GO Content Meeting Notes Aug 22, 2004
Carnegie, Stanford, CA

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Contents

MINUTES

Purpose of the meeting: To bring together GO group members and a few domain experts in person. To review and discuss three problematic areas in the GO process ontology; metabolism, pathogenesis, and cell cycle; in order to come up with acceptable solutions and specific action items to resolve the problems.

Various proposals for change have been submitted and these are included in the appendix sections. A summary is included in the appendix called: 'Background reading from Jane on all three topics.'

The first topic involved improvements to the terms around 'host-pathogen interaction'. As a consequence of this we discussed the definition of pathogenesis, but we also discussed in some depth the ways of defining situations where two organisms have physiological interaction. (e.g. parasitic relationships, and symbiotic relationships.)

Pathogenesis and interactions between organisms.

See also the appendices:
Background Reading From Jane On All Three Topics
Alex Diehl's Pre-Meeting Proposal On Pathogenic Terms
Comments From Matt Berriman On The Pathogenesis Proposals
Pathogenesis Powerpoint Presentation.
PAMGO Powerpoint Presentation.
Alex's Proposal On Pathogenic Terms To Change Or Eliminate From The GO
Suparna's Proposal On Host-Pathogen Interactions. (Url)

Problems to be addressed:

Problem I: Intelligibility
The meaning of 'pathogenesis' is unclear from the name. It should be used for pathogen annotations only, but, from AmiGO we find that there are currently annotated: 5 human gene products, 5 mouse, 1 rat.

Problem II: True path
Terms specific for viral proteins have incorrect ancestry. This violates the true path, and creates odd GO slims.

Problem III: Which organism?

'Cytolysis' can occur by multiple mechanisms e.g. as a result of exposure to a exogenous toxin, or by the immune system to destroy an infected cell. Therefore two completely different processes would be annotated to the same term. There is a problem of univocity, which means that terms should mean the same wherever they're used.

Problem IV: Symbiosis
Interactions between symbiont and host may be destructive to host (parasitism), they may also be mutualistic or commensalistic. No terms in GO currently cover these processes. Biological processes to establish these states (symbiosis or parasitism) often conserved so common terms will be needed to cover the same processes within different types of relationships (e.g. the initiation of pathogenesis versus the initiation of mutualism by a microbe both have some processes in common, and it would be helpful to be able to see this through GO terms and tree structure).

Discussion of symbiosis

from Jane's Pathogenesis presentation:
(ftp://ftp.geneontology.org/pub/go/meeting/minutes/20040822_Stanford_Content/pathogenesis.pdf
ftp://ftp.geneontology.org/pub/go/meeting/minutes/20040822_Stanford_Content/pathogenesis.ppt)

There was some discussion about how, on one hand, PAMGO really wanted general terms for processes that could apply to organisms involved in either pathogenesis or symbiosis (because seeing these common processes across different end results would be really useful). Others at the meeting, really wanted the terms under the separate processes of pathogenesis and symbiosis, because people who wanted to use GO to annotate genes in pathogens or symbionts would naturally tend to search using those familiar categories. In the end, we came up with a compromise. We would make, as children, under the parent term "interaction between host and other organism", all of the general terms as proposed by PAMGO (e.g. "recognition of host" etc.), but other children under that parent term would also be "pathogenesis" and "symbiosis", and children under each of these would include the general terms as specified for those processes (e.g. under "pathogenesis" you would have the child term "recognition of host during pathogenesis", and under "symbiosis" you would have "recognition of host during symbiosis." In addition, under the general term "recognition of host" you would find the children "recognition of host during pathogenesis" and "recognition of host during symbiosis." That should allow the needs of all to be met.

Action 1. Establish common parents and replicate subtrees for symbionts and pathogens as appropriate, e.g.

[i]acquisition of nutrients from host
---[i]acquisition of nutrients from host during symbiosis

---[i]acquisition of nutrients from host during pathogenesis

We discussed the difficulties in referring to, and in defining, the partners in the symbiotic and parasitic relationships.

It is difficult to define symbioses. They may be mutualistic or commensalistic. There are no terms in GO to cover these processes. The biological processes to establish these states are often conserved so common terms are needed for the various types of symbioses. Does symbiosis include pathogenesis (and therefore parasitism)? This problem of exactly what "symbiosis" means seems to exist across biology - where it is used differently by different texts, people, etc. The way it is used below, and the way PAMGO thought about it when they were working on their tree, is that "symbiosis" does not include "pathogenesis" or parasitism", but only mutualism and commensalism - i.e. when one or both organisms benefits, but neither is harmed. It seems that it is important to get this matter of how we are using "symbiosis" in GO straightened out. Should PAMGO define symbiosis to exclude parasitism or pathogenesis in their modified proposal?

Action 2. Should PAMGO define symbiosis to exclude parasitism or pathogenesis in their modified proposal? This remains a point for further discussion.

We considered how to define 'host'. PAMGO suggest that it is an organism from which another organism obtains nutrition, shelter, dispersal, protection etc. Although this does describe a host accurately, it could also apply
equally well to either individual in a mutualistic relationship in which
neither organism would be called a host.

Action 3. Define host based on PAMGO definition (To be taken from:
% interaction with host organism
Def: any interaction between an organism, usually a parasite or symbiont, and another organism from which it may obtain nourishment, protection, and/or a means of dispersal.

Action 4. We need a name and a definition for the 'hostee'; the dependent organism in a relationship, e.g. a parasite.

Action 5. Remove 'interaction with non-host organism' and move sub-terms up one level.

i.e. get rid of the non-host terms so the proposed tree goes from this:

[i]interaction with other organism
---[i]interaction with non-host organism
---[i]interaction with host organism

to this:

[i]physiological interaction with other organism
---[i]interaction between host and other organism

The word 'physiological' excludes interactions such as one animal hunting and eating another animal. (Michelle and Candace agreed after the content meeting to change the higher order term in the revised PAMGO proposal to "interaction between host and other organism".) Any gene products that needed the 'non-host' concept will be annotated to the parent term.

Action 6. Change 'competition with non-host' to 'competition with other'. N.B Michelle and Alex exchanged email after the meeting and settled on the phrase "another, non-host, organism" to describe better what "non-host" means. PAMGO agree with this. See https://sourceforge.net/tracker/?func=detail&aid=1012931&group_id=36855&atid=440764

If you have 'interaction with host' terms, you may also need 'interaction with hostee' terms. We need to incorporate this concept as needed. Idea: Taxon field can take one or more entries. Usually you are annotating from the perspective of one organism. But you can annotate from the perspective of more than one. For example, Plasmodium takes gene products from other organisms and converts them to its own use.

Action 7. Suparna will look into adding 'host-side' processes or using taxonID to clarify reciprocal terms as needed.

Action 8. Change definition of 'cell-cell signaling' to mean between cells in the same species.

Action 9. Add 'within the same species' qualifier to the definition of 'pollen-pistil interaction'

Action 10. Consider adding 'within the same species' to the definition of terms for all children of 'cell communication'.

Pathogenesis
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Having discussed the term 'host-pathogen interaction' with reference to symbiosis, we also discussed the use of the word 'pathogen'.

Background: The distinction of 'pathogenic' processes from 'normal' processes is quite ambiguous; from the point of view of the infecting organism, all processes are quite normal and yet we designate them pathogenic.

The PAMGO representatives suggested that the results for the host are something different from health. On the host side, there are natural processes that occur in an attempt by the host to prevent the pathogenic state from developing. Therefore "pathogenesis" is a natural process and terms relating to it are appropriate for GO. (N.B. symptoms do not belong in GO, although the underlying responses that happen to give rise to symptoms may be valid GO processes. A 'candidate' for a response term would have to be evaluated individually by curators. Gene products involved in such host responses should not be annotated to 'pathogenesis'.) In addition, many of the processes involved in establishing a symbiotic interaction and establishing a pathogenic interaction are identical, so we needed to create common terms.

Current structure (Michelle Gwinn):
Pathogenesis is currently under 'physiological process', and 'host-parasite interaction' is in a different node, under 'cell process'. The virus terms are throughout both ontologies, again in their own nodes.

B. Outline of problem (Jane Lomax): There are lots of potential true path violations e.g. viruses are not cells, but virus-specific terms are ancestors of cellular processes. This will become more of a problem as more pathogen groups join and want terms e.g. the plant microbe group. It also means these groups will have some strange GO slims. We need a systematic way of adding new terms that are specific to pathogens in a similar way to the term 'host'.

The biological use of the word 'pathogenesis' was discussed. At least to some of the plant people present, there is a clear difference between the concept of pathogenesis as it is defined in plant and in mammal research fields. In mammals there are many bacterial strains that live in the gut, and these may cause disease in some individuals but not in others. This means that these bacterial strains are sometimes pathogenic and sometimes not. However, some of the plant biologists present stated that in plant biology a pathogen is considered to be a species that will always cause disease in its target species, and that is adapted to fit this niche. They said that plant pathogens are identified by their ability to inject virulence factors into the cells of the target species as one of the first steps in the infection process. By this view of things there would be a considerable difference in the way that the plant research community and the mammal research community view pathogenesis. As a caveat however, to this apparently clear distinction in viewpoint, it was noted that the plant experts present were divided on the subject. Some of those present stated that this view of plant pathogenesis is not a concept that all plant pathologists would

agree with.

To clarify the point, further information has been contributed after the meeting by the PAMGO group:

"There are incredibly diverse ways in which various microbes interact with plants. It is true that many of the best studied pathogens are dedicated pathogens whose virulence depends on injecting virulence proteins into plant cells (the bacterium Pseudomonas syringae is a good example). However, there are some very devastating pathogens that appear to rely on diffusible low-MW toxins to defeat plant defenses (the fungus Cochliobolus victoriae is a good example). There are also some P. syringae strains that are able to inject 'virulence' proteins into plant cells, but they do not cause disease on any plants tested. To further confuse things, the protein injection system used by gram-negative bacterial pathogens (the type III secretion system) shows up in some plant-associated bacteria that are mutualistic symbionts or commensals. Also, the 'disease triangle' is a very real factor in many plant diseases, such that environmental conditions can determine whether the interaction results in a symptomless latent infection or active pathogenesis leading to symptoms. To summarize, even a bacterium that is specialized to be able to inject virulence factors into plants does not always do that - sometimes it just sits on the surface of leaves without becoming a pathogen. As we learn more about plant pathogens, it is likely that the truth will be very much as expressed by Alex re: mammalian pathogens."

Action 11. PAMGO would feel comfortable defining pathogenesis in line with the mammal model as explained by Alex and wish this to be considered in the continuing discussion of this topic.

A proposal was made that in the term 'defense response to pathogenic bacteria', and related terms, we should remove the word 'pathogenic', since 'defense response' by itself implies that the thing is pathogenic so the two words are redundant. A further proposal was made to replace the existing terms 'pathogenesis' and 'host-pathogen interaction': Candace Collmer's suggestion is to create a tree where we don't specify whether an interaction between two organisms is pathogenic or not, with top term 'interaction with other organism', to be a replacement for the existing terms pathogenesis and host-pathogen interaction. (This term, 'interaction with other organism' has been modified since the content meeting to be "interaction between organisms" in the PAMGO revised)

Action 12. Consider removing 'pathogenic' from defense terms as proposed and clarifying definitions. This would also mean include 'response to pathogen' as synonym and still keeping defense response of bacteria, fungi, etc. Terms would be normalized to 'defense response to x' rather than 'pathogenic response to x'. There was a general majority agreement that this should be implemented.

Action 13. The new term "interaction with other organism" should be a child of the parent term "physiological process" and the definition of this new term ("interaction with other organism") should be "the physiological process by which different organisms act on, affect, or influence each other." [Michelle Gwinn and Candace have agreed, since the content meeting, that they will propose, in the modified PAMGO proposal, to alter this term to "interaction between organisms", so that it will be ready to later include terms related to the host side of the interaction (as was discussed at the content meeting)].

Alex proposed replacing 'defense to pathogenic bacteria' with 'response to foreign biotic stimulus' i.e., foreign detected things.

Action 14. Update definitions to include a definition of 'biotic' i.e. includes parts derived from living organisms if not living organism itself.

The use of the word 'response' was discussed. We had difficulty defining the borderline between the defense response and the immune response. For example, is the skin a defense response? It is certainly a defense. Likewise is the presence of antibodies a 'defense response' acted out over the evolutionary timescale? The example was given of the 'castle wall vs. the archers on castle wall'. The existence of the castle wall is not a spur-of-the-moment response in the same way that sending archers on to the castle wall is, but rather a pre-existing defense. However, you wouldn't build a wall in the first place if you had not already perceived the need for defense. Do we annotate castle wall situations as 'defense response'? Putting 'archers on the castle wall' is certainly a defense response.

