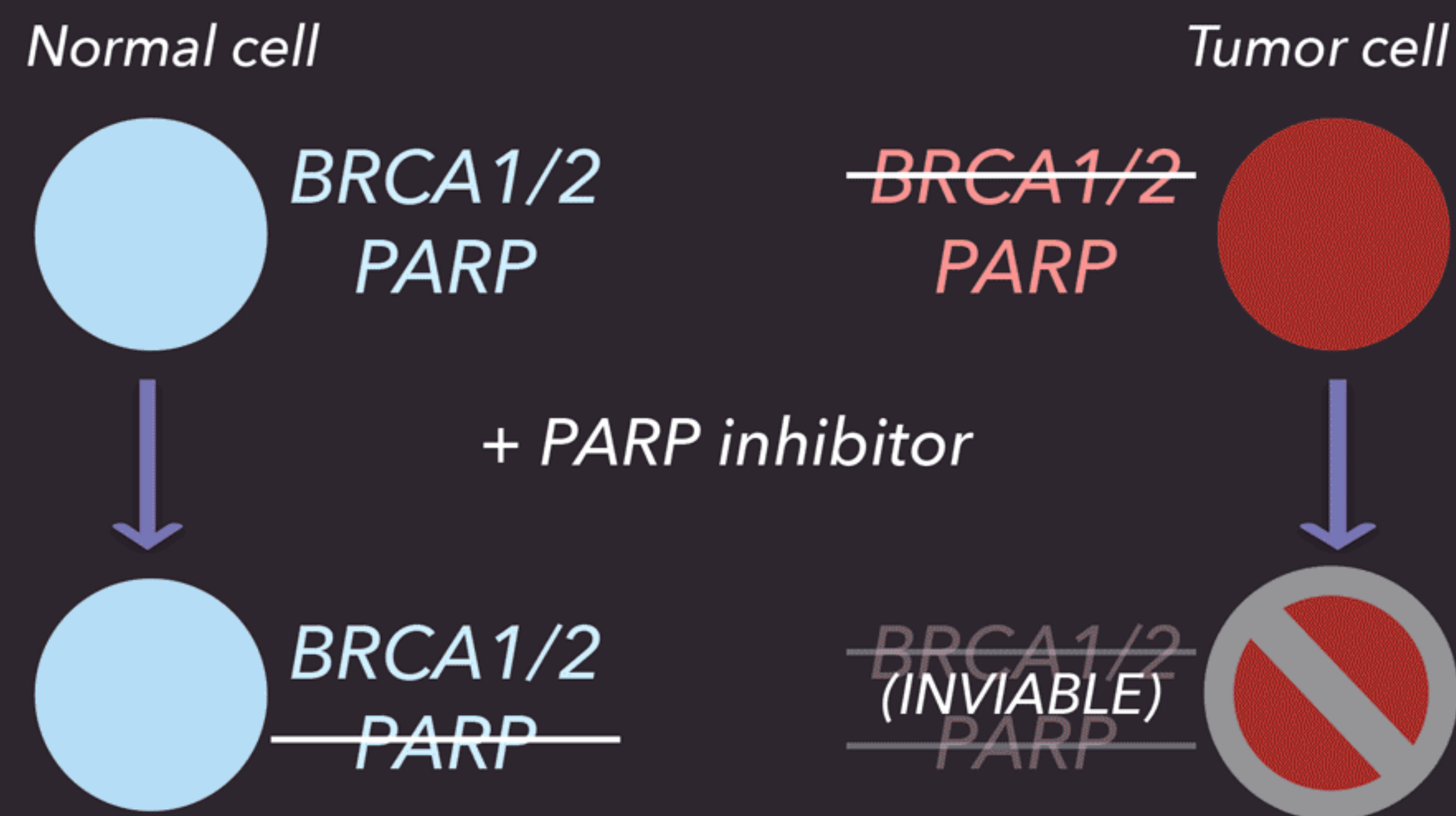


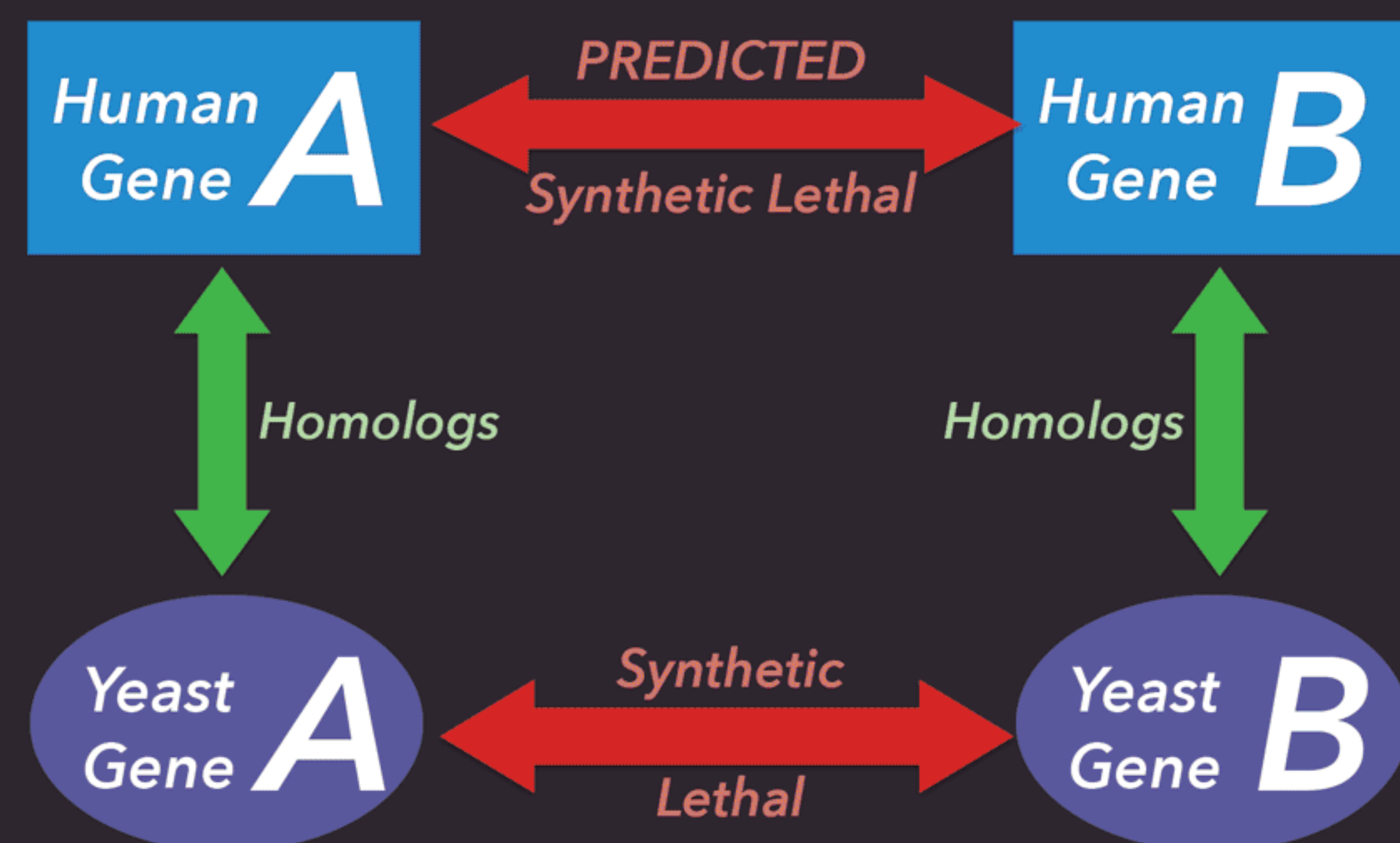
## Background



Synthetic lethality is a type of genetic interaction where loss of two or more genes, such as PARP and BRCA1/2, results in loss of cell viability.

Some tumors lose BRCA1/2 function. Because of the synthetic lethal interaction between PARP and BRCA1/2, drugs that inhibit PARP can be used to specifically target & kill tumor cells.

Synthetic lethal interactions are therefore of great interest to precision medicine, but not all interactions of this type are known in humans.

