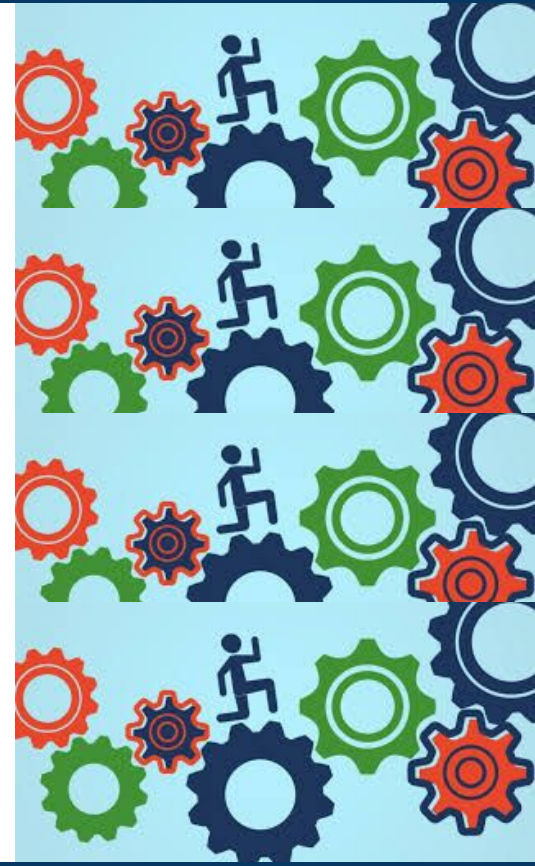




Extending the Gene Ontology for Biological Network Modeling

Pascale Gaudet
SIB Swiss Institute of Bioinformatics
GO Central

Gene Ontology Knowledgebase: Contents and optimization



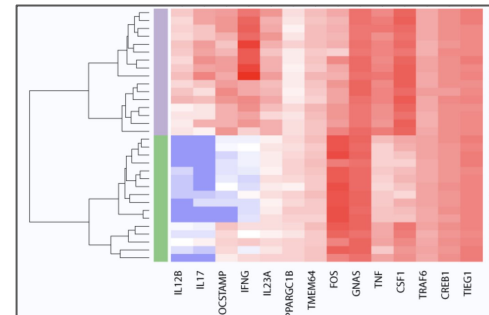
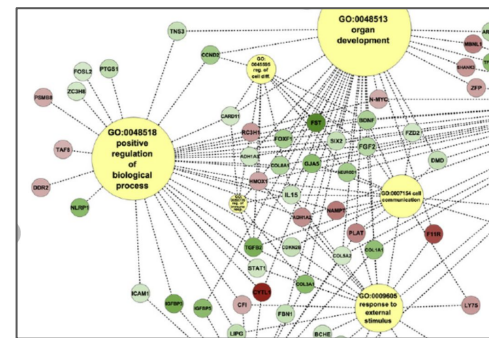
The Gene Ontology (GO)

Provides a computational model of **gene function** at every level:

- molecular activities
- signaling and metabolic pathways
- cellular organism-level systems

Consists of:

- 1) **ontology**: a framework to describe the biological concepts
- 2) **annotations**: associations between genes and GO terms



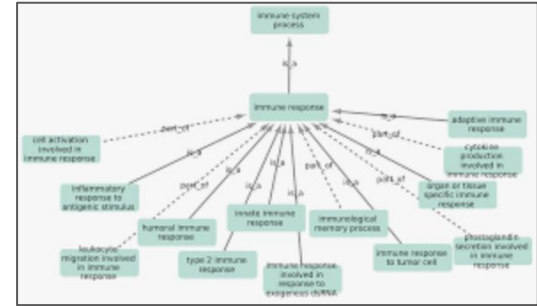
Current GO knowledgebase content

January 2026 release

Ontology

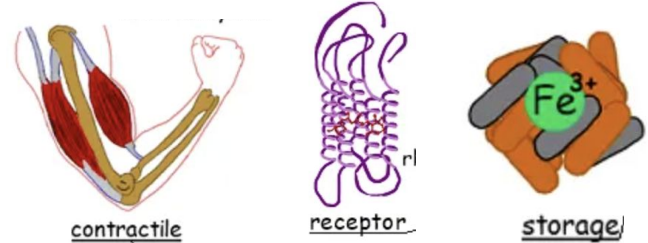
38,739 terms

- 24,547 BP
- 10,123 MF
- 4,069 CC



Annotations

- > 1 M annotations based on experimental data
- Millions of annotations by phylogenetic and electronic methods (800M in QuickGO/UniProt)



The 3 aspects of GO

Molecular Function (MF)

- **Biochemical activity** that a gene product performs
- Examples: enzymatic activity, adaptor activity, transcription factor activity

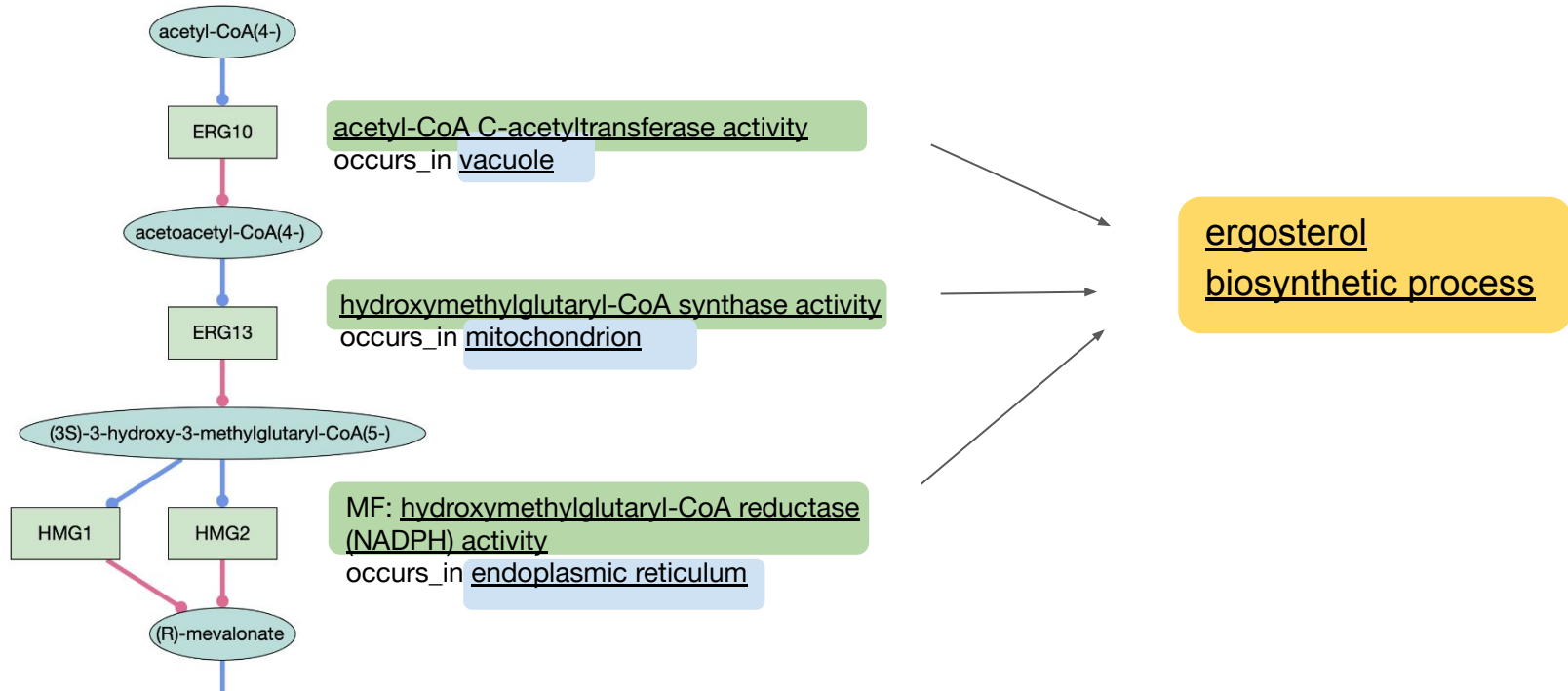
Cellular Component (CC)

- Cellular location where a gene product performs its activity (MF)
- Example: nucleus, cytoskeleton, ribosome

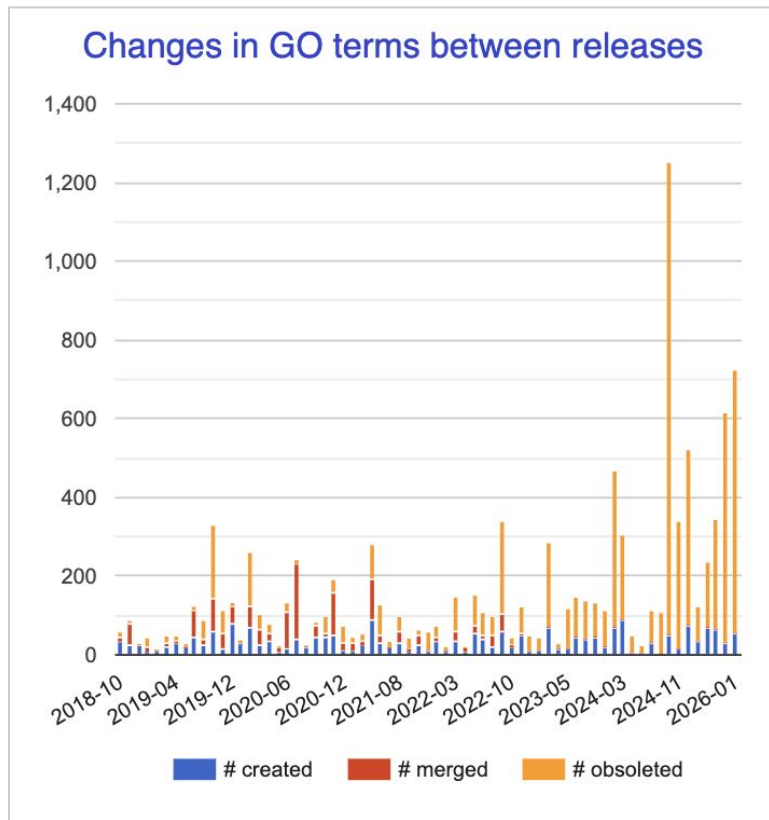
Biological Process (BP)

