# **ONTOLOGY DEVELOPMENT AND INTEGRATION**

# **Tutorial exercise: A preview**

http://www.gramene.org



# What's in a name/vocabulary?

- How do we define "cell"?
  - the basic structural and functional unit of all living organisms
  - a device that delivers an electric current as the result of a chemical reaction
  - a room where a prisoner is kept
  - any small compartment (eg. *cells* of a honeycomb)
  - a small unit serving as part of or as the nucleus of a larger political movement
- A cell can be a whole organism or a part of it



# What is an Ontology?

An Ontology is a glossary of keywords arranged in a structured order or a network based on the biological concepts

- The problem:
  - Vast amounts of biological data
  - Different names/terms for the same concepts

 $\rightarrow$ Cross-species comparison is difficult

- A (part of the) solution:
  - Ontology : "a controlled vocabulary that can be applied to either all organisms or at least with in a kingdom/sub-class/family even as knowledge of phenotypes and the associated gene and their roles in cells is accumulating and changing"



# What is an Ontology?

- NOT a system of nomenclature or a list of gene products/phenotypes
- It doesn't attempt to cover all aspects of biology or evolutionary relationships
- NOT a dictated standard
- NOT a way to unify databases.
- It allows the users to query the different databases using the same keywords and query strings provided those different databases have implemented the commonly adopted ontologies.



# How does it work?

In Gramene we have ontologies describing three different types of biological concepts.

•Gene Ontology (GO) to describe a protein/gene's biochemical property

- Molecular Function (e.g. transporter, enzyme)
- Role in a Biological Process (e.g. photosynthesis, defense response)
- Localization in a Cellular Component (e.g. plastid, cell wall)

•Plant Ontology (PO) to describe a protein/gene/phenotype expression

- In a Plant Structure (e.g. panicle, flower, xylem, phloem)
- At a Growth Stage (e.g. germination, embryo development)

•<u>Trait Ontology (TO)</u> to describe the observable feature assayed to determine the phenotype.

• Plant traits (e.g. leaf color, plant height, disease resistance)



# Anatomy of an ontology

- Ontology terms are composed of
  - Term name
  - Unique ID
  - Definition (more than 75% of terms defined)
  - Synonyms (optional)
  - Database references (optional)
  - Relationships to other terms in the same ontology
- 16600+ Gene Ontology terms (from GO consortium)
- 400+ Trait Ontology terms (from Gramene)
- 400+ plant structure terms (from PO consortium)
- 200+ cereal plant growth stages terms (from Gramene)



Each 'child term' has a unique relationship to its 'parent term'.

# Instance of (is a, type of):

Used to describe the relationship between a child term that represents a specific type of a more general parent term. For example: a *caryopsis* is a type of *fruit*; a *panicle* is an *inflorescence*.

## Part of:

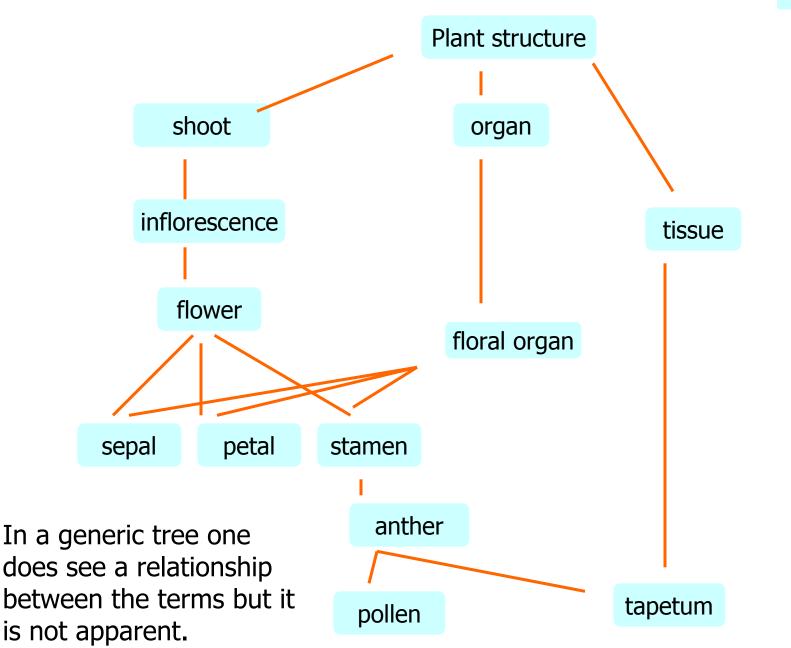
Used to indicate the relationship between a child term that is a part of the parent term. For example: the *ectocarp* is a part of the *pericarp*, which in turn is part of the *fruit*.

# Develops from: (used only in plant structure ontology)

Used to describe the relationship between a child term that develops from its parent term. For example: the *root hair* develops from *trichoblast* 