Action 15. Clarify use of 'Response to' (define carefully)

e.g. Can a response be pre-emptive or does it happen after the event?
Are antibodies part of the response evolutionarily?

Evasion

With reference to 'defense response' we also discussed evasion. A nematode living in the lymph node to avoid the immune response could be considered to be using evasion as a tactic. Do we need separate evasion and suppression terms, and a parent to use for annotation if neither child is obviously appropriate?

Action 16.

original PAMGO proposal suggests:

```
        [i] interaction with host organism
        ---[i] evasion or suppression of host defenses
        ------[i] evasion of host defense response GO:0030682
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changed to:

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          [i] interaction between host and other organism
        ---[i] avoidance of host defenses
          ---------[i]evasion of host defenses
          -----------------[i] evasion of host defense response GO:0030682
          ---------[i]suppression of host defenses
          -----------------[i] suppression of host defense response GO:new
```

[N.B. It was also agreed in the meeting that 'evasion of host defenses' and 'suppression of host defenses' should be exact synonyms of 'avoidance of host defenses' but Midori pointed out after the meeting that this would be redundant with the child terms. Michelle, Candace and Alan have agreed to implement only the child terms and not the synonyms.]

Action 17. Alex was to provide a new proposal based on discussion of 'defense' response and see what PAMGO think. Since the meeting this has become a further discussion item rather than an action item. He closed SF 1013068 on 9/20/2004 and submitted a new proposal, Response and Detection Terms (http://sourceforge.net/tracker/?func=detail&aid=1031159&group_id=36855&atid=440764). To see the post-meeting developments please read this item.

General concern was expressed that synonyms cannot be accessed with many tools.

Action 18. Check for all tools that synonyms can be queried and displayed easily.

Summary

The general consensus for the pathogenesis and symbiosis section was that the PAMGO proposal was very good, and would be implemented pending some modifications (as outlined above). Candace to submit an ammended version of the proposal to SF for further comment.

The cell killing proposal

See also the appendices:
Background Reading From Jane On All Three Topics
Alex Diehl's Pre-Meeting Proposal On Cell Killing Terms
Alex's Cell Killing Proposal And Terms
Cell Killing Terms Incorporating The Discussion At The Go Content Meeting

This was a general discussion of cell killing, following on from Alex's proposal.

Michelle Gwinn asked where bacterial autolysis would fit in with the proposed cytolysis terms, as the definition of 'cell killing, self' excludes this process. Autolysis is a normal process for bacteria under conditions of environmental stress, and may serve to e.g. disseminate its DNA so it gets taken up by other cells.

Action 19. It was decided to add a new term (possibly microbial autolysis) directly under cell death.

There is a difficulty in distinguishing between necrosis and apoptosis. David pointed out that apoptosis involves destruction of plasma membrane earlier by the cell itself, and Michelle confirmed this saying that necrosis was from outside while apoptosis was internally controlled. Alex pointed out that a virus may cause apoptosis and that a host may kill itself. He said he felt we needed to do more reading of reviews to see how people are using the terms. Plant folks stated that the distinctions in plant biology were quite murky but that it would be useful to have general term of 'cell killing' at the moment. David mentioned that some biologists use the term 'apoptosis' it to talk about the death of tissues but other groups use it as self-cell death. If necrosis is looked at it from a tissue level, necrotic cell death is looking at it from a self-referential level. David further elaborated, explaining that necrosis was originally defined pathologically, by watching the cell break up. Late stage apoptosis = necrosis.

Further points made by Alex:

- Cytolysis can mean self-killing or non-self-killing.
- Cytotoxicity is not the same as cytolysis.
- We could have a 'cell-mediated cell death during development' term.

Action 20. Autolysis should be an is-a child of cytolysis. Cytolysis remains a child of cell death rather than becoming a child of cell killing, although some of its child terms will have multiple parentage.

cell death
[i]programmed cell death

[i]cytolysis
---[i]autolysis
[i]cell killing

Action 21. Change definition of cell killing to explicitly state the induction of cell death in another cell. It was decided that the definition of 'cell killing' should include some of the information currently assigned to the comment.

Action 22. Remove 'cell killing, self', move up 'immune cell mediated cytotoxicity', make consistency changes.

There was some discussion as to whether 'cell killing, self' and 'cell killing, non-self' were split too low (see tree in handout).

Action 23. It was decided that many of the processes involved were common to both self and non-self, so the level of the split suggested by Alex was okay.

Action 24. 'cell invasion' is to be moved. We did not decide where to.

Finally: To incorporate all of these changes into a single plan and to prepare them for consideration at the consortium meeting:

Action 25. Alex will update the existing 'cell killing' SF entry (https://sourceforge.net/tracker/?func=detail&aid=1012931&group_id=36855&atid=440764) (Done on 17/9/2004.)

To reiterate, following on from the three discussions above there are three SourceForge Proposals: the PAMGO proposal (965023), "Response and Detection Terms" (1031159), and "Cell Killing Proposal" (1012931). The further conclusions in these items will be considered at the Consortium Meeting at Chicago in October.

Metabolism:

See also the appendices:
Background Reading From Jane On All Three Topics
Metabolism Explanation Power-point Presentation.
Metabolism Proposal Power-point Presentation.

Current Structure - Midori

[i]physiological process
---[i]metabolism
[i]behavior
[i]cellular process
[i]development
[i]regulation of biological process
[i]viral life cycle

The big question is: What is the scope of the 'metabolism' concept? Metabolism can be thought of as physiology at the biochemical level (or indeed the physiology of biochemicals), so does fit under 'physiological process'.

At present, many children of 'metabolism' do not have 'cellular process' parentage but biologists would expect to find them under cellular process.

Problems:
- We need to define where metabolism (of a particular substance, or generally) begins and ends.
- For unicellular organisms there is essentially a complete overlap between cellular and physiological processes.
- Is 'cellular physiological processes' the same as 'cell growth and maintenance'?
- Right now, metabolism includes a subset of physical changes but not transport activity and it should include anabolic and catabolic process.

David gave a presentation using glucose metabolism as an example. Much of glucose metabolism, such as glycolysis and gluconeogenesis, occurs within the cell, but in multicellular organisms, glucose homeostasis is systemic. We need to decide if the regulation of blood glucose levels by insulin and glucagon count as components of glucose metabolism, and what is the relationship between glucose homeostasis and glucose metabolism?

(More details in appendix: Metabolism explanation power-point presentation. ftp://ftp.geneontology.org/pub/go/meeting/minutes/20040822_Stanford_Content/metabolism_explanation.pdf and ftp://ftp.geneontology.org/pub/go/meeting/minutes/20040822_Stanford_Content/metabolism_explanation.ppt)

We considered some of the defining features of metabolism concepts. Most, but not

all, metabolism involves production or consumption of energy. Metabolic processes are not necessarily essential for cell growth or maintenance (consider secondary metabolism). The current MetaCyc definition has 'all chemical reactions and interactions in a biological system', but even Peter Karp thinks it's not wholly satisfactory. Should we include or exclude things like protein phosphorylation, and is post-translational modification a kind of protein metabolism? What about metabolic pathways that require transport?

Action 26. We agreed to include such instances of transport, but not transport generally, under metabolism. Reactome considers where a process can be localized (including whether it's within a single cell or not).

We considered the relationship between metabolism and physiology. Some examples of non-metabolic physiological processes include neurophysiology and transport.

However, transport has same issue as metabolism, e.g. transport within vs. between cells, also long-range intracellular transport in multicellular organisms.

The same question extends to other physical changes. At present the definition of 'metabolism' in GO (which came from the Oxford Dictionary of Biochemistry and Molecular Biology) includes physical changes, but Michael recommended, and the group agreed, to restrict metabolism to chemical changes. (Michael spoke of 'transformation of substances', but we will use the wording 'chemical changes' to avoid ambiguity -- e.g. a substance moving from outside the cell to inside could be said to be 'transformed'.)

This change will mean that fewer supracellular processes will count as metabolism, but will not remove all of them from consideration.

Sue proposed that the criterion for 'organismal' process should be that they require more than one cell type.

We discussed these things and agreed on some new definitions and a new structure.

Action 27. This is the agreed structure:

physiological process
[i]metabolism (GO:0008152)
---[i]organismal metabolism (new)
---[i]cellular metabolism (new)
---[i]primary metabolism (new)
---[i]secondary metabolism (GO:0019748)

---[i]anabolism (GO:0009058)
---[i]catabolism (GO:0009056)
---[i]regulation of metabolism
---[i]generation of precursor metabolites and energy (rename energy pathways, needs definition, consult MetaCyc def)

This is the agreed cellular metabolism parentage:

[i]Physiological process
---[i]Cellular physiological process
------[i]Cellular metabolism
---[i]Metabolism (GO:0008152)
------[i]Cellular metabolism
[i]Cellular process
---[i]Cellular physiological process
------[i]Cellular metabolism

Action 28. 'cellular physiological process' is to merge with 'cell growth and maintenance'

Action 29. This is the agreed 'organismal metabolism' parentage:

[i]Physiological process
---[i]organismal physiological process
------[i]organismal metabolism
---[i]Metabolism (GO:0008152)
------[i]organismal metabolism

The new definitions proposed are detailed below:

Action 30. The definition of 'metabolism' was discussed, and will be altered. At a minimum, references to physical changes will be deleted. If no further changes are made, the definition would be:

'The chemical reactions that occur in living organisms, comprising anabolism and catabolism; may be qualified to mean the chemical reactions undergone by a particular substance, or class of substances, in a living organism.' [ISBN:0198547684]

A more extensive rewording also came about, and generally found favor:

Processes that cause many of the chemical changes in living organisms, including anabolism and catabolism. Metabolic processes typically transform small molecules, but also include macromolecular processes such as DNA repair and replication, and

protein synthesis and degradation. [comment or to be revisited: Metabolic processes do not include single functions (or processes?) such as protein-protein interactions, protein-nucleic acids, nor recepter-ligand interactions.]

Action item 31: Change the definition of 'metabolism'. The group prefers the second option; if it is used, we must discuss whether to include a statement (as a comment) about what processes are NOT considered metabolism, and, if so, how it should be worded.

Action 32. Secondary metabolism:

The current definition is:

Chemical reactions and physical changes that generate diverse byproducts that are often unique to a taxon, are generally not essential for survival, and have no known metabolic role. In multicellular organisms secondary metabolism is generally carried out in specific cell types, and may be useful for the organism as a whole. In unicellular organisms, secondary metabolism is often used for the production of antibiotics or for the utilization and acquisition of unusual nutrients.' [GO:curators]

Action 33: Consider changing the definition; make sure everyone involved in the discussion on the existing definition sees the proposal and approves. Also check the old SF item (https://sourceforge.net/tracker/?func=detail&atid=440764&aid=896576&group_id=36855).

There are two proposals for the new def. The first is a slight rewording of the current one:

def 1: Processes that result in many of the chemical changes of compounds that are not required for growth and maintenance of cells, and are often unique to a taxon. In multicellular organisms secondary metabolism is generally carried out in specific cell types, and may be useful for the organism as a whole. In unicellular organisms, secondary metabolism is often used for the production of antibiotics or for the utilization and acquisition of unusual nutrients.

The second is the MetaCyc definition:

def 2: Metabolism of secondary compounds, defined simply as compounds other than primary compounds. A compound is classified as a secondary metabolite if it does not seem to directly function in the processes of growth and development. Even though secondary compounds are a normal part of the metabolism of an organism, they are often produced in specialized cells, and tend to be more complex than primary compounds. Examples of secondary compounds include antibiotics and plant chemical defenses such as alkaloids and steroids.

Also in this def: change 'byproducts' to 'products'

Action 34. These further definitions were agreed:

Organismal metabolism: Metabolic processes in multicellular organisms that occur at the tissue, organ, or organismal level. These processes, unlike cellular metabolism, can include transport of substances between cells when that transport is required.

Cellular metabolism: Metabolic processes by which individual cells transform chemical substances.

Primary metabolism: Primary metabolism encompasses reactions involving those compounds which are formed as a part of the normal anabolic and catabolic processes. These processes take place in most, if not all, cells of the organism.
MetaCyc (www.metacyc.org): Taiz, Lincoln, and Eduardo Zeiger. 'Surface Protection and Secondary Defense Compounds.' Plant Physiology. New York: Benjamin/Cummings Publishing Company, Inc., 1991: 320-345.

The question was asked: 'Where should the following terms go?'

- Energy pathways: Not defined.

Action 35. Reword to 'generation of precursor metabolites and energy'; add def based on MetaCyc; put directly under metabolism.

- Electron transport: The transport of electrons from an electron donor to an electron acceptor.
- Oxidative phosphorylation: The phosphorylation of ADP to ATP that accompanies the oxidation of a metabolite through the operation of the respiratory chain. Oxidation of compounds establishes a proton gradient across the membrane, providing the energy for ATP synthesis.

