



CARNEGIE
SCIENCE

Plant Biology

www.plantcyc.org



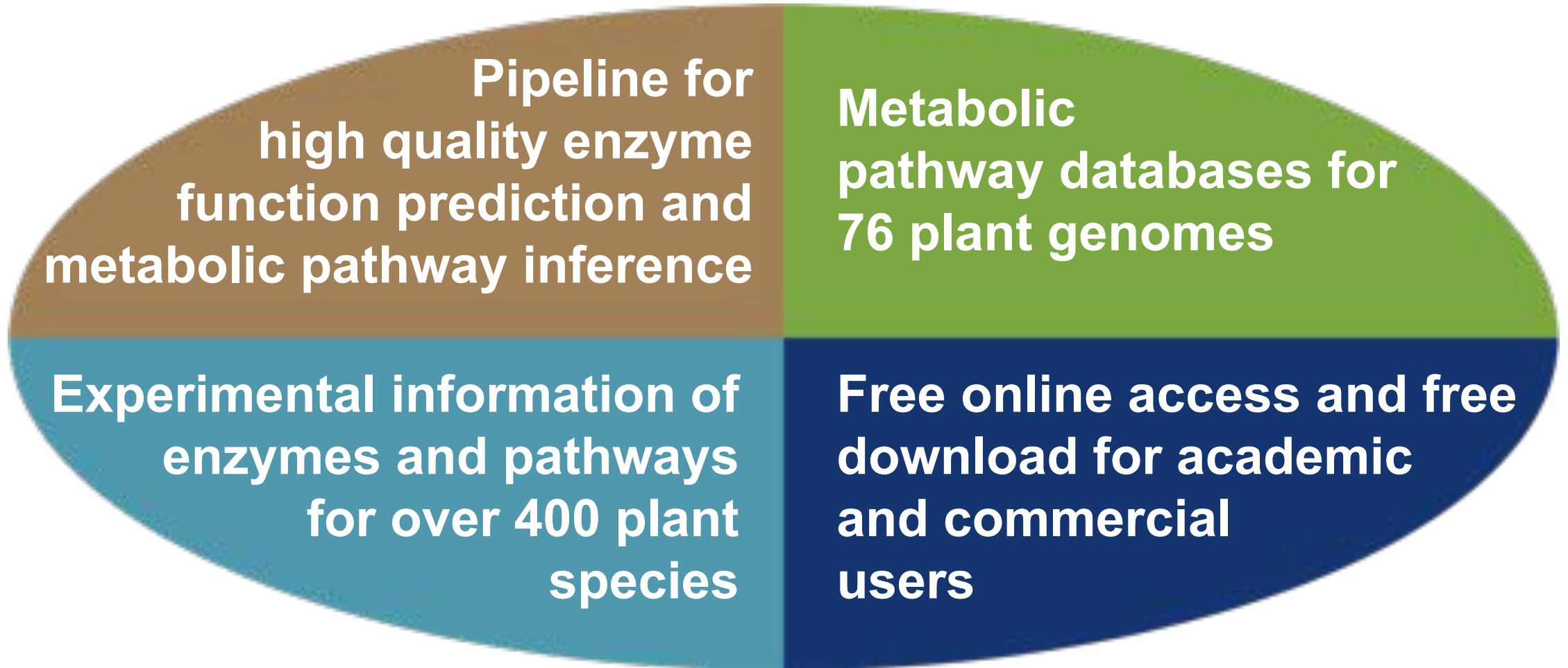
Plant Metabolic Network, a unified resource for studying plant metabolism

