

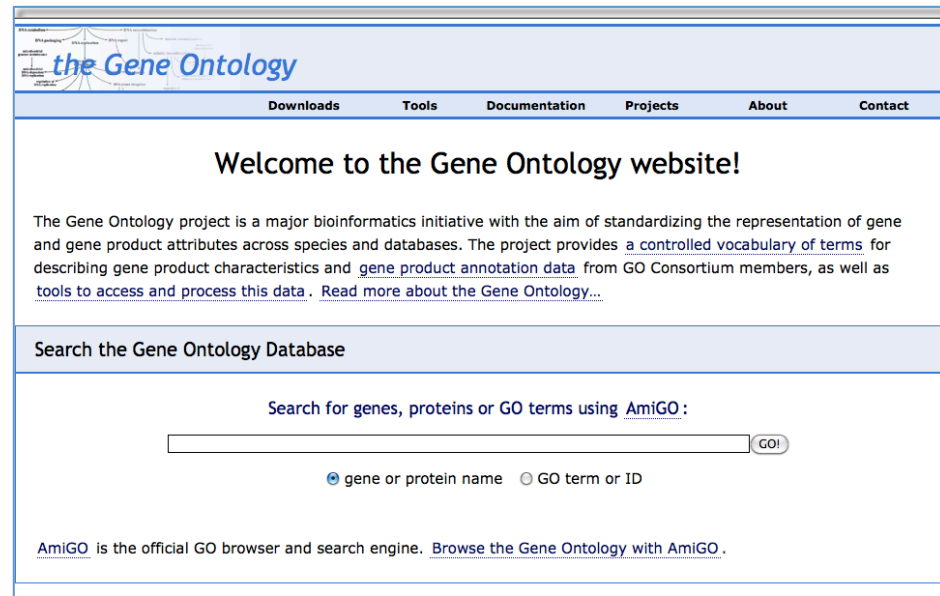
Apply SBGN-AF in the LEGO Project

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Gene Ontology

- The first ontology that was designed as a formal representation of biological knowledge
- Three knowledge domains:
 - molecular function
 - biological process
 - cellular component.



Hexokinase

Molecular function: GO:0004396 : hexokinase activity

Biological process: GO:0006096 : glycolysis

Cellular component: GO:0005829 : cytosol

Ashburner, M. et al. (2000) Gene ontology: tool for the unification of biology. The Gene Ontology Consortium. *Nat Genet.* **25**: p. 25-9.

The Gene Ontology Consortium (2012) The Gene Ontology: enhancements for 2011. *Nucleic Acids Res.* 40:D559

- ▣ all : all [377130 gene products]
 - + ⓘ GO:0008150 : biological_process [272439 gene products]
 - + ⓘ GO:0009987 : cellular process [155181 gene products]
 - + ⓘ GO:0044237 : cellular metabolic process [102936 gene products]
 - + ⓘ GO:0044262 : cellular carbohydrate metabolic process [5325 gene products]
 - ▣ ⓘ **GO:0044275 : cellular carbohydrate catabolic process [1748 gene products]**
 - + ⓘ GO:0019405 : alditol catabolic process [66 gene products]
 - + ⓘ GO:0046176 : aldonic acid catabolic process [3 gene products]
 - ▣ ⓘ GO:0051692 : cellular oligosaccharide catabolic process [4 gene products]
 - + ⓘ GO:0044247 : cellular polysaccharide catabolic process [157 gene products]
 - + ⓘ GO:0046352 : disaccharide catabolic process [80 gene products]
 - ▣ ⓘ GO:0019391 : glucuronoside catabolic process [1 gene product]
 - + ⓘ **GO:0006096 : glycolysis [1063 gene products]**
 - + ⓘ GO:0016139 : glycoside catabolic process [72 gene products]
 - + ⓘ GO:0006098 : pentose-phosphate shunt [367 gene products]
 - + ⓘ GO:0043471 : regulation of cellular carbohydrate catabolic process [71 gene products]
 - + ⓘ GO:0006258 : UDP-glucose catabolic process [1 gene product]
- + ⓘ GO:0044248 : cellular catabolic process [11927 gene products]
 - + ⓘ GO:0044265 : cellular macromolecule catabolic process [6698 gene products]
 - ▣ ⓘ **GO:0044275 : cellular carbohydrate catabolic process [1748 gene products]**
 - + ⓘ GO:0019405 : alditol catabolic process [66 gene products]
 - + ⓘ GO:0046176 : aldonic acid catabolic process [3 gene products]
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 - + ⓘ GO:0016139 : glycoside catabolic process [72 gene products]

GO biological process viewed in AmiGO

What is LEGO Project?

