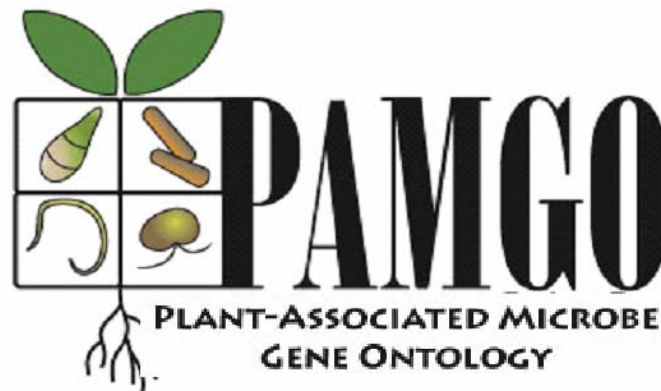


Plant-Associated Microbe Gene Ontology (**PAMGO**):  
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(<http://pamgo.vbi.vt.edu>)

# Outline of the PAMGO Workshop (1:30-3:40 P.M.)

- Candace Collmer: Getting started with PAMGO – Creating a tree of new GO terms about microbe-host interactions and forming a GO Interest Group
- Trudy Torto-Alalibo: Continuing GO term development – A PAMGO jamboree, a wiki, and beyond
- Michelle Gwinn-Giglio: Annotation using GO terms – theory and practice

## Questions:

How can comparative genomics be used to study microbial pathogenesis of plants and animals?

How is the **Gene Ontology** essential to this effort?

As more and more complete genome sequences of microbes become available,

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1) Can do obvious structural comparisons:

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e.g. What genes are present, altered, or missing in related pathovars that correlate with changes in host range or virulence?

e.g. BLAST for single gene comparisons, once a gene is known to be important,

Tools like the Artemis Comparison Tool (ACT) for whole-genome comparisons

2) Would like to do functional comparisons:

e.g. a) What biological processes (i.e. genes involved in them) differ significantly between pathogens and non-pathogens?

b) What gene products are used by different pathogens (bacteria, fungi, nematodes) to suppress host defenses?

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(Here, annotation could provide an opportunity to not only show info you know, but also find things you don't know)

2) Would like to do functional comparisons:

e.g. a) What biological processes differ significantly between pathogens and non-pathogens?

b) What gene products are used by different pathogens (bacteria, fungi, nematodes) to suppress host defenses?

But, comparisons of functions of gene products across genomes require that:

1) functions be assigned to genes via annotation,

2) the vocabulary for describing such functions be universally understandable

Annotation approaches prior to GO don't allow good functional comparisons:

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- 3) “Name” or “comment” fields reflect only a subset of the multiple roles of any gene product
- 4) Terminology often has specific and different meanings in different areas (e.g. “attachment,” “adhesion,” “prepenetration activity” could be used to describe similar events, or not)

Annotation approaches prior to GO don't allow good functional comparisons:

- 5) No way to add systematically new information about function of gene products that supports cross-genome comparisons
- 6) No way to tell the nature of the evidence –
  - low level of BLAST similarity?
  - extensive experimental confirmation?

## **Type II secretion in pathogenic bacteria as an illustration of the limitations of traditional annotation:**

The biological process is variously referred to as

“Type II secretion”,

“Type II secretory pathway”,

“general secretion pathway”, and

"main terminal branch"

Three letter gene and product names are as different as

Xcp,

Out,

Xps, and

Gsp

Many type II secretion genes are also required for type IV pilus biogenesis, but the **dual function is rarely noted** in individual annotations

The solution to the problem:

the **Gene Ontology (GO)**!

**GO** is a set of controlled vocabularies

---

# GO is a set of controlled vocabularies

---

The vocabularies are used to describe 3 aspects of a gene product's existence:

**what** it does (**molecular function**),

**why** it does what it does (**biological process**),

and **where** it does what it does (**cellular component**)

# What is a controlled vocabulary?

- a set of precisely defined terms
- used to attach meaningful descriptions (a k a annotations) to objects

Thus, **GO** allows all biologists to speak the same biological language, to:

- Describe gene products ( a k a annotate them)
- Search annotation data across genomes to answer biological questions

GO offers an annotation capture system that:

- allows the unambiguous communication of annotation information,
- is in a format readable by both computers and humans,
- facilitates data exchange

# The structure of GO

The GO consists of three controlled vocabularies stored as ontologies.