Pascal Schlapfer

Carnegie Institution for Science

ASPB 2017

PMN: offering resources to scientists

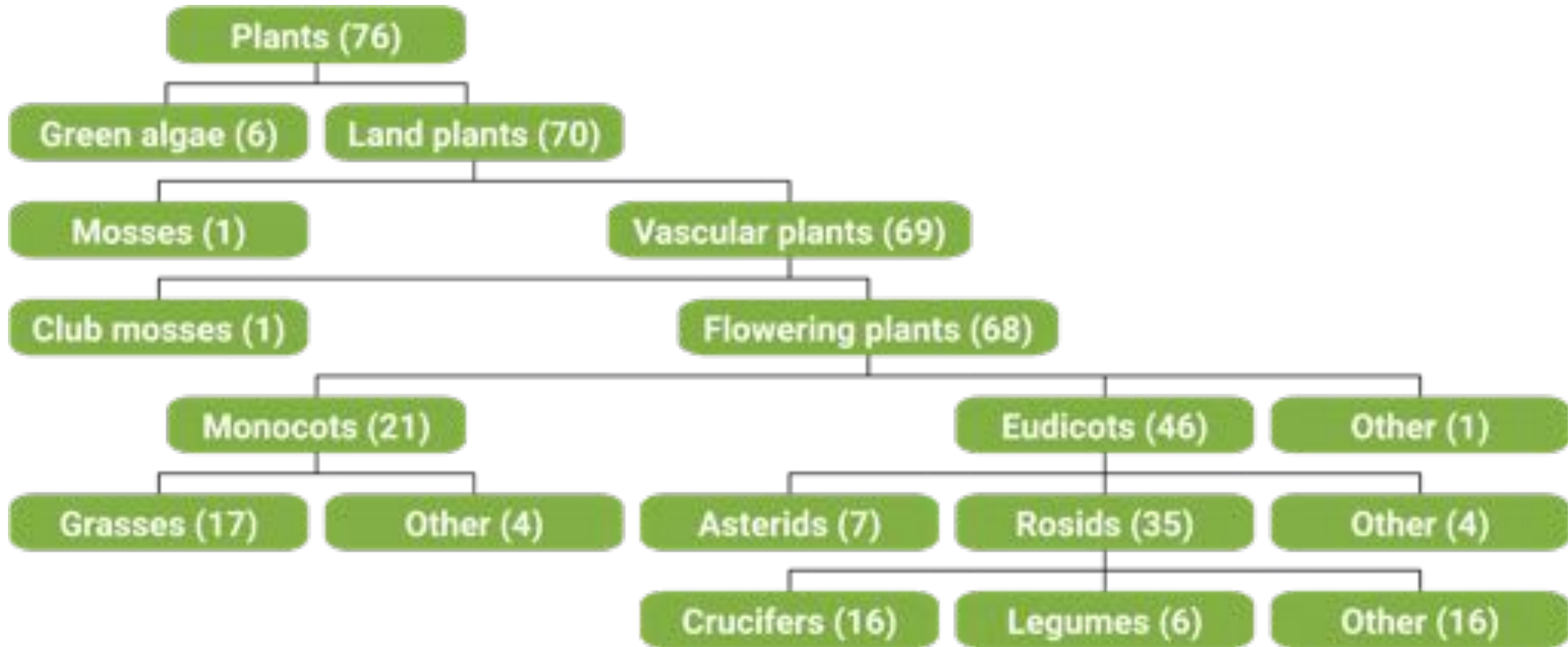


High quality enzyme function prediction and pathway inference

- Ensemble voting machine: (blast, PRIAM), >50k enzyme and >90k non-enzyme sequences → >10k enzyme functions
- Schlapfer et al 2017, Plant Physiology
- Pathway-tools software suite (SRI): using MetaCyc) and PlantCyc as pathway resource
- Semi automated decision tree to improve predictions



Genome wide metabolic pathway databases for plants



Find out more about your gene of interest



Find out more about your gene of interest

▼ MONOMER-12033 | Uniprot: Q8G7B6 | THCA synthase | Species: Cannabis sativa | Gene: G-0017 1/200