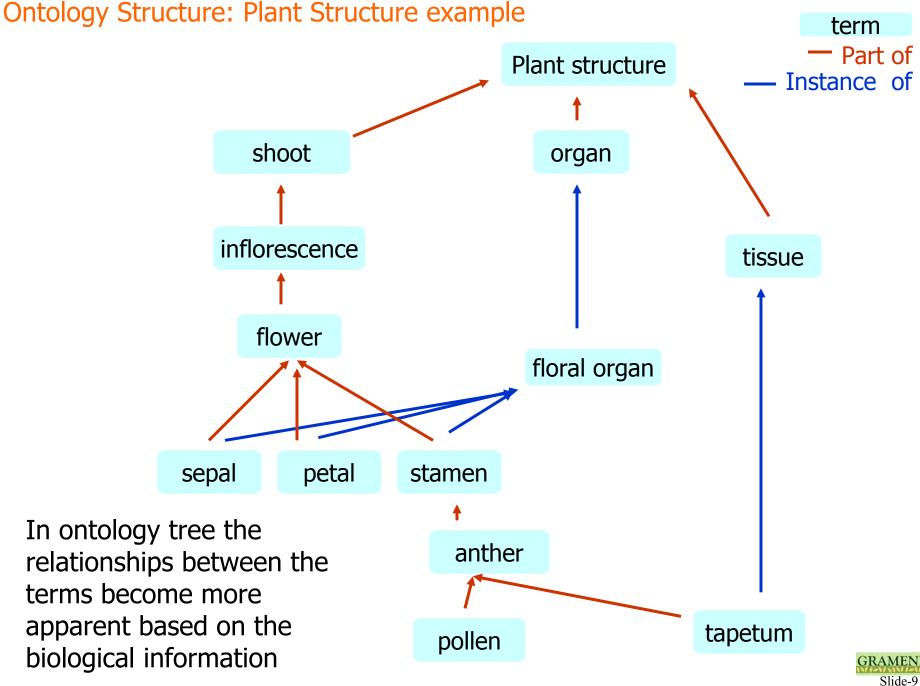


# **Ontology Structure: Plant structure example**

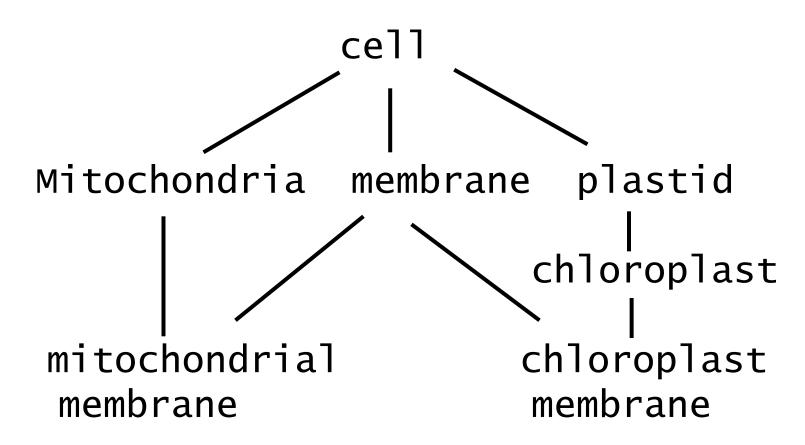




term



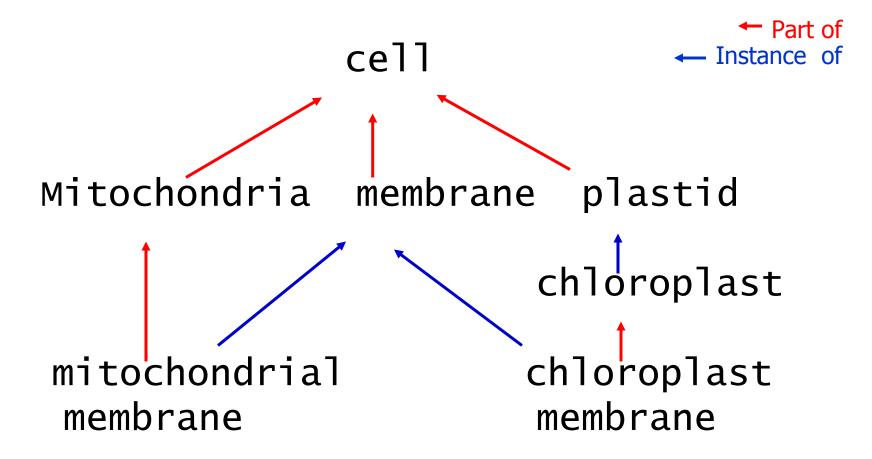
Ontology Structure: Cellular component example from GO



Similarly, in a generic tree one does see a relationship between the cellular component terms but it is NOT clear how they are related. This becomes important because if a user does not know about all the detail components of an organelle he/she will not be able to search/find all the appropriate annotations to a parent organ. The information remains scattered with no single way to find them all or cluster them.

Slide-10

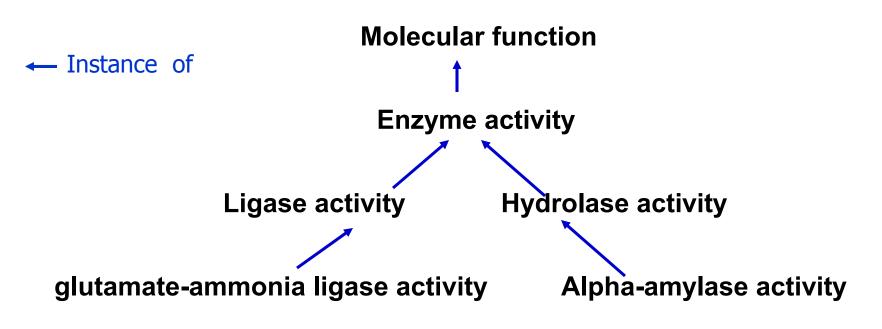
# Ontology Structure: Cellular component example from GO

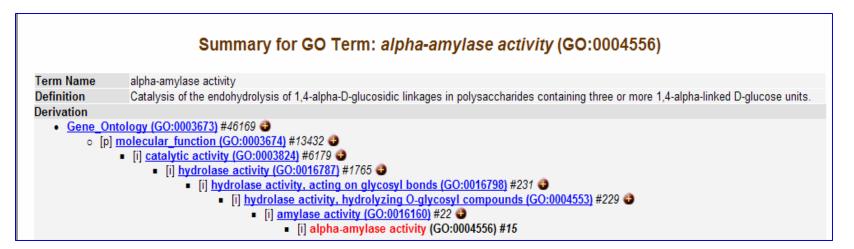


Whereas if the relationship types are established, then it is easy to browse up or down in a tree based on the biological knowledge. Lower down in the tree are finer components, whereas as we go upwards the gross level components are organized.