- molecular function (what)
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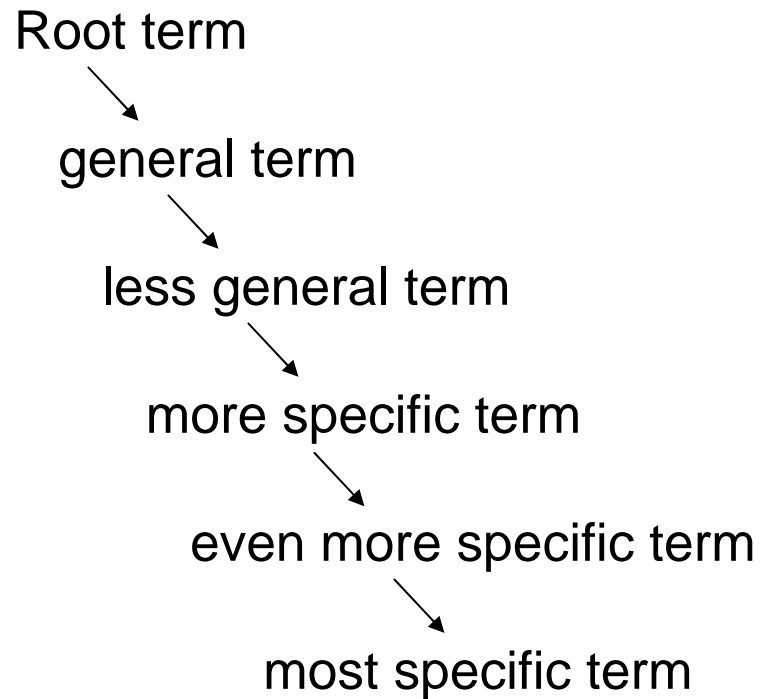
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Each term has a name and a detailed definition - these are understandable by humans.

Each term also has a unique id number - this makes the term easily understandable and searchable by a computer.

Each term is related to other terms in a “parent-child” relationship where the child term is more specific than the parent term.

# General GO tree structure



## One branch example:

biological process (root)

cellular process

metabolic process

carbohydrate metabolic process

ribose metabolic process

## Two branch example:

molecular function (root)

transporter  
activity

catalytic activity

carbohydrate  
transporter  
activity

kinase activity

ribose transporter  
activity

carbohydrate kinase  
activity

ribokinase activity

# Elements of a GO term

- ID number:** GO:0044247
- ontology:** biological process
- Name:** cellular polysaccharide catabolic process
- Definition:** The chemical reactions and pathways resulting in the breakdown of polysaccharides, polymers of more than 10 monosaccharide residues joined by glycosidic linkages, as carried out by individual cells.
- synonyms:** cellular polysaccharide breakdown, cellular polysaccharide degradation
- parent term:** cellular carbohydrate catabolic process; cellular polysaccharide metabolic process; polysaccharide catabolic process
- child terms:** xylan catabolic process, glucan catabolic process; etc. (many more)



- GO began as a collaboration among scientists working on eukaryotic model organisms: mouse (MGI), fruit fly (FlyBase), and baker's yeast (SGD)
- Terms relevant to prokaryotic organisms added later, spearheaded by scientists at TIGR
- GO term development is a continuous process

## The Start of PAMGO

By 2003, full genome sequences of diverse plant pathogens (microbes) were becoming available:

- Bacteria
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- Oomycetes
- Nematodes

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We realized the power of GO annotation for asking important biological questions across organisms

e.g. What gene products in different pathogens are involved in suppressing host defenses?

But few GO terms were available for annotating genes involved in the different processes of pathogenesis.