- Series of events making up a **biological module or program**, accomplished by a specific set of molecular functions, in a specific order
- Examples: glycolysis, transcription, photosynthesis

Example: function, component and process



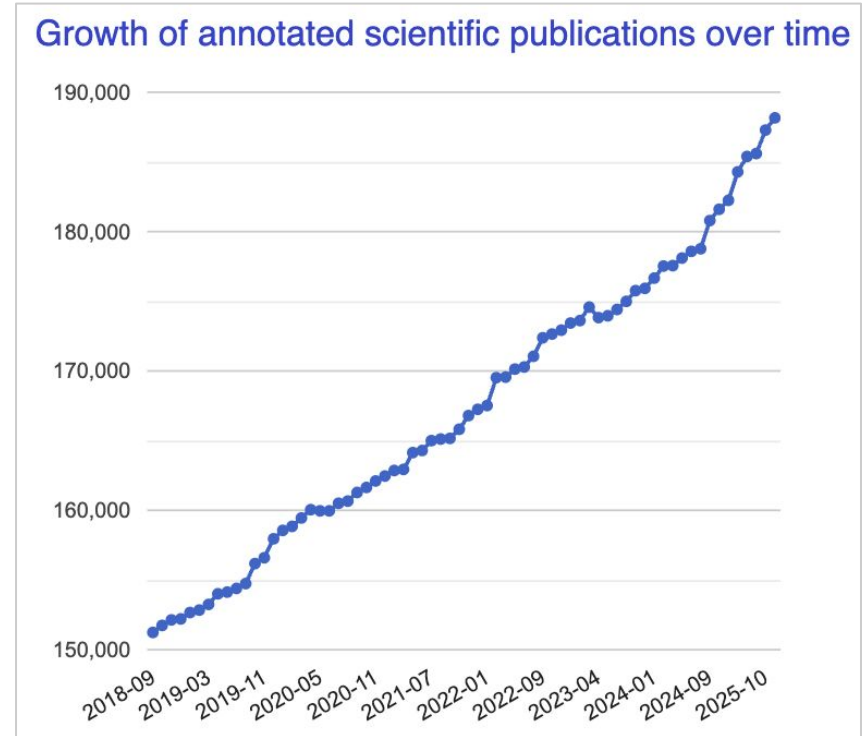
GO is dynamic



- GO aims to represent the current state of knowledge in biology
- Constantly revised as knowledge evolves
- Most change requests come from biocurators when annotating papers
- Large refactorings are made collaboratively with domain experts in particular areas of biology

Annotations are added and removed to represent current state of knowledge

- A GO annotation is a statement that links a gene product and a GO term
- These are linked via relations from the Relations Ontology
- GO aims to represent the **current state of knowledge** in biology, hence it is constantly revised and expanded as biological knowledge accumulates





















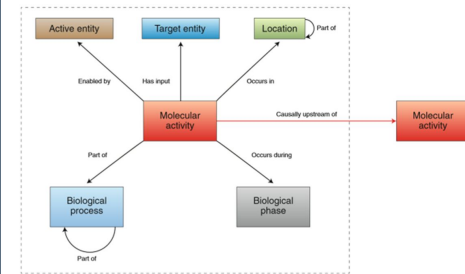
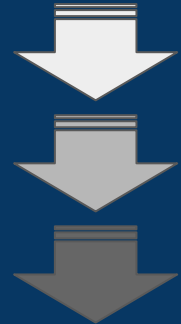
GO annotations

- Each gene can have any number of annotations to represent:
 - its function(s) and substrates
 - the cellular locations where it is active
 - the roles it plays in any process
 - each paper and evidence
- Both a feature and a limitation



Representing the complexity of biology: from lists to models

Gene Product	Symbol	Qualifier	GO Term	Evidence	Reference
UniProtKB:P42987	DRP1A	acts_upstream_of_or_within	GO:0009181   cytokinesis by cell plate formation	ECO:0000316  KGI	PMID:12671086
UniProtKB:P42987	DRP1A	acts_upstream_of_or_within	GO:0009789   embryo development ending in seed dormancy	ECO:0000316  KGI	PMID:12671086
UniProtKB:P42987	DRP1A	acts_upstream_of_or_within	GO:0009005   cell plate formation involved in plant-type cell wall biogenesis	ECO:0000316  KGI	PMID:12671086
UniProtKB:P42987	DRP1A	acts_upstream_of_or_within	GO:0105011   xylem and phloem pattern formation	ECO:0000315  BAP	PMID:15925323
UniProtKB:P42987	DRP1A	acts_upstream_of_or_within	GO:0105011   trichome branching	ECO:0000315  BAP	PMID:12671086
UniProtKB:P42987	DRP1A	acts_upstream_of_or_within	GO:0046786   root hair initiation	ECO:0000315  BAP	PMID:27251533



From function to GO annotation

P46934 · NEDD4_HUMAN

Proteinⁱ | E3 ubiquitin-protein ligase NEDD4

Geneⁱ | NEDD4



Molecular activity

Functionⁱ

E3 ubiquitin-protein ligase which accepts ubiquitin from an E2 ubiquitin-conjugating enzyme in the form of a thioester and then directly transfers the ubiquitin to targeted substrates. Specifically ubiquitinates 'Lys-63' in target proteins (PubMed:[19920177](#), PubMed:[21399620](#), PubMed:[23644597](#)).

Involved in the pathway leading to the degradation of VEGFR-2/KDR, independently of its ubiquitin-ligase activity. Monoubiquitinates IGF1R at multiple sites, thus leading to receptor internalization and degradation in lysosomes (By similarity).

Many substrates with roles in various cellular processes

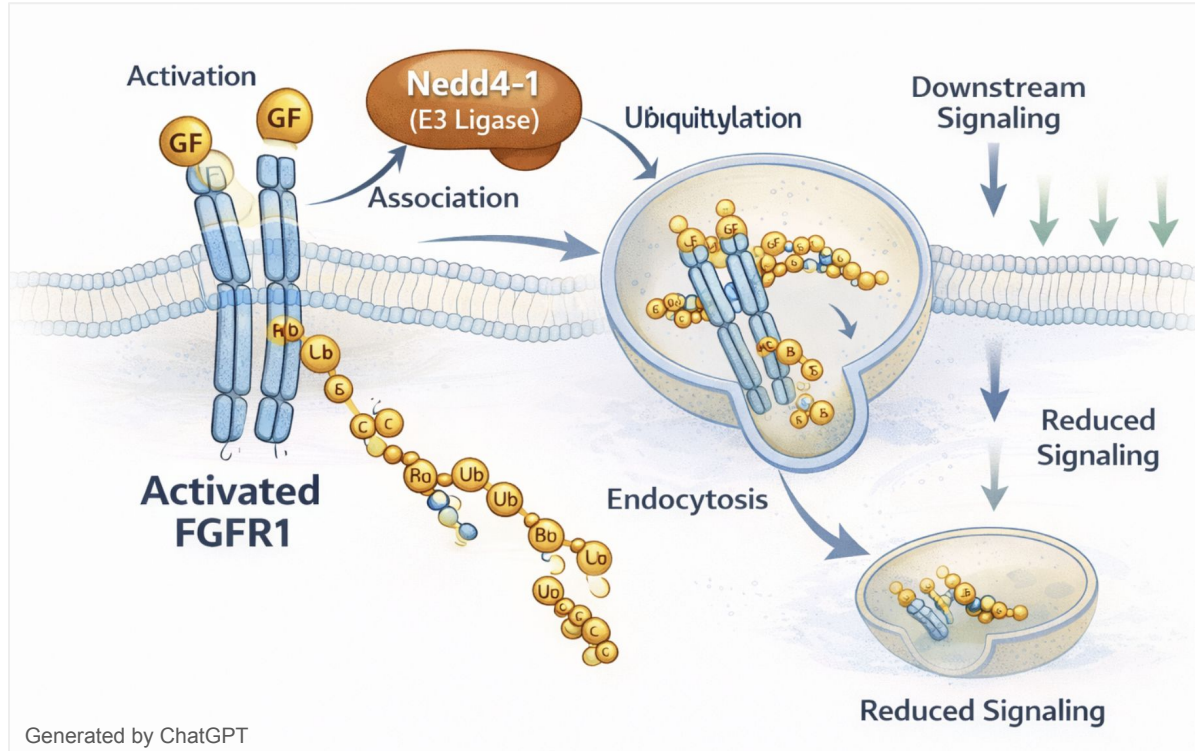
Ubiquitinates TNK2 and regulates EGF-induced degradation of EGFR and TNF2 (PubMed:[20086093](#)).

Ubiquitinates BRAT1 and this ubiquitination is enhanced in the presence of NDFIP1 (PubMed:[25631046](#)).