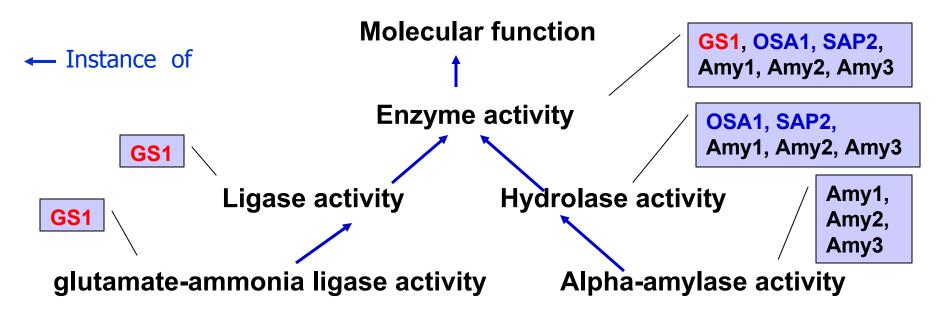
# Ontology Structure: Molecular function example from GO







# How ontology helps find your favorite gene/phenotype?



As one moves upwards in a tree, the associations (based on annotations) from the children terms are accumulated by the parent terms based on their relationship. Thus you see two types of associations

<u>Direct associations:</u> which are exact finer level association to a ontology term. e.g. Amy genes are directly associated to Alpha-amylase activity.

*Indirect association:* which are accumulated by the parents from their children terms. e.g. Amy genes are indirectly associated to Alpha-amylase activity, because it is an instance of hydrolase activity.

Thus if a user enters the ontology search/browse using the <u>hydrolase activity</u>, the results will return not only the *OSA1* and *SAP1* genes that are directly associated to this term but also the indirectly associated *Amy* genes. From this point onwards the user has an option to find the finer level of annotations by going downwards in the tree or get a collective info at gross level by going upwards.



# Ontology Structure: Biological process example with associations

	Summary for GO Term: photosynthesis, light reaction (GO:	0019684)
Term Name Derivation	photosynthesis, light reaction	
<u>Gene_Or</u>	<ul> <li>htology (GO:0003673) #46169</li> <li>biological_process (GO:0008150) #11570</li> <li>[i] physiological processes (GO:0007582) #11356</li> <li>[i] photosynthesis (GO:0015979) #45</li> <li>[p] photosynthesis, light reaction (GO:0019684) #6</li> <li>[p] NADP+ reduction (GO:0009780) #0</li> <li>[p] photosynthetic electron transport (GO:0009767) #0</li> <li>[p] photosynthesis light harvesting (GO:0009765) #4</li> <li>[p] photosynthetic phosphorylation (GO:0009777) #0</li> <li>[p] photosynthetic water oxidation (GO:0009781) #0</li> <li>[p] primary charge separation (GO:0009766) #0</li> <li>[p] regulation of photosynthesis, light reaction (GO:0042548) #0</li> </ul>	
	<ul> <li>[i] metabolism (GO:0008152) #6182</li> <li>[i] energy pathways (GO:0006091) #132</li> <li>[i] photosynthesis, light reaction (GO:0019684) #6</li> <li>[p] NADP+ reduction (GO:0009780) #0</li> <li>[p] photosynthetic electron transport (GO:0009767) #0</li> <li>[p] photosynthesis light harvesting (GO:0009765) #4</li> <li>[p] photosynthetic phosphorylation (GO:0009777) #0</li> <li>[p] photosynthetic water oxidation (GO:0009781) #0</li> <li>[p] pintosynthetic water oxidation (GO:0009781) #0</li> <li>[p] pintosynthetic separation (GO:0009766) #0</li> <li>[p] pintosynthetic water oxidation (GO:0009781) #0</li> <li>[p] pintosynthetic separation (GO:0009766) #0</li> <li>[p] regulation of photosynthesis, light reaction (GO:0042548) #0</li> </ul>	
Gene Product	Association ( 6 records found )	Download

Associated Gene Product Name (sort)

OSJNBa0036B21.6 protein

Putative low molecular mass early light-induced protein,chloroplast

Putative low molecular mass early light-induced protein,chloroplast

# Associated Term (sort)

1 photosynthesis light harvesting

2 photosynthesis light harvesting

3 photosynthesis light harvesting



Evidence Codes

IEA

IEA

IFA

Gene Product Symbol (sort)