Only these GO parent terms:

“pathogenesis”

“host-pathogen interaction”

In 2004, formation of the **Plant-Associated Microbe Gene Ontology (PAMGO)** interest group

Collaborators from:

Cornell University

North Carolina State University

TIGR

University of Wisconsin at Madison

Virginia Bioinformatics Institute (VPI)

Wells College

.... working on genome projects of plant pathogens:

bacteria -- *Pseudomonas syringae* pathovars,  
*Erwinia chrysanthemi*  
*Agrobacterium tumefaciens*

oomycetes -- *Phytophthora sojae*  
*Phytophthora ramorum*

fungus -- *Magnaporthe grisea*

nematode -- *Meloidogyne hapla*

Original goal of PAMGO:

To develop higher order GO Biological Process terms for  
annotating genes of microbes implicated in plant  
pathogenesis

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But soon realized the broader utility of developing **general terms** to serve:

- diverse microbes (prokaryotic and eukaryotic)  
*(All face same challenges vis-à-vis the host)*
- plant and animal hosts  
*(Some microbial processes used for both – e.g. type III secretion system in bacterial pathogens of plants and animals)*
- all intimate relationships (mutualistic to parasitic)  
*(Attachment to host is necessary for both a mutualistic Rhizobium [nitrogen fixation] or a pathogenic Agrobacterium [plant disease])*

The last realization –

that we wanted terms for describing the full range of intimate interactions between microbes and their hosts –

led to the most discussion with the GO Consortium (at meetings) and among GO friends (over email).

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Will return to that....

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.... for annotating genes in microbes that had been implicated in interactions with their hosts

# Original PAMGO-developed Biological Process GO terms

## **GO:0051701 : interaction with host**

GO:0044002 : acquisition of nutrients from host

GO:0044406 : adhesion to host

GO:0044413 : avoidance of host defenses

GO:0044415 : evasion of host defenses

GO:0044414 : suppression of host defenses

GO:0044007 : dissemination or transmission of organism from host

GO:0044409 : entry into host

GO:0044408 : growth on or near host surface

GO:0044412 : growth within host

GO:0044416 : induction of host defense response

GO:0044003 : modification of host morphology or physiology

GO:0044004 : disruption of host cells

GO:0044005 : induction in host of tumor, nodule, or growth

GO:0044000 : movement within host

GO:0044405 : recognition of host

GO:0044417 : translocation of molecules into host

- Proposal generated intensive discussion before, during, and after its presentation by PAMGO members (C. Collmer, M. Gwinn-Giglio, A. Collmer) at a GO Content meeting in August, 2004.

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- **\*\*By this time PAMGO had become an official GO Interest Group**





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## GO Curator Interest Groups

The Gene Ontology covers a wide range of biological topics and to facilitate development of the ontologies, interest groups have been set up for discussion of areas within the ontologies that are likely to require extensive additions or revisions, or where proposed changes crop up frequently.

### About Interest Groups

#### Interest groups with a mailing list

- Cell cycle (process)
- Developmental biology (process)
- Farm animals
- Metabolism
- Neurobiology
- Pathogens and Pathogenesis
- Protein kinases
- Response to drug

#### Other interest groups

### About Interest Groups

Interest groups are organized by topics that roughly correspond to GO terms, usually high-level terms that might appear in [GO slim](#) sets. Organism-specific (*sensu*) terms are not listed because these would be redundant with model organism database affiliations, but such terms should be treated in an analogous manner to interest group topics: the relevant model organism database curators should be consulted.

#### Joining an existing group or creating a new group

Membership of an Interest group is open to anyone, and all members are listed on the web site. To join a group or to suggest a new group, please send your request to [Midori Harris](#).

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\*\*Some in the GO Consortium wanted all of our proposed terms to be children of the parent term “pathogenesis”

e.g. pathogenesis

... acquisition of nutrients from host *during* pathogenesis

...adhesion to host *during pathogenesis*

...avoidance of host defenses *during pathogenesis*

etc.

etc.

\*\*Others, including PAMGO, wanted the terms as children of a general term, encompassing all types of intimate relationships

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**\*\*Others, including PAMGO, wanted the terms as children of a general term, encompassing all types of intimate relationships**

- 1) We wanted to capture all genes in microbes known to be involved in attachment, irregardless of outcome (mutualism, pathogenesis, whatever)
- 2) The outcome of microbial attachment (adhesion) by a particular microbe is not always the same -- it may or may not lead to pathogenesis, depending on environmental conditions, the strength of the host's defenses, etc.