Hit length: 545 Select Sequence FASTA PlantCyc 12.0 UniProt

1. Score	E value	Identities	Gaps	Positives
1133.63 (2937)	0.00	545/545 (100.00)	0/545 (0.00)	545/545 (100.00)
Query 1		MHCSAFSPFVCKIIPFPLSPHIDQISIANPRENFKCFSEHIFMVAAMPKLVYTDQDGLY		60
Subject 1		MHCSAFSPFVCKIIPFPLSPHIDQISIANPRENFKCFSEHIFMVAAMPKLVYTDQDGLY		60
Query 61		HSILNSTIQNLRPIISDITPFPPLVIVTPSNNSHIQATILCSKRYVQLQRTASGGHDAEGRS		120
Subject 61		HSILNSTIQNLRPIISDITPFPPLVIVTPSNNSHIQATILCSKRYVQLQRTASGGHDAEGRS		120
Query 121		YISQVPPFVVVQLRHTMSIKIDVHSQTAVVEASATLSEVYYMINERKNEMLSPFQDHCPTVE		180
Subject 121		YISQVPPFVVVQLRHTMSIKIDVHSQTAVVEASATLSEVYYMINERKNEMLSPFQDHCPTVE		180
Query 181		VDSHPISGGYQALHRENYGLAADNIIIDAKLVNVDGKVLDRKSPGDELFWAIRGGGSENFQI		240
Subject 181		VDSHPISGGYQALHRENYGLAADNIIIDAKLVNVDGKVLDRKSPGDELFWAIRGGGSENFQI		240
Query 241		IAAWIKLVAVPSKSTIIPSEKRNRIHGLVCLPKEVQNDIAYKFDKDLVLRTHPIITENITD		300
Subject 241		IAAWIKLVAVPSKSTIIPSEKRNRIHGLVCLPKEVQNDIAYKFDKDLVLRTHPIITENITD		300
Query 301		MSDEKTTVHGVFLLTPHSDVDCLVGLNKKCFPELQIKYTDCEFFSLDITTTIPFQVVSR		360

Find out more about your gene of interest

The screenshot shows the PMN website interface. At the top, there is a search bar with the text "Enter a gene, protein, metabolite or pathway" and a "Quick Search" button. Below the search bar, the text "Searching PlantCyc" and "change organism database" are visible. The search results for *Cannabis sativa* are displayed, showing the gene name "G-9317 (PlantCyc)" and its synonym "Δ⁹-tetrahydrocannabinolic acid synthase". The reaction is listed as "cannabigerolate + oxygen → Δ⁹-tetrahydrocannabinolate + hydrogen peroxide". The pathway is identified as "cannabinoid biosynthesis". The summary section provides a detailed description of the gene and its function, mentioning its isolation from a cDNA pool and its role in the biosynthesis of tetrahydrocannabinolic acid (THCA). The unification links section lists various database identifiers for the gene, including Entrez, UniProt, and others. A gene-reaction schematic is also shown at the bottom, illustrating the conversion of cannabigerolate to Δ⁹-THCA.

PMN

LOGIN | Why Login? | Create New Account

Enter a gene, protein, metabolite or pathway
Searching PlantCyc [change organism database](#)

Cannabis sativa

Synonym Δ^9 -tetrahydrocannabinolic acid synthase

Accession G-9317 (PlantCyc)

IDs NIL
NIL
Q8GTB6 (UniProt)

Reaction cannabigerolate + oxygen → Δ^9 -tetrahydrocannabinolate + hydrogen peroxide

Pathway [cannabinoid biosynthesis](#)

Summary

A gene encoding a protein with tetrahydrocannabinolic acid (THCA) synthase activity was isolated from a cDNA pool generated using RNA from expanding leaves of *Cannabis sativa* [Sirikantaramas04]. When the gene was heterologously expressed in insect cells, the protein, purified to homogeneity, was shown to covalently bind FAD in a 1:1 molar ratio [Sirikantaramas04]. The binding site of FAD has been determined to be at His-114 in the consensus sequence for flavinylation (Arg¹¹⁰-Ser-Gly-Gly-His¹¹⁴). This enzyme belongs to FAD-dependent oxidases. The enzyme could also be successfully heterologously expressed in tobacco.