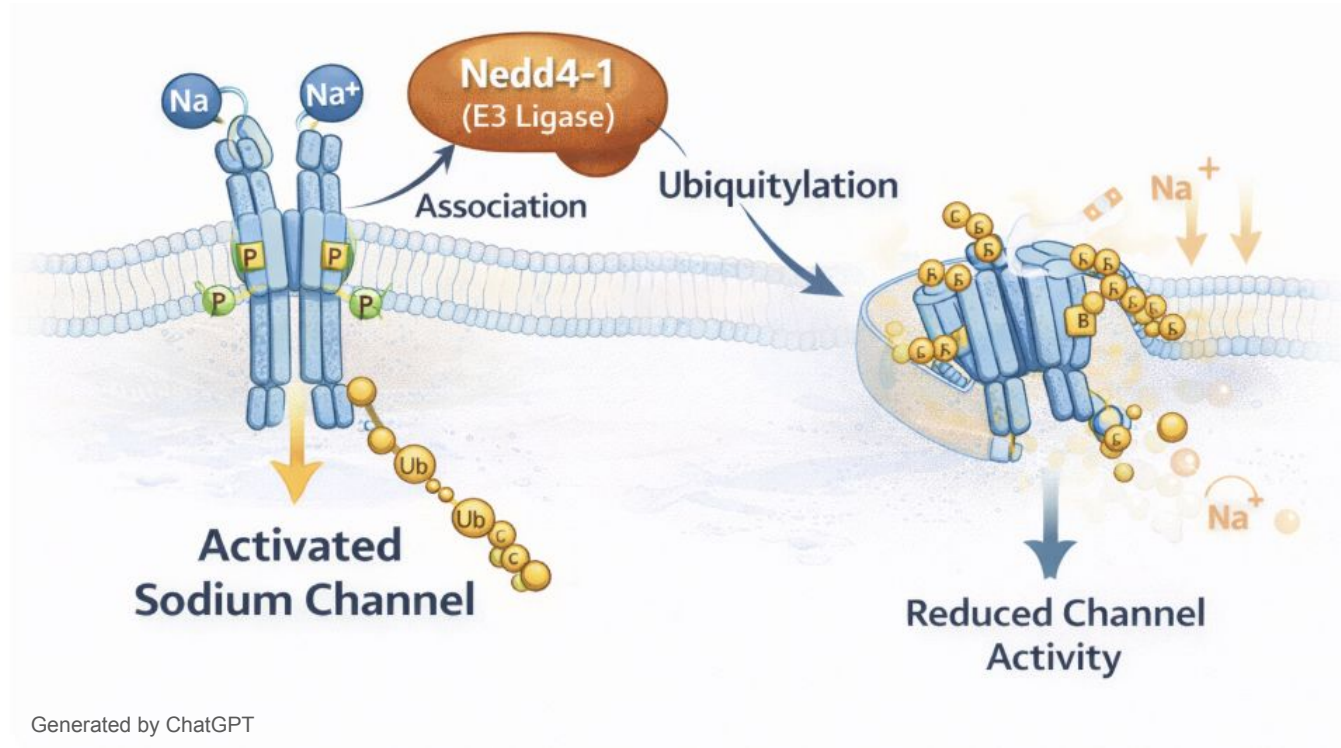
Ubiquitinates DAZAP2, leading to its proteasomal degradation (PubMed:[11342538](#)).

Ubiquitinates POLR2A (PubMed:[19920177](#)).

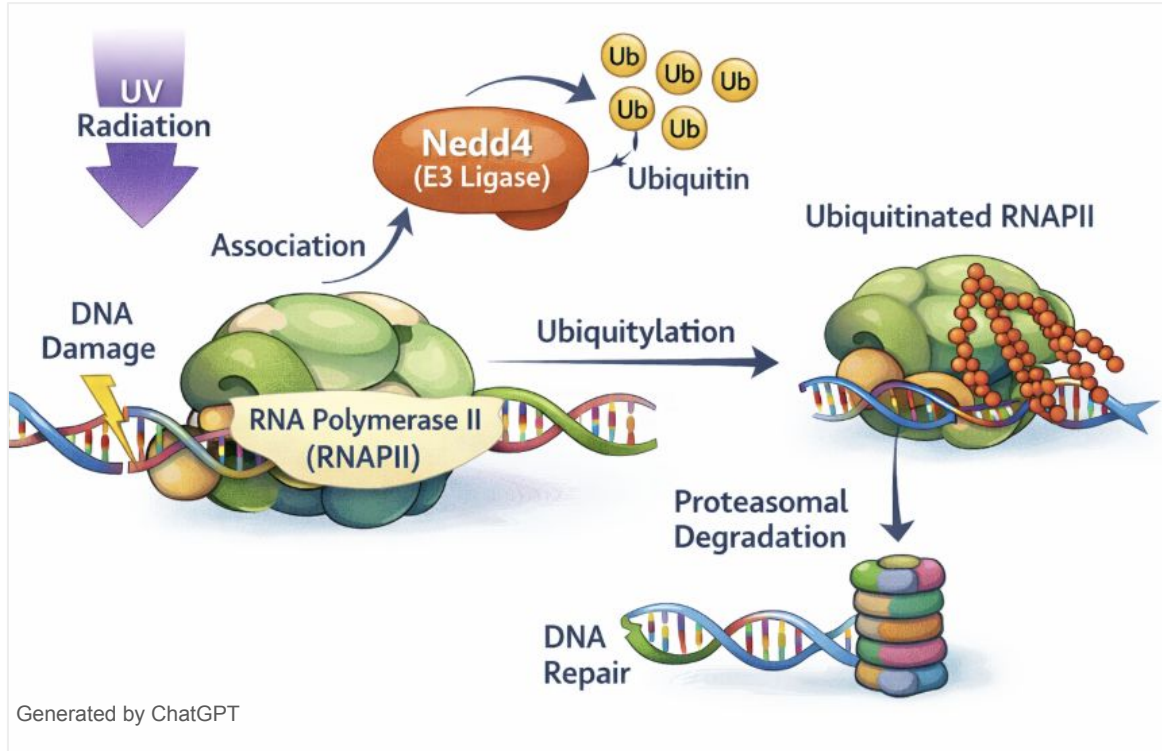
NEDD4 downregulates FGFR1 signaling



NEDD4 downregulates Na^{2+} channels



NEDD4 inhibits gene transcription in the presence of DNA damage



Standard annotations are unconnected and lack context

Molecular Function

- ubiquitin-protein ligase activity
- sodium channel inhibitor activity
- RNA polymerase binding
- fibroblast growth factor binding

Cellular Component

- cytosol
- plasma membrane
- nucleus

Biological Process

- ubiquitin-dependent protein catabolic process
- positive regulation of endocytosis
- negative regulation of sodium ion transport
- cellular response to UV
- negative regulation of transcription from RNA polymerase II promoter
- negative regulation of fibroblast growth factor receptor signaling pathway



















Dissecting the biology

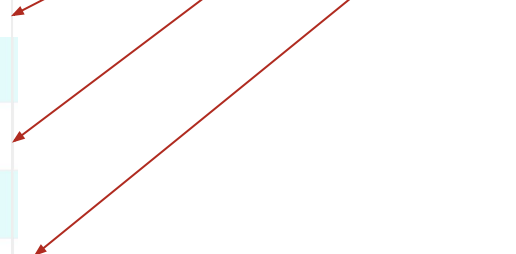
Molecular function (33 annotations + 75 'protein binding')

substrates

UniProtKB:P46934	NEDD4	enables	GO:0061630    ubiquitin protein ligase activity	ECO:0000314  IDA	PMID:17116753	9606 Homo sapiens	ARUK-UCL	has_input (UniProtKB:Q9NZ52)
UniProtKB:P46934	NEDD4	enables	GO:0061630    ubiquitin protein ligase activity	ECO:0000314  IDA	PMID:17996703	9606 Homo sapiens	BHF-UCL	part_of (GO:0000122) more...
UniProtKB:P46934	NEDD4	enables	GO:0061630    ubiquitin protein ligase activity	ECO:0000314  IDA	PMID:20086093	9606 Homo sapiens	BHF-UCL	has_input (UniProtKB:Q07912)
UniProtKB:P46934	NEDD4	enables	GO:0061630    ubiquitin protein ligase activity	ECO:0000314  IDA	PMID:26006083	9606 Homo sapiens	ARUK-UCL	has_input (UniProtKB:P08183) more...
UniProtKB:P46934	NEDD4	enables	GO:0061630    ubiquitin protein ligase activity	ECO:0000314  IDA	PMID:34880843	9606 Homo sapiens	UniProt	has_input (UniProtKB:Q7Z434) more...

