

# FungiDB Metabolic Pathways

## Learning objectives:

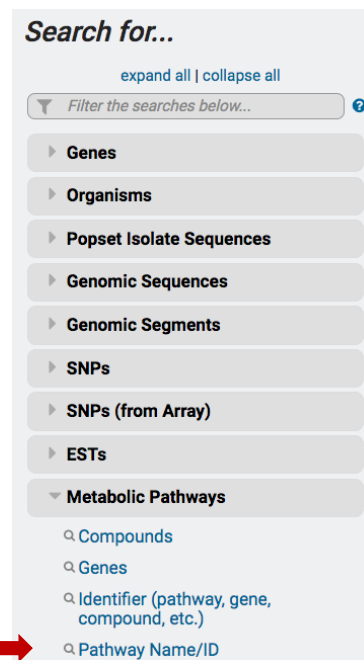
- Explore the metabolic pathways searches and visualization tools
- Search for a pathway using the name or pathway identifier
- Paint data onto pathway maps to explore:
  - a. Which enzymes in a pathway are present in different genera
  - b. How transcriptional abundance of enzymes in a pathway differs under experimental conditions
- Explore secondary metabolite searches using InterPro domain data

## 1. Find and explore the metabolic pathway for glycolysis.

Navigate to the search page for Identify Metabolic Pathways based on Pathway Name/ID.

- Find the metabolic pathway searches on the home page. You can look under “Metabolic Pathways” or use the search filter. You can find metabolic pathways based on the pathway name or identifier, or using genes or compounds involved in the pathway. Search for the **glycolysis** pathway using the Pathway Name/ID option.

This search is equipped with a type-ahead function for finding the metabolic pathway name. Begin typing glycolysis and then choose the pathway name from the list that appears.



The screenshot shows the FungiDB search interface. At the top, it says "Search for..." with links to "expand all" and "collapse all". Below this is a search bar with the placeholder text "Filter the searches below...". A list of search categories is shown, each with a dropdown arrow: Genes, Organisms, Popset Isolate Sequences, Genomic Sequences, Genomic Segments, SNPs, SNPs (from Array), ESTs, and Metabolic Pathways. The "Metabolic Pathways" category is expanded, showing a list of search options: Compounds, Genes, Identifier (pathway, gene, compound, etc.), and Pathway Name/ID. A red arrow points to the "Pathway Name/ID" option.

- Examine the Glycolysis / Gluconeogenesis pathway.