Additional Citations: [Sirikantaramas05]

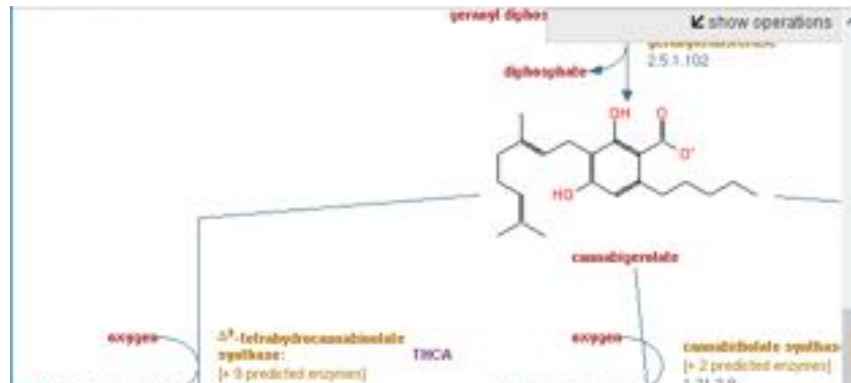
Gene-Reaction Schematic

1.21.3.7: cannabigerolate + oxygen → Δ^9 -THCA

Unification Links

Entrez	BAC41376
Entrez-Nucleotide	AB07805
ModBase	Q8GTB6
Swiss-Model	Q8GTB6
UniProt	Q8GTB6

Find out more about a metabolic pathway



Summary

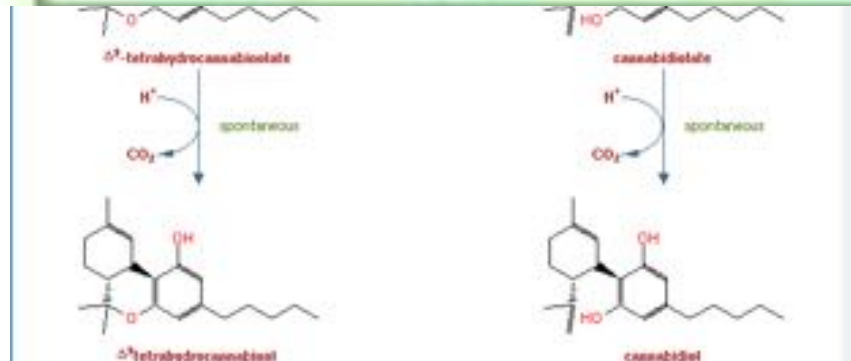
General Background

Cannabinoids are terpenophenolics found in Indian hemp *Cannabis sativa*. They accumulate in considerable amounts in glandular trichomes of hemp. Several compounds of this class have been the subject of extensive studies due to their psychotomimetic effects in humans, in preparations such as marijuana and hashish. Amongst the reported effects of the drugs are: changes in mood and perception, increased appetite and tachycardia. The compound responsible for these activities is Δ^9 tetrahydrocannabinol (THC). In addition to its psychoactivity, THC has been shown to act as an analgesic, appetite stimulant and antiemetic (for review, see [Page06]). Many cannabinoids are devoid of psychoactivity but sometimes possess notable pharmacological properties. For example, cannabidiol (CBD), a cannabinoid present in high amount in low-THC hemp varieties, has anti-convulsive, anti-inflammatory, anti-anxiety and anti-nausea properties.

About This Pathway

Enter a gene, protein, metabolite or pathway...
Searching PlantCyc change organism database

Quick Search Gene Search



If an enzyme name is shown in bold, there is experimental evidence for this enzymatic activity.