Biological process (52 annotations)

UniProtKB:P46934	NEDD4	involved_in	GO:0000122    negative regulation of transcription by RNA polymerase II
UniProtKB:P46934	NEDD4	involved_in	GO:0006511    ubiquitin-dependent protein catabolic process
UniProtKB:P46934	NEDD4	involved_in	GO:0006974    DNA damage response
UniProtKB:P46934	NEDD4	involved_in	GO:0007041    lysosomal transport
UniProtKB:P46934	NEDD4	involved_in	GO:0010766    negative regulation of sodium ion transport
UniProtKB:P46934	NEDD4	involved_in	GO:0016567    protein ubiquitination



Early 2000's solution: Precomposition

Precomposed terms aimed to provide more expressive terms

cellular response to UV + negative regulation of transcription
from RNA polymerase II promoter

=

negative regulation of transcription from RNA polymerase II
promoter in response to UV-induced DNA damage

Examples obsolete pre-composed terms

- regulation of planar cell polarity pathway involved in axis elongation
- regulation of transcription involved in G1/S transition of mitotic cell cycle
- cell morphogenesis involved in differentiation
- regulation of the force of heart contraction involved in baroreceptor response to decreased systemic arterial blood pressure
- regulation of cytosolic calcium ion concentration involved in phospholipase C-activating G protein-coupled signaling pathway

Precomposition

cellular response to UV + negative regulation of transcription
from RNA polymerase II promoter

- Combinatorially unmanageable
- Complexity in the ontology leads to errors and inconsistencies
- Most have already been obsoleted

cellular response to UV-induced DNA damage
negative regulation of transcription from RNA polymerase II promoter

Annotation extensions

- AE provide additional context for annotations by linking MF, BP, CC annotations, as well as inputs/substrates, cell types and anatomical structures

<input type="checkbox"/> Gene/product	Gene/product name	Annotation qualifier	GO class (direct)	Annotation extension
<input type="checkbox"/> NEDD4	E3 ubiquitin-protein ligase NEDD4		ubiquitin protein ligase activity	part of negative regulation of transcription by RNA polymerase II part of DNA damage response

Annotation extensions

- AE provide additional context for annotations
- Limited scope because extensions are not easily exploitable by GO tools
- Not amenable to pathway-like representation

Annotation extensions \neq pathways

<input type="checkbox"/> Gene/product	Gene/product name	Annotation qualifier	GO class (direct)	Annotation extension
<input type="checkbox"/> NEDD4	E3 ubiquitin-protein ligase NEDD4		ubiquitin protein ligase activity	part of negative regulation of transcription by RNA polymerase II part of DNA damage response

allowed extension

negatively regulates RNA polymerase activity

disallowed extension
(logic too complex for format)

negatively regulates RNA polymerase activity of **POL2A**

GO causal activity models (GO-CAMs)

Provides a system to extend GO annotations

✓ provides context

- CC: in which cellular component, cell, tissue the function/process take place
- MF: capture substrates
- BP: which BP is a MF part of
- BPs can also be part of broader BPs

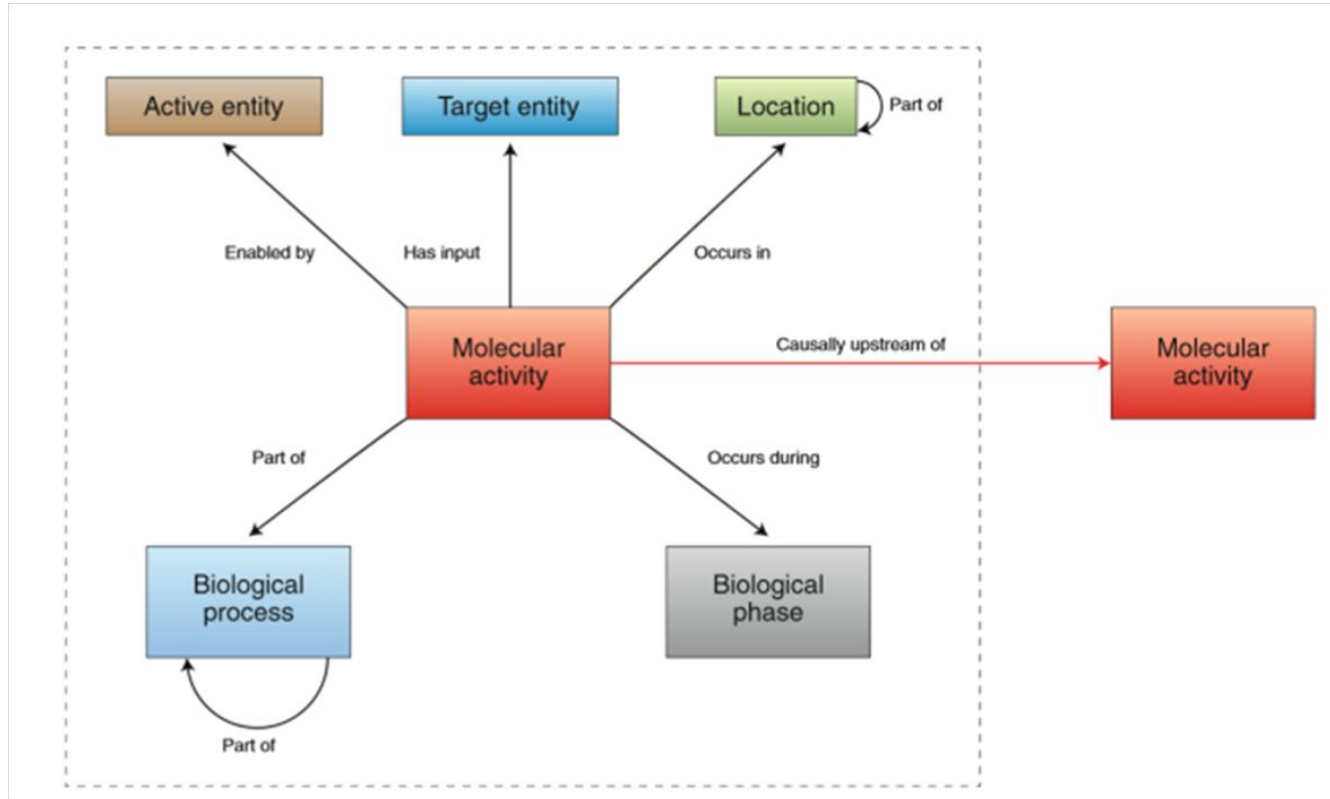
✓ defines causal connections between activities (MFs)

- allows network representation
- enables pathway visualization & analysis

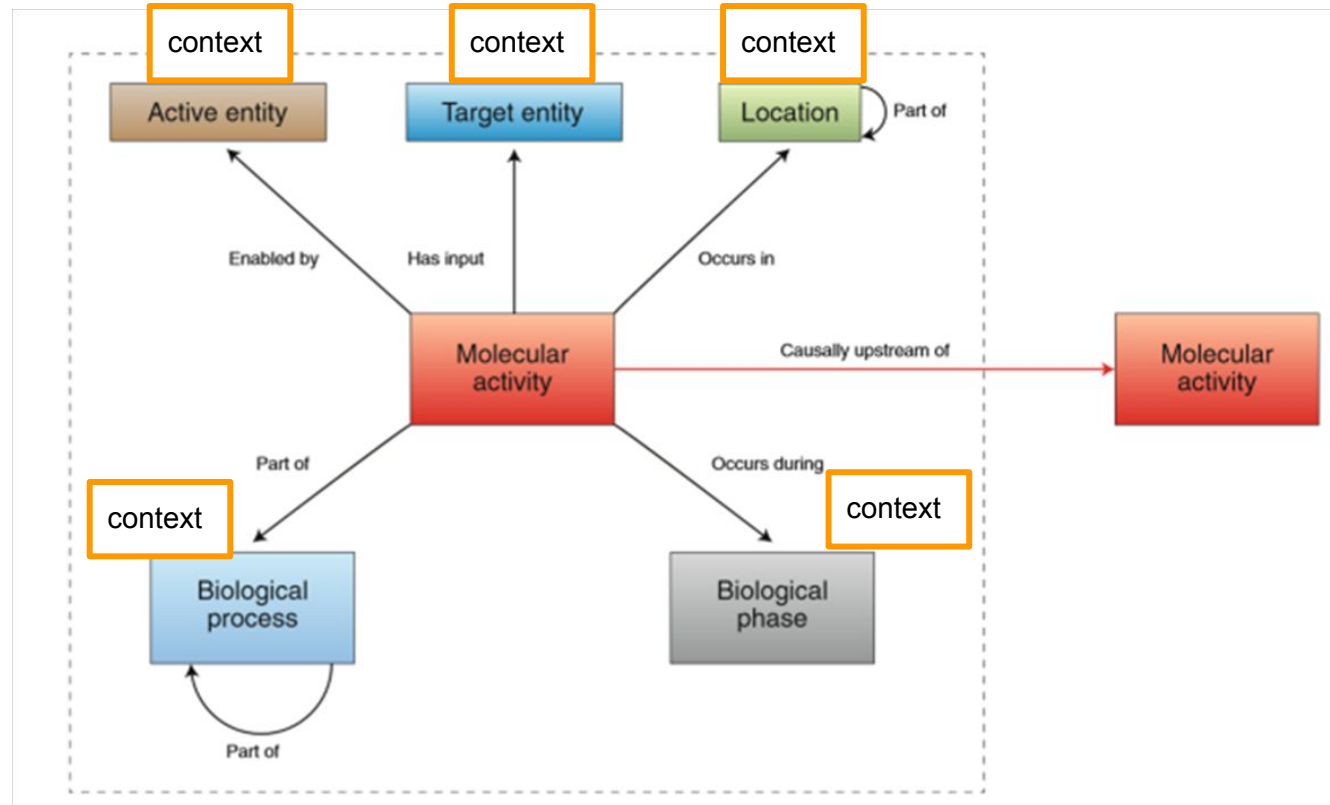
Published in Thomas & al, [Nat Genet. 2019](#)

See also [GO documentation](#)