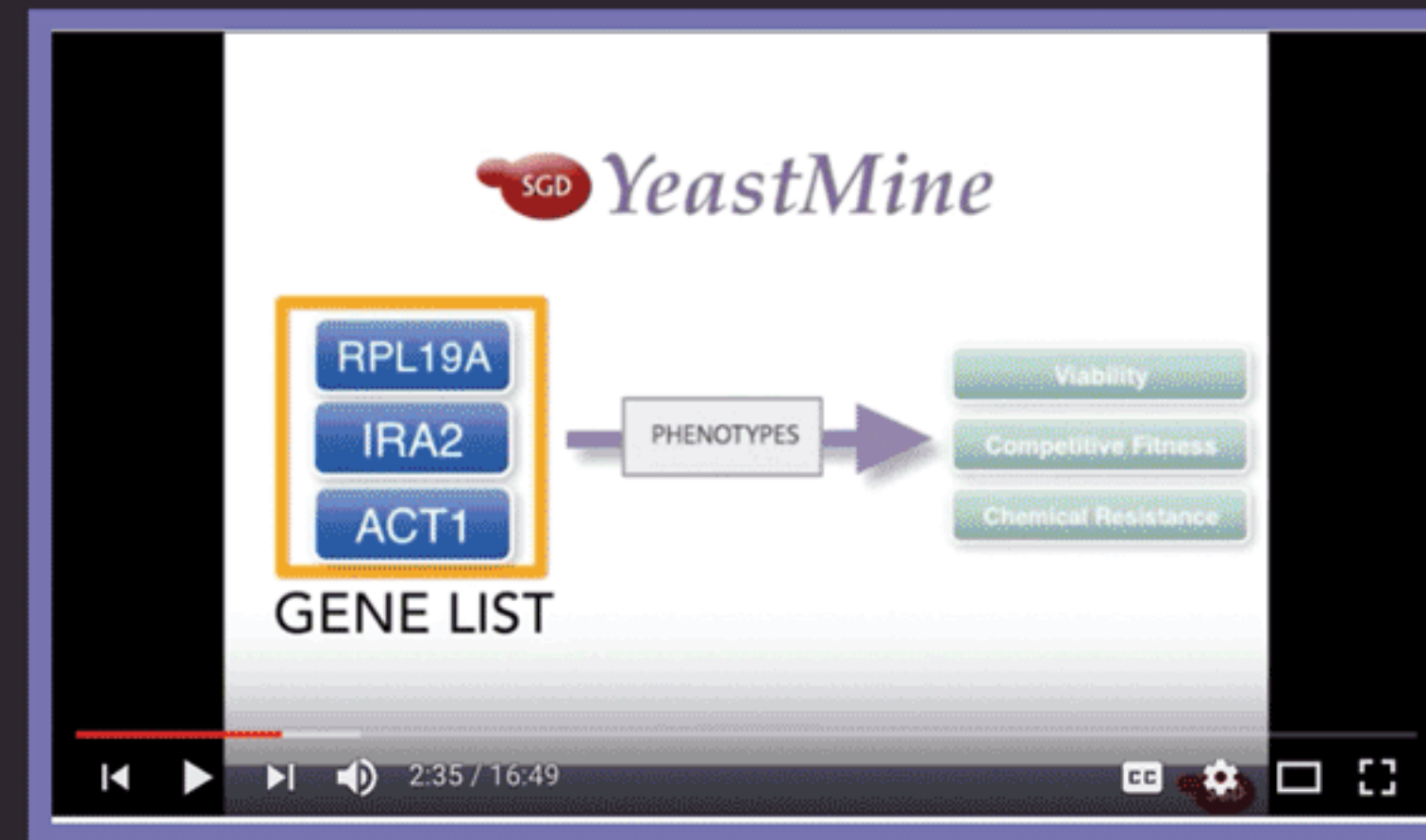


To predict cancer-relevant synthetic lethal interactions in the human genome, we can turn to the wealth of data available on *S. cerevisiae*.

In the following tutorial, we will import a list of human tumor suppressors into YeastMine in order to identify yeast homologs with potentially conserved synthetic lethal interactions.

## yeastmine.yeastgenome.org

The YeastMine tutorial presented here is also available as a YouTube video:



<http://bit.ly/SGDchemotherapy>

For more step-by-step help on YeastMine, check out:



SGD YouTube • Video Tutorials  
[youtube.com/SaccharomycesGenomeDatabase](https://www.youtube.com/SaccharomycesGenomeDatabase)

Or contact us directly:



Questions, suggestions?  
[sgd-helpdesk@lists.stanford.edu](mailto:sgd-helpdesk@lists.stanford.edu)

YeastMine is populated by the *Saccharomyces* Genome Database (SGD; [yeastgenome.org](http://yeastgenome.org)) and powered by InterMine ([intermine.org](http://intermine.org))



*Saccharomyces*  
GENOME DATABASE



## Quick Guide



### Predicting Chemotherapy Targets



[yeastmine.yeastgenome.org](http://yeastmine.yeastgenome.org)



## Step 1: Import human tumor suppressors

ATR  
CHUK  
RAD51C  
FLCN

Analyse  
Enter a list of identifiers.  
Gene  
H. sapiens  
ATR  
CHUK  
RAD51C  
FLCN  
advanced  
ANALYSE

On the YeastMine homepage, import human tumor suppressor genes through the “**Analyse**” feature. You can try the four genes listed here as an example. Name this list: “**LIST 1: Human TS Genes**”