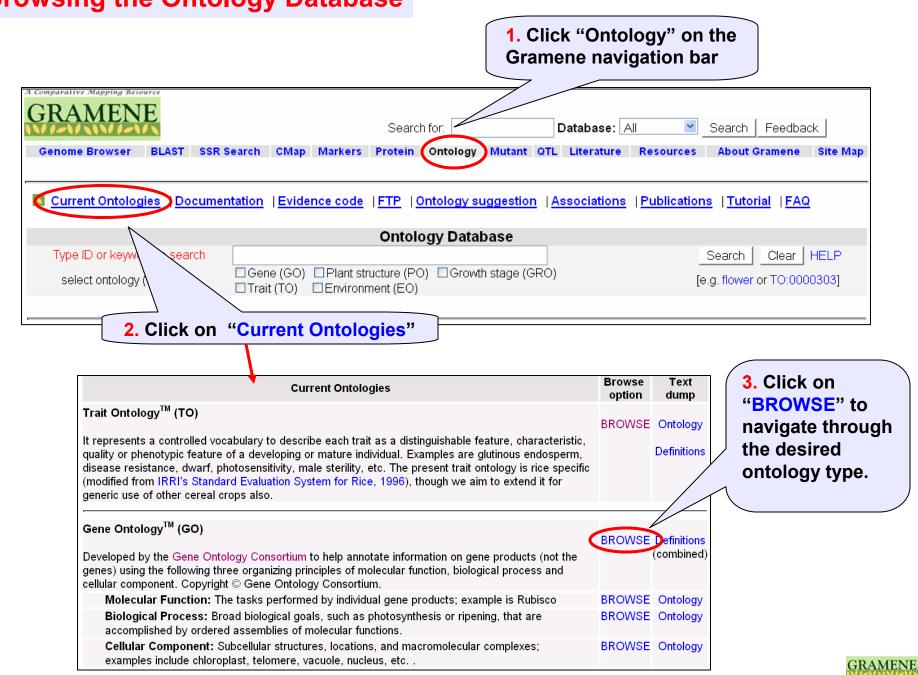
OJ1361 E02.9

OJ1361 E02.10

OSJNBA0036B21.6

# How to search or browse ontologies on the Gramene website at <u>www.gramene.org</u> ?

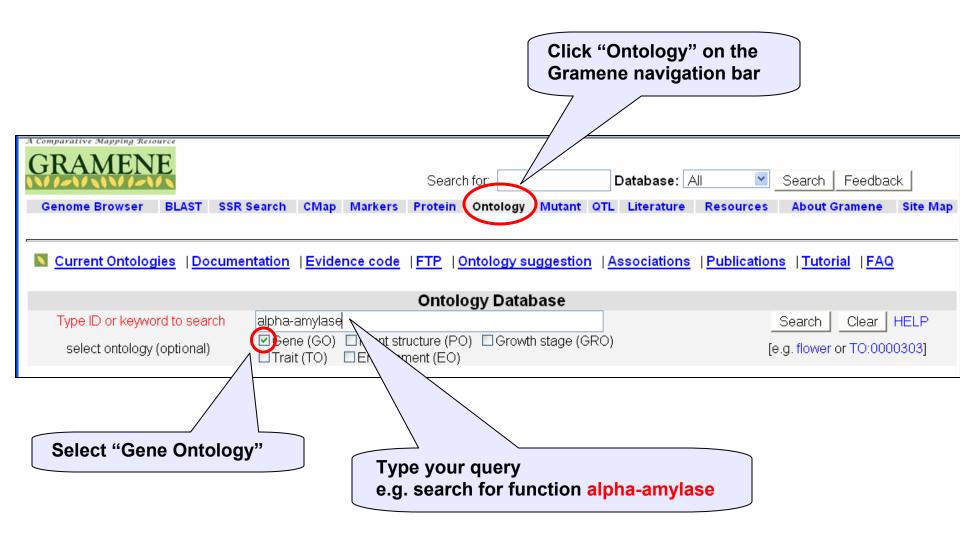
Please follow the instructions / pointers in the following slides.