Action 36: Put these two under the reworded energy pathways term.

- Metabolism resulting in cell growth: The chemical reactions and physical changes that occur in living organisms that result in an increase in the mass (size) of a cell.

Action 37: Delete this term.

- long-term maintenance of gene activation: Any mechanism, at the level of transcription or post-transcription, maintaining gene activation in the long-term.

Action 38: move this term to correct parent(s).

Action 39. Check through the metabolism terms and decide which are organismal and which are cellular.

Examples of organismal metabolism:
- C4 photosynthesis
- Salivary polysaccharide metabolism
- Lignification
- Starch metabolism
- organismal lipid metabolism
- Hibernation

We discussed the possibility of continuing to improve this node and to arrange all the terms in their correct places in the new structure.

Action 40. Expand Metabolism Interest Group to include MetaCyc and Reactome folks.

Action 41. General Action Item: Work on new approaches to supporting Interest Groups.

(Current support for interest groups: Current support is restricted to listing the members and their contact details on the GO website. A plan was formed that the groups should communicate via the GO mailing list with the subject lines beginning with the name of their interest group and a hyphen e.g. subject: 'development - gametophyte development'. However, this generated a great deal of traffic on the list an caused frustration for the many peripheral GO users who are subscribed. Consequently this plan was abandoned and so the discussions of interest groups are currently either on sourceforge or off-list. Off-list discussion are not archived and so it is hoped that the conclusions of these discussions should be sent to the list or added to sourceforge items. However, it is not clear that this occurs, or that it would be sufficient even if it did.)

Action 42. Archived mailing lists will be created for the the interest groups:
1. cell cycle,
2. metabolism,
3. pathogenesis/cell killing/immunology
4. development

We discussed the regulation terms and the possible implementation of the 'regulates' relationship.

Action 43. Suzi to talk to Chris about a presentation on this (again). Presentation is to make a specific proposal and outline methods/processes for implementation. Also to present what the current problems are.

Action 44. We'd like to implement the new relationship type 'regulates' if this is agreed to at the October meeting.

e.g. 'regulation of metabolism' regulates 'metabolism'.

If 'regulates' was represented by '*' then this DAG would look like this:

```
-%metabolism
--*regulation of metabolism.
```

(the star wasn't agreed in the meeting, I just did that in my notes. Ed.)

Cell cycle

See also the appendices:
Background Reading From Jane On All Three Topics
Cell Cycle Power-point Presentation.

Amelia: presentation on Cell Cycle

Summary of the current situation from Amelia's power-point presentation:

```
[p]cytokinesis
[p]cell cycle (under cell proliferation)
---[p]M phase
------[p]nuclear division
---------[i]meiosis
---------[i]mitosis
---[i]mitotic cell cycle
------[p]phases of the mitotic cell cycle - G1, G2, S
------[p]M phase of mitotic cell cycle
---------[p]cytokinesis after mitosis
---------[p]mitosis
------------[p]phases of mitosis: anaphase, metaphase, etc.
---------------[p]events occurring during each phase
```

Problems:
1) Current structure is based on yeast paradigm, which results in true path problems

for any species without paradigmatic mitosis and meiosis cycles.
2) Anything in 'resting' phase occurs under cell proliferation. Solution: split out new high-level term of 'cell cycle phase'.
3) Timed events were under phases but this didn't work. solution: add terms such as meiotic cell cycle phase progression.

Action 45. Split out the temporal elements of the cell cycle and have them stand alone

Action 46. Create the physical processes related to the cell cycle but do not relate them to temporal components.

Action 47. Do not obsolete 'cytokinesis'

Action 48. Add the words 'phase progression' to the end of the 'high level' phase terms.

Action 49. 'x during cell cycle' terms are to be added.

Action 50. Look out for GO generic slim terms when making adjustments.

Action 51. Finish redefinition of 'cell cycle' in SourceForge.

Action 52. Find a good location for 'nuclear division'.

Action 53. The final proposal:

The proposal that came from the meeting can be downloaded at the sourceforge item page: http://sourceforge.net/tracker/index.php?func=detail&aid=1025157&group_id=36855&atid=440764. A few further improvements have been made since the meeting. Details are provided on that page.

Component ontology:

There was a bit of spare time in the meeting during which a short presentation was made by Peifen Zhang about work she has done on considering potential improvements to the component ontology.

Action 54.

1) MetaCyc will make sourceforge requests for CC terms.
2) Will form Interest Group on revision of cellular component.
3) Will plan to have Content Meeting on CC to include MetaCyc and Reactome groups and Chris Mungall at least.

APPENDICES

The remainder of this document contains the appendices. These are are the list of action items, and the text files that were given as handouts at the meeting.

List of appendices:

1. Action items
2. Agenda.
3. Background reading from Jane on all three topics.
4. The pre-meeting PAMGO obo file.
5. Alex Diehl's pre-meeting proposal on pathogenic terms (sourceforge url).
6. Alex Diehl's pre-meeting proposal on Cell Killing terms (sourceforge url).
7. Comments from Matt Berriman on the pathogenesis proposals.
8. Pathogenesis powerpoint presentation.
9. PAMGO powerpoint presentation.
10. Metabolism explanation powerpoint presentation.
11. Metabolism proposal powerpoint presentation.
12. Cell Cycle powerpoint presentation.
13. Alex's proposal: Pathogenic Terms I want to change or eliminate from the GO.
14. Alex's Cell Killing Proposal and Terms
15. Alex's Cell Killing Terms incorporating the discussion at the GO Content meeting
16. Suparna's proposal on host-pathogen interactions. (url)

Action items.

Action 1. Establish common parents and replicate subtrees for symbionts and pathogens as appropriate, e.g.

```
[i]acquisition of nutrients from host
---[i]acquisition of nutrients from host during symbiosis
---[i]acquisition of  nutrients from host during pathogenesis
```

Action 2. Should PAMGO define symbiosis to exclude parasitism or pathogenesis in their modified proposal? This remains a point for further discussion.

Action 3. Define host based on PAMGO definition (To be taken from:

% interaction with host organism
Def: any interaction between an organism, usually a parasite or symbiont, and another organism from which it may obtain nourishment, protection, and/or a means of dispersal.

Action 4. We need a name and a definition for the 'hostee'; the dependent organism in a relationship, e.g. a parasite.

Action 5. Remove 'interaction with non-host organism' and move sub-terms up one level.

i.e. get rid of the non-host terms so the proposed tree goes from this:

[i]interaction with other organism
---[i]interaction with non-host organism
---[i]interaction with host organism

to this:

[i]physiological interaction with other organism
---[i]interaction between host and other organism

Action 6. Change 'competition with non-host' to 'competition with other'. N.B Michelle and Alex exchanged email after the meeting and settled on the phrase "another, non-host, organism" to describe better what "non-host" means. PAMGO agree with this. See https://sourceforge.net/tracker/?func=detail&aid=1012931&group_id=36855&atid=440764

Action 7. Suparna will look into adding 'host-side' processes or using taxonID to clarify reciprocal terms as needed.

Action 8. Change definition of 'cell-cell signaling' to mean between cells in the same species.

Action 9. Add 'within the same species' qualifier to the definition of 'pollen-pistil interaction'

Action 10. Consider adding 'within the same species' to the definition of terms for all children of 'cell communication'.

Action 11. PAMGO would feel comfortable defining pathogenesis in line with the mammal model as explained by Alex and wish this to be considered in the continuing discussion of this topic.

Action 12. Consider removing 'pathogenic' from defense terms as proposed and clarifying definitions. This would also mean include 'response to pathogen' as synonym and still

keeping defense response of bacteria, fungi, etc. Terms would be normalized to 'defense response to x' rather than 'pathogenic response to x'. There was a general majority agreement that this should be implemented.

Action 13. The new term "interaction with other organism" should be a child of the parent term "physiological process" and the definition of this new term ("interaction with other organism") should be "the physiological process by which different organisms act on, affect, or influence each other." [Michelle Gwinn and Candace have agreed, since the content meeting, that they will propose, in the modified PAMGO proposal, to alter this term to "interaction between organisms", so that it will be ready to later include terms related to the host side of the interaction (as was discussed at the content meeting)].

Action 14. Update definitions to include a definition of 'biotic' i.e. includes parts derived from living organisms if not living organism itself.

Action 15. Clarify use of 'Response to' (define carefully)

e.g. Can a response be pre-emptive or does it happen after the event?
Are antibodies part of the response evolutionarily?

Action 16.

original PAMGO proposal suggests:

```
[i] interaction with host organism
---[i] evasion or suppression of host defenses
------[i] evasion of host defense response GO:0030682
```

changed to:

```
  [i] interaction between host and other organism
---[i] avoidance of host defenses
  ---------[i]evasion of host defenses
  -----------------[i] evasion of host defense response GO:0030682
  ---------[i]suppression of host defenses
  -----------------[i] suppression of host defense response GO:new
```

Action 17. Alex was to provide a new proposal based on discussion of 'defense' response and see what PAMGO think. Since the meeting this has become a further discussion item rather than an action item. He closed SF 1013068 on 9/20/2004 and submitted a new proposal, Response and Detection Terms (http://sourceforge.net/tracker/?func=detail&aid=1031159&group_id=36855&atid=440764). To see the post-meeting developments please read this item.

Action 18. Check for all tools that synonyms can be queried and displayed easily.

Action 19. It was decided to add a new term (possibly microbial autolysis) directly under cell death.

Action 20. Autolysis should be an is-a child of cytolysis. Cytolysis remains a child of cell death rather than becoming a child of cell killing, although some of its child terms will have multiple parentage.

```
cell death
   [i]programmed cell death
   [i]cytolysis
   ---[i]autolysis
   [i]cell killing
```

Action 21. Change definition of cell killing to explicitly state the induction of cell death in another cell. It was decided that the definition of 'cell killing' should include some of the information currently assigned to the comment.

Action 22. Remove 'cell killing, self', move up 'immune cell mediated cytotoxicity', make consistency changes.

Action 23. It was decided that many of the processes involved were common to both self and non-self, so the level of the split suggested by Alex was okay.

Action 24. 'cell invasion' is to be moved. We did not decide where to.

Action 25. Alex will update the existing 'cell killing' SF entry (https://sourceforge.net/tracker/?func=detail&aid=1012931&group_id=36855&atid=440764) (Done on 17/9/2004.)

To reiterate, following on from the three discussions above there are three SourceForge Proposals: the PAMGO proposal (965023), "Response and Detection Terms" (1031159), and "Cell Killing Proposal" (1012931). The further conclusions in these items will be considered at the Consortium Meeting at Chicago in October.

Action 26. Metabolic pathways that require transport:
We agreed to include such instances of transport, but not transport generally, under metabolism. Reactome considers where a process can be localized (including whether it's within a single cell or not).

Action 35. Reword to 'generation of precursor metabolites and energy'; add def based on MetaCyc; put directly under metabolism.

- Electron transport: The transport of electrons from an electron donor to an electron acceptor.
- Oxidative phosphorylation: The phosphorylation of ADP to ATP that accompanies the oxidation of a metabolite through the operation of the respiratory chain. Oxidation of compounds establishes a proton gradient across the membrane, providing the energy for ATP synthesis.

Action 36: Put these two under the reworded energy pathways term.

- Metabolism resulting in cell growth: The chemical reactions and physical changes that occur in living organisms that result in an increase in the mass (size) of a cell.

Action 37: Delete this term.

- long-term maintenance of gene activation: Any mechanism, at the level of transcription or post-transcription, maintaining gene activation in the long-term.

Action 38: move this term to correct parent(s).

Action 39. Check through the metabolism terms and decide which are organismal and which are cellular.

Action 40. Expand Metabolism Interest Group to include MetaCyc and Reactome folks.

Action 41. General Action Item: Work on new approaches to supporting Interest Groups.

Action 42. Archived mailing lists will be created for the the interest groups:

1. cell cycle,
2. metabolism,
3. pathogenesis/cell killing/immunology
4. development

Action 43. Suzi to talk to Chris about a presentation on this (again). Presentation is to make a specific proposal and outline methods/processes for implementation. Also to present what the current problems are.

Action 44. We'd like to implement the new relationship type 'regulates' if this is agreed to at the October meeting.

Action 45. Split out the temporal elements of the cell cycle and have them stand alone

Action 46. Create the physical processes related to the cell cycle but do not relate them to temporal components.

Action 47. Do not obsolete 'cytokinesis'

Action 48. Add the words 'phase progression' to the end of the 'high level' phase terms.

Action 49. 'x during cell cycle' terms are to be added.

Action 50. Look out for GO generic slim terms when making adjustments.

Action 51. Finish redefinition of 'cell cycle' in SourceForge.

Action 52. Find a good location for 'nuclear division'.

Action 53. The final proposal:

The proposal that came from the meeting can be downloaded at the sourceforge item page: http://sourceforge.net/tracker/index.php?func=detail&aid=1025157&group_id=36855&atid=440764. A few further improvements have been made since the meeting. Details are provided on that page.

