

Representation of apoptosis in the Gene Ontology

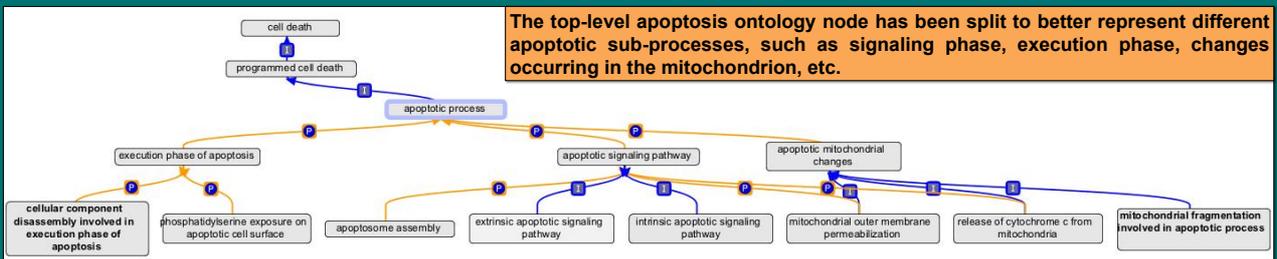


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The **Gene Ontology (GO)** (<http://www.geneontology.org>) is a freely available bioinformatics resource that classifies protein function using structured, controlled vocabularies. Currently, these contain >38,000 terms, used to annotate proteins from ~350,000 species. GO annotations are invaluable tools to the scientific community because they aid representation and interpretation of biological data, especially from high-throughput experiments.

Recently, the GO Consortium worked with apoptosis experts to expand and refine this area of the ontology. **Apoptosis** is a type of programmed cell death; it's a key biological process in development and is altered in various diseases such as cancer and disorders of the cardiovascular, neurological and autoimmune systems. The **Apoptosis GO project** stemmed from a dual need: a thorough revision of existing terms, and an expansion of the ontology with new terms to fully capture up-to-date biological knowledge. Upon discussion with experts, we **revisited 183 existing terms and added 88 new ones**.



The top-level apoptosis ontology node has been split to better represent different apoptotic sub-processes, such as signaling phase, execution phase, changes occurring in the mitochondrion, etc.

The 'molecular function' ontology now contains terms to represent activity of **caspase** proteins acting at various steps.

- Synonym: **initiator caspase**
- Synonym: **effector caspase**
- Plant and fungal metacaspases

- ← cysteine-type peptidase activity
- ← cysteine-type endopeptidase activity
- ← calcium-dependent cysteine-type endopeptidase activity
- ← cysteine-type endopeptidase activity involved in apoptotic process
- ← cysteine-type endopeptidase activity involved in apoptotic signaling pathway
- ← cysteine-type endopeptidase activity involved in execution phase of apoptosis
- ← cysteine-type endopeptidase activity involved in plant-type hypersensitive response

The ontology work is being paralleled by a significant **annotation effort** to increase the breadth (number of gene products) and depth (granularity of the GO term) of apoptosis-related annotations. Initial annotation focused on human proteins involved in apoptosis and displaying protein-protein interactions.

Apoptosis ontology and annotation statistics, as of March 2013:

Publications manually curated during the annotation effort	86
Terms under "cell death" (GO:0008219)	382
Newly created / modified terms	271
Number of gene products manually annotated with any term under "cell death"	3000
Apoptosis-relevant newly annotated gene products	206
Number of manual annotations currently under "cell death" or its children	5442
Number of new manual annotations	682
Number of protein annotations potentially affected by the re-structuring (both manual and computational)	78980

This preliminary annotation effort allowed a **pilot enrichment analysis**. Results show that, following the Apoptosis GO project, **enriched terms are more informative due to added granularity**.

As part of the Apoptosis GO project, types of cell death other than apoptosis are also being considered, e.g. **necroptosis**.



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induction of apoptosis	regulation of execution phase of apoptosis
induction of programmed cell death	regulation of apoptotic process
apoptosis	regulation of cell death
programmed cell death	regulation of programmed cell death
activation of pro-apoptotic gene products	apoptotic signaling pathway
induction of apoptosis by intracellular signals	regulation of cysteine-type endopeptidase activity involved in apoptotic process
positive regulation of apoptosis	positive regulation of cysteine-type endopeptidase activity involved in apoptotic process
cell death	execution phase of apoptosis
positive regulation of programmed cell death	cellular component disassembly involved in execution phase of apoptosis
death	intrinsic apoptotic signaling pathway
positive regulation of cell death	activation of cysteine-type endopeptidase activity involved in apoptotic process
cellular process	extrinsic apoptotic signaling pathway
activation of caspase activity	apoptotic mitochondrial changes
positive regulation of caspase activity	cell-type specific apoptotic process
induction of apoptosis by extracellular signals	extrinsic apoptotic signaling pathway via death domain receptors
regulation of apoptosis	release of cytochrome c from mitochondria
regulation of programmed cell death	glial cell apoptotic process
regulation of cell death	neuron apoptotic process
regulation of caspase activity	neuron death
cellular component disassembly involved in apoptosis	apoptotic DNA fragmentation

Further plans to increase number of apoptosis-related annotations, and to make the existing ones more specific, involve participation from other members of the GO Consortium. To aid in this wider annotation and re-curation effort, an **apoptosis curation manual** has been drafted and made available to curators.

See Poster n.134 by Pablo Porras Millán

The ultimate goal is to present the scientific community with a powerful resource to highlight cell death mechanisms altered in some conditions (e.g. cancer or drug treatment) and hopefully aid in discovering specific cell functions involved in apoptosis and cancer.

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