Superclasses: Biosynthesis → Secondary Metabolites Biosynthesis → Terpenophenolics Biosynthesis

Summary

General Background

Cannabinoids are terpenophenolics found in Indian hemp *Cannabis sativa*. They accumulate in

pathway involves the prenylation of olivetolic acid with geranylpyrophosphate (GPP). A hemp enzyme (NPP olivetolate neryltransferase / GPP olivetolate geranyltransferase) has been identified that can perform this reaction. The product of the reaction is the central branch-point intermediate: cannabigerolate (CBGA). The same enzyme was also shown to be able to use nerylpyrophosphate instead of GPP as prenyl chain although it prefers GPP. Enzymes have been identified that can catalyze the cyclization of CBGA, each forming a different cannabinoid cyclization product. Each of these enzymes was shown to be able to use cannabigerolate instead of CBGA, leading to the same cyclization product as CBGA [Morimoto58a, Taura96]. The last step (decarboxylation) of this pathway occurs spontaneously in a non-enzymatic reaction during storage or smoking but is also found in vivo [Baker81, Bosy00].

Addendum

The biosynthetic route to olivetolate has been elucidated in more detail. It has been demonstrated that hexanoyl-CoA originates from hexanoate. This step is catalyzed by a hexanoyl CoA synthetase which has been found in glandular trichomes on female flowers of *Cannabis sativa*. That is a rare occurrence as most plant polyketides are usually synthesized from fatty acyl-CoA's [Stout12]. Furthermore, two enzymes, i.e. tetraketide synthase/olivetol synthase (TKS/OLS) and olivetol acid cyclase (OAC) catalyze in a unique and concerted manner the conversion of hexanoyl-CoA to olivetolate ([Taura09] [Gagne12]). Only the coordinated interplay of those two enzymes generates the cannabinoid biosynthesis key intermediate olivetolate which cannot be catalyzed by either enzyme alone. OAC by itself shows no polyketide synthase activity and the unaided OLS only produces α -pyrone and olivetol by-products (see olivetol biosynthesis (olivetol synthase by-products synthesis)) which have not been found in *Cannabis sativa*.

Overlay and analyze omics data sets

SmartTable: Enriched from Expression Ratios

Click to add description

211 rows of pathways from AraCyc col

Owner: Peifen Zhang, Created: 08-Jul-2016 15:31:42, Last Modified: 08-Jul-2016 15:31:44, Source:

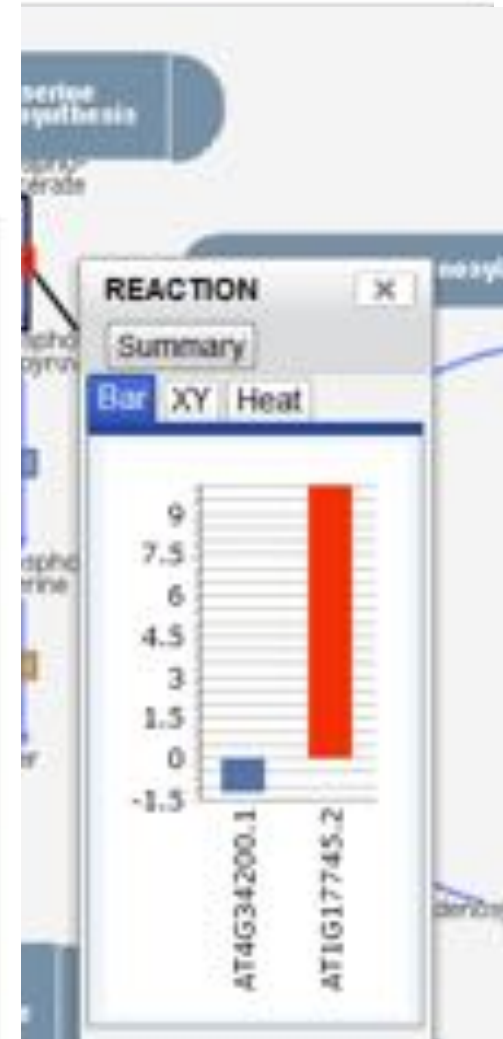
ENRICHED Genes enriched for pathways from Expression Ratios

ADD TRANSFORM COLUMN
choose a transform...