Slide-16

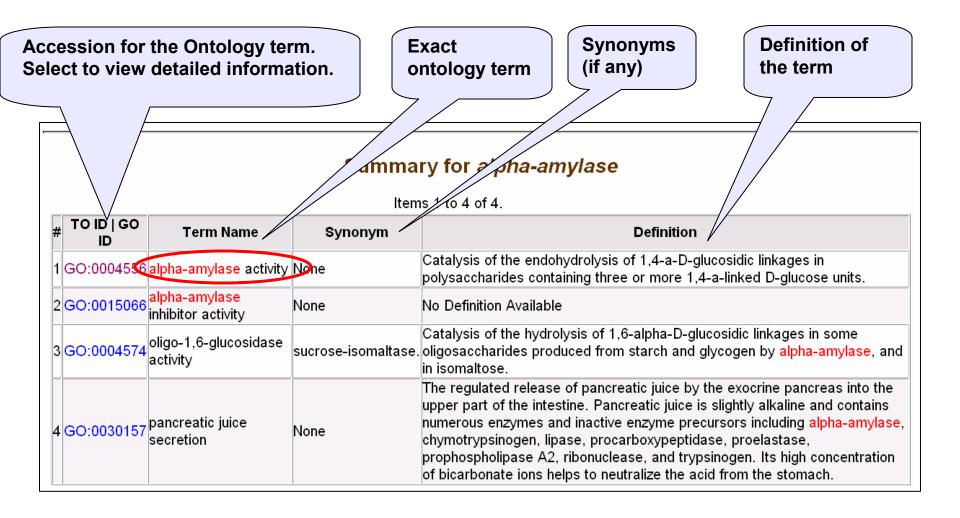
## **Browsing the Ontology Database**

# Searching the Gene Ontology (GO) Database



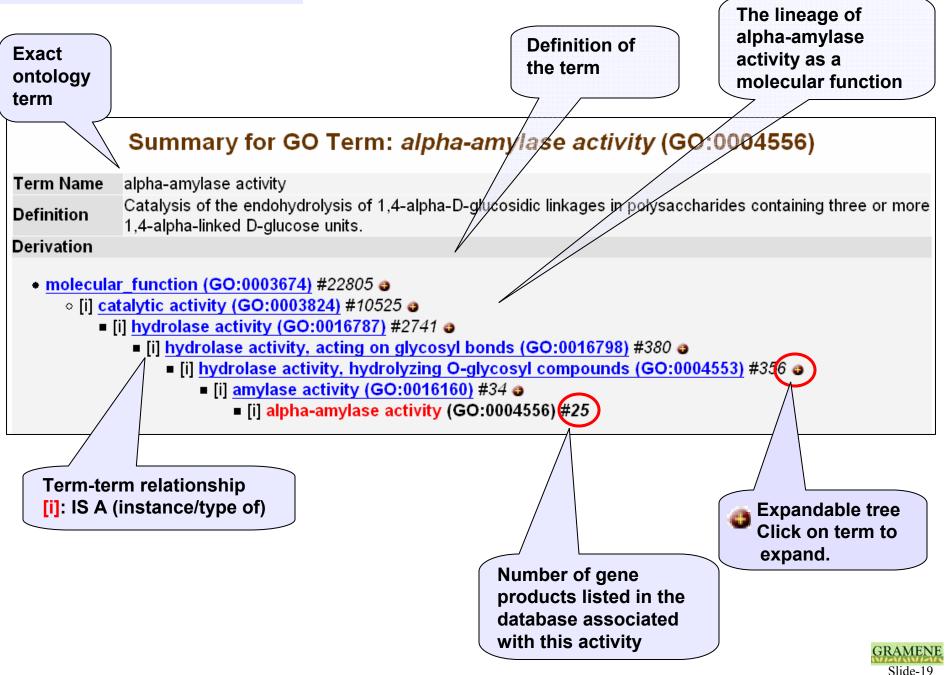


# Gene Ontology (GO) search results

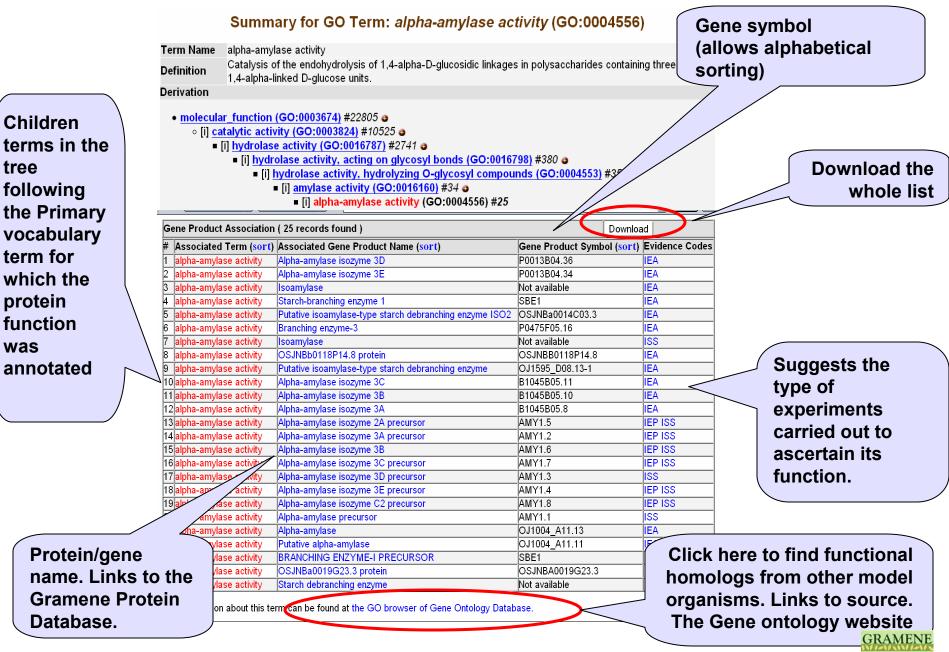


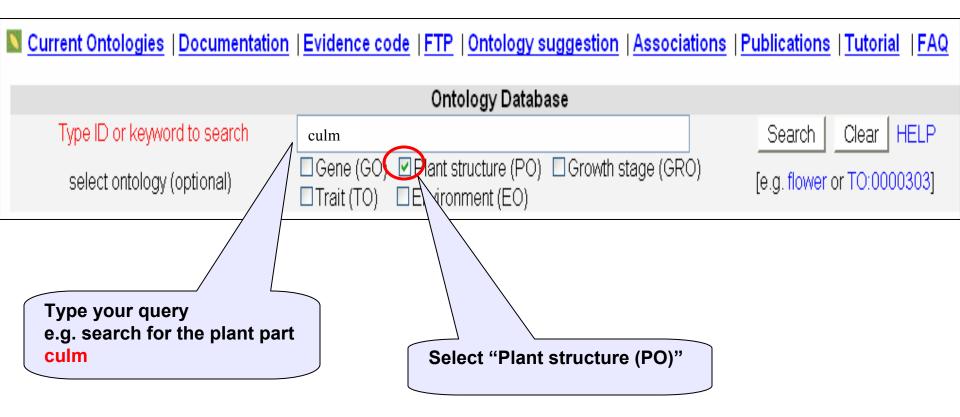


# Features of a GO term



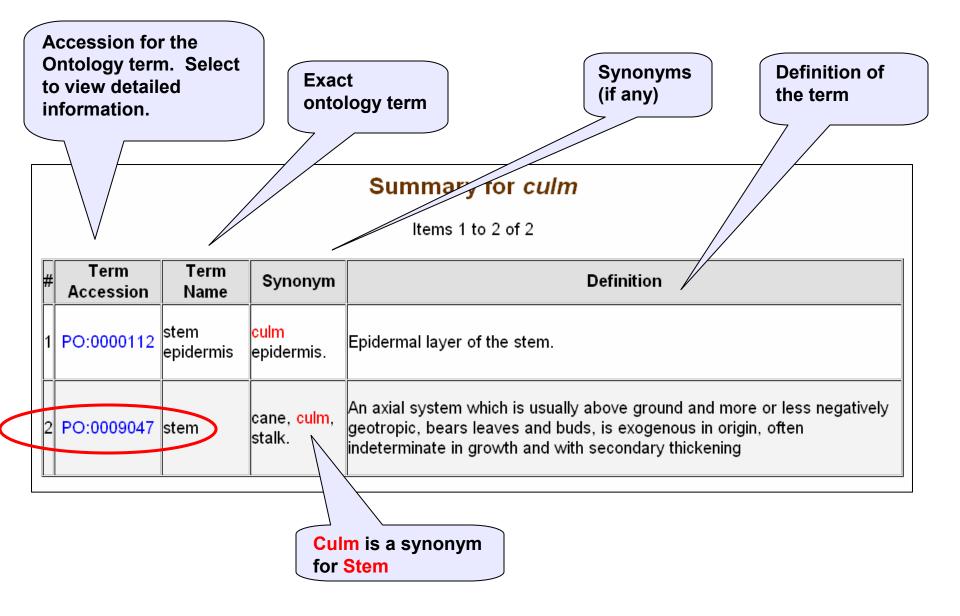
# **GO** Associations





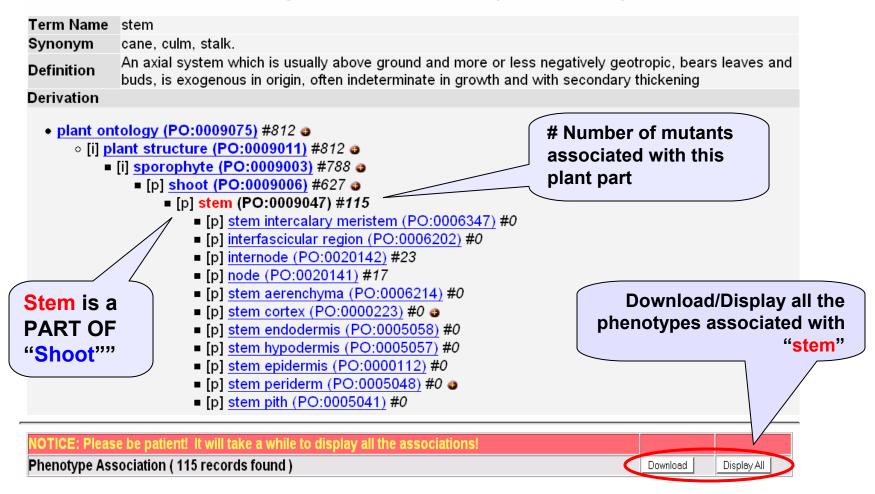


# Plant Ontology (PO) search results





#### Summary for PO Term: stem (PO:0009047)





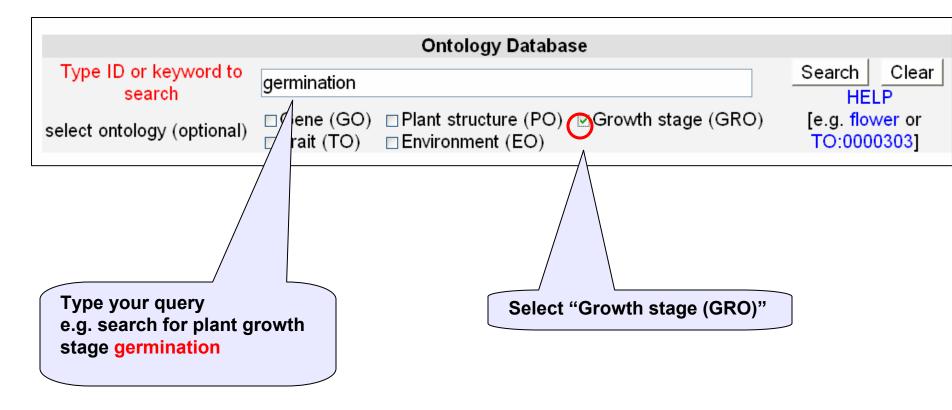
Mutant gene symbol (allows alphabetical sorting				
Phe	enotype Association ( 115 rec	cords found )		Download
#	Associated Term ( <mark>sort</mark> )	Associated Gene Name ( <mark>sort</mark> )	Gene Symbol ( <mark>sort</mark> )	Evidence Codes
1	internode	accerelated overgrowth of internode	ao	TAS