- LEGO is a new development under the Gene Ontology project.
- It is an extension of the existing GO by capturing relationships among various GO terms during the curation of genes.
- Current annotations take a very simple form:
 - Gene_product *implied_relation* GO_class
 - For MF, relation is *has_function*
 - For BP, relation is *involved_in*
 - For CC, relation is *located_in*
- LEGO will enable curators to use the GO to express rich biological statements from the literature
 - Maximize biological knowledge captured by curator
 - Represent complex biology in an accurate, computable manner
 - Prevent
 - “kludges” that use existing terms misleadingly or inconsistently
 - Combinatorial explosion of GO terms

GO annotation 2010

NEDD4

MF

- Ubiquitin-protein ligase activity
- RNA polymerase binding

BP

- Ubiquitin-dependent protein catabolic process
- Cellular response to UV
- Negative regulation of transcription from RNA polymerase II promoter

NEDD4

Fuction

Process

GO:0004842	ubiquitin-protein ligase activity	F	ID	GO:0000122	negative regulation of transcription from RNA polymerase II promoter	P	IEA	Ensembl Compara
GO:0004842	ubiquitin-protein ligase activity	F	ID	GO:0002250	adaptive immune response	P	IEA	Ensembl Compara
GO:0005515	protein binding	F	IP	GO:0003151	outflow tract morphogenesis	P	IEA	Ensembl Compara
GO:0005515	protein binding	F	IP	GO:0003197	endocardial cushion development	P	IEA	Ensembl Compara
GO:0005515	protein binding	F	IP	GO:0006513	protein monoubiquitination	P	IEA	Ensembl Compara
GO:0005515	protein binding	F	IP	GO:0006622	protein targeting to lysosome	P	IDA	PMID:17116753
GO:0005515	protein binding	F	IP	GO:0007041	lysosomal transport	P	IDA	PMID:18544533
GO:0005515	protein binding	F	IP	GO:0007399	nervous system development	P	IEA	UniProt Keywords2GO (UniProtKB/Swiss-Prot entries)
GO:0005515	protein binding	F	IP	GO:0007528	neuromuscular junction development	P	IEA	Ensembl Compara
GO:0005515	protein binding	F	IP	GO:0010766	negative regulation of sodium ion transport	P	IEA	Ensembl Compara
GO:0005515	protein binding	F	IP	GO:0010766	negative regulation of sodium ion transport	P	IDA	PMID:10642508
GO:0005515	protein binding	F	IP	GO:0010768	negative regulation of transcription from RNA polymerase II promoter in response to UV-induced DNA damage	P	IMP	PMID:17996703
GO:0005515	protein binding	F	IP	GO:0014068	positive regulation of phosphatidylinositol 3-kinase cascade	P	IMP	PMID:17218260
GO:0005515	protein binding	F	IP	GO:0016567	protein ubiquitination	P	IEA	Ensembl Compara
GO:0005515	protein binding	F	IP	GO:0016567	protein ubiquitination	P	IEA	UniPathway2GO
GO:0016874	ligase activity	F	IE	GO:0016567	protein ubiquitination	P	IDA	PMID:18305167
GO:0019871	sodium channel inhibitor activity	F	IE	GO:0019048	modulation by virus of host morphology or physiology	P	IEA	UniProt Keywords2GO (UniProtKB/Swiss-Prot entries)
GO:0019871	sodium channel inhibitor activity	F	ID	GO:0019089	transmission of virus	P	IMP	PMID:15126635
GO:0019904	protein domain specific binding	F	IP	GO:0019221	cytokine-mediated signaling pathway	P	TAS	Reactome:REACT_25229
GO:0031698	beta-2 adrenergic receptor binding	F	ID	GO:0030948	negative regulation of vascular endothelial growth factor receptor signaling pathway	P	IEA	Ensembl Compara
GO:0043130	ubiquitin binding	F	ID	GO:0030948	negative regulation of vascular endothelial growth factor receptor signaling pathway	P	ISS	GO_REF:0000024
GO:0050815	phosphoserine binding	F	IE	GO:0031175	neuron projection development	P	IEP	PMID:9990509
GO:0050815	phosphoserine binding	F	IS	GO:0031623	receptor internalization	P	IDA	PMID:18544533
GO:0050816	phosphothreonine binding	F	IE					
GO:0050816	phosphothreonine binding	F	IS					
GO:0070063	RNA polymerase binding	F	IP					
GO:0070064	proline-rich region binding	F	IE					