## Step 2: Find yeast homologs (of human tumor suppressors)

GENOME PROTEINS FUNCTION PHENOTYPES INTERACTIONS REGULATION **HOMOLOGY** EXPRESSION LITERATURE

Read more

Query for homology:

- Yeast gene → OMIM human homolog(s)
- Human Gene → Yeast Homolog(s)
- Gene → Non-Fungal organism
- Gene → Functional Complex
- OMIM Disease Phenotype(s)
- Gene → Fungal Homolog(s)
- Human Gene → Fungal Homolog(s)
- Organism → All S. cerevisiae

Human Gene → Yeast Homolog(s) → OMIM Disease Phenotype  
For a given human gene(s) retrieve associated OMIM disease phenotype(s) and yeast homolog(s).

Gene  
LOOKUP: POMT1  
constrain to be IN saved Gene list LIST 1: Human TS Genes  
Show Results  
web service URL Perl Python Ruby Java help export XML

I) Open the **HOMOLOGY** tab in the query toolbar.

Select the query:  
• Human Gene → Yeast Homolog(s) → OMIM Disease Phenotype

Input: **LIST 1: Human TS Genes** and hit “Show Results”

Save as List

Gene (4 Genes)  
Gene > Cross References (4 Cross References)  
Gene > Homologues > Homologue (4 Genes)  
Gene > Diseases (9 Diseases)

II) After the results table is produced, click on the “**Save as List**” button. Save the yeast homologs as: “**LIST 2: Yeast Homologs**”

## Step 3: Find synthetic lethal interactors (of the yeast homologs)

GENOME PROTEINS FUNCTION PHENOTYPES **INTERACTIONS** REGULATION HOMOLOGY EXPRESSION LITERATURE

Read more

Query for interactions:

- Gene → Interaction
- Gene → Complex
- Complex → Details
- Literature → Interaction

Gene → Interaction  
Retrieve all interactions for a specified gene.

Gene  
LOOKUP: act1  
constrain to be IN saved Gene list LIST 2: Yeast Homologs  
Show Results  
web service URL Perl Python Ruby Java help export XML

I) Open the **INTERACTIONS** tab in the query toolbar.

Select the query: • Gene → Interaction

Then, input: **LIST 2: Yeast Homologs** and run the query.