2	internode	Big uppermost culm	Buc	TAS, IAGP
3	internode	dwarf-1	dwf1	TAS, IAGP
4	internode	dwarf-9	dwf9	TAS
5	internode	elongated uppermost internode-1	eui1	TAS, IAGP
6	internode	gold hull and internode-1	gh1	TAS, IAGP
7	internode	gold hull and internode-3	gh3	TAS, IAGP
8	internode N	Inhibitor for purple leaf-2	IPI2	TAS, IAGP

Children terms in the tree following the Primary vocabulary term for which the mutant gene was annotated

Mutant gene name. Links to the Gramene Mutant Database.



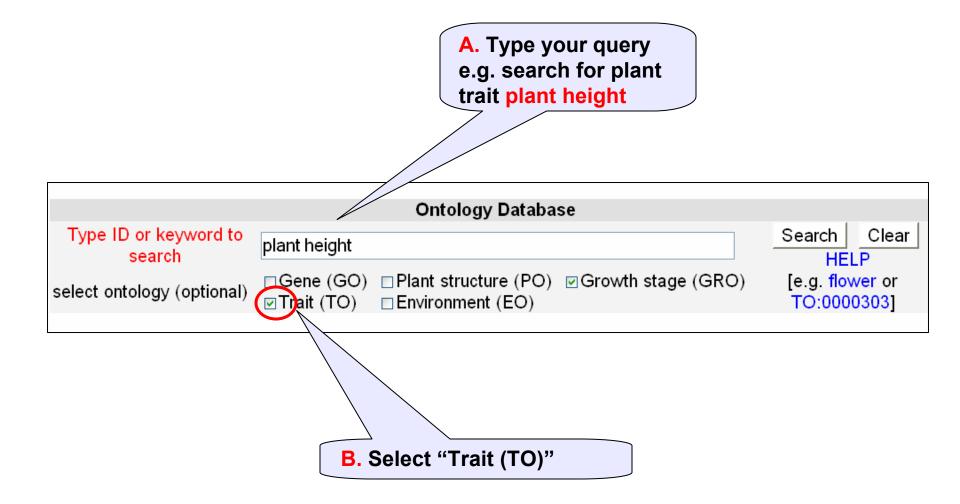
# **Searching Plant Ontology: Growth stages**



Follow the search results by selecting the term e.g. "germination" in rice (GRO:0007051). Display / download all associations to view associated phenotypes.