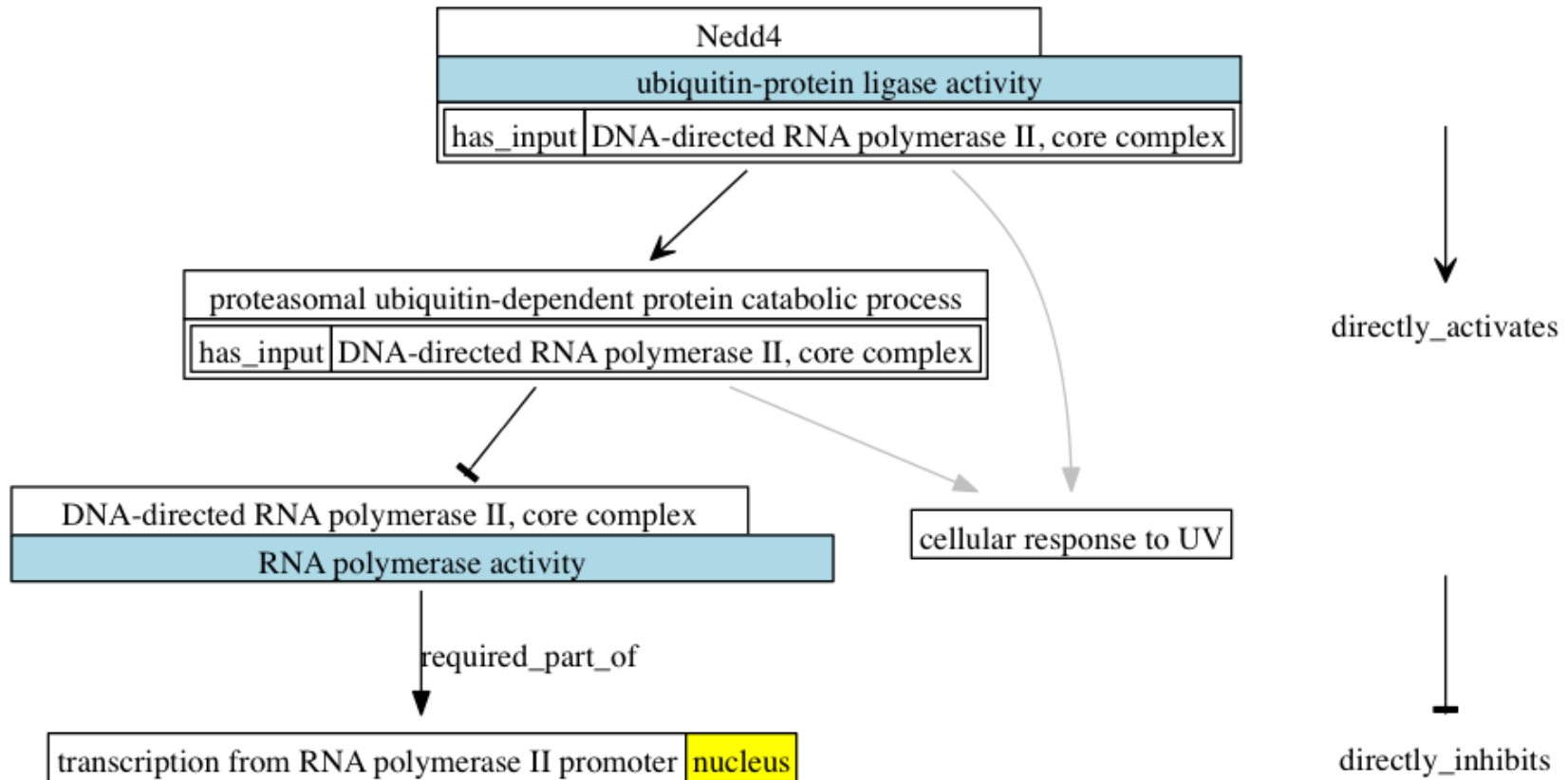
NEDD4

Fuction

Process

GO:0004842 ubiquitin-protein ligase activity	F	ID	GO:0009122 negative regulation of transcription from RNA polymerase II promoter	P	IEA	Ensembl Compara
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GO:0019904 protein domain specific binding	F	IP	GO:0019221 cytokine-mediated signaling pathway	P	TAS	Reactome:REACT_25229
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GO:0043130 ubiquitin binding	F	ID	GO:0030948 negative regulation of vascular endothelial growth factor receptor signaling pathway	P	ISS	GO_REF:0000024
GO:0050815 phosphoserine binding	F	IE				
GO:0050815 phosphoserine binding	F	IS				
GO:0050816 phosphothreonine binding	F	IE				
GO:0050816 phosphothreonine binding	F	IS				
GO:0070063 RNA polymerase binding	F	IP	GO:0031175 neuron projection development	P	IEP	PMID:9990509
GO:0070064 proline-rich region binding	F	IE	GO:0031623 receptor internalization	P	IDA	PMID:18544533

LEGO viewer plugin for Protege

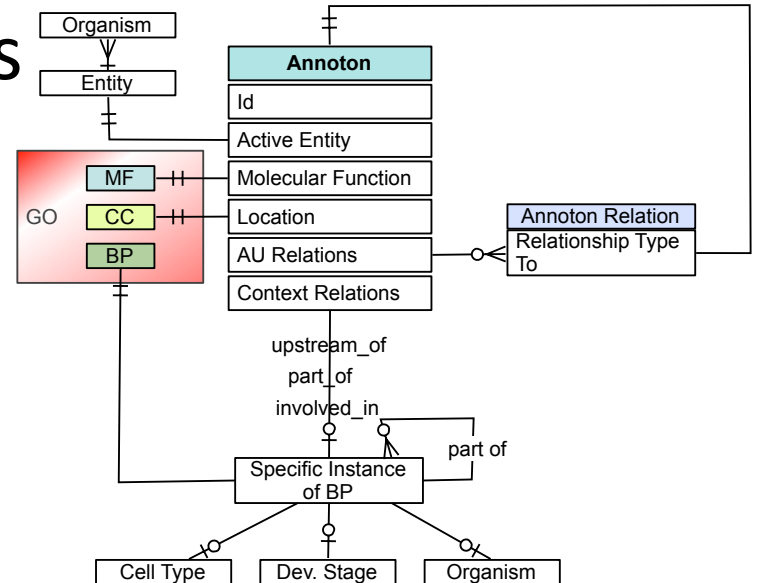


NEDD4 ubiquitin protein ligase activity acting on RNAPII complex involved in positive regulation of proteasomal ubiquitin-dependent catabolic process
 acting on RNAPII complex involved in negative regulation of RNAPII complex
 RNA polymerase II activity involved in negative regulation of transcription from RNAPII promoter during cellular response to UV

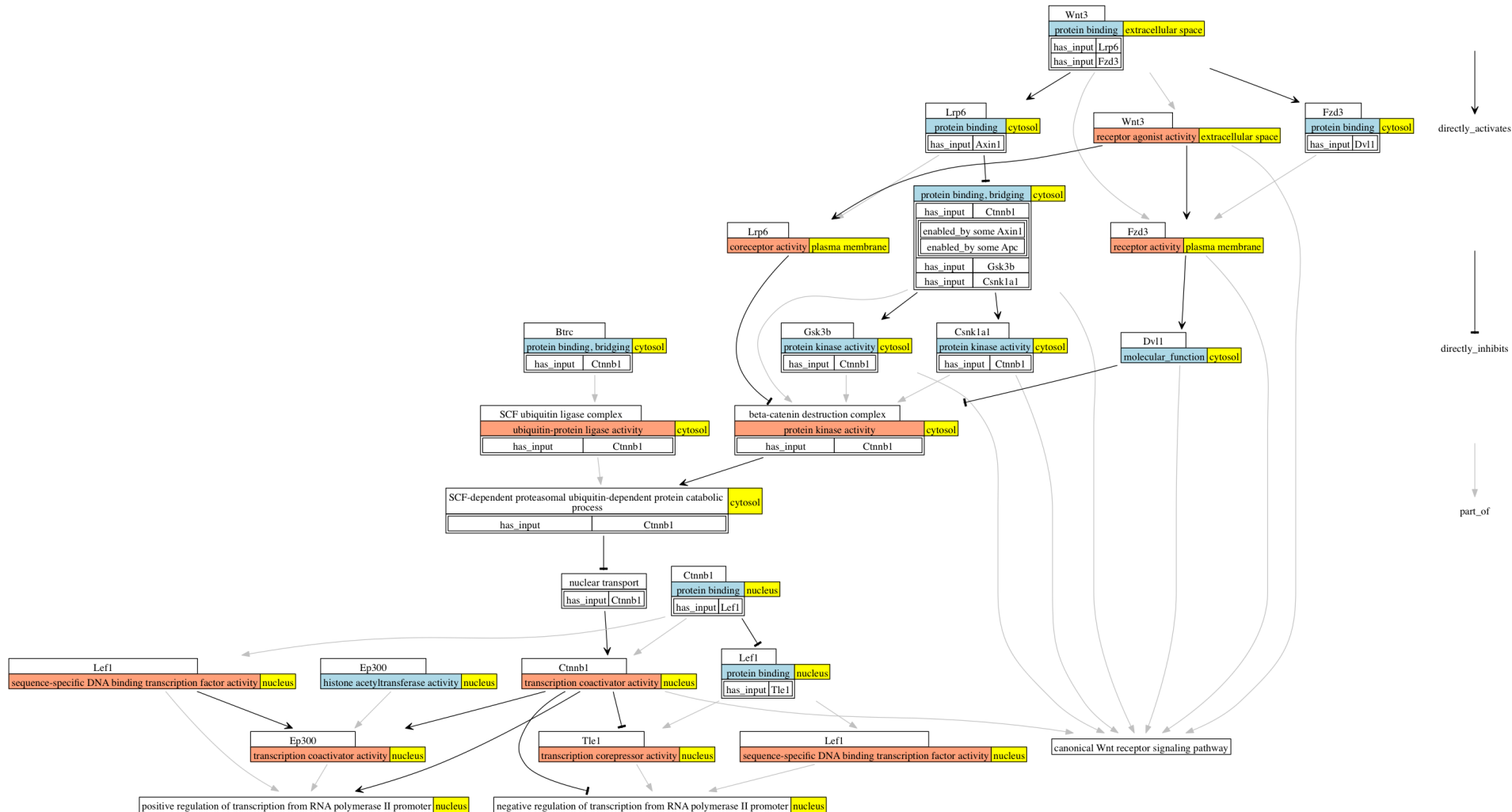
part_of

Progress

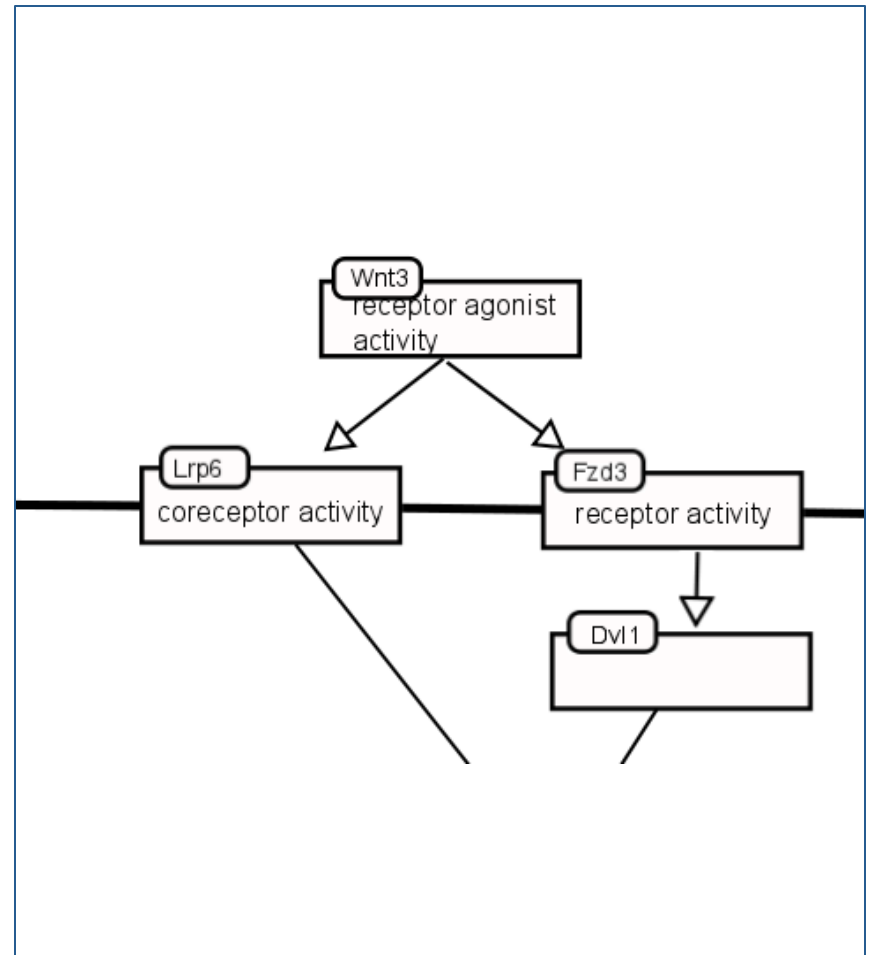
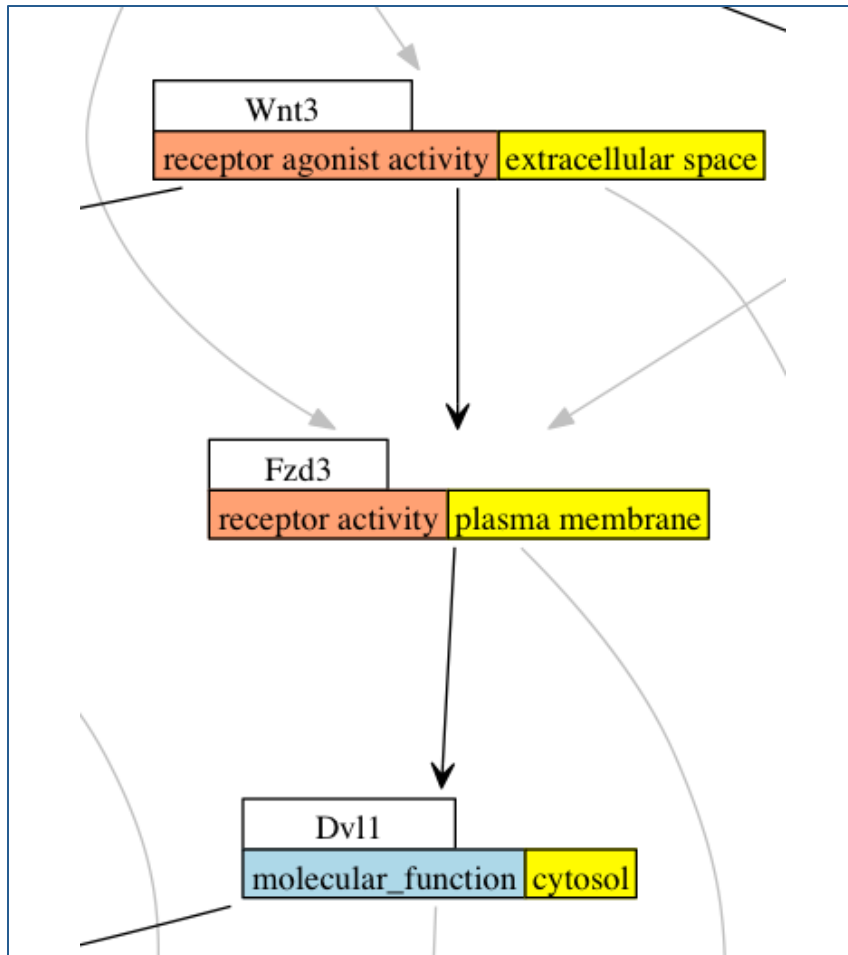
- Formal spec for construction of LEGO annotation
- Developed plugin for Protégé to enable use as prototype LEGO annotation tool
- Tested with several papers, including review articles on entire pathways



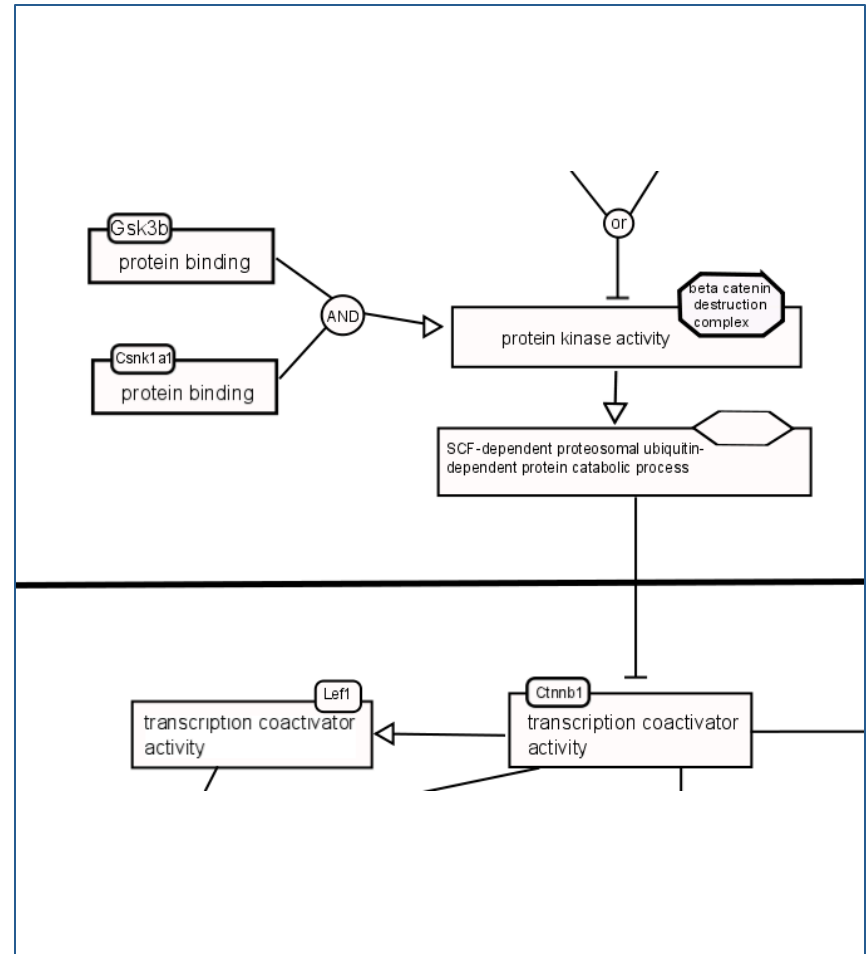
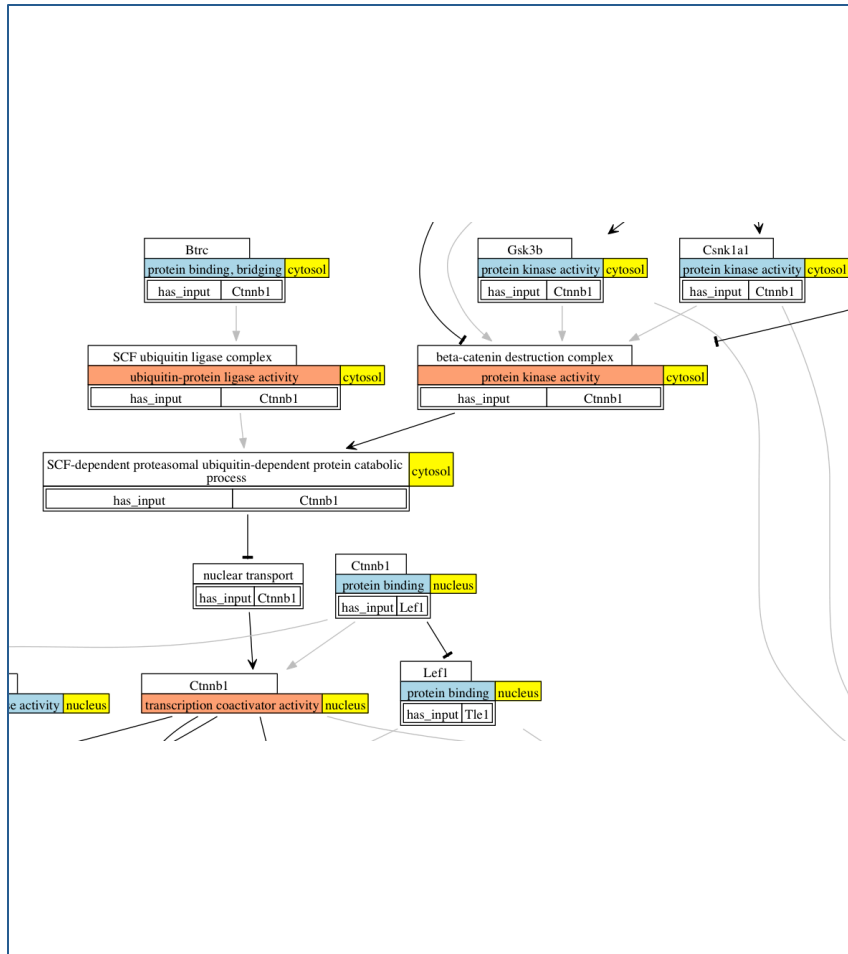
Wnt signaling pathway



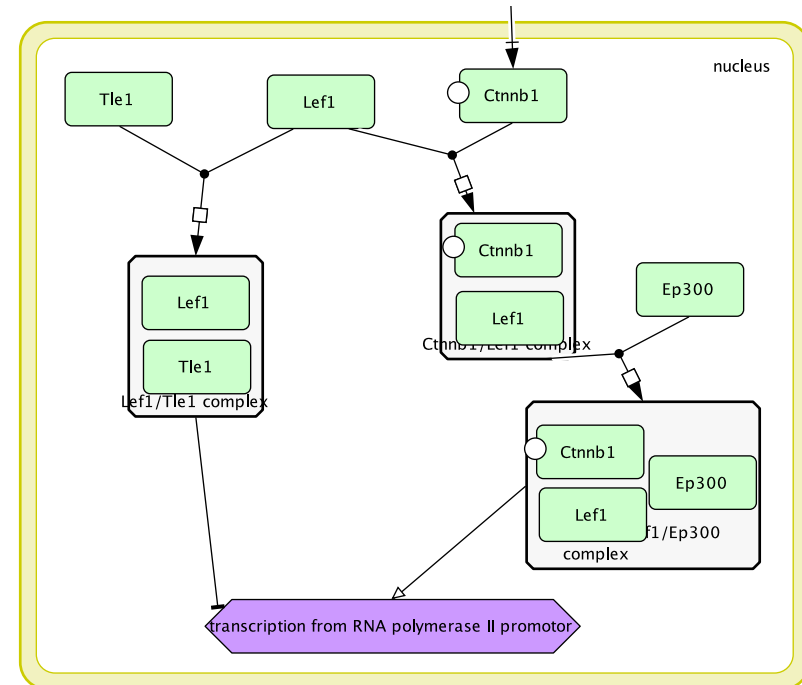
