Search strategies in FungiDB

1. Finding genes using the Gene Text Search box

The Gene Text query searches gene records for the text you specify. You can use the text search from two places. At the top right side of any FungiDB webpage (this searches all genomes and a predefined set of fields within the gene record) or from the gene text search page where you are able to specify the organisms and fields to search.

	Organism	w	nere you	r criteria	were matched
Initiate a search	 Conjunction 125 selected, out of 125 Filter list below Ornyoetes Find select all [collapse all Tax select all [collapse all [collapse all Text term (use * as wildcard) your text description Fields Fields Gene product Gene name Go terms and definitions Metabolic pathway names and descriptions Phenotype Protein domain names and descriptions Photomedic pathway names and descriptions Photomedic pathway names and descriptions PubMed	onomy →Output sociated cords		➡ Transcript ID NCU04173-28_1 NCU04173-28_2 SIMAC_02416-28_1 PTG_02462-28_1 AN2276-T AN6542-T AN5275-T A0090701000065-T CNB1210-28_1 NCU01756-28_1 NCU01756-28_1 NCU01756-28_1 YFL030C-28_1 YFL030C-28_1 YFL030C-28_1 YFL030C-28_1 AN4999-T AN831-T P174DRART_43990- U7_1	Crossa OR74A N. crassa OR74A N. crassa OR74A N. crassa OR74A S. macrospora k-hell P. infestans T30-4 A. nickulans FGSC A4 A. nickulans FGSC A4 A. nickulans FGSC A4 A. nickulans FGSC A4 A. nocorrans var. neoformans B- 3501A C. neoformans var. neoformans B- 3501A N. crassa OR74A N. crassa OR74A S. crevisiae S288c S. cerevisiae S288c S. cerevisiae S288c S. cerevisiae S288c A. nickulans FGSC A4 A. nickulans

- a. Find all genes containing the term actin.
 - Use the keyword **actin** in the **Gene Text Search** box (top right of the webpage) and click on the search icon or simply press the Enter key.

Note: When using this shortcut, the search identifies your input term in all FungiDB organisms and in a predefined lists of gene record fields (e.g. Gene name, description, user comments, GO terms, etc.).

The text search in FungiDB is an exact match search, which makes the wild card option particularly useful when trying to find complex terms (see below).



• How many genes were returned by your search?



Note: Due to frequent database updates, the results shown here may not match exactly to your search result.

• How many of those genes are in *Aspergillus nidulans*?

Note: Use the filter table located between the strategy panel and the result table that shows the distribution of results across the various organisms. Scroll to the right, click on a number under the Neurospora crassa to 'filter' the results.

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- Do you believe all of these genes encode actin?
- Find the **Product Description** and the **Found in** columns in the Gene Results table to understand your results.

Note: Some genes are annotated with GO terms (internal curation or uploaded from the GO consortium), while other genes have predicted protein function annotated with domains from InterPro scan, product description from the gene model functional annotations, etc. Understanding why these genes are associated with the term actin is important when interpreting your results.

• Can you revert the display back to showing all genes across all organisms?

Hint: Scroll back to the beginning of the horizontal display and click on the **All Results** number in blue. Note that the search strategy display has also changed (hour glass is no longer visible), which means that you are no longer displaying species-specific results.



b. Search ubiquitin-related gene products (*e.g.* ubiquitin carboxyl-terminal hydrolase, ubiquitinprotein ligase, small ubiquitin-like modifier) using a wild card

Rather than searching for individual terms, try using a wild card (*).

- Search for **ubiquitin*** in *Gene product in Oomycetes*
 - How many genes were returned?
 - What happens if you search for ***ubiquitin**?

0	Organism
	20 selected, out of 129
	Filter list below T
•	☑ Oomycetes □ Fungi
	select all clear all expand all collapse all
0	Text term (use * as wildcard)
	ubiauitin
0	Fields
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0	Fields Alias Community annotation EC descriptions
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c. Search for a two-word term

- Search for "Histone H3" (including quotations) using *Search for Genes > Text* approach and select *Oomycetes* in the *Organism* search parameter and leave *Fields* selections at default.
 - How many results are returned?
 - Notice that hypothetical and unspecified products are also returned in this search? Why do you think that is? How would you go about finding out where the "Histone H3" term may be mentioned for this gene to be included in your search results?

Hint: Look in the Found in column for the source of Histone H3 annotation. Navigate to the gene record page by clicking on the GeneID to learn more about why this gene has been returned in your search. Try using web text search (Ctrl F (Windows); Command F (Mac)) to see where Histone H3 is mentioned within the gene records page.

- How would you go about finding out where the "Histone H3" term may be mentioned for this gene to be included in your search results?
- Save your strategy with the name "Histone H3" (you would need to be logged in to your account to so this; also see below).

2. Modify an existing search strategy or add a new step

a. Rename a text search step in the previously saved "Histone H3" strategy

- Click on the step to highlight it in yellow if you navigated away from it.
- Hover over the box to select to reveal the edit link.
- Click on the edit function within the yellow box, then click on 'Rename'
- Click on the Save As link again and then replace the strategy to keep your latest edits.