# **Searching the Trait Ontology (TO) Database**





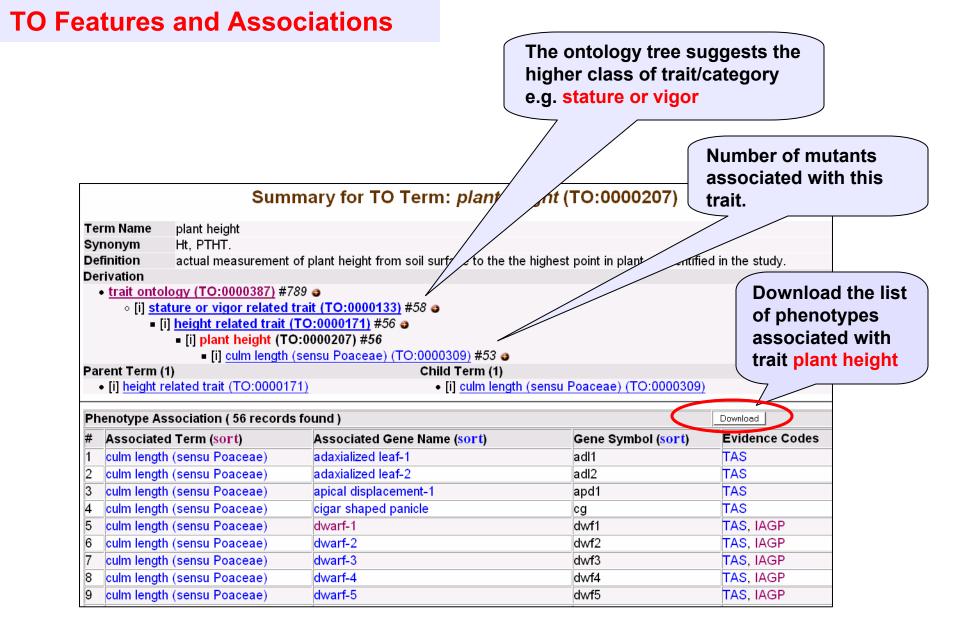
Accession for the Ontology term. Select to view detailed information.

#### Summary for *plant height*

Items 1 to 5 of 5

#	Tenn Accession	Term Name	Synonym	Definition
1		os-rapid stem	malze growth stage-s, mid-whorl stage, stem	After tassel initiation, stem length begins to increase rapidly, through elongation of cells formed by the intercalary meristem at the base of above-ground internodes. The rate of elongation decreases prior to anthesis, but plant height may continue to increase until after flowering
2	GRO:0007048	-	internode elongation, jointing stage, rice growth stage-4.	Begins about the same time panicle initiation is occurring. It continues until full plant height is reached.
3	TO:0000207	plant height		actual measurement of <mark>plant height</mark> from soil surface to the the highest point in plant as identified in the study.
4			elongation of <mark>plant height</mark> , SHELRATE.	No Definition Available
5	TO:0000296	-	vegetative growth vigor, Vg, VGVIG.	Represents the growth of plant. Used to evaluate genetic material under stress and non-stress conditions, several factors may interact, influencing the seedling vigor (e.g. tillering ability, plant height, etc),



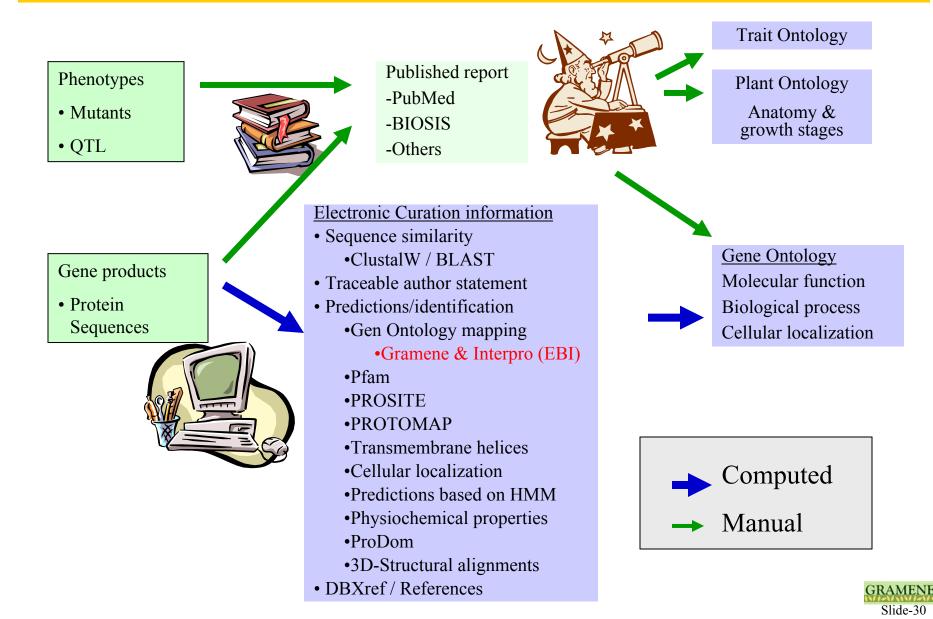


#### GRAMENE Slide-28

# How are associations built in an annotation process?

- The following slides will guide you through the methodologies used by Gramene on associating
  - Gene products to Gene Ontology terms for molecular function, biological process and localization (expression) in a cellular component.
  - Phenotypes to the plant ontology terms where (plant part) and when (growth stage) the phenotype is expressed.

# Annotation-I: How are associations built in an annotation process? Manual Vs Electronic (computed)



# How are associations built as part of annotation exercise?

Nature. 2002 Apr 18;416(6882):701-2.

### nature

#### Green revolution: a mutant gibberellin-synthesis gene in rice.

Sasaki A, Ashikari M, Ueguchi-Tanaka M, Itoh H, Nishimura A, Swapan D, Ishiyama K, Saito T, Kobayashi M, Khush GS, Kitano H, Matsuoka M.

Bioscience Center, Nagoya University, Nagoya 464-8601, Japan. makoto@nuagr1.agr.nagoya-u.ac.jp

The chronic food shortage that was feared after the rapid expansion of the world population in the 1960s was averted largely by the development of a high-yielding semi-dwarf variety of rice known as IR8, the so-called rice 'green revolution'. The short stature of IR8 is due to a mutation in the plant's sd1 gene, and here we identify this gene as encoding an <u>oxidase enzyme involved</u> in the <u>biosynthesis of gibberellin</u>, a plant growth hormone. Gibberellin is also implicated in green-revolution varieties of wheat, but the <u>reduced height</u> of those crops is conferred by defects in the hormone's signalling pathway.