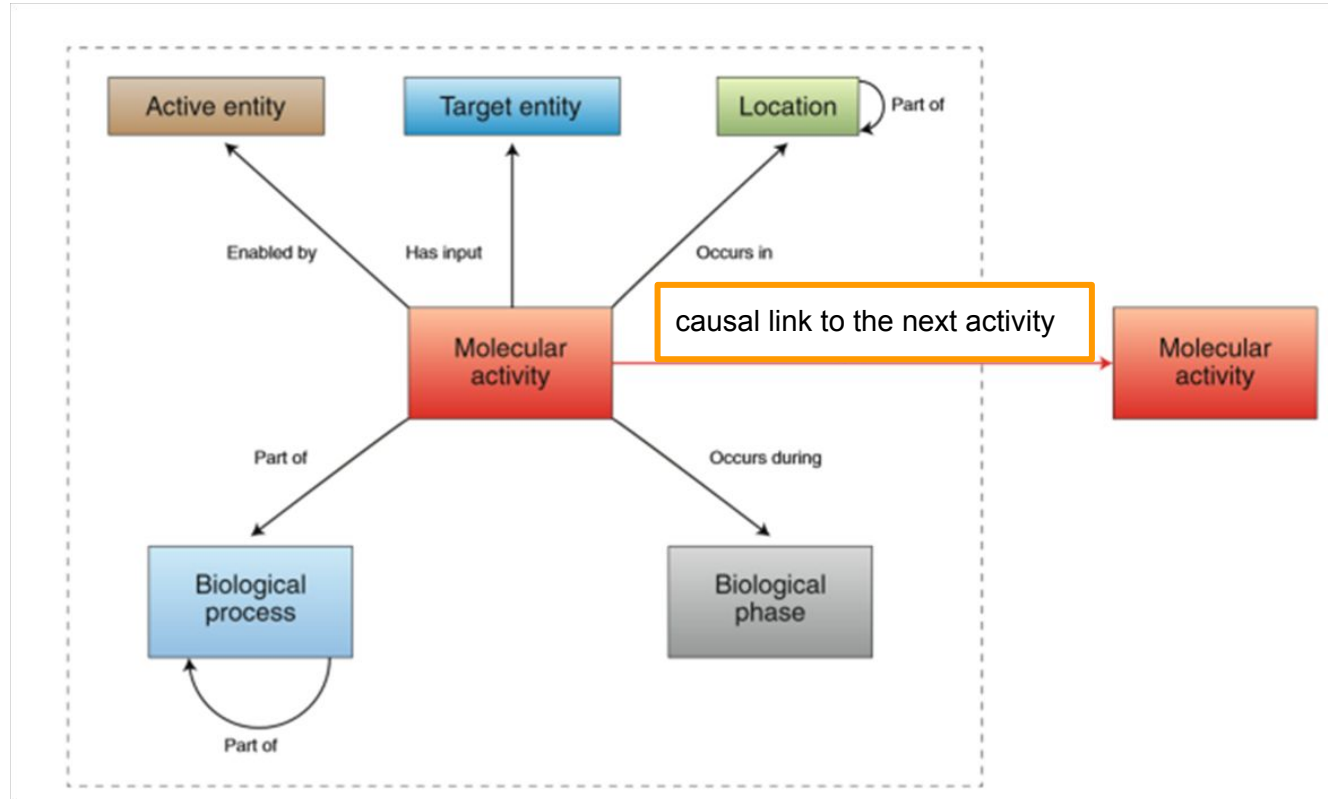
GO-CAM model specifications



GO-CAM model specifications



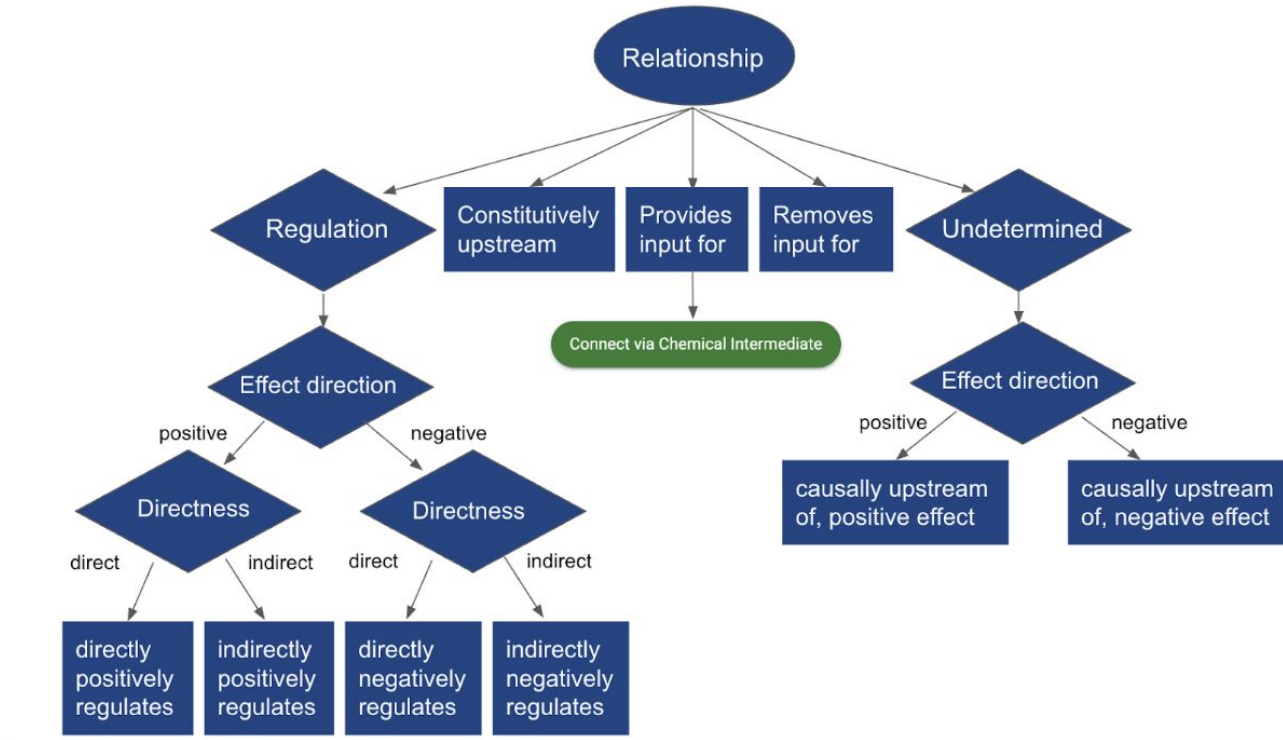
GO-CAM model specifications



Causal relations

- Link a MF to a MF
- Can be positive or negative

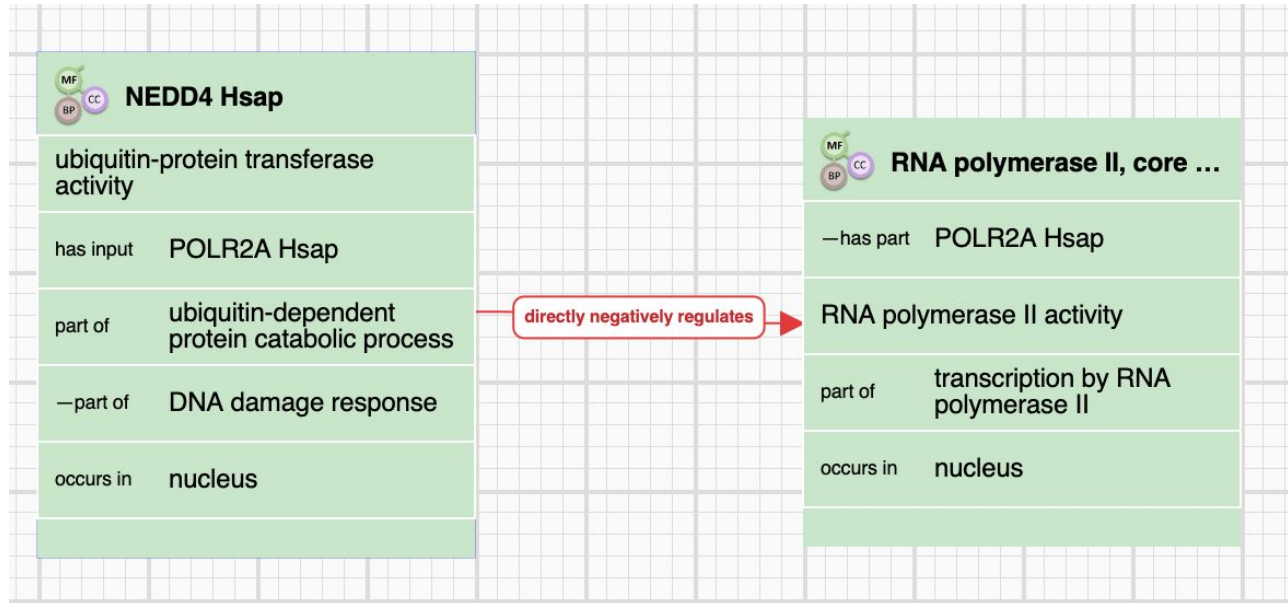
GO-CAM causal relations



See also the [Noctua User Guide](#)

directly negatively regulates	Links two activities when the upstream activity has a negative causal effect (decreasing or inhibiting) on an immediately downstream activity. Immediately means there is no intervening activity. The mechanism by which the upstream activity controls the downstream activity must be known.
directly positively regulates	Links two activities when the upstream activity has a positive causal effect (increasing or activating) on an immediately downstream activity.
indirectly negatively regulates	Links two activities when the upstream activity has a negative regulatory effect (decreasing or inhibiting) on the downstream activity via a larger process (e.g. proteasome-mediated protein degradation) that is reused in many contexts and the curator does not want to reproduce that process in the GO-CAM. The mechanism by which the upstream activity controls the downstream activity must be known.
indirectly positively regulates	Links two activities when the upstream activity has a positive regulatory effect (increasing or activating) on the downstream activity via a larger process (e.g. transcription) that is reused in many contexts and the curator does not want to reproduce that process in the GO-CAM. The mechanism by which the upstream activity controls the downstream activity must be known.
provides input for	Links two successive activities when the product (output) of the upstream activity is the substrate (input) for the downstream activity, and the product is a macromolecule (i.e. DNA, RNA, protein).
removes input for	Links two activities when the upstream activity has a negative causal effect (decreasing or inhibiting) on the downstream activity and the two activities act on or modify the same molecular target at the same site(s).
constitutively upstream of	Links two activities when the upstream activity is required for the downstream activity, but does not regulate the downstream activity.
causally upstream of, negative effect	Links two activities when the upstream activity has a negative causal effect (decreasing or inhibiting) on the downstream activity but the mechanism is not known.
causally upstream of, positive effect	Links two activities when the upstream activity has a positive causal effect (increasing or activating) on the downstream activity but the mechanism is not known.