Action 54.

1) MetaCyc will make sourceforge requests for CC terms.
2) Will form Interest Group on revision of cellular component.
3) Will plan to have Content Meeting on CC to include MetaCyc and Reactome groups and Chris Mungall at least.

End of action item list.

---

2. Agenda for content meeting
Seminar room, Carnegie Institution, Stanford, CA.

Sunday 22nd August

(Those staying at SLAC meet at 8.15am in the lobby to organise cars to Carnegie Institution).

8.30 - 9.00am continental breakfast
9.00 - 9.30am introductions/logistics
9.30am pathogenesis/cell killing

1. Current structure - Michelle
2. Outline of problem - Jane

10.30 - 11am tea and coffee break

11am pathogenesis/cell killing cont.

3. Proposals - Candace (PAMGO) - see proposal in SF.
- Suprana
4. Discussion

1pm - 2pm lunch

2pm pathogenesis/cell killing cont.

4. Discussion cont.
5. Action items

3.30pm - 4pm tea and coffee break

4pm metabolism

1. Current structure - Midori
2. Outline of problem - David

5.30pm end

7pm - dinner at local Gordon Biersch microbrew pub, where there will be 2 hrs of all you can drink beer with a set menu (salad choices, main choices, dessert choices).

Monday 23rd August

8.30 - 9.00am continental breakfast

9.00 - 9.30am logistics/introductions

9.30am metabolism cont.

3. Proposals:
Jane
Sue
4. Discussion

10.30 - 11am tea and coffee break

11am metabolism cont.

4. Discussion cont.
5. Action itmes

1pm - 2pm lunch

2pm cell cycle

1. Current structure - Amelia
2. Outline of problem - Amelia
3. Proposals - Amelia
4. Discussion

3.30pm - 4pm tea/coffee break

4pm cell cycle cont.

5. Action items

4.30pm summary/future directions

5.30pm end

Dinner in San Fransisco if enough interest.

---

3. Background reading from Jane on all three topics:

First GO Content Meeting
August 22-23, 2004
Carnegie Institution, Department of Plant Biology, Stanford, CA 94305
Organizers: Jane Lomax (jane@ebi.ac.uk), Sue Rhee (rhee@acoma.stanford.edu)

Purpose: To bring together GO group members and a few domain experts in person to review and discuss three problematic areas in the GO process ontology, metabolism, pathogenesis, and cell cycle, in order to come up with acceptable solutions and specific action items to resolve the problems.

Agenda:

I. Pathogenesis summary

A. Current structure (Michelle Gwinn): pathogenesis is currently under 'physiological process', and 'host-parasite interaction' is in a different node, under 'cell process'. The virus terms are throughout both ontologies, again in their own nodes.

B. Outline of problem (Jane Lomax): Lots of potential true path violations e.g. viruses are not cells, but virus-specific terms are ancestors of cellular processes. Will become more of a problem as more pathogen groups join and want terms e.g. the plant microbe group. It also means these groups will have some strange GO slims. We need a systematic way of adding new terms that are specific to pathogens in a similar way to the term 'host'. See the email thread:

http://www.geneontology.org/email-go/go-arc/go-2004/0560.html

and the SF items:

cell killing:
https://sourceforge.net/tracker/index.php?func=detail&aid=900600&group_id=36855&atid=440764

viral parasite terms relationship to host:
https://sourceforge.net/tracker/index.php?func=detail&aid=895787&group_id=36855&atid=440764

The distinction of 'pathogenic' processes is quite artificial; from the point of view of the infecting organism, all processes are quite normal and yet we designate them pathogenic. In addition, many of the processes involved in establishing a symbiotic interaction and establishing a pathogenic interaction are very identical, so we need to create common terms (see PAMGO proposal attached).

C. Proposals:
1. Candace Collmer (PAMGO) - create a tree where we don't specify whether an interaction between two organisms is pathogenic or not, with top term 'interaction with other organism', to replace existing terms pathogenesis and host-pathogen interaction. See SF item:

https://sourceforge.net/tracker/?group_id=36855&atid=440764&func=detail&aid=965023

and Appendix I.

2. Suparna Mundodi (TAIR) - integrating 'response to' terms into the proposed PAMGO tree.

3. Alex Diehl (MGI) - cell killing hierarchy proposal. See SF item:

http://sourceforge.net/tracker/?func=detail&aid=960898&group_id=36855&atid=440764

D. Additional questions:

- Can the 'response to parasite' etc terms be incorporated into this new structure?
- Pathogenic v/s non-pathogenic xxx responses. Are these still useful classifications?
- Are the proposed terms intuitive - will annotators understand them?
- What about component terms? We currently use 'host'.

II. Metabolism summary

A. Current Structure (Midori Harris): Metabolism is a child of 'physiological process' only. Children of metabolism are grouped by type of metabolism (catabolism or anabolism) and by substrate (e.g. lipid metabolism). Although there is 'secondary metabolism' term, there is not 'primary metabolism' term.

The metabolism branch can be found at:
http://www.godatabase.org/cgi-bin/amigo/go.cgi?open_1=GO:0003673&open_1=GO:0008150&open_1=GO:0007582

B. Original Problem (David Hill): Metabolism is a child of physiological processes, but not cellular process.

SourceForge thread illustrating the initial communications about this issue:
https://sourceforge.net/tracker/index.php?func=detail&aid=814460&group_id=36855&atid=440764

Subsequent GO email communication about this issue:
http://www.geneontology.org/email-go/go-arc/go-2004/subject.html
(Go to 'metabolism split' section)

C. Proposals (not necessarily mutually exclusive)
1. Jane: split into cellular and organismal metabolism and put cellular metabolism under cellular process.
2. Sue: put metabolism at a higher node at the same level as physiological processes and put a bit more structure under it.

D. Additional Questions:
- Is metabolism really a child of physiological processes? What is the rationale for either view?
- Does metabolism occur only at the cellular level? Are there any examples of metabolism that occur at the supracellular (organismal/tissue) level? Are there any examples of metabolism that occurs ONLY at the cellular level?
- Do these questions also apply to transport processes?

III. Cell cycle summary

A. Original problem: cytokinesis is not part of the cell cycle but it seems as if it should be. This then brought up other issues involving cell division / replication events that occur in organisms which do not have a canonical cell cycle.

Sourceforge thread illustrating the initial communications about this issue:

cytokinesis (0000910)/cell cycle relationship
https://sourceforge.net/tracker/index.php?func=detail&aid=815892&group_id=36855&atid=440764

A couple of other related SourceForge items on the cell cycle:

[931134] meiosis, mitosis and the cell cycle
http://sourceforge.net/tracker/?group_id=36855&atid=440764&func=detail&aid=931134

[822657] M phase of meiotic cell cycle
http://sourceforge.net/tracker/?group_id=36855&atid=440764&func=detail&aid=822657

GO email communication about this issue:
http://www.geneontology.org/email-go/go-arc/go-2004/1029.html and subsequent thread.

B. Current structure:
cell cycle and cytokinesis are siblings; all the events in the cell cycle are
underneath the cell cycle stages.

cell proliferation
[p]cytokinesis
[p]cell cycle
---[p]M phase
------[i]M phease of mitotic cell cycle
---------[p]mitosis
------[p]nuclear division
---------[i]meiosis
---------[i]mitosis
---[p]mitotic cell cycle
------[p]phases of the mitotic cell cycle - G1, G2, S
------[p]M phase of mitotic cell cycle
------[p]mitosis
---------[p]cytokinesis after mitosis
---------[p]phases of mitosis: anaphase, metaphase, etc.
------------[p]events occurring during each phase

C. Proposal:
1. Split cell cycle into cell cycles stages - eg. M phase, prophase, leptotene -
and cell cycle events - eg. meiosis, chromosome segregation, cytokinesis.

D. (Additional) Questions/Issues:
-Cell cycle events are currently all children of cell proliferation, the rapid
division and multiplication of cells. Do we need a term to encompass non-rapid
cell replication? I would suggest a generic parent of 'cell division' for cell
cycle and cell proliferation.

Appendix I - PAMGO suggested changes.

The bare tree of the proposed PAMGO terms (with some existing GO terms integrated):

biological process - physiological process (GO:0007582)
-%interaction with other organism

--%interaction with non-host organism
---%Competition with non-host organism
----%killing of non-host cells
---%biofilm formation (GO:0042710)
--%interaction with host organism
---%virus-host interaction (GO:0019048)
----%viral host cell process manipulation (GO:0019054)
----%viral host defense evasion (GO:0019049)
----%viral induction of host immune response (GO:0046730)
---%recognition of host
---%adhesion to host
----%cytoadherence to microvasculature (GO:0020035)
---%growth on or near host surface
---%entry into host
----%entry into host through natural portals
----%entry into host through host barriers
----%cell invasion (GO:0030260)
-----%viral entry (GO:0046718)
---%evasion or suppression of host defenses
----%evasion of host defense response (GO:0030682)
-----%evasion of host immune response (GO:0020012)
-----%viral host defense evasion (GO:0019049)
---%induction of host defense response
----%viral induction of host immune response (GO:0046730)
---%translocation of molecules into host
----%translocation of DNA into host
----%translocation of protein into host
-----%type III protein secretion system (GO:0030254)
---%movement within host
----%migration within host
----%viral spread within host (GO:0046739)
---%acquisition of nutrients from host
---%modification of host morphology or physiology
----%viral host cell process manipulation (GO:0019054)
----%viral transformation (GO:0019087)
-----%viral immortalization (GO:0019088)
----%disruption of host cells
-----%killing of host cells
------%hemolysis (GO:0019836)
------%necrosis (GO:0008220)
----%induction in host of a tumor, nodule, or growth
-----%induction in host of a tumor, nodule, or growth containing transformed cells
-----%induction in host of a tumor, nodule, or growth not containing transformed cells

---%dissemination or transmission of an organism from a host
----%dissemination or transmission of an organism from a host by a vector
----%viral transmission (GO:0019089)
-%cell killing
--%killing of non-host cells
--%killing of host cells

DRAFT -- New GO terms from PAMGO - from 4/23/04 PAMGO meeting, plus all changes via email discussion among PAMGO members since then, plus some integrations of existing GO terms - as of end of day, 6/01/04

biological process - physiological process (GO:0007582)

---% interaction with other organism
------% interaction with non-host organism
---------% competition with non-host organism
----------% killing of non-host cells
---------% biofilm formation (GO:0042710
------% interaction with host organism -
---

interaction with other organism
def: the processes by which organisms act on, affect, or influence each other
interaction with non-host organism
def: any process in which an organism interacts with another organism that does not act as its host
competition with non-host organism
def: any process by which one community member gains an advantage in growth or survival over another community member
killing of non-host cells
def: any process in an organism that results in the death of another, non-host organism or its cells
biofilm formation (GO:0042710
def: A process whereby microorganisms irreversibly attach to and grow on a surface and produce extracellular polymers that facilitate attachment and matrix formation, resulting in an alteration in the phenotype of the organisms with respect to growth rate and gene transcription)
interaction with host organism
def: any interaction between an organism, usually a parasite or symbiont, and another organism from which it may obtain nourishment, protection, and/or a means of dispersal

[NOTE: we suggest that this Physiological Process term replace both the Cellular Process term "GO:0030383 = host-pathogen interaction", and the Physiological Process term "GO:0009405 = pathogenesis" in order to more easily group processes related to pathogenesis (and symbiosis) that may be difficult to cleanly define as either cellular or physiological. We also hope to make this new term more broad, thus incorporating interactions between host and pathogen as well as between host and symbiont (as many of the processes involved are shared by both, and sometimes the outcome [pathogenesis vs. symbiosis] can vary depending on other conditions [e.g. environment, host defense response, etc.], as previously discussed on the GO Consortium discussion list. Thus, the outcome should not be pre-judged.) We feel this will better serve the needs of those searching across organisms for gene products involved in this more broadly-defined process of inter-organismic interactions. However, this now brings us into the realm of a discussion on the GO Consortium email that took place earlier this year - whether "pathogenesis" should include gene products like the human protein huntingtin, which can cause disease in humans - Huntington's disease - when it is mutated. While I did not think that GO currently annotates functions of proteins that are true only when they are mutated, that particular gene product (huntingtin) is currently annotated under the current GO term "pathogenesis." If our suggested new term "interaction with host organism" and its suggested children now serve as terms to use in annotating disease-causing molecules in pathogens (and symbionts), GO will need a new term and definition to accommodate the annotation of gene products such as huntingtin.]