**Identify Metabolic Pathways based on Pathway Name/ID**

**Pathway Source**

Any

**Pathway Name or ID**

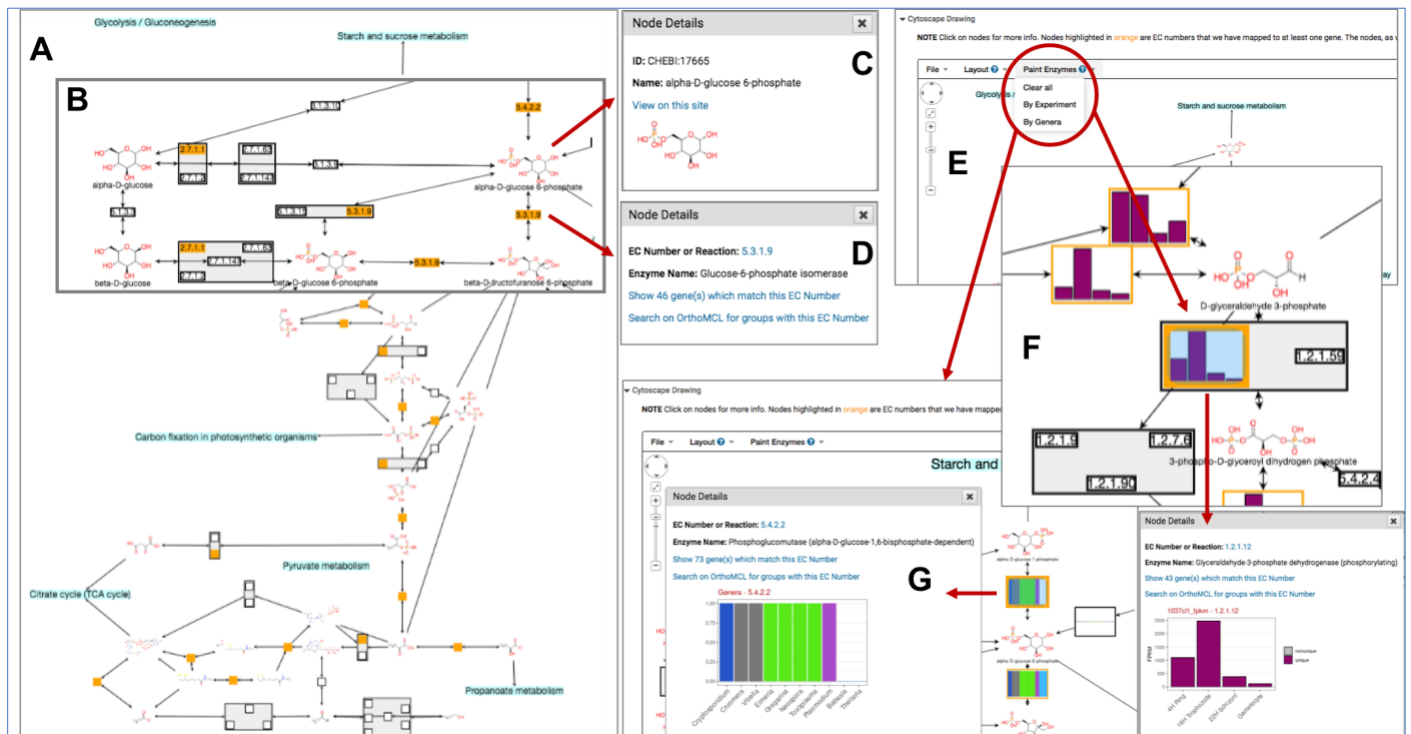
Glyco[

- C-glycosylflavone biosynthesis I (PWY-6602) (MetaCyc)
- C-glycosylflavone biosynthesis II (PWY-7188) (MetaCyc)
- C-glycosylflavone biosynthesis III (PWY-7189) (MetaCyc)
- CMP-N-glycolylneuramate biosynthesis (PWY-6144) (MetaCyc)
- Glycolysis / Gluconeogenesis (ec00010) (KEGG)**
- Glycosaminoglycan biosynthesis - chondroitin sulfate / dermatan sulfate (ec00532) (KEGG)
- Glycosaminoglycan biosynthesis - heparan sulfate / heparin (ec00534) (KEGG)
- Glycosaminoglycan degradation (ec00531) (KEGG)
- Glycosphingolipid biosynthesis - ganglio series (ec00604) (KEGG)
- Glycosphingolipid biosynthesis - globo and isoglobo series (ec00603) (KEGG)

The search takes you straight to the record page for the Glycolysis / Gluconeogenesis (ec00010) metabolic pathway from KEGG. The overview section of the record page contains an interactive graphical representation of the pathway. The pathway map and the legend can be repositioned.

Overview of the metabolic pathway interface:

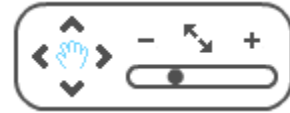
- Initial pathway view is zoomed out.
- Zoom in to see more details including EC numbers and metabolite structures.
- Click on a metabolite structure to get additional information.
- Click on the EC number to get more info about the enzyme including links to retrieve all genes in the database assigned to this EC number.



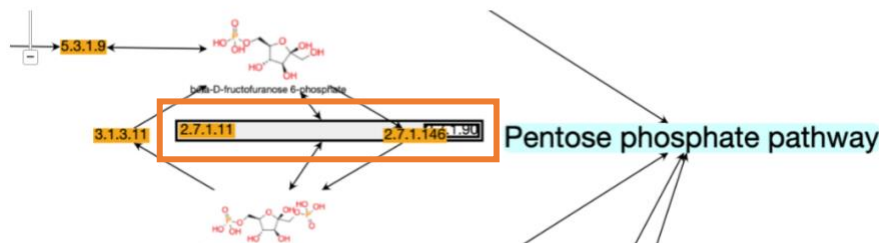
- The drop-down menu under the heading “Paint Enzymes” allows you to paint the pathway based on experimental data or phyletic pattern.

- F. Painting pathway by experiment provides a graphical representation of experimental results. Click on the graph to see more details.
- G. Painting pathway based on phyletic pattern provides a graphical representation of phyletic distribution. Clicking on the phyletic pattern graphic provides additional information.