GO-CAM model view fo regulation of RNA polymerase by NEDD4



GO-CAM impact on the ontology

Ontology refactoring

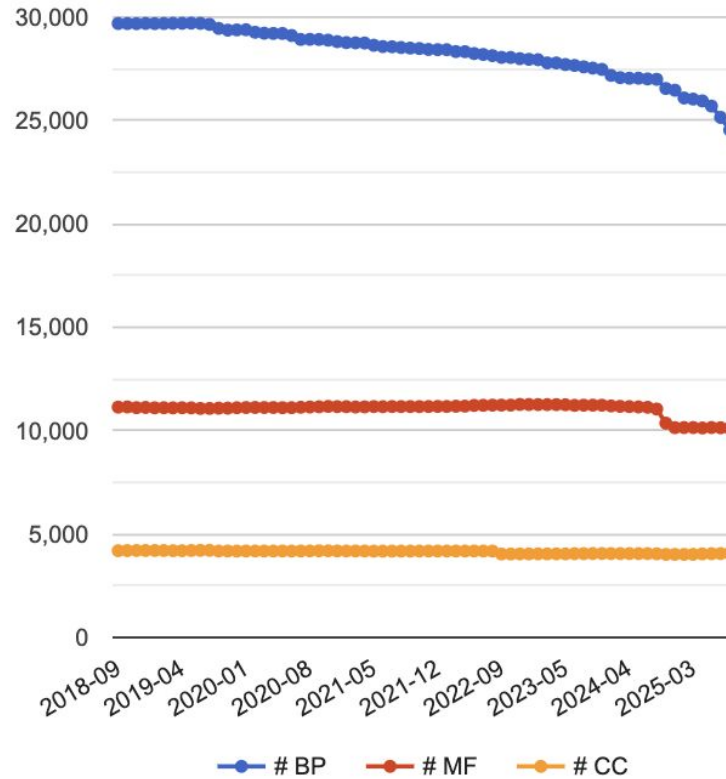
Started a major ontology refactor in 2019 to address issues caused by old ontology practices

- Proactive introduction of terms to anticipate potential curator needs (but never used)
- Excessive intermediate-level grouping terms
- Precomposed terms
- Single step reactions in the BP aspect of the ontology
- Terms that refer to more than one ontological aspect
- Experimental assays and non-physiological substrates

Examples obsoleted terms

Reason for obsoletion	Examples
Phenotype of perturbation experiments	<i>negative regulation of necrotic cell death</i> (GO:0060547)
BP terms that represent a MF	<i>histone H2A acetylation</i> (GO:0043968)
Pre-composed terms that are now represented by GO-CAMs	<i>histone H4 acetylation involved in response to DNA damage stimulus</i> (GO:2000776)
Sub-reaction and reaction mechanisms	<i>formation of peptidyl-cystine persulfide by sulphur transfer from free cysteine</i> (GO:0044526)
Substrates beyond the specificity of known enzymes or not physiologically relevant	<i>4,4'-diapophytoene desaturase</i> (4,4'-diapolycopene-forming) (GO:0140868)

Number of GO terms by aspect



WELCOME TO NOCTUA

Noctua is a web-based, collaborative Gene Ontology (GO) annotation tool developed by the GO Consortium to create standard GO annotations as well as GO-CAMs (Gene Ontology Causal Activity Models).

Noctua allows to view, create and edit GO annotations

Noctua



Help

Pascale Gaudet
GO Central



Filter by

Clear

Annotations

☐ Exact Term

Filter by Any Ontology Term

Filter by Obsolete GO Term

Filter by Gene Product

Filter by Chemical

Filter by Reference



Filter by Organism

Contributor

Filter by Contributor

Filter by Group

Date last modified

☐ Date Range

WELCOME TO NOCTUA

Noctua is a web-based, collaborative Gene Ontology (GO) annotation tool developed by the GO Consortium to create standard GO annotations as well as GO-CAMs (Gene Ontology Causal Activity Models).

CREATE

STANDARD ANNOTATIONS
EDITOR

GO-CAM VISUAL PATHWAY
EDITOR

HELP

USER GUIDE

Filtered By:

Results: 54720



GO CAMs per page: 50

1 - 50 of 54720



Title	Saved	State	Date Modified	Contributors
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Vesicle fusion in cytotoxic T cell degranulation (Human)



Production

2026-02-04

LB Lionel Breuza

Actions

CD36 transport to the plasma membrane for muscle regeneration (Human)



Production

2026-02-04

LB Lionel Breuza

Actions

NMDAR-triggered AMPAR recruitment to AP2/PICK1 machinery enables clathrin-mediated endocytosis and LTD



Development

2026-02-04

JB Job Berkhout

Actions

Two main workbenches

Standard Annotations Editor (SAE)

GENE PRODUCT	RELATIONSHIP	TERM *	EVIDENCE	REFERENCE	WITH	EXTENSION	DATE MODIFIED
STXBP2 Hsap UniProtKB:Q15833	enables	protein-macromolecule adaptor activity GO:0030674	direct assay evidence used in manual assertion ECO:0000314	PMID:28265073		has input SNARE complex GO:0031201 occurs in immunological synapse GO:0001772 part of SNARE complex assembly GO:0035493	Feb 4, 2026
SNARE complex GO:0031201	enables	fusogenic activity GO:0140522	direct assay evidence used in manual assertion ECO:0000314	PMID:28265073		occurs in immunological synapse GO:0001772 part of vesicle fusion GO:0006906	Feb 4, 2026

Visual Pathway Editor (VPE)

Title: Vesicle fusion in cytotoxic T cell ... ✎ 🗨 📄 🔄 Production

TOOLBOX Automatic Layout Layout Detail : Default Spacing

ACTIVITY UNIT

PROTEIN COMPLEX

CHEMICAL

STXBP2 Hsap

protein-macromolecule adaptor activity

- has input SNARE complex
- part of SNARE complex assembly
- part of cytotoxic T cell degranulation
- occurs in immunological synapse
- part of cytotoxic T cell

directly positively regulates

SNARE complex

- has part SNAP23 Hsap
- has part STX11 Hsap
- has part VAMP8 Hsap

fusogenic activity


- part of vesicle fusion
- part of cytotoxic T cell degranulation
- occurs in immunological synapse
- part of cytotoxic T cell

Standard Annotations Editor - creating annotations

☐ NOT

Gene Product	GP to Term Relation ▼	GO Term	⋮
--------------	-----------------------	---------	---

Evidence

Evidence	Reference 	With/From
----------	---	-----------

Extensions

Add Extension

Comments

Add Comment

Clear

Save

Visual Pathway Editor - new annotation

Left Sidebar:

- ACTIVITY UNIT (MF, BP, CC)
- PROTEIN COMPLEX (GP, GP)
- CHEMICAL (hexagon)

Main Workspace:

- STXBP2 Hsap** (protein, molecule, adaptor, activity)
 - has input SNARE complex
 - part of SNARE complex assembly
 - part of cytotoxic T cell degranulation
 - occurs in immunological synapse
 - part of cytotoxic T cell
- SNARE complex**
 - has part SNAP23 Hsap
 - has part STX11 Hsap
 - has part VAMP8 Hsap
 - fusogenic activity
 - part of vesicle fusion
 - part of cytotoxic T cell degranulation
 - occurs in immunological synapse
 - part of cytotoxic T cell

Activity Unit Form

Close

Gene Product

enabled by (GP)

Function Description

Molecular Function	Evidence	Reference	With	
(MF) part of (BP)	Evidence	Reference	With	
(MF) occurs in (CC)	Evidence	Reference	With	

GO-CAM status

- ~ 2,000 models ('production')
- > 10,000 distinct genes
- 5 major contributing groups: UniProt, PomBase, FlyBase, SGD, MGI

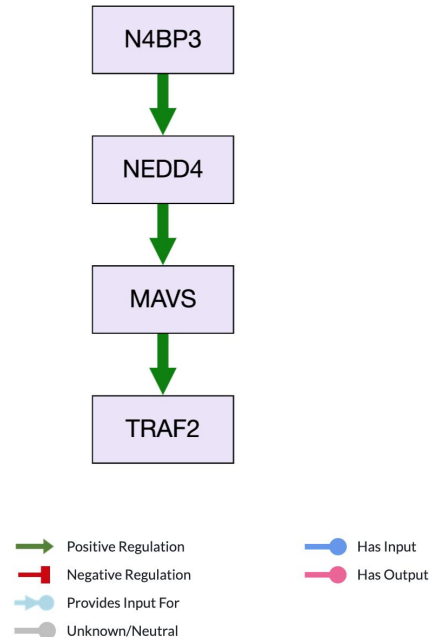
GO-CAM model availability

- GO-CAM model in OWL-type formats (ttl)
- conversion to standard annotations, with extensions if appropriate


<input type="checkbox"/> Gene/product	Gene/product name	Annotation qualifier	GO class (direct)	Annotation extension
<input type="checkbox"/> NEDD4	E3 ubiquitin-protein ligase NEDD4		ubiquitin protein ligase activity	part of negative regulation of transcription by RNA polymerase II part of DNA damage response

GO-CAM Pathway Viewer widget

- Widget can be embedded in any website
- Available in AmiGO, Alliance of Genomes, UniProt, PomBase, FlyBase



GO-CAMs are also available at NDEx

v2.5.8

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Login/Register

Latest Networks

Featured Networks

Search Examples

Search for networks, users, and groups

☐ Perform Search Term Expansion (Genes and Proteins only)

Featured Content

NDEx IQuery: a multi-method network gene set analysis leveraging the Network Data Exchange

NDEx IQuery is a new web tool for network and pathway-based gene set interpretation

NDEx Integrated Query

Powered by NDEx and integrated with Cytoscape, IQuery uses selected pathway and a variety of interactome networks to power gene set analysis. The networks come from many different sources and new networks will be continuously added.