---------% virus-host interaction (GO:0019048
------------% viral host cell process manipulation (GO:0019054)
------------% viral host defense evasion (GO:0019049)
------------% viral induction of host immune response (GO:0046730)
---------% recognition of host
---------% adhesion to host
------------% cytoadherence to microvasculature (GO:0020035
---------% growth on or near host surface
---------% entry into host
------------% entry into host through natural portals
------------% entry into host through host barriers
------------% cell invasion (GO:0030260
---------------% viral entry (GO:0046718
---------% evasion or suppression of host defenses

```
------------% evasion of host defense response (GO:0030682
---------------% evasion of host immune response (GO:0020012)
---------------% viral host defense evasion (GO:0019049)
---------% induction of host defense response
------------%viral induction of host immune response (GO:0046730)
---------% translocation of molecules into host
------------% translocation of DNA into host
------------% translocation of protein into host
---------------% type III protein secretion system (GO:0030254
---------% movement within host
------------% migration within host
------------%viral spread within host (GO:0046739)
---------% acquisition of nutrients from host
---------% modification of host morphology or physiology
------------% viral host cell process manipulation (GO:0019054
------------% viral transformation (GO:0019087
---------------% viral immortalization (GO:0019088)
------------% disruption of host cells
---------------% killing of host cells
-------------------% hemolysis (GO:0019836)
-------------------% necrosis (GO:0008220
------------% induction in host of a tumor, nodule, or growth
---------------% induction in host of a tumor, nodule, or growth containing transformed cells
---------------% induction in host of a tumor, nodule, or growth not containing transformed cel
---------% dissemination or transmission of an organism from a host
------------% dissemination or transmission of an organism from a host by a vector
------------% viral transmission --  (GO:0019089
---% cell killing
------% killing of non-host cells
------% killing of host cells


---
defs:


% virushost interaction (GO:0019048)
def:interactions, directly with the host cell macromolecular machinery, to allow virus
replication)

% recognition of host
def:the specific processes that allow an organism to detect the presence of a host via
physical or chemical signals
```

% adhesion to host
def:the attachment of an organism to its host via adhesion molecules, general stickiness, etc., either directly or indirectly

% cytoadherence to microvasculature (GO:0020035)
def:adherence of parasiteinfected erythrocytes to microvascular endothelium. [NOTE: this GO term has been moved, unchanged, from its place as a child of "hostpathogen interactions" to a child of newly proposed term "adhesion to host," which is itself a child of newly proposed term "interaction with host organism"]

% growth on or near host surface
def:an increase in size or number of an organism on or near the exterior of its host.

% entry into host
def:penetration by an organism into the body, cells, or tissues of the host
(Question: make "invasion into host" a synonym???)

% entry into host through natural portals -
def: penetration by an organism to the inside of a host via naturally occurring openings in the host

% entry into host through host barriers
def: penetration by an organism to the inside of a host via active breaching of physical barriers

% cell invasion (GO:0030260
def:invasion of a host cell by another cell (microorganism) or virus.)

% viral entry (GO:0046718
def:the process by which a virion enters a host cell, including virion attachment and penetration. [NOTE: We suggest that this term be made a child of "cell invasion" in addition to its current place as a child of "initiation of viral infection")

(NOTE: We propose that currently existing GO term, GO:0001404
-Invasive growth (currently a child of "pathogenesis"), should be deleted. That term is used differently for plant and animal pathogens, and there are currently no gene products annotated to this term in GO.)

% evasion or suppression of host defenses
def: any process by which an organism avoids, minimizes, or suppresses the effects of a host defense(s), which can be either basal or induced

[NOTE: we suggest that this term become a broader parent term to "GO:0030682
-evasion of host defense response" [currently a child of "hostpathogen interaction"]
in order to define this process more broadly and to serve both pathogens and
symbionts, etc. Also, we wanted to broaden the definition beyond a host "response,"
as some defenses are preformed rather than responsive. We think this will work in
all current trees. The term "GO:0030682
-evasion of host defense response" then becomes a child of this new term, and this
GO term's currently existing children terms "GO:0020012
-evasion of host immune response" and "GO:0019049
-viral host defense evasion", as well as their respective children terms, should be
able to stay at their current places in the tree under GO:0030682, as seen below.]

% evasion of host defense response (GO:0030682
def:any process by which a pathogen evades or minimizes the effects of a defense
response mounted against it by its host.

% induction of host defense response
def:the triggering by an organism of reactions in a host that can act to protect
the host cell(s) or host organism

% translocation of molecules into host
def:the directed movement of a molecule(s) produced by an organism to a location
inside the host

% type III protein secretion system (GO:0030254
def:a bacterial secretion system in which secretion occurs in a continuous process
without the distinct presence of periplasmic intermediates; does not involve
proteolytic processing of secreted proteins [Note: the definition of this term
needs correction in order to differentiate it from the other protein secretion
systems in bacteria. We'll send in a request to do that very soon.]

% movement within host
def:the process by which an organism or its progeny spreads from one location
to another within a host

% migration within host
def:the directional movement of an organism from one place to another within a host

% acquisition of nutrients from host
def:the production of structures and/or molecules in an organism that are required
for the acquisition and/or utilization of nutrients obtained from its host

% modification of host morphology or physiology

def:the process of effecting a change in the structure or function of a host by means of molecules produced by an associated organism

% viral host cell process manipulation (GO:0019054
def:alteration of defined cellular processes that viruses target during replication)

% viral transformation (GO:0019087
def:any virus-induced change in the morphological, biochemical, or growth parameters of a cell)

% disruption of host cells
def:any process in an organism that results in damage to the structure or function of the cell

% killing of host cells
def:any process in an organism that results in the death of its host or cells of its host

% hemolysis (GO:0019836)
def:"the processes that cause hemolysis, the lytic destruction of red blood cells with the release of intracellular hemoglobin, in another organism." [Note: This term is currently a child of "pathogenesis"
- we suggest it be moved to here.]

% necrosis (GO:0008220
def:"the processes that cause necrosis, the death of tissues, in another organism". [Question: What to do with this current GO term, currently a child of "pathogenesis"?? Should the 13 terms currently annotated here be transferred to "killing of host cell(s)" and the "necrosis" term obsoleted? "Necrosis" could be made a synonym of this term, or they could be merged and "necrosis" become a secondary term under the new one ???]

% induction in host of a tumor, nodule, or growth
def:the process by which an associated organism causes the formation of an abnormal mass of cells in the host

% induction in host of a tumor, nodule, or growth containing transformed cells
def:the process by which an associated organism causes the formation in a host of an abnormal growth whose cells have been transformed and continue to exist in the absence of the inducing organism. [NOTE: We suggest this should replace the current GO term "host cell immortalization" (GO:0020021
- the modification of a host cell into an immortal cell line as a consequence of infection), which currently has no genes annotated to it.]

% induction in host of a tumor, nodule, or growth not containing transformed cells
def:the process by which an associated organism causes the formation in a host of an abnormal growth whose cell size or number has increased but which is not sustained in the absence of the inducing organism

% dissemination or transmission of an organism from a host
def:the movement of an organism from a host to another host or another place in the environment

% viral transmission -- (GO:0019089
def: the transfer of virions in order to create new infection)

% cell killing
def:any process in an organism that results in the death of another organism or its cells

% killing of non-host cells
def:any process in an organism that results in the death of another, non-host organism or its cells

% killing of host cells
def:any process in an organism that results in the death of its host or cells of its host

---

4. The pre-meeting PAMGO obo file can be downloaded from
[965023] new terms requested by PAMGO
https://sourceforge.net/tracker/?group_id=36855&atid=440764&func=detail&aid=965023
The file is just called 'pango'

---

5. Alex Diehl's pre-meeting proposal on pathogenic terms
[1013068] Pathogenic Terms
https://sourceforge.net/tracker/?group_id=36855&atid=440764&func=detail&aid=1013068

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6. Alex Diehl's pre-meeting proposal on Cell Killing terms
[1012931] Cell Killing Proposal
https://sourceforge.net/tracker/?group_id=36855&atid=440764&func=detail&aid=1012931

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7. Comments from Matt Berriman on the pathogenesis proposals:

Some comments on the pathogenesis proposals by Matt Berriman.

biofilm formation
==========
appears as a child of interaction with non-host organism. However, bio-film formation plays a major role in the pathogenesis of many candida species.

the definition of biofilm formation mentions alteration in growth rate and gene expression. This seems to me to be unnecessarily restrictive.

interaction with host organism
==========
I agree that host-pathogen interactions can be quite easily be changed to the proposed interaction with host organism.

pathogenesis
==========
the case of the huntingtin protein seems to me ato be a miss-annotation. What is the normal role of that gene product in a human without huntington's? If it is not known, there are terms for that.

entry into host
==========
I don't think that this is synonymous with "invasion into host". I use invasion to describe a complex series of events leadiong to the penetration of host cells by a pathogen. This is very different to simply entering the body, rather than individual cells, of a host. A more suitable synonym for invasion into host looks like cell invasion.

invasive growth
==========
what terms should be used to annotate invasive growth of Aspergillus into human cells when it uses them as a nutrient source?

Viral terms
==========
it is not clear to me why distinctions need to be made for viral terms e.g...

Viral host defense evasion
==========
why does the term need to include "viral"? I presume the term means evasion of host by a virus, not evasion of a viral host However, still don't see why the distinction between defence by viruses and by other pathogens needs to be made.

also,

viral immortailzation (which presumably should be written immortalisation by a virus)
==========
is this different to immortalisation by a protozoan (e.g. Theileria). Answer is that we don't know yet.

---

8. Pathogenesis powerpoint presentation.

ftp://ftp.geneontology.org/pub/go/meeting/minutes/20040822_Stanford_Content/pathogenesis.pdf
ftp://ftp.geneontology.org/pub/go/meeting/minutes/20040822_Stanford_Content/pathogenesis.ppt

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9. PAMGO powerpoint presentation.

ftp://ftp.geneontology.org/pub/go/meeting/minutes/20040822_Stanford_Content/PAMGO.pdf
ftp://ftp.geneontology.org/pub/go/meeting/minutes/20040822_Stanford_Content/PAMGO.ppt

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10. Metabolism explanation powerpoint presentation.

ftp://ftp.geneontology.org/pub/go/meeting/minutes/20040822_Stanford_Content/
metabolism_explanation.pdf
ftp://ftp.geneontology.org/pub/go/meeting/minutes/20040822_Stanford_Content/
metabolism_explanation.ppt

---

11. Metabolism proposal powerpoint presentation.

ftp://ftp.geneontology.org/pub/go/meeting/minutes/20040822_Stanford_Content/
metabolism_proposal.pdf

ftp://ftp.geneontology.org/pub/go/meeting/minutes/20040822_Stanford_Content/metabolism_proposal.ppt

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12. Cell Cycle powerpoint presentation.

ftp://ftp.geneontology.org/pub/go/meeting/minutes/20040822_Stanford_Content/cell_cycle.pdf
ftp://ftp.geneontology.org/pub/go/meeting/minutes/20040822_Stanford_Content/cell_cycle.ppt

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13. Alex's proposal on Pathogenic Terms to change or eliminate from the GO

Basically, I want to eliminate all references to pathogens, pathogenic, or pathogenesis from all GO terms and definitions.

The following is a excerpt of part of my email of 4 March 2004:

What we call "pathogenesis" is a human perspective to normal behavior by microorganisms. What we need in the GO is a class of terms that refer to processes induced in a host organism by a microorganism or parasite. Many of these processes may well be benign for the host, some may be considered pathogenic, but the GO terms used should be neutral on this point.

In fact, the PAMGO proposal accords well with this viewpoint.

In most cases below where no replacement term is offered, annotations can be directly transferred to the parent terms.

There are some references to "pathogen" in some plant related terms (GO:0009689, GO:0009626, GO:0009627, perhaps some others). I recommend changing the word to "microbial" or "microbe" where appropriate.

We can work out the DAG at the GO Content Meeting or after.

Thanks,

Alex

1) Obsolete: GO:0009613 ; response to pest, pathogen or parasite
Replace by "response to foreign biotic stimulus"

Definition: A change in state or activity of an organism (in terms of movement, secretion, enzyme production, gene expression, etc.) as a result of the perception of a foreign biotic stimulus. Foreign implies recognition of non-self components through both dedicated (TLRs etc) and adaptive (antibodies or TCRs) components. No distinction is made between "pathogenic" and "non-pathogenic" bacteria etc. (Note that the meaning of "biotic stimulus" needs to be expanded to mean any stimulus derived from a biological origin, such a soluble protein, as well as whole cells, living or dead)

2) Obsolete: GO:0009596 ; detection of pest, pathogen or parasite
Replace by "detection of foreign biotic stimulus"
Definition: The series of events by which a stimulus from a foreign biotic stimulus is received and converted into a molecular signal.