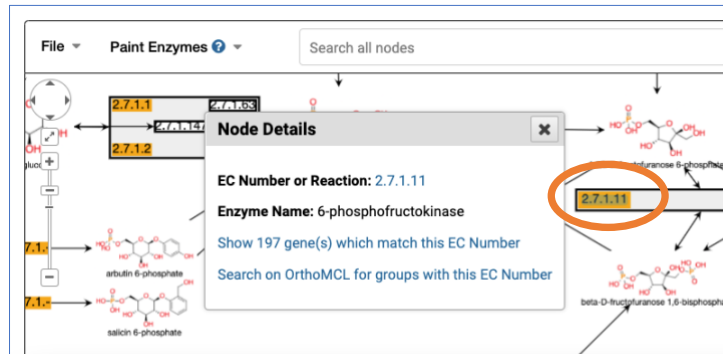
- Use the Tool Box to move (drag) the map and individual nodes. Zoom in and out to help explore the map.



- Click on nodes for more info. Nodes highlighted in orange are represent enzymes where there is at least one gene encoding that enzyme in the database (in this case, in FungiDB). If you click on the node, the pop-up window contains a link to a search that finds all genes encoding this enzyme. The nodes, as well as the info box, can be repositioned by dragging.
- What is the difference between the rectangular nodes that are orange and those that are not? White enzyme nodes mean that KEGG or BioCyc or another source are documenting that an enzyme with the displayed EC number catalyses the reaction shown, but there are no genes in the database (in this case, in FungiDB that encode an enzyme with that EC number. White nodes may occur because of the missing annotation or, sometimes, it can be an indication the enzymes are doing something different from the canonical KEGG/BioCyc pathway.
- Why are some enzymes grouped? Two or more enzyme nodes together in a box are called a node group. This indicates that BioCyc/KEGG suggests that any of the enzymes in the box could catalyse this reaction. This can be a result of redundancy, or it can be differential enzyme usage by different organisms, different developmental stages etc. In this example, EC2.7.1.11 and the white node on the right that ends in 1.90 could both catalyse the reaction, but the one that ends in 1.90 is not annotated in any of the fungi.



- Find the node representing 6-phosphofructokinase (EC number = 2.7.1.11). You may need to zoom and reposition the map to find the node. Click on the 2.7.1.11 node to open a popup with information about this enzyme.

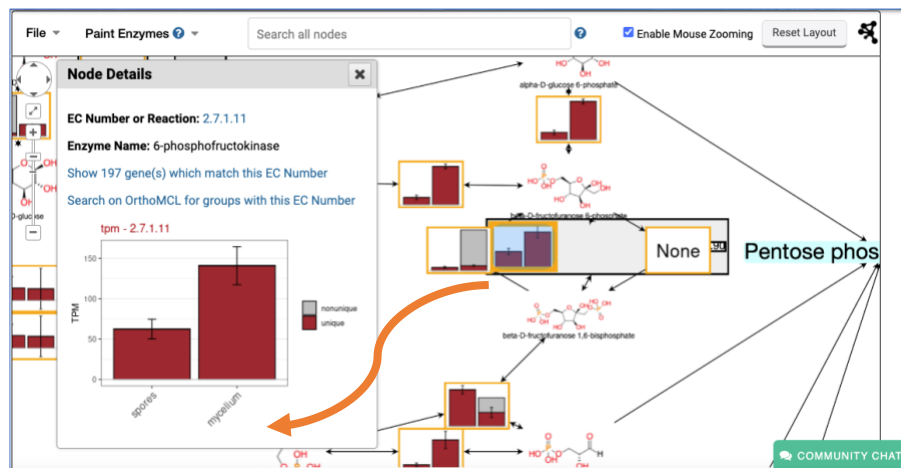


- How many genes in the database matched this EC number?
- Try the link “Show 197 gene(s) which match this EC Number”. Where did you end up? What do the 197 genes in the result list represent? Is 6-phosphofructokinase unique to one or many species? Notice the two columns called “EC numbers” and “EC numbers from OrthoMCL”.

**EC numbers** provided by annotation centers or other data providers

**EC numbers from OrthoMCL** are derived based on consistency of annotated EC numbers withing OrthoMCL ortholog group. OrthoMCL provides a scalable method for constructing orthologous groups across multiple eukaryotic taxa, using a Markov Cluster algorithm to group (putative) orthologs and paralogs (<https://genome.cshlp.org/content/13/9/2178.full>).

- Use your Browser’s back button to return to the glycolysis pathway record page and open the Paint Experiment menu. Choose the experiment “F. graminearum PH-1 Genome-wide gene expression analysis of spores and mycelium (Zhao et al. 2014)”. Be patient while the graphs appear in place of the EC numbers.
- What can you tell about 6-phosphofructokinase expression in spores and mycelium?



- Use the Paint Genera option to determine whether 6-phosphofructokinase has orthologs across oomycetes.