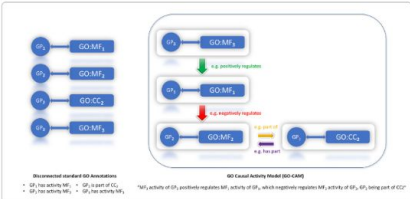
By doing many simultaneous queries, we present the biologist with a Google-like experience and immediate actionable results; any IQuery hit can be seamlessly opened in Cytoscape for additional analysis or saved to NDEx for later use. Alternatively, users can explore the master networks that originated those results and perform additional queries or other operations.

Enter your gene set here...

Examples: [Death Receptors](#) [PTC](#) [Beta Cell](#)

Enter your gene set in the text box above or use one of the

GO-Causal Activity Models



GO-Causal Activity Models (GO-CAMs) use a defined "grammar" for linking multiple GO annotations into larger models of biological function (such as "pathways") in a semantically structured manner. GO-CAMs are created by expert biocurators from the GO Consortium, using the Noctua Curation Platform. GO-CAMs can be used as "pathway diagrams" that can be browsed and visualized, as full GO-CAM graphs that can be downloaded or as "reduced" pairwise GO annotations, included in the GO annotation files for backward compatibility with the broader GO communities. Human GO-CAMs are available in NDEx

<https://www.ndexbio.org>

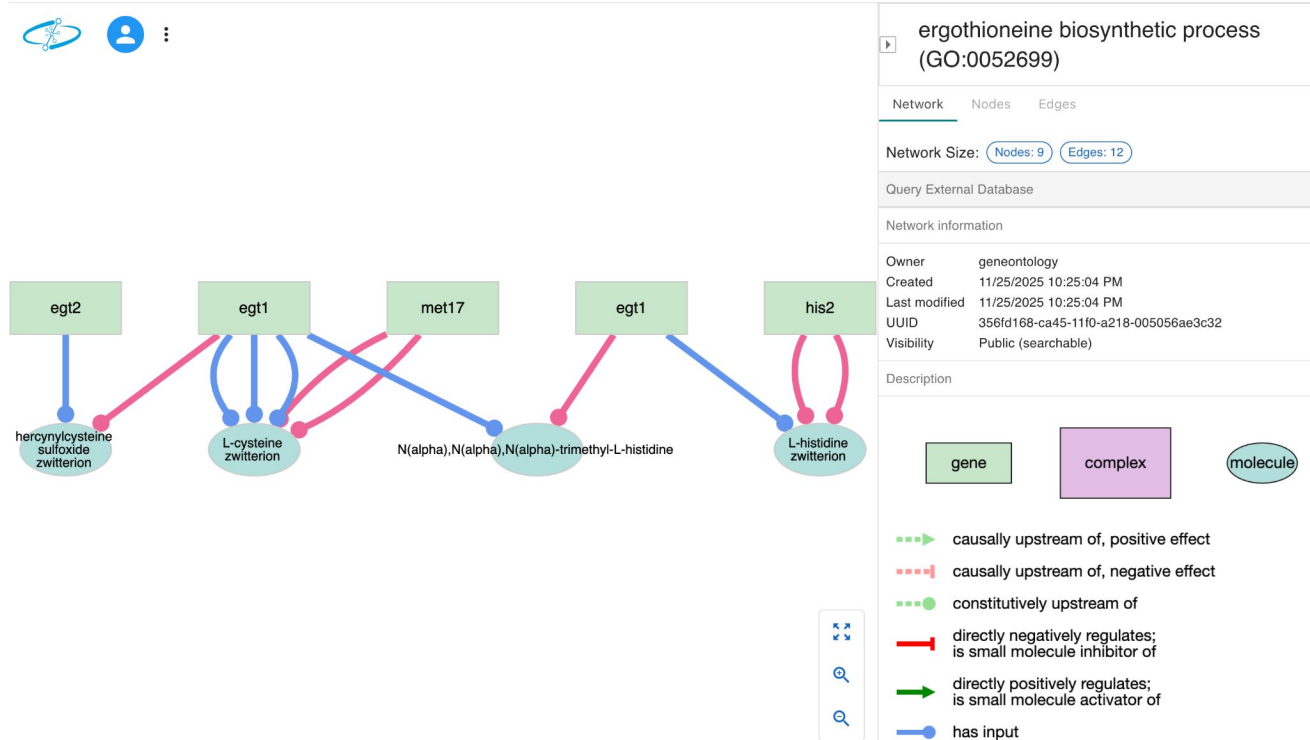
"The NDEx Project provides an open-source framework where scientists and organizations can store, share, manipulate, and publish biological network knowledge."

can help researchers understand the interplay among these genes, and explore the different biological processes they participate in to enable hypothesis generation and drive experimental validation.


However, LLMs can make mistakes, so we recommend users to perform their due diligence and always verify the results.



For additional information, GSAI is described and

NDEx GO-CAM pathway viewer




NDEx IQuery


 NDEx Integrated Query

Powered by
 

One search finds a variety of pathways and interaction networks relevant to your set of genes. Powered by **NDEx** and integrated with **Cytoscape**.



NDEx Integrated Query
v1.4

 Enter gene list (or click an example below)

Query gene set examples:

[PANCREATIC BETA CELL](#) [DEATH RECEPTORS](#) [COMPLEMENT](#)

Send us [feedback](#).

NDEx Integrated Query uses selected pathway and interactome networks in NDEx to power gene set analysis. The networks come from many different sources and new networks will be continuously added. Do you have a pathway

<https://www.ndexbio.org/iquery>

IQuery provides a form of gene set enrichment analysis by indexing certain NDEx network sets and allowing users to find networks by searching over Human gene sets

NDEx IQuery tests pathway representation for lists of genes

NDEx Integrated Query

APAF1 BCL2 BID BIRC2 BIRC3 CASP10 CASP3 CASP6 CASP7 CFLAR CHUK DFFA DFFB FADD GAS2

Powered by NDEx

CURATED PATHWAYS PATHWAY FIGURES INDRA GO CANCER CELL MAP INITIATIVE **GO-CAMS** INTERACTOMES

Sort by ☐ Similarity ☒ p-Value ☐ Overlap

GO-CAMS: Involvement of CASP7 in apoptosis, its acti...

Involvement of CASP7 in apoptosis, its activation by initiator caspases (CASP8, CASP9 and CASP10) and regulation by XIAP and PAK2 (Human)
3 / 6 unique genes Similarity: 0.32 p-Value: **8.95e-4**

CASP10	CASP7	XIAP	APAF1
BCL2	BID	BIRC2	BIRC3
CASP3	CASP6	CFLAR	CHUK
DFFA	DFFB	FADD	GAS2
LMNA	MAP3K14	NFKB1	RELA
RIPK1	SPTAN1	TNFRSF25	TNFSF10
TRADD	TRAF2		

Poxvirus-CRMB inhibition of TNF signaling pathway (Human-Poxvirus)
3 / 5 unique genes Similarity: 0.33 p-Value: **8.95e-4**
FADD TRADD TRAF2

TRAIL/TRAILR1 interaction leading to apoptosis
3 / 6 unique genes Similarity: 0.33 p-Value: **8.95e-4**
FADD TNFSF10 TRADD

TRAIL/TRAILR2 interaction leading to apoptosis
3 / 5 unique genes Similarity: 0.36 p-Value: **8.95e-4**
FADD TNFSF10 TRADD

TRAF7 modulation of NF-kappa-B via IKBKG and NEMO K-29 ubiquitination (Human)
3 / 7 unique genes Similarity: 0.23 p-Value: **1.23e-3**
CHUK NFKB1 RELA

Cleavage and inactivation of PARP1 by CASP3 and/or CASP7 during the execution phase of apoptosis (Human)

```
graph TD; CASP10 -- green --> CASP7; CASP8 -- green --> CASP7; CASP9 -- green --> CASP7; XIAP -- red --> CASP7; PAK2 -- red --> CASP9; style CASP7 stroke:#f08080,stroke-width:2px; style CASP10 stroke:#f08080,stroke-width:2px; style CASP8 stroke:#f08080,stroke-width:2px; style CASP9 stroke:#f08080,stroke-width:2px; style XIAP stroke:#f08080,stroke-width:2px; style PAK2 stroke:#f08080,stroke-width:2px;
```

- Query set: NDex 'Death receptor' test list
- Over-represented GO-CAMS show up on the left
- For each model, hits are highlighted

Exploring AI to enhance GO

GO tasks

- Ontology development
 - create new terms, obsolete terms
 - fix hierarchy to align with external resources (EC, RHEA, etc)
 - apply design patterns
- Annotation
 - add new annotation
 - remove incorrect annotations
 - annotation reviews
 - new GO-CAMs
 - review GO-CAMs
- QC

AI-generated annotation review

Gene Annotation Review Browser

GENE: APO1

REVIEW: [Review](#)

LINK: [Link](#)

ID: Q9XIR4

GENE PRODUCT TYPE: PROTEIN

REVIEW STATUS: COMPLETE

GO TERM: regulation of gene expression

GO ID: [GO:0010468](#)

EVIDENCE: IMP

PATHWAY: [Pathway](#)

ORIG REF: [PMID:21421812](#)

ORIG TITLE: APO1 promotes the splicing of chloroplast group II introns and harbors a plant-specific zinc-dependent RNA binding domain.

