

FungiDB: Secondary Metabolites and clusters

1. Finding secondary metabolites and gene clusters

There are several main classes of secondary metabolites in fungi: the non-ribosomal peptides and amino acid-derived compounds, polyketides and fatty acid-derived compounds, and terpenes (Hoffmeister and Keller, 2007). The secondary metabolites can be segregated into groups based on the first step of their biosynthesis, more specifically, the “key enzymes” that are required: Non-Ribosomal Peptide Synthetases (NRPS), PolyKetide Synthases (PKS), followed by Terpene synthases (TS). (Read more: <https://www.ncbi.nlm.nih.gov/pubmed/24692239>)

- a) Initiate a text search in *A. nidulans*. Find all genes annotated with *terpene*.
- Use wild cards to cast a wide search for any combinations of the word *terpene*

The screenshot shows the FungiDB search interface. The 'Organism' section is set to 'nidu' (Aspergillus nidulans). The 'Text term' field contains '*terpene*'. The 'Fields' section is checked for 'Gene name', 'Gene product', and 'Gene notes'. The search results show 178 genes. A table of results is displayed, showing the sequence, chromosome, organism, number of genes, and length for three entries: ChrVII_A_nidulans_FGSC_A4, ChrVIII_A_nidulans_FGSC_A4, and ChrII_A_nidulans_FGSC_A4. A 'Gene Locations' visualization is shown below the table, highlighting regions with multiple genes in close proximity. A legend indicates that blue bars represent genes on the forward strand and red bars represent genes on the reversed strand. A 'Region on ChrVIII_A_nidulans_FGSC_A4 (3,275,172 - 3,287,961) forward strand, with 3 genes. Click to view detail.' is highlighted in the visualization.

Sequence	Organism	Chromosome	#Genes	Length
ChrVII_A_nidulans_FGSC_A4	Aspergillus nidulans FGSC A4	ChrVII	40	4550218
ChrVIII_A_nidulans_FGSC_A4	Aspergillus nidulans FGSC A4	ChrVIII	28	4934093
ChrII_A_nidulans_FGSC_A4	Aspergillus nidulans FGSC A4	ChrII	26	4070060

- b) What can you tell about the chromosomal locations of these genes?

- Can you identify regions with multiple genes?

Hint: Shaded areas are highlighting areas with multiple genes in close proximity. These are not programmatically determined clusters but rather a visual representation of gene dense areas

c) Next, navigate to *AN3277* gene record page in FungiDB.

Gene ID	Transcript ID	Organism	Genomic Location (Gene)	Product Description	Found in	Score
AN3277	AN3277-T	<i>A. nidulans</i> FGSC A4	ChrVI_A_nidulans_FGSC_A4:1,253,459..1,254,638(+)	Has domain(s) with predicted magnesium ion binding, terpene synthase activity	GO Terms, Product, Metabolic Pathways	3

- Note that the product description is referring to domains associated with a specific function, however this gene is not directly annotated to terpene synthesis pathway.
- Investigate further by navigating to the *Protein feature and properties* section of the record page, look through associated documentation about domains, etc., and select *STRING: functional protein association networks*:

▼ **STRING: functional protein association networks**

Please select the organism:

- Look through available information and click on the Databases, which provides a summary of annotation from curated resources:
 - i. Do you think this gene may be a part of terpenoid synthesis pathway?

DATABASE KNOWLEDGE	
Relevant datasets in <i>Aspergillus nidulans</i>:	
annotated pathway (KEGG) <i>Inter-pathway connection between 'Steroid biosynthesis' and 'Terpenoid backbone biosynthesis'</i>	AN3376.2 AN8143.2 AN0654.2 AN1592.2 AN8012.2 AN2002.2 AN8878.2 AN3867.2 AN5600.2
annotated pathway (KEGG) <i>Name: Terpenoid backbone biosynthesis</i>	AN8143.2 AN0654.2 AN1592.2 AN8012.2 AN2002.2 AN8878.2 AN3867.2 AN5600.2 [... and 12 other proteins]
annotated pathway (KEGG) <i>Name: Biosynthesis of antibiotics</i>	AN3376.2 AN8143.2 AN0654.2 AN1592.2 AN8012.2 AN2002.2 AN3867.2 [... and 256 other proteins]
annotated pathway (KEGG) <i>Name: Sesquiterpenoid and triterpenoid biosynthesis</i>	AN3277.2 AN3376.2
annotated pathway (KEGG) <i>Inter-pathway connection between 'Terpenoid backbone biosynthesis' and 'Sesquiterpenoid and triterpenoid biosynthesis'</i>	AN3277.2 AN3376.2 AN8143.2 AN0654.2 AN1592.2 AN8012.2 AN2002.2 AN8878.2 AN3867.2 AN5600.2
Relevant information transferred from other organisms:	
curated complex (Gene Ontology) <i>protein farnesyltransferase complex</i>	Schizosaccharomyces pombe: cpp1 cwp1

- Look through available information and click on the Databases, which provides a summary of annotation from curated resources:

d) Navigate to *AN3277* gene record page in JGI MycoCosm.

- Identify protein domains and their function.