3) Obsolete: GO:0009680 ; response to non-pathogenic bacteria
4) Obsolete: GO:0009681 ; detection of non-pathogenic bacteria
5) Obsolete: GO:0042828 ; response to pathogen
6) Obsolete: GO:0042829 ; defense response to pathogen
7) Obsolete: GO:0009814 ; defense response to pathogen, incompatible interaction
(replace with "defense response, incompatible interaction," defined as "A response of an organism to a microbiotic stimulus that prevents the occurrence or spread of the microbe.")
8) Obsolete: GO:0009618 ; response to pathogenic bacteria
9) Obsolete: GO:0009598 ; detection of pathogenic bacteria
10) Obsolete: GO:0042830 ; defense response to pathogenic bacteria
11) Obsolete: GO:0009816 ; defense response to pathogenic bacteria, incompatible interaction
(replace with "defense response to bacteria, incompatible interaction")
12) Obsolete: GO:0009621 ; response to pathogenic fungi
13) Obsolete: GO:0009599 ; detection of pathogenic fungi
14) Obsolete: GO:0016047 ; detection of parasitic fungi
15) Obsolete: GO:0042831 ; defense response to pathogenic fungi
16) Obsolete: GO:0009817 ; defense response to pathogenic fungi, incompatible interaction
(replace with "defense response to fungi, incompatible interaction")
17) Obsolete: GO:0042833 ; response to pathogenic protozoa
18) Obsolete: GO:0042832 ; defense response to pathogenic protozoa
19) Obsolete: GO:0009818; defense response to pathogenic protozoa, incompatible interaction
(replace with "defense response to protozoa, incompatible interaction")
20) Obsolete: GO:0043019 ; response to pathogenic insects

(Definition: "A change in state or activity of an organism (in terms of movement, secretion, enzyme production, gene expression, etc.) as a result of the perception of a pathogenic (disease-causing) insect." Personally, I kill all mosquitoes regardless of their West Nile Virus status.)
21) Obsolete: GO:0030383 ; host-pathogen interaction
(agree with PAMGO on this)
22) Obsolete: GO:0009405 ; pathogenesis
(agree with PAMGO on this)
23) GO:0012504 ; induction of non-apoptotic programmed cell death by pathogen
(currently undefined, probably best replaced by PAMGO's necrosis term)

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14. Alex's Cell Killing Proposal and Terms

I have incorporated terms from Candace Collmer's PAMGO proposal and my own SourceForge entry 960898 (Cytolysis Terms) into a larger cell killing DAG intended to cover the killing of both self and foreign cells. I feel this is necessary to unite all mechanisms of cell killing in the GO under one larger umbrella, and recognize that certain mechanisms such as the activation of the terminal pathway of complement are used against both self and non-self (i.e. what might be considered 'non host' in the PAMGO proposal) cells. Naturally the PAMGO hierarchy is mostly unaffected itself, except for a few term name modifications. The GO should be written to cover all biology from both microbial and host perspectives, and thus a unified cell killing hierarchy is needed. This is not intended as a finished proposal, more like a stimulus for discussion. But the cytotoxicity terms are sorely needed for immunology, so I hope we can resolve this at the content meeting. Some definitions of new terms are from PAMGO, others from SF 960898 (shown after the DAG view below), and others from me today (listed before DAG). Sensible regulation terms and other things may be added as needed.

-- Alex

A) New Term: cell killing
Definition: Any process in an organism that results in the killing of its own cells or those of another organism, including in some cases the death of the other organism.
Comment: Killing here refers to the induction of death in one cell by another cell, not cell-autonomous death due to internal or other environmental conditions.

B) New Term: cell killing, other organism (called 'cell killing' in PAMGO)

Definition: Any process in an organism that results in the death of another organism or its cells.

C) New Term: cell killing, self

Definition: Any process in an organism that results in the killing of its own cells.
Comment: Killing here refers to the induction of death in one cell by another cell, not cell-autonomous death due to internal or other environmental conditions.

D) New Term: activation of the membrane attack complex

Synonym: activation of the terminal complement cascade
Synonym: activation of MAC
Synonym: activation of TCC
Definition: The activation of the membrane attack complex components of the complement cascade which can result in death of a target cell through cytolysis.

The new DAG:

GO:0008219 ; cell death
--< GO:0007569 ; cell aging +
--% GO:0012501 ; programmed cell death +
--% GO:0010198 ; synergid cell death +
--% GO:NewTerm ; cell killing
----% GO:0019835 ; cytolysis
------< GO:0042268 ; regulation of cytolysis
--------% GO:0045918 ; negative regulation of cytolysis
--------% GO:0045919 ; positive regulation of cytolysis
------% GO:0019835 ; cytolysis of host cells
--------% GO:0019836 ; hemolysis
------< GO:0042268 ; regulation of cytolysis of host cells
--------% GO:0045918 ; negative regulation of cytolysis
--------% GO:0045919 ; positive regulation of cytolysis
------% GO:NewTerm ; activation of the membrane attack complex
----% GO:NewTerm ; cell killing, other organism
------% GO:NewTerm ; killing of host cells
--------% GO:0019835 ; cytolysis of host cells
----------% GO:0019836 ; hemolysis
--------< GO:0042268 ; regulation of cytolysis of host cells
----------% GO:0045918 ; negative regulation of cytolysis

```
----------% GO:0045919 ; positive regulation of cytolysis
------% GO:NewTerm killing of non host cells
----% GO:NewTerm ; cell killing, self
------% GO:NewTerm ; immune cell mediated cytotoxicity
--------% GO:NewTerm ; T-cell mediated cytotoxicity
----------< GO:NewTerm ; regulation of T-cell mediated cytotoxicity
------------% GO:NewTerm ; negative regulation of T-cell mediated cytotoxicity
------------% GO:NewTerm ; positive regulation of T-cell mediated cytotoxicity
--------% GO:0042267 ; natural killer cell mediated cytotoxicity [as renamed]
----------< GO:0042269 ; regulation of natural killer cell mediated cytotoxicity [as renamed]
------------% GO:0045953 ; negative regulation of natural killer cell mediated cytotoxicity [as
renamed]
--------------% GO:0042270 ; protection from natural killer cell mediated cytotoxicity [as
renamed]
------------% GO:0045954 ; positive regulation of natural killer cell mediated cytotoxicity [as
renamed]
--------------% GO:0042271 ; susceptibility to natural killer cell mediated cytotoxicity [as
renamed]
--------% GO:0001788 ; antibody-dependent cellular cytotoxicity
----------< GO:0001813 ; regulation of antibody-dependent cellular cytotoxicity
------------% GO:0001814 ; negative regulation of antibody-dependent cellular cytotoxicity
------------% GO:0001815 ; positive regulation of antibody-dependent cellular cytotoxicity
--------< GO:NewTerm ; regulation of immune cell mediated cytotoxicity
----------% GO:NewTerm ; negative regulation of immune cell mediated cytotoxicity
------------% GO:NewTerm ; negative regulation of T-cell mediated cytotoxicity
------------% GO:0045953 ; negative regulation of natural killer cell mediated cytotoxicity [as
renamed]
--------------% GO:0042270 ; protection from natural killer cell mediated cytotoxicity [as
renamed]
------------% GO:0001814 ; negative regulation of antibody-dependent cellular cytotoxicity
----------% GO:NewTerm ; positive regulation of immune cell mediated cytotoxicity
------------% GO:NewTerm ; positive regulation of T-cell mediated cytotoxicity
------------% GO:0045954 ; positive regulation of natural killer cell mediated cytotoxicity [as
renamed]
--------------% GO:0042271 ; susceptibility to natural killer cell mediated cytotoxicity [as
renamed]
------------% GO:0001815 ; positive regulation of antibody-dependent cellular cytotoxicity
----------% GO:NewTerm ; regulation of T-cell mediated cytotoxicity
------------% GO:NewTerm ; negative regulation of T-cell mediated cytotoxicity
------------% GO:NewTerm ; positive regulation of T-cell mediated cytotoxicity
----------% GO:0042269 ; regulation of natural killer cell mediated cytotoxicity [as renamed]
--------------% GO:0045953 ; negative regulation of natural killer cell mediated cytotoxicity |
renamed]
```

----------% GO:0042270 ; protection from natural killer cell mediated cytotoxicity [as renamed]
----------% GO:0045954 ; positive regulation of natural killer cell mediated cytotoxicity | renamed]
----------% GO:0042271 ; susceptibility to natural killer cell mediated cytotoxicity [as renamed]
----------% GO:0001813 ; regulation of antibody-dependent cellular cytotoxicity
----------% GO:0001814 ; negative regulation of antibody-dependent cellular cytotoxicity
----------% GO:0001815 ; positive regulation of antibody-dependent cellular cytotoxicity

The terms from SF 960898 (as revised in that thread):

1) New Term: immune cell mediated cytotoxicity
Synonym: immune cell mediated cell killing [=]
Synonym: immune cell mediated cell death [=]
Definition: The directed killing of a target cell by a by an immune cell.
Parentage: is-a to GO:0008219 cell death and is-a to GO:0042087 cell-mediated immune response.
Comment: This term and its children are meant to describe contact-dependent killing of target cells by lymphocytes and myeloid cells of the immune system.
Reference: ISBN:0781735149, PMID:11911826

2) New term: regulation of immune cell mediated cytotoxicity
Synonym: regulation of immune cell mediated cell killing [=]
Synonym: regulation of immune cell mediated cell death [=]
Definition: Any process that modulates the frequency, rate, or extent of immune cell mediated cytotoxicity.
Parentage: part-of to "immune cell mediated cytotoxicity," above
Reference: ISBN:0781735149, PMID:11911826

3) New term: negative regulation of immune cell mediated cytotoxicity
Synonym: negative regulation of immune cell mediated cell killing [=]
Synonym: negative regulation of immune cell mediated cell death [=]
Definition: Any process that stops, prevents, or reduces the rate of immune cell mediated cytotoxicity.
Parentage: is-a to "regulation of immune cell mediated cytotoxicity," above
Reference: ISBN:0781735149, PMID:11911826

4) New term: positive regulation of immune cell mediated cytotoxicity

Synonym: positive regulation of immune cell mediated cell killing [=]
Synonym: positive regulation of immune cell mediated cell death [=]
Definition: Any process that activates or increases the rate of immune cell mediated cytotoxicity.
Parentage: is-a to "regulation of immune cell mediated cytotoxicity," above
Reference: ISBN:0781735149, PMID:11911826

5) New Term: T-cell mediated cytotoxicity
Synonym: T cell mediated cytotoxicity [=]
Synonym: T-cell mediated apoptosis [=]
Synonym: T cell mediated apoptosis [=]
Synonym: T-cell mediated cell killing [=]
Synonym: T cell mediated cell killing [=]
Synonym: T-cell mediated cell death [=]
Synonym: T cell mediated cell death [=]
Synonym: T-cell mediated cytolysis [~]
Synonym: T cell mediated cytolysis [~]

Definition: The directed killing of a target cell by a T-cell through the release of granules containing cytotoxic mediators or through the engagement of death receptors.
Parentage: is-a to immune cell mediated cytotoxicity and is-a to GO:00069174 induction of apoptosis.
Comment: Note that either or both mechanisms mentioned in the definition may be used in this process.
Comment: Note that both granule release and the engagement of death receptors on target cells result in the induction of apoptosis in the target cell.
Comment: Note that both CD4 and CD8 positive T-cells can mediate apoptosis of target cells, independently of their definition as "helper" T-cells or not.
Reference: ISBN:0781735149, PMID:11911826

[Editorial note: although isolated perforin has been shown to induce cytolysis directly when applied to target cells at high concentrations, experimental evidence shows that the function of perforin is to allow access of granzymes into the cytoplasm of the target cell, followed by the granzyme mediated cleavage of caspase and non-caspase components of the apoptotic pathway leading to the induction of apoptosis.]