SUMMARY: Too general - should use more specific RNA processing term

ACTION: MODIFY

REASON: APO1 regulates gene expression through RNA splicing, not transcriptional regulation. The more specific term "chloroplast group II intron splicing" (GO:0000373) better captures the mechanism

REF TEXT: APO1 promotes the splicing of chloroplast group II introns and harbors a plant-specific zinc-dependent RNA binding domain.

REFIDS: [PMID:21421812](#)

REPLACEMENTS: GO:0006397:mRNA processing

GO term & evidence

Justification

Suggested GO term

AI-generated new annotation suggestions

Gene Annotation Review Browser

Browse AI reviews

GENE: ELF4
REVIEW: [Review](#)
LINK: [Link](#)
ID: O04211
GENE PRODUCT TYPE: PROTEIN

REVIEW STATUS: DRAFT
GO TERM: transcription regulator complex
GO ID: [GO:0005667](#)

EVIDENCE: IDA
ORIG REF: [PMID:21753751](#)
ORIG TITLE: The ELF4-ELF3-LUX complex links the circadian clock to diurnal control of hypocotyl growth.
SUMMARY: ELF4 is a component of the Evening Complex (EC), a tripartite transcriptional repressor complex. This is documented in ComplexPortal (CPX-1291) and demonstrated experimentally by co-immunoprecipitation and ChIP experiments.
ACTION: NEW

REASON: This annotation captures ELF4's role as part of the Evening Complex, which is central to its function. The EC is a well-characterized transcription regulator complex that represses target genes.

REF TEXT: Here we identify a protein complex (called the evening complex)--composed of the proteins encoded by EARLY FLOWERING 3 (ELF3), ELF4 and the transcription-factor-encoding gene LUX ARRHYTHMO (LUX; also known as PHYTOCLOCK 1)--that directly regulates plant growth | We found that ELF4-HA could co-immunoprecipitate both ELF3 and LUX

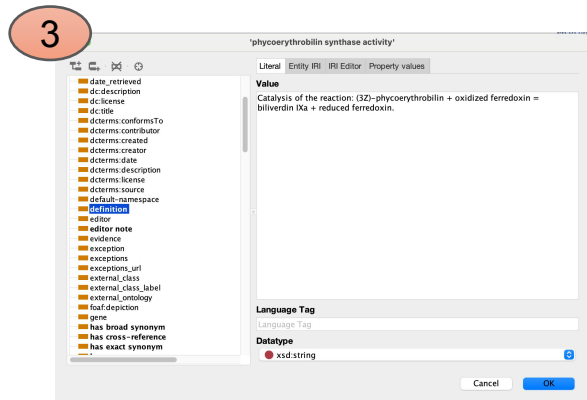
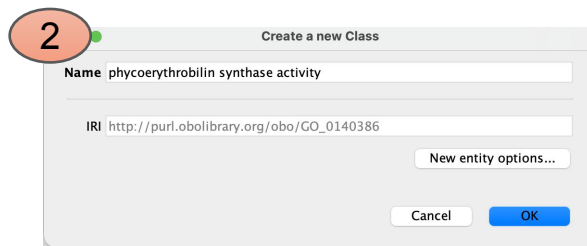
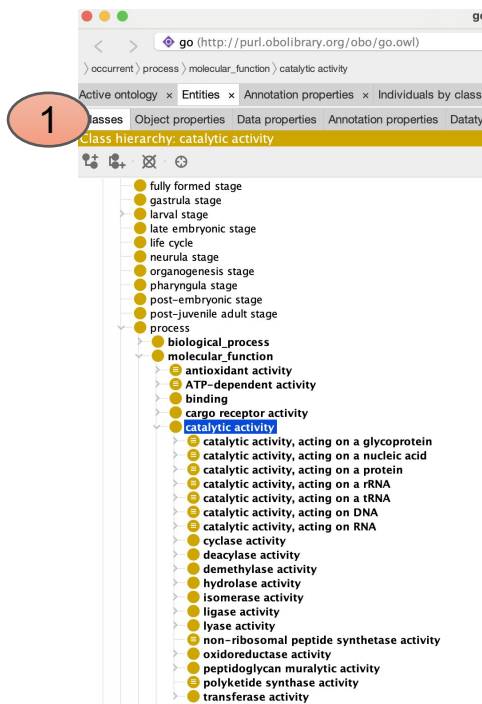
REFIDS: [PMID:21753751](#); [PMID:21753751](#)
ISOFORM: false
TAGS:

GO term & evidence

Justification

Conventional workflow for ontology editing

- GO uses Protégé as ontology editing tool, hooked to GitHub actions for QC



4 add namespace

5 add cross-reference #1

6 add cross-reference #2

7 add synonym

etc

8 save

9 commit, push

10 create pull request, merge

Agentic workflow

User request in GitHub

NTR: Phycoerythrobilin synthase [Rhea:25359], EC 1.3.7.6 #31443

Closed #31452

AndreaAuchincloss opened last week Member ...

Hello,
This reaction is missing from GO, can it be made please?
[Rhea:25359], EC 1.3.7.6
Label:
Phycoerythrobilin synthase

Description:
Catalysis of the reaction: (3Z)-phycoerythrobilin + oxidized ferredoxin = biliverdin IXa + reduced ferredoxin.

PMIDs 18356052, 18662988 and 21050180 show the reaction, the last one in particular shows the product is the 3Z isomer of PEB.

Cyanobacteria do this reaction with 2 proteins (PebA 1.3.7.2 GO:0050617 Q02189) and (PebB 1.3.7.3 GO:0050618 Q02190), but there are a number of viruses (including characterized Q58MU6) that have a protein that does it all in one swoop.

It is a child of GO:0016636.


Editor asks agent to do the task

raymond91125 5 days ago Member ...

@dragon-ai-agent please add the new term phycoerythrobilin synthase activity. Use RHEA:25359 and PMID:18662988, and no others, as the definition references. Add RHEA and EC as exact match general cross references.

1

Agentic workflow - new term created !

 dragon-ai-agent 5 days ago Member ...

I have created the new term **phycoerythrobilin synthase activity** (GO:7770044).

Term Summary


- **ID:** GO:7770044
- **Name:** phycoerythrobilin synthase activity
- **Parent:** GO:0016636 (oxidoreductase activity, acting on the CH-CH group of donors, iron-sulfur protein as acceptor)
- **Definition:** "Catalysis of the reaction: biliverdin IXalpha + 2 reduced ferredoxin + 4 H+ = (3Z)-phycoerythrobilin + 2 oxidized ferredoxin."
- **Definition references:** PMID:18662988, RHEA:25359
- **Cross-references:** EC:1.3.7.6 (exactMatch), RHEA:25359 (exactMatch)
- **Synonyms:**
 - "(3Z)-phycoerythrobilin:ferredoxin oxidoreductase activity" (RELATED)
 - "PebS" (RELATED)

Background



Phycoerythrobilin synthase (PebS, EC 1.3.7.6) is a ferredoxin-dependent bilin reductase found in marine cyanophages. The enzyme performs a four-electron reduction of biliverdin IXalpha to (3Z)-phycoerythrobilin in a single step, combining the activities of PebA (EC 1.3.7.2) and PebB (EC 1.3.7.3) that are required in cyanobacteria.

The reaction direction in the definition follows the biosynthetic (physiological) direction, consistent with the enzyme's name as a synthase.

PR: [#31452](#)

 raymond91125 5 days ago

@dragon-ai-agent please remove the synonyms. They are not required.

  1

Editor asks agent to make corrections if needed

Summary

- GO is a computational model of gene function that aims to be comprehensive, species-agnostic and current
- The ontology is continually updated, with recent major updates to better capture biology rather than experimental results
- Annotations exist in both standard and GO-CAM flavors
- GO-CAMs are now disseminated across various resources
- GO strives to be efficient and accurate

Ressources

- GO Handbook
- GO-CAM paper (2019)
- Gene Ontology website
 - General ontology documentation
 - General annotation documentation
- Annotation Relations documentation
- EBI Gene Ontology tutorial on YouTube (general)

Contributors



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Contributing groups

CGD, CACAO, EcoWiki, ComplexPortal, dictyBase, DisProt, EcoCyc, EcoliWiki, Ensembl, FlyBase, HGCN, HUGO, IntAct, InterPro, JaponicusDB, MGI, PANTHER, PHI-base, PomBase, RGD, Reactome, RHEA, RNACentral, SGD, SignatureScience, TAIR, HPA, Matrisome, SynGO, UniProt, WormBase, ZFIN