	Rename View Analyze Revise Make Nested Strategy Insert Step Before Orthologs Delete
Text Add Step 2649 Genes Step 1 Show Results. Click Edit to make changes.	STEP 1 : Text Organism : Coprinopsis, Phanerochaete, Albugo candida, Albugo laibachii, Albugo candida 2VRR, Albugo laibachii Nc14, Allomyces macrogynus, Allomyces macrogynus ALCO 38327, Aphanomyces astaci Aphanomyces astaci strain APO3, Aphanomyces invadans, NJM9701, Aspergillus aculeatus, Aspergillus brasiliensis, Aspergillus campestris, Aspergillus carbonarius, Aspergillus brasiliensis, Aspergillus fischeri,
	"Histone H3" Text 26-Step:As
	Histone H3 2649 Genes Step 1

Other functions of the Edit tool include:

• Analyze – redirects you to the Analyse results section:

alyze your Gene results with a tool below.		
		kinase phosphatase exported membrane
Gene Ontology Enrichment	Metabolic Pathway Enrichment	Word Enrichment

• **Revise** – revise your strategy. Practice revising your strategy (*e.g.* "Histone H3") by limiting your search to *Aspergillus* (Fungi) and *Gene description* only:

2 Organism				
	26 selected, out of 129			
	Filter list below			
Þ	Oomycetes			
ŀ	Fungi			
	select all clear all expand all collapse all			
3	Text term (use * as wildcard)			
•	Text term (use * as wildcard) "Histone H3"			
3	Text term (use * as wildcard) "Histone H3"			
	Text term (use * as wildcard) "Histone H3"			
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	Text term (use * as wildcard) "Histone H3" Fields Alias Community annotation			
•	Text term (use * as wildcard) "Histone H3" Fields Community annotation EC descriptions			
	Text term (use * as wildcard) "Histone H3" Fields Alias Community annotation EC descriptions Gene ID			
2	Text term (use * as wildcard) *Histone H3* Fields Alias Community annotation EC descriptions Gene ID Gene notes			

- **Insert Step Before** allows to revise your strategy by adding steps before the step you are modifying
- **Orthologs** allows to add a step after the one you are modifying that will find orthologs according to your selections in the orthologs parameter pop-up window. For example, choose to find all orthologs of "Histone H3" results in *Fusarium*:



• Delete function deletes the step that is being modified

3. Finding genes using the Gene ID search box

Let's say you are working with *Candida auris* and studying the process of biofilm formation. B9J08_001462, annotated as hypothetical protein product, piqued your interest because it came up in your genetic screen and you would like to know more about the function of this gene.

• Enter B9J08_001462 in the *Gene ID* search box and press Enter:

,)	Fungi	DR		1033			A Euf	PathDB Project
V	Fungal and Oomycete Geno	imics Resources			Gene II	B9J08_001	462 Gene Text Search:	Q,
		100 Aug 100				About	rungiDB Help Login Register	Contact Us 🛛 🔚 🔛
	New Search 👻	My Strategies	My Basket (0)	Data Summary 👻	Downloads -		Analyze My Experiment	

- Examine the **Orthology and Synteny** section of the gene record page.
 - Does the provided information support its putative function as a cyclin?

Hint: Navigate to the Orthology and Synteny section of the gene record page and examine orthologs' function.

• What can you say about this gene's expression in biofilm in C. auris?

Hint: Navigate to the Transcriptomics section of the gene record page to evaluate the expression of this gene in biofilm forming conditions (plank = planktonic cells; 4, 12, 24hr = biofilm forming conditions).

• Does this gene have syntenic orthologs in *Candida* species?



• Does the protein have any identifiable domains?

Hint: Use the Contents menu section to navigate to the **Protein features and properties** *section of the gene record page.*

Search this table		Q Sh	owing 6 rows					
↓† Transcript ID(s)	↓† Name	↓† Interpro ID	↓↑ Primary ID	↓↑ Secondary ID	↓† Description	↓† Start Min	↓† End Min	¢† <mark>E-</mark> va
B9J08_001462-t37_1	PFAM	IPR006671	PF00134	Cyclin_N	Cyclin, N-terminal domain	43	162	5.0E-
B9J08_001462-t37_1	PFAM	IPR004367	PF02984	Cyclin_C	Cyclin, C-terminal domain	209	259	6.7E-
B9J08_001462-t37_1	PIRSF		PIRSF001771		Cyclin, A/B/D/E types	9	258	1.7E-
B9J08_001462-t37_1	SMART	IPR013763	SM00385	cyclin_7		70	156	2.3E-
B9J08_001462-t37_1	SUPERFAMILY	IPR036915	SSF47954	0054835	Cyclin-like	26	165	1.7E-3
B9J08 001462-t37 1	SUPERFAMILY	IPR036915	SSF47954	0054835	Cyclin-like	212	255	2.8E-



- Cross-reference the search results with what is known in other model organisms.
 - Navigate to the Orthology and Synteny section
 - Click on the CR_02920C_A in Camdida albicans SC5314 to be redirected to an ortholog gene record page.
 - Navigate to the *Link outs* section on the C5_01680C_A gene record page and click on the CGD *External ID* link

3	ink outs		
▼ E:	kternal Links 🕹 Download 🛢 Data sets		
	Search this table	Q Showing 3	rows
	↓↑ Database	↓↑ External ID	
	CGD	CR_02920C_A	
	Entrez Gene	3642587	
	The Universal Protein Resource (UniProt)	Q5A1Z4	

- Navigate to the **Phenotype** tab on the CGD record page for CR_02920C_A.
- Is the deletion mutant viable?
- What can you say about growth phenotype (filamentous and invasive growth) or biofilm formation in the null mutant?