PMID: 11961544 [PubMed - indexed for MEDLINE]

from abstract (manual/compated)				
Oxidase enzyme	oxidoreductase activity	GO:0016491		Oxidase enzyme
Biosynthesis of gibbrellin	gibberellic acid biosynthesis	GO:0009686		Biosynthesis of gibbrellin
Reduced height	Plant height	TO:0000207		Reduced height

# From abstract (manual/computed) From manual curation and further reading

Oxidase enzyme	gibberellin 20- oxidase activity **	GO:0045544	-Function
Biosynthesis of gibbrellin	gibberellic acid biosynthesis	GO:0009686	-Process
Reduced height	Culm length**	TO:0000309	-Trait

Related Articles, Lin

\*\* Annotations were modified based on further reading<sub>Slide-31</sub>

# Ontology Exercise TRY ON YOUR OWN !

#### 🗖 1: Proc Natl Acad Sci U S A. 2004 Jan 7 [Epub ahead of print].

Full text article at www.pnas.org

#### PLASTOCHRON1, a timekeeper of leaf initiation in rice, encodes cytochrome P450.

Miyoshi K, Ahn BO, Kawakatsu T, Ito Y, Itoh JI, Nagato Y, Kurata N.

\*Plant Genetics Laboratory, National Institute of Genetics, Yata 1111, Mishima, Shizuoka 411-8540, Japan.

During postembryonic development of higher plants, the shoot apical meristem produces lateral organs in a regular spacing (phyllotaxy) and a regular timing (plastochron). Molecular analysis of mutants associated with phyllotaxy and plastochron would greatly increase understanding of the developmental mechanism of plant architecture because phyllotaxy and plastochron are fundamental regulators of plant architecture. pla1 of rice is not only a plastochron mutant showing rapid leaf initiation without affecting phyllotaxy, but also a heterochronic mutant showing ectopic shoot formation in the reproductive phase. Thus, pla1 provides a tool for analyzing the molecular basis of temporal regulation in leaf development. In this work, we isolated the PLA1 gene by map-based cloning. The identified PLA1 gene encodes a cytochrome P450, CYP78A11, which potentially catalyzes substances controlling plant development. PLA1 is expressed in developing leaf primordia, bracts of the panicle, and elongating internodes, but not in the shoot apical meristem. The expression pattern and mutant phenotype suggest that the PLA1 gene acting in developing leaf primordia affects the timing of successive leaf initiation and the termination of vegetative growth.

PMID: 14711998 [PubMed - as supplied by publisher]

Make your own assertions on which of the ontology terms from either the GO, PO or TO vocabularies appropriately match to the function and phenotype traits associated to PLASTOCHRON1 gene.



Related Articles, Links

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Related Articles, Links

Full text article at www.pnas.org

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#### PMID: 14711998 [PubMed - as supplied by publisher]

For clues, please see the underlined portions of the text, to make your own assertions on the use of either the GO, PO or TO vocabularies.



Ontology Annotation includes various experimental evidence codes suggesting how the ontology term to gene/phenotype association was made.

- ISS Inferred from Sequence/Structural Similarity
- IDA Inferred from Direct Assay
- IPI Inferred from Physical Interaction
- TAS Traceable Author Statement
- NAS Non-traceable Author Statement
- IMP Inferred from Mutant Phenotype
- IGI Inferred from Genetic Interaction
- IEP Inferred from Expression Pattern
- IC Inferred by Curator
- ND No Data available



IEA Inferred from electronic annotation



GRAMEN Slide-34

BLAST

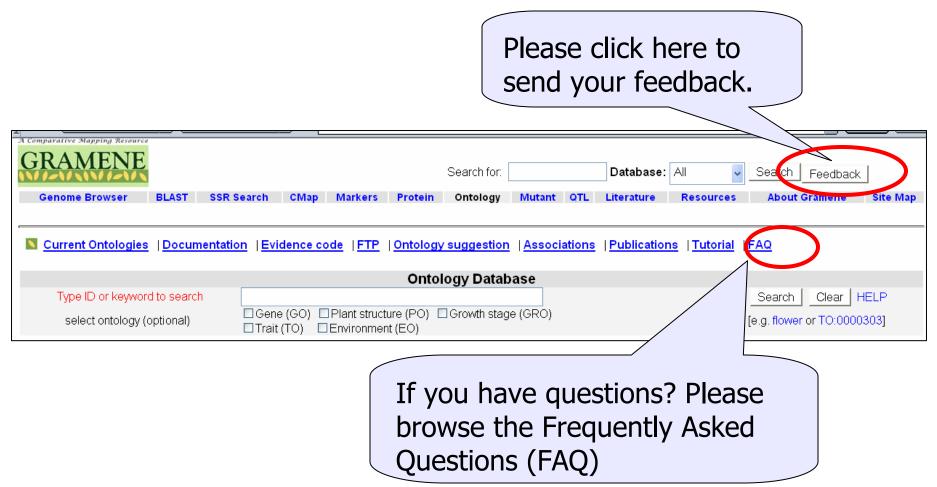
# What else can YOU do?

- Send us your review of the terms, definitions and relationships to ensure accuracy.
- Suggest new terms, definitions, or improvements to the structures.
- Use the terms in describing data in publications and databases.
- If your project on cereal plants is generating data sets that may require these kinds of annotations and associations, please feel free to reach us at gramene@gramene.org. We will be happy to help guide you through the annotation process and if necessary in setting up an Ontology database.



# Thank you for using this tutorial.

We appreciate your comments or suggestions.



You can also reach us by sending e-mail at gramene@gramene.org