6) New Term: regulation of T-cell mediated cytotoxicity
Synonym: regulation of T cell mediated cytotoxicity [=]
Synonym: regulation of T-cell mediated apoptosis [=]
Synonym: regulation of T cell mediated apoptosis [=]

Synonym: regulation of T cell mediated cell killing [=]
Synonym: regulation of T-cell mediated cell killing [=]
Synonym: regulation of T-cell mediated cell death [=]
Synonym: regulation of T cell mediated cell death [=]
Synonym: regulation of T-cell mediated cytolysis [~]
Synonym: regulation of T cell mediated cytolysis [~]
Definition: Any process that modulates the frequency, rate, or extent of T-cell mediated cytotoxicity.
Parentage: part-of to "T-cell mediated cytotoxicity" and is-a to "regulation of immune cell mediated cytotoxicity," above.
Reference: ISBN:0781735149

7) New Term: negative regulation of T-cell mediated cytotoxicity
Synonym: negative regulation of T cell mediated cytotoxicity [=]
Synonym: negative regulation of T-cell mediated apoptosis [=]
Synonym: negative regulation of T cell mediated apoptosis [=]
Synonym: negative regulation of T cell mediated cell killing [=]
Synonym: negative regulation of T-cell mediated cell killing [=]
Synonym: negative regulation of T-cell mediated cell death [=]
Synonym: negative regulation of T cell mediated cell death [=]
Synonym: negative regulation of T-cell mediated cytolysis [~]
Synonym: negative regulation of T cell mediated cytolysis [~]
Definition: Any process that stops, prevents, or reduces the rateof T-cell mediated cytotoxicity.
Parentage: is-a to "regulation of T-cell mediated cytotoxicity" and is-a to "negative regulation of immune cell mediated cytotoxicity," above.
Reference: ISBN:0781735149

8) New Term: positive regulation of T-cell mediated cytotoxicity
Synonym: positive regulation of T cell mediated cytotoxicity [=]
Synonym: positive regulation of T-cell mediated apoptosis [=]
Synonym: positive regulation of T cell mediated apoptosis [=]
Synonym: positive regulation of T cell mediated cell killing [=]
Synonym: positive regulation of T-cell mediated cell killing [=]
Synonym: positive regulation of T-cell mediated cell death [=]
Synonym: positive regulation of T cell mediated cell death [=]
Synonym: positive regulation of T-cell mediated cytolysis [~]
Synonym: positive regulation of T cell mediated cytolysis [~]
Definition: Any process that activates or increases the rate of T-cell mediated cytotoxicity.
Parentage: is-a to "regulation of T-cell mediated cytotoxicity" and is-a to "positive regulation of immune cell mediated cytotoxicity," above.
Reference: ISBN:0781735149

9) GO:0042267 natural killer cell mediated cytolysis
This term needs to be renamed and redefined to parallel the T-cell mediated cytotoxicity term, because the mechanisms of cell killing used by NK cells are nearly identical to those of T cell and involve the induction of apoptosis in the target cells.
Proposed new name: natural killer cell mediated cytotoxicity
Synonym (new): NK cell mediated cytotoxicity [=]
Synonym (new): natural killer cell mediated cytolysis [~]
Synonym (old): NK cell mediated cytolysis [~]
Synonym (old): natural killer-cell mediated cytolysis [~]
Proposed new definition: The directed killing of a target cell by a natural killer cell throu the release of granules containing cytotoxic mediators or through the engagement of death receptors.
Revised parentage: is-a to "immune cell mediated cytotoxicity," above, and is-a to GO:0006917 induction of apoptosis
Comment: Note that either or both mechanisms mentioned in the definition may be used in this process.

Comment: Note that both granule release and the engagement of death receptors on target cells result in induction of apoptosis in the target cell.

10) GO:0042269 regulation of natural killer cell mediated cytolysis
Proposed new name: regulation of natural killer cell mediated cytotoxicity
Synonym (new): regulation of NK cell mediated cytotoxicity [=]
Synonym (new): regulation of natural killer cell mediated cytolysis [~]
Synonym (old): regulation of NK cell mediated cytolysis [~]
Synonym (old): regulation of natural killer-cell mediated cytolysis [~]
Proposed new definition: Any process that modulates the frequency, rate, or extent of natural killer cell mediated cytotoxicity.
Revised parentage: part-of to GO:0042267 natural killer cell mediated cytotoxicity [as renamed and to "regulation of immune cell mediated cytotoxicity," above.
Reference: ISBN:0781735149

11) GO:0045953 negative regulation of natural killer cell mediated cytolysis
Proposed new name: negative regulation of natural killer cell mediated cytotoxicity
Synonym (new): negative regulation of NK cell mediated cytotoxicity [=]
Synonym (new): negative regulation of natural killer cell mediated cytolysis [~]
Synonym (old): negative regulation of NK cell mediated cytolysis [~]
Proposed new definition: Any process that stops, prevents, or reduces the rate of natural kill mediated cytotoxicity.
Revised parentage: is-a to GO:0042269 regulation of natural killer cell mediated cytotoxicity [as renamed] and to "negative regulation of immune cell mediated cytotoxicity," above.
Reference: ISBN:0781735149

12) GO:0045954 positive regulation of natural killer cell mediated cytolysis
Proposed new name: positive regulation of natural killer cell mediated cytotoxicity
Synonym (new): positive regulation of NK cell mediated cytotoxicity [=]
Synonym (new): positive regulation of natural killer cell mediated cytolysis [~]
Synonym (old): positive regulation of NK cell mediated cytolysis [~]
Proposed new definition: Any process that activates or increases the rate of natural killer ce
mediated cytotoxicity.
Revised parentage: is-a to GO:0042269 regulation of natural killer cell mediated cytotoxicity
[as renamed] and to "positive regulation of immune cell mediated cytotoxicity," above.
Reference: ISBN:0781735149

13) GO:0042270 protection from natural killer cell mediated cytolysis
Proposed new name: protection from natural killer cell mediated cytotoxicity
Synonym (new): protection from NK cell mediated cytotoxicity [=]
Synonym (new): protection from natural killer cell mediated cytolysis [~]
Synonym (old): protection from NK cell mediated cytolysis [~]
Proposed new definition: The process of protecting a cell from natural killer cell mediated
cytotoxicity.
Revised parentage: is-a to GO:0045953 negative regulation of natural killer cell mediated
cytotoxicity [as renamed above].
Comment: Note that this term is intended for cell-surface molecules on a target cell which
interact with inhibitory receptors on a natural killer cell to prevent natural killer cell
mediated cytotoxicity.
[Editorial note: This is clearly a type of negative regulation of NK cell cytotoxicity and its
position in the DAG should reflect that.]

14) GO:0042271 susceptibility to natural killer cell mediated cytolysis
Proposed new name: susceptibility to natural killer cell mediated cytotoxicity
Synonym (new): susceptibility to NK cell mediated cytotoxicity [=]
Synonym (new): susceptibility to natural killer cell mediated cytolysis [~]
Synonym (old): susceptibility to NK cell mediated cytolysis [~]
Proposed new definition: The process of causing a cell to become susceptible to natural killer
cell mediated cytotoxicity.
Revised parentage: is-a to GO:0045954 positive regulation of natural killer cell mediated
cytotoxicity [as renamed above].
Comment: Note that this term is intended for cell-surface molecules on a target cell which
interact with activating receptors on a natural killer cell to promote natural killer cell
mediated cytotoxicity.
[Editorial note: This is clearly a type of positive regulation of NK cell cytotoxicity and its
position in the DAG should reflect that.]

15) GO:0001788 antibody-dependent cellular cytotoxicity

Proposed new definition: Killing of target cells by natural killer cells, eosinophils, neutrophils, monocytes, or macrophages following engagement of antibodies bound to the target cells by Fc receptors on the effector cells.
Revised parentage: is-a to "immune cell mediated cytotoxicity," above, and is-a to GO:0006917 induction of apoptosis

16) GO:0001813 regulation of antibody-dependent cellular cytotoxicity
Revised parentage: part-of to GO:0001788 antibody-dependent cellular cytotoxicity and is-a to "regulation of immune cell mediated cytotoxicity," above.

17) GO:0001814 negative regulation of antibody-dependent cellular cytotoxicity
Revised parentage: is-a to GO:0001813 regulation of antibody- dependent cellular cytotoxicity and is-a to "negative regulation of immune cell mediated cytotoxicity," above.

18) GO:0001815 positive regulation of antibody-dependent cellular cytotoxicity
Revised parentage: is-a to GO:0001813 regulation of antibody- dependent cellular cytotoxicity and is-a to "positive regulation of immune cell mediated cytotoxicity," above.

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15. Cell Killing Terms incorporating the discussion at the GO Content meeting

I have made changes to the DAG and terms according to the discussion at the GO content meeting (including the elimination of the term "cell killing, self"). However, I am still unsure of ho to rename the PAMGO term "killing of non host cells," and whether the term "cytolysis of non-ho cells" and its children need to be created.

Additional comments are welcome,

Alex

A) New Term: cell killing
Definition: Any process in an organism that results in the killing of its own cells or those o another organism, including in some cases the death of the other organism. Killing here refers to the induction of death in one cell by another cell, not cell-autonomous death due to interna or other environmental conditions.

B) New Term: cell killing, other organism (called 'cell killing' in PAMGO)
Definition: Any process in an organism that results in the death of another organism or its cells.

C) New Term: activation of the membrane attack complex

Synonym: activation of the terminal complement cascade
Synonym: activation of MAC
Synonym: activation of TCC
Definition: The activation of the membrane attack complex components of the complement cascade which can result in death of a target cell through cytolysis.

D) New Term: autolysis
Definition: The spontaneous death by lysis of bacteria in response to environmental conditions

The revised DAG:

GO:0008219 ; cell death
--< GO:0007569 ; cell aging +
--% GO:0012501 ; programmed cell death +
--% GO:0010198 ; synergid cell death +
--% GO:0019835 ; cytolysis
----% GO:NewTerm ; autolysis
----< GO:0042268 ; regulation of cytolysis
------% GO:0045918 ; negative regulation of cytolysis
------% GO:0045919 ; positive regulation of cytolysis
----% GO:NewTerm ; cytolysis of host cells
------% GO:0019836 ; hemolysis
------< GO:NewTerm ; regulation of cytolysis of host cells
--------% GO:NewTerm ; negative regulation of cytolysis of host cells
--------% GO:NewTerm ; positive regulation of cytolysis of host cells
----% GO:NewTerm ; cytolysis of non host cells
------< GO:NewTerm ; regulation of cytolysis of non host cells
--------% GO:NewTerm ; negative regulation of cytolysis of non host cells
--------% GO:NewTerm ; positive regulation of cytolysis non host cells
----% GO:NewTerm ; activation of the membrane attack complex
--% GO:NewTerm ; cell killing
----% GO:NewTerm ; cell killing, other organism
------% GO:NewTerm ; killing of host cells
--------% GO:NewTerm ; cytolysis of host cells
----------% GO:0019836 ; hemolysis
----------< GO:NewTerm ; regulation of cytolysis of host cells
------------% GO:NewTerm ; negative regulation of cytolysis of host cells
------------% GO:NewTerm ; positive regulation of cytolysis host cells
------% GO:NewTerm killing of non host cells
--------% GO:NewTerm ; cytolysis of non host cells
----------< GO:NewTerm ; regulation of cytolysis of non host cells
------------% GO:NewTerm ; negative regulation of cytolysis of non host cells
------------% GO:NewTerm ; positive regulation of cytolysis non host cells

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----% GO:NewTerm ; immune cell mediated cytotoxicity
------% GO:NewTerm ; T-cell mediated cytotoxicity
--------< GO:NewTerm ; regulation of T-cell mediated cytotoxicity
----------% GO:NewTerm ; negative regulation of T-cell mediated cytotoxicity
----------% GO:NewTerm ; positive regulation of T-cell mediated cytotoxicity
------% GO:0042267 ; natural killer cell mediated cytotoxicity [as renamed]
--------< GO:0042269 ; regulation of natural killer cell mediated cytotoxicity [as renamed]
----------% GO:0045953 ; negative regulation of natural killer cell mediated cytotoxicity [as
renamed]
------------% GO:0042270 ; protection from natural killer cell mediated cytotoxicity [as rename
----------% GO:0045954 ; positive regulation of natural killer cell mediated cytotoxicity [as
renamed]
------------% GO:0042271 ; susceptibility to natural killer cell mediated cytotoxicity [as
renamed]
------% GO:0001788 ; antibody-dependent cellular cytotoxicity
--------< GO:0001813 ; regulation of antibody-dependent cellular cytotoxicity
----------% GO:0001814 ; negative regulation of antibody-dependent cellular cytotoxicity
----------% GO:0001815 ; positive regulation of antibody-dependent cellular cytotoxicity
------< GO:NewTerm ; regulation of immune cell mediated cytotoxicity
--------% GO:NewTerm ; negative regulation of immune cell mediated cytotoxicity
----------% GO:NewTerm ; negative regulation of T-cell mediated cytotoxicity
----------% GO:0045953 ; negative regulation of natural killer cell mediated cytotoxicity [as
renamed]
------------% GO:0042270 ; protection from natural killer cell mediated cytotoxicity [as rename
----------% GO:0001814 ; negative regulation of antibody-dependent cellular cytotoxicity
--------% GO:NewTerm ; positive regulation of immune cell mediated cytotoxicity
----------% GO:NewTerm ; positive regulation of T-cell mediated cytotoxicity
----------% GO:0045954 ; positive regulation of natural killer cell mediated cytotoxicity [as
renamed]
------------% GO:0042271 ; susceptibility to natural killer cell mediated cytotoxicity [as
renamed]
----------% GO:0001815 ; positive regulation of antibody-dependent cellular cytotoxicity
--------% GO:NewTerm ; regulation of T-cell mediated cytotoxicity
----------% GO:NewTerm ; negative regulation of T-cell mediated cytotoxicity
----------% GO:NewTerm ; positive regulation of T-cell mediated cytotoxicity
--------% GO:0042269 ; regulation of natural killer cell mediated cytotoxicity [as renamed]
----------% GO:0045953 ; negative regulation of natural killer cell mediated cytotoxicity [as
renamed]
------------% GO:0042270 ; protection from natural killer cell mediated cytotoxicity [as rename
----------% GO:0045954 ; positive regulation of natural killer cell mediated cytotoxicity [as
renamed]
------------% GO:0042271 ; susceptibility to natural killer cell mediated cytotoxicity [as
renamed]
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--------% GO:0001813 ; regulation of antibody-dependent cellular cytotoxicity
----------% GO:0001814 ; negative regulation of antibody-dependent cellular cytotoxicity
----------% GO:0001815 ; positive regulation of antibody-dependent cellular cytotoxicity