Note: you can also download the phenotype table and open it in Excel or save it for later use.

4. Combining text search results with results from other types of searches

- a. Find kinase genes that are likely secreted.
 - Let's go back to the *kinase* kinase search strategy.



• **Insert a step** before current Step 2 to identify kinases that have a predicted Signal Peptide.

Hint: Select to revise the strategy and then navigate to the Insert Step Before tab.

Note: Signal Prediction is made with the SignalP program that predicts the presence and location of signal peptide cleavage sites in amino acid sequences.

Rename View Analyze Revise Open Nested Strategy Unnest Strategy	Insert Step Before Orthologs Delete	
STEP 2 : Copy of kinase The nested strategy gets opened be	low.	
Results: 176 Genes		
□ Give this search a we	ight	
10		
Assign Optionally give this search a 'weight' for examp in a search strategy, unions and intersects will sum the weights, giving higher	Hun a new Search for Ganes I oct Producted Sign Hun a new Search for Ganes Ganes Ganes Ganes In a new Search for Sanes Ganes Ganes Ganes Ganes In a new Search for Sanes Ganes	nal Peptide
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Combine	Genes in Step 1 with Genes in Step 2: COD 1 Intersect 2 COD 1 Union 2 COD 2 Minus 1 Helative to 2, using genomic colocation	
	(Genes)	
	Signal Pep Copy of kinase 975 Genes 0 Genes 187 Genes 9 Genes Step 1 Step 2 Step 3	

Search operator selection can be edited at any time by clicking on the edit link within the operator window:



		Operator	:	Combined Result will contain:
	-	© (1) 1 INTERSECT 2	:	IDs in common between the two lists
1		① ① ① ① ① ① ① ① ① ① ① ① ① ① ① ① ① ① ①	:	IDs from list 1 and list 2
		© 🚺 1 MINUS 2	:	IDs unique to 1
	-		:	IDs unique to 2
2	-	I Relative to 2	:	IDs whose features are near each other (colocated) in the genome

The top four operators (1) are used when both searches produce the same type of genomic feature results and therefore are used for direct comparison of similar types of data (*e.g.* gene list 1 and gene list 2 obtained from proteomics and RNA-Seq evidence searches, respectively).

When two search steps are run against different types of data (e.g. genes and chromosomal sequences or SNPs), the colocation feature (2) allows combining these different types of data (e.g. searching for a list of SNPs or transposable elements colocating to the upstream/downstream regions of genes).

How many kinases are predicted to have a signal peptide?

Can you identify genes that have predicted signal peptides but are not kinases? *Hint: Hover over the operator selection to select the Edit function.*

5. Creating Nested Strategies

Nesting a strategy allows you to control the order in which your search result sets are combined. Consider the difference between two mathematical equations:

- A. Equation with nesting:B. Equation without nesting: $2 \times (3+5) = 16$
- $2 \times 3 + 5 = 11$

Here is how the sample equations above translate into search results in FungiDB queries:



Note that nested (A) and non-nested (B) strategies return results that are quite different. The final number of genes returned in nested vs non-nested strategy is 3417 and 436, respectively.

Let's go back to the search in C. neoformans KN99 we just ran and delete the very last step to display the search results for *kinase* and signal peptide query:



• How can you define kinases that have either a secretory signal peptide <u>AND/OR</u> a transmembrane domain(s) (option A above)?

Hint: You would need to create a nested strategy because search operators allow combining steps in subsequent fashion only. Start by revising the Step 2 to create a nested strategy as shown below.



• Close the **Expanded View of Step Signal Pep** window as shown above, and you should have a nested strategy as follows:



- Save your strategy (rename it if necessary)
- Modify your strategy to scenario B to return kinases that have predicted signal peptide as well as a transmembrane domain.
 - First duplicate the strategy and then delete the second step in the duplicated strategy:

My Strategies: New Opened (1)	All (664) Basket Public Strategies (48) Help
⊟ Hide search strategy panel	Rename View Analyze Revise Open Nested Strategy Unnest Strategy Insert Step Before Orthologs Delete 🗵
(Genes)	STEP 2 : Signal Pep The nested strategy gets opened below.
Text	Results: 1932 Genes
187 Genes 12 Genes Add Step 1 Step 2	

Hint: To return kinases that have predicted signal peptide as well as a transmembrane domain, add two steps (searching for secreted and transmembrane proteins, respectively).

• Compare the A and B strategies. Do the results make sense?