Therefore, annotating to the adhesion term, as a child term of the parent term pathogenesis, would imply that the adhesion was always part of pathogenesis (i.e. the “true path” rule in GO), but would not be true

pathogenesis

...adhesion to host *during pathogenesis*

The final solution was an excellent compromise, where

1) “symbiosis” was adopted as a general term,  
with the broad definition that encompasses  
mutualism through parasitism

## Example of the precise GO definition:

“symbiosis” = An interaction between two organisms living together in more or less intimate association. The term host is usually used for the larger (macro) of the two members of a symbiosis. The smaller (micro) member is called the symbiont. Microscopic symbionts are often referred to as endosymbionts. The various forms of symbiosis include parasitism, in which the association is disadvantageous or destructive to one of the organisms; mutualism, in which the association is advantageous, or often necessary to one or both and not harmful to either; and commensalism, in which one member of the association benefits while the other is not affected. **However, mutualism, parasitism, and commensalism are often not discrete categories of interactions and should rather be perceived as a continuum of interaction ranging from parasitism to mutualism. In fact, the direction of a symbiotic interaction can change during the lifetime of the symbionts due to developmental changes as well as changes in the biotic/abiotic environment in which the interaction occurs.**

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2) the term “pathogenesis” was retained as a sibling term to our broad terms,

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1) “symbiosis” was adopted as a general term, with the broad definition that encompasses mutualism through parasitism

2) the term “pathogenesis” was retained as a sibling term to our broad terms,

...and a gene shown to function in attachment (a synonym of “adhesion”) that sometimes leads to pathogenesis could be annotated to **both** GO terms

- [-] all : all [179191] 🌐
  - [-] ⓘ GO:0008150 : biological\_process [138785]
    - [-] ⓘ GO:0051704 : interaction between organisms [1595]
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          - ➡ [-] ⓘ GO:0051816 : acquisition of nutrients from other organism during symbiotic interaction [1]
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          - [-] ⓘ GO:0051821 : dissemination or transmission of organism from other organism during symbiotic interaction [12]
          - [-] ⓘ GO:0051828 : entry into other organism during symbiotic interaction [75]
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          - [-] ⓘ GO:0051702 : interaction with symbiont [0]
          - [-] ⓘ GO:0051708 : intracellular protein transport in other organism during symbiotic interaction [3]
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          - [-] ⓘ GO:0044399 : multi-species biofilm formation [0]
          - [-] ⓘ GO:0009877 : nodulation [5]
          - ➡ [-] ⓘ GO:0009405 : pathogenesis [455]
          - [-] ⓘ GO:0051824 : recognition of other organism during symbiotic interaction [0]
          - [-] ⓘ GO:0051836 : translocation of molecules into other organism during symbiotic interaction [54]

This GO tree shows how a gene can be annotated to different levels of specificity, depending on what is known about the gene product

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e.g. For annotating a gene in a microbe known to be the symbiont (smaller organism) interacting with a host (larger organism), we can use the terms that are children of GO term GO:0051701 - “interaction with host”

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# PAMGO-developed Children Terms of GO:0051701

## **GO:0051701 : interaction with host ( 297 )**

GO:0044002 : acquisition of nutrients from host ( 1 )

### **GO:0044406 : adhesion to host ( 88 )**

GO:0044413 : avoidance of host defenses ( 22 )

GO:0044415 : evasion of host defenses ( 21 )

GO:0030682 : evasion of host defense response ( 10 ) \*\*

GO:0044414 : suppression of host defenses ( 0 )

GO:0044007 : dissemination or transmission of organism from host (12 )

GO:0044409 : entry into host ( 75 )

GO:0044408 : growth on or near host surface ( 0 )

GO:0044412 : growth within host ( 10 )

GO:0044416 : induction of host defense response ( 22 )

GO:0044003 : modification of host morphology or physiology ( 66 )

GO:0044004 : disruption of host cells ( 62 )

GO:0044005 : induction in host of tumor, nodule, or growth ( 0 )



GO:0044000 : movement within host ( 3 )

GO:0044405 : recognition of host ( 0 )

GO:0044417 : translocation of molecules into host ( 0 )

(1/5/07)

\*\* Could use a child term of GO:0051701 plus GO:0009405

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As genome annotation using the new GO terms began in 2005-2006 for genes implicated in the virulence of the plant pathogens:

- *Pseudomonas syringae* pathovars
- *Erwinia chrysanthemi* 3937
- *Phytophthora* spp.

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It soon became evident that additional, more specific GO terms were necessary to capture information available in the published literature

We had originally planned to use the Gene Ontology SourceForge site to request new GO terms as literature curation revealed their need

## SourceForge open to all...

- SourceForge site used to submit requests for new terms or for changes to existing terms
  - [https://sourceforge.net/tracker/?func=add&group\\_id=36855&atid=440764](https://sourceforge.net/tracker/?func=add&group_id=36855&atid=440764)
- Anyone can submit a SF item
- GO maintains a 4-person full-time staff to maintain the ontologies and respond to SF items
- Anyone can join “interest groups” to participate in ontology development in specific areas of biological interest

# The Gene Ontology SourceForge Tracker for Ontology Development

SF.net » Projects » Gene Ontology » Tracker » Curator requests » [Submit New Tracker Item](#)

**Gene Ontology**   [Advanced](#)

[Project](#) [Tracker](#) [Mailing Lists](#) [Forums](#) [Code](#) [Download](#) [Documentation](#) [Tasks](#) [Project Web Site](#)

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Use this tracker to suggest changes in GO content. Please provide an **informative** description in the "Summary" field (note: summary lines like "new term request" are not informative, please provide more information). If you mention any existing terms, please **include both the text string and the ID**.

**"New term request"**: Request that a new term be added to the Gene Ontology. Please be as detailed as possible: include the term name, a suggested **definition** and **database reference** for that definition (e.g. FB:ma), a suggestion of **where it should appear in the GO hierarchy**, and any pertinent literature references, synonyms, etc..

**"Other term-related request"**: suggest modifications to existing terms, movement of existing terms to correct paths; suggest definitions, or any other changes to the GO vocabularies.

**"Term obsolescence"**: recommend that an existing term be made obsolete. Please include the reason(s).

**For Project:**  
Gene Ontology

**Category: (?)**  
 (admin)

**Summary: (?)**

**Detailed Description:**

**Private: (?)**

**Group: (?)**  
 (admin)

[https://sourceforge.net/tracker/?func=add&group\\_id=36855&atid=440764](https://sourceforge.net/tracker/?func=add&group_id=36855&atid=440764)

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Related terms did exist in GO, i.e.

GO:0012501 – programmed cell death

GO:0009626 – hypersensitive response

But some needs were quite complex, and required more general GO discussion

e.g. Needed a term for annotating a bacterial gene shown to induce the hypersensitive response in a plant host

Related terms did exist in GO, i.e.

GO:0012501 – programmed cell death

GO:0009626 – hypersensitive response

But their current definitions indicated they were to be used to annotate host genes, not microbial (symbiont) genes

**“programmed cell death”** = "Cell death resulting from activation of endogenous cellular processes"

**“programmed cell death”** = “Cell death resulting from activation of endogenous cellular processes”

and

**“hypersensitive response”** = “The rapid death of plant cells in response to invasion by a pathogen”

Again, this need led to a broad discussion among GO Consortium members,  
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.... where the GO Consortium adopted the concept of using “dual taxon” annotation for gene products that are made by one organism, but act in another,

... which can be used for GO terms that are children of GO:0051704 - “interaction between organisms”

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By summer 2006, given the number of new terms PAMGO members wanted to propose (originally **over 50**) as children of “interaction between organisms,”

we held a 3-day PAMGO term jamboree in July, 2006, at TIGR with

- 5 PAMGO members
- 2 members of GO editorial board

to expedite the creation and integration of the new terms within GO



PAMGO term  
jamboree at TIGR,  
July 2006

Left to right:  
Bryan Biehl,  
Trudy Torto-Alalibo  
Michelle Gwinn Giglio  
Candace Collmer  
Jane Lomax - GO  
Marcus Chibucos  
Amelia Ireland - GO

and of course, TIGR's  
tiger

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Trudy Torto-Alalibo will tell more about these.....

# Current PAMGO Collaborators

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Dr. Trudy Torto-Alalibo (Virginia Bioinformatics Institute) – **Coordinator**

Dr. Brett Tyler (Virginia Bioinformatics Institute) - **PI**

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Dr. Jeremy Glasner (University of Wisconsin)

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Dr. Ralph Dean (North Carolina State University)

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Dr. Linda Hannick (TIGR)

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