ADD PROPERTY COLUMN
choose a property

1 2 3 4 5 6 7 8 9 Next Show all

	Pathways	p-values
1	Proteinogenic Amino Acids Biosynthesis	1.7923744e-14
2	Amino Acids Biosynthesis	7.283686e-13
3	L-cysteine Biosynthesis	3.5492891e-7
4	Autotrophic CO ₂ Fixation	1.0414992e-6
5	Calvin-Benson-Bassham cycle	1.0414992e-6
6	Sugars Biosynthesis	1.8024729e-6
7	CO ₂ Fixation	1.8949237e-6
8	sucrose biosynthesis I (from photosynthesis)	1.8949237e-6
9	C1 Compounds Utilization and Assimilation	5.3437448e-6
10	Sucrose Biosynthesis	5.595559e-6

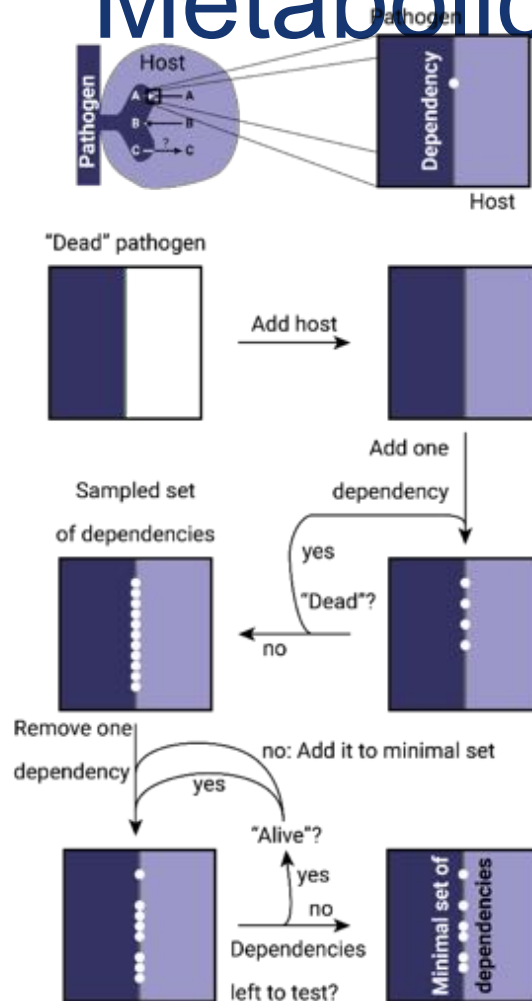


Come to my poster:

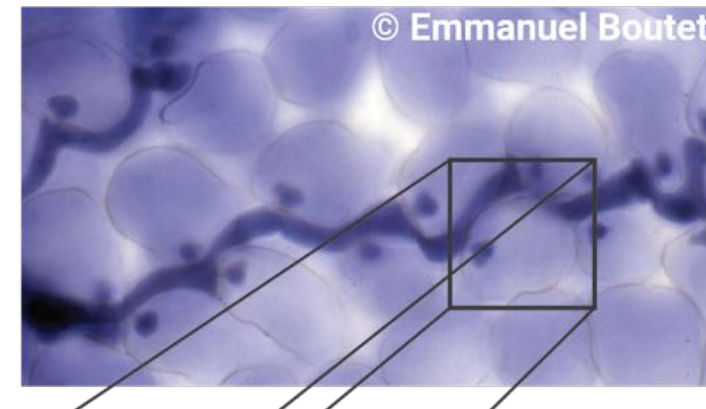
1000-024, Weaning pathogens off their host

Metabolic modeling using PMN resources

- Time today: 6:30 PM – 7:15 PM



Obligate biotrophic pathogens live exclusively on living hosts



Thank you!

- The PMN Crew
 - Sue Rhee (PI)
 - Peifen Zhang
 - Bo Xue
 - Arvind Chavali
 - Garret Huntress
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 - MaizeGDB at USDA-ARS
- Editorial board members
- Users for data submission and correction



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