The terms from SF 960898 (as revised in that thread):

1) New Term: immune cell mediated cytotoxicity
Synonym: immune cell mediated cell killing [=]
Synonym: immune cell mediated cell death [=]
Definition: The directed killing of a target cell by a by an immune cell.
Parentage: is-a to GO:0008219 cell death and is-a to GO:0042087 cell-mediated immune response.
Comment: This term and its children are meant to describe contact-dependent killing of target cells by lymphocytes and myeloid cells of the immune system.
Reference: ISBN:0781735149, PMID:11911826

2) New term: regulation of immune cell mediated cytotoxicity
Synonym: regulation of immune cell mediated cell killing [=]
Synonym: regulation of immune cell mediated cell death [=]
Definition: Any process that modulates the frequency, rate, or extent of immune cell mediated cytotoxicity.
Parentage: part-of to "immune cell mediated cytotoxicity," above
Reference: ISBN:0781735149, PMID:11911826

3) New term: negative regulation of immune cell mediated cytotoxicity
Synonym: negative regulation of immune cell mediated cell killing [=]
Synonym: negative regulation of immune cell mediated cell death [=]
Definition: Any process that stops, prevents, or reduces the rate of immune cell mediated cytotoxicity.
Parentage: is-a to "regulation of immune cell mediated cytotoxicity," above
Reference: ISBN:0781735149, PMID:11911826

4) New term: positive regulation of immune cell mediated cytotoxicity
Synonym: positive regulation of immune cell mediated cell killing [=]
Synonym: positive regulation of immune cell mediated cell death [=]
Definition: Any process that activates or increases the rate of immune cell mediated cytotoxicity.
Parentage: is-a to "regulation of immune cell mediated cytotoxicity," above
Reference: ISBN:0781735149, PMID:11911826

5) New Term: T-cell mediated cytotoxicity
Synonym: T cell mediated cytotoxicity [=]
Synonym: T-cell mediated apoptosis [=]
Synonym: T cell mediated apoptosis [=]
Synonym: T-cell mediated cell killing [=]
Synonym: T cell mediated cell killing [=]
Synonym: T-cell mediated cell death [=]
Synonym: T cell mediated cell death [=]
Synonym: T-cell mediated cytolysis [~]
Synonym: T cell mediated cytolysis [~]
Definition: The directed killing of a target cell by a T-cell through the release of granules containing cytotoxic mediators or through the engagement of death receptors.
Parentage: is-a to immune cell mediated cytotoxicity and is-a to GO:00069174 induction of apoptosis.
Comment: Note that either or both mechanisms mentioned in the definition may be used in this process.
Comment: Note that both granule release and the engagement of death receptors on target cells result in the induction of apoptosis in the target cell.
Comment: Note that both CD4 and CD8 positive T-cells can mediate apoptosis of target cells, independently of their definition as "helper" T-cells or not.
Reference: ISBN:0781735149, PMID:11911826
[Editorial note: although isolated perforin has been shown to induce cytolysis directly when applied to target cells at high concentrations, experimental evidence shows that the function of perforin is to allow access of granzymes into the cytoplasm of the target cell, followed by the granzyme mediated cleavage of caspase and non-caspase components of the apoptotic pathway leading to the induction of apoptosis.]

6) New Term: regulation of T-cell mediated cytotoxicity
Synonym: regulation of T cell mediated cytotoxicity [=]
Synonym: regulation of T-cell mediated apoptosis [=]
Synonym: regulation of T cell mediated apoptosis [=]
Synonym: regulation of T cell mediated cell killing [=]
Synonym: regulation of T-cell mediated cell killing [=]
Synonym: regulation of T-cell mediated cell death [=]
Synonym: regulation of T cell mediated cell death [=]
Synonym: regulation of T-cell mediated cytolysis [~]
Synonym: regulation of T cell mediated cytolysis [~]
Definition: Any process that modulates the frequency, rate, or extent of T-cell mediated cytotoxicity.
Parentage: part-of to "T-cell mediated cytotoxicity" and is-a to "regulation of immune cell mediated cytotoxicity," above.

Reference: ISBN:0781735149

7) New Term: negative regulation of T-cell mediated cytotoxicity
Synonym: negative regulation of T cell mediated cytotoxicity [=]
Synonym: negative regulation of T-cell mediated apoptosis [=]
Synonym: negative regulation of T cell mediated apoptosis [=]
Synonym: negative regulation of T cell mediated cell killing [=]
Synonym: negative regulation of T-cell mediated cell killing [=]
Synonym: negative regulation of T-cell mediated cell death [=]
Synonym: negative regulation of T cell mediated cell death [=]
Synonym: negative regulation of T-cell mediated cytolysis [~]
Synonym: negative regulation of T cell mediated cytolysis [~]
Definition: Any process that stops, prevents, or reduces the rate of T-cell mediated cytotoxicity.
Parentage: is-a to "regulation of T-cell mediated cytotoxicity" and is-a to "negative regulation of immune cell mediated cytotoxicity," above.
Reference: ISBN:0781735149

8) New Term: positive regulation of T-cell mediated cytotoxicity
Synonym: positive regulation of T cell mediated cytotoxicity [=]
Synonym: positive regulation of T-cell mediated apoptosis [=]
Synonym: positive regulation of T cell mediated apoptosis [=]
Synonym: positive regulation of T cell mediated cell killing [=]
Synonym: positive regulation of T-cell mediated cell killing [=]
Synonym: positive regulation of T-cell mediated cell death [=]
Synonym: positive regulation of T cell mediated cell death [=]
Synonym: positive regulation of T-cell mediated cytolysis [~]
Synonym: positive regulation of T cell mediated cytolysis [~]
Definition: Any process that activates or increases the rate of T-cell mediated cytotoxicity.
Parentage: is-a to "regulation of T-cell mediated cytotoxicity" and is-a to "positive regulation of immune cell mediated cytotoxicity," above.
Reference: ISBN:0781735149

9) GO:0042267 natural killer cell mediated cytolysis
This term needs to be renamed and redefined to parallel the T-cell mediated cytotoxicity term, because the mechanisms of cell killing used by NK cells are nearly identical to those of T cells, and involve the induction of apoptosis in the target cells.
Proposed new name: natural killer cell mediated cytotoxicity
Synonym (new): NK cell mediated cytotoxicity [=]
Synonym (new): natural killer cell mediated cytolysis [~]
Synonym (old): NK cell mediated cytolysis [~]

Synonym (old): natural killer-cell mediated cytolysis [~]
Proposed new definition: The directed killing of a target cell by a natural killer cell through the release of granules containing cytotoxic mediators or through the engagement of death receptors.
Revised parentage: is-a to "immune cell mediated cytotoxicity," above, and is-a to GO:00069174 induction of apoptosis
Comment: Note that either or both mechanisms mentioned in the definition may be used in this process.
Comment: Note that both granule release and the engagement of death receptors on target cells result in induction of apoptosis in the target cell.

10) GO:0042269 regulation of natural killer cell mediated cytolysis

Proposed new name: regulation of natural killer cell mediated cytotoxicity
Synonym (new): regulation of NK cell mediated cytotoxicity [=]
Synonym (new): regulation of natural killer cell mediated cytolysis [~]
Synonym (old): regulation of NK cell mediated cytolysis [~]
Synonym (old): regulation of natural killer-cell mediated cytolysis [~]
Proposed new definition: Any process that modulates the frequency, rate, or extent of natural killer cell mediated cytotoxicity.
Revised parentage: part-of to GO:0042267 natural killer cell mediated cytotoxicity [as renamed] and to "regulation of immune cell mediated cytotoxicity," above.
Reference: ISBN:0781735149

11) GO:0045953 negative regulation of natural killer cell mediated cytolysis
Proposed new name: negative regulation of natural killer cell mediated cytotoxicity
Synonym (new): negative regulation of NK cell mediated cytotoxicity [=]
Synonym (new): negative regulation of natural killer cell mediated cytolysis [~]
Synonym (old): negative regulation of NK cell mediated cytolysis [~]
Proposed new definition: Any process that stops, prevents, or reduces the rate of natural killer mediated cytotoxicity.
Revised parentage: is-a to GO:0042269 regulation of natural killer cell mediated cytotoxicity [as renamed] and to "negative regulation of immune cell mediated cytotoxicity," above.
Reference: ISBN:0781735149

12) GO:0045954 positive regulation of natural killer cell mediated cytolysis
Proposed new name: positive regulation of natural killer cell mediated cytotoxicity
Synonym (new): positive regulation of NK cell mediated cytotoxicity [=]
Synonym (new): positive regulation of natural killer cell mediated cytolysis [~]
Synonym (old): positive regulation of NK cell mediated cytolysis [~]
Proposed new definition: Any process that activates or increases the rate of

natural killer cell mediated cytotoxicity.
Revised parentage: is-a to GO:0042269 regulation of natural killer cell mediated cytotoxicity [as renamed] and to "positive regulation of immune cell mediated cytotoxicity," above.
Reference: ISBN:0781735149

13) GO:0042270 protection from natural killer cell mediated cytolysis
Proposed new name: protection from natural killer cell mediated cytotoxicity
Synonym (new): protection from NK cell mediated cytotoxicity [=]
Synonym (new): protection from natural killer cell mediated cytolysis [~]
Synonym (old): protection from NK cell mediated cytolysis [~]
Proposed new definition: The process of protecting a cell from natural killer cell mediated cytotoxicity.
Revised parentage: is-a to GO:0045953 negative regulation of natural killer cell mediated cytotoxicity [as renamed above].
Comment: Note that this term is intended for cell-surface molecules on a target cell which interact with inhibitory receptors on a natural killer cell to prevent natural killer cell mediated cytotoxicity.
[Editorial note: This is clearly a type of negative regulation of NK cell cytotoxicity and its position in the DAG should reflect that.]

14) GO:0042271 susceptibility to natural killer cell mediated cytolysis
Proposed new name: susceptibility to natural killer cell mediated cytotoxicity
Synonym (new): susceptibility to NK cell mediated cytotoxicity [=]
Synonym (new): susceptibility to natural killer cell mediated cytolysis [~]
Synonym (old): susceptibility to NK cell mediated cytolysis [~]
Proposed new definition: The process of causing a cell to become susceptible to natural killer cell mediated cytotoxicity.
Revised parentage: is-a to GO:0045954 positive regulation of natural killer cell mediated cytotoxicity [as renamed above].
Comment: Note that this term is intended for cell-surface molecules on a target cell which interact with activating receptors on a natural killer cell to promote natural killer cell mediated cytotoxicity.
[Editorial note: This is clearly a type of positive regulation of NK cell cytotoxicity and its position in the DAG should reflect that.]

15) GO:0001788 antibody-dependent cellular cytotoxicity
Proposed new definition: Killing of target cells by natural killer cells, eosinophils, neutrophils, monocytes, or macrophages following engagement of antibodies bound to the target cells by Fc receptors on the effector cells.
Revised parentage: is-a to "immune cell mediated cytotoxicity," above, and is-a to GO:00069174 induction of apoptosis

16) GO:0001813 regulation of antibody-dependent cellular cytotoxicity
Revised parentage: part-of to GO:0001788 antibody-dependent cellular cytotoxicity and is-a to "regulation of immune cell mediated cytotoxicity," above.

17) GO:0001814 negative regulation of antibody-dependent cellular cytotoxicity
Revised parentage: is-a to GO:0001813 regulation of antibody-dependent cellular cytotoxicity and is-a to "negative regulation of immune cell mediated cytotoxicity," above.

18) GO:0001815 positive regulation of antibody-dependent cellular cytotoxicity
Revised parentage: is-a to GO:0001813 regulation of antibody-dependent cellular cytotoxicity and is-a to "positive regulation of immune cell mediated cytotoxicity," above.

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16. Suparna's proposl on host-pathogen interactions. (url)

ftp://ftp.geneontology.org/pub/go/meeting/minutes/20040822_Stanford_Content/host-pathogen_proposal.doc
ftp://ftp.geneontology.org/pub/go/meeting/minutes/20040822_Stanford_Content/host-pathogen_proposal.pdf