Save as List Generate Python code

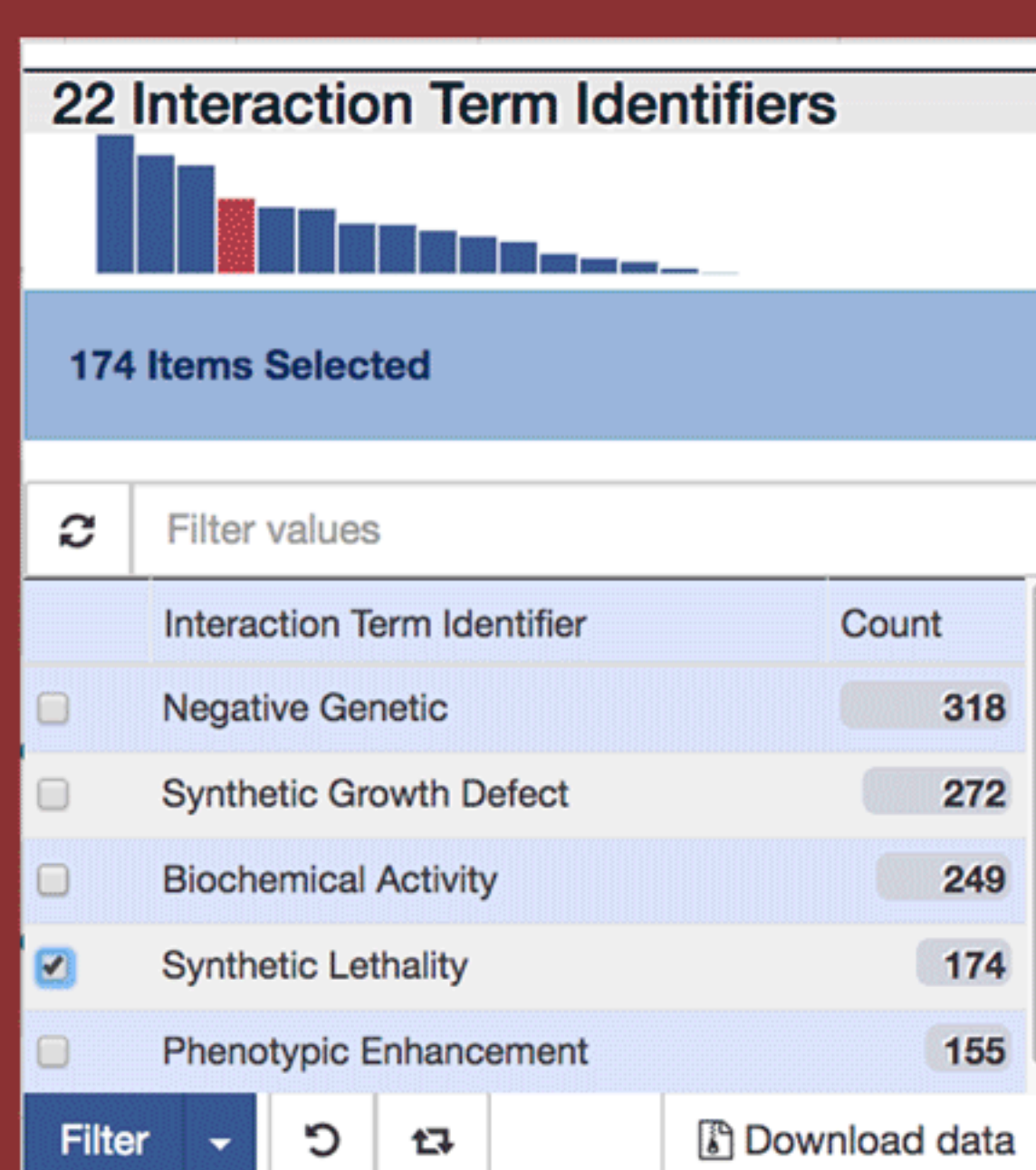
25

View column summary

Participant 1	Participant 2	Interaction	Experiment
Standard Name	Secondary Identifier	Detection Methods	Experiment Name
Bait	CDC73	YLR418C	Synthetic Lethality
			van Pel DM, et al. (2013)-23390603-Synthetic Lethality

II) In the results table, find the column shown here:

Click on the  icon.



III) Filter the table for “**Synthetic Lethality**” as shown here.

Undo Save as List

Gene (4 Genes)  
Gene > Organism (1 Organism)  
Gene > Interactions > Details (174 Interaction Details)  
Gene > Interactions > Participant 2 (143 Genes)  
Gene > Interactions > Details > Experiment > Interaction Detection Methods (1 Interaction Term)

IV) Save the synthetic lethal interactors as: “**LIST 3: Yeast SL Interactors**”

## Step 4: Find human homologs (of the yeast synthetic lethal interactors)

GENOME PROTEINS FUNCTION PHENOTYPES INTERACTIONS REGULATION **HOMOLOGY** EXPRESSION LITERATURE

Read more

Query for homology:

- Yeast gene → OMIM human homolog(s)
- Human Gene → Yeast Homolog(s)
- Gene → Non-Fungal organism
- Gene → Functional Complex
- OMIM Disease Phenotype(s)
- Gene → Fungal Homolog(s)
- Human Gene → Fungal Homolog(s)
- Organism → All S. cerevisiae

Yeast gene → OMIM human homolog(s) → OMIM Disease Phenotype(s)  
Retrieve human homolog(s) of yeast gene(s) and any of their associated OMIM disease phenotypes.

Gene  
LOOKUP: PMT3  
constrain to be IN saved Gene list LIST 3: Yeast SL Interactors  
Show Results  
web service URL Perl Python Ruby Java help export XML

I) Open the **HOMOLOGY** tab in the query toolbar.

Then, select the query:

• Yeast gene → OMIM human homolog(s) → OMIM Disease Phenotype(s)

Input **LIST 3: Yeast SL Interactors** and hit “Show Results”

Save as List

Gene (127 Genes)  
Gene > Homologues > Homologue (251 Genes)  
Gene > Homologues > Homologue > Organism (1 Organism)  
Gene > Homologues > Homologue > Cross References (251 Cross References)

II) Save the human homologs as: “**LIST 4: Human SL Interactors**”

## Interpreting Results

To predict synthetic lethal interactions for the human tumor suppressors, browse through each of the query results that were produced during steps 2-4.

### Example findings from each step:

#### Step 2

Human **ATR** is homologous to yeast MEC1.

#### Step 3

Yeast MEC1 has a synthetic lethal interaction with yeast POL3.

#### Step 4

Yeast POL3 is homologous to human **POLD1**.

### Conclusion:

Because yeast MEC1 and POL3 have a synthetic lethal interaction, their human homologs (**ATR** and **POLD1**) are predicted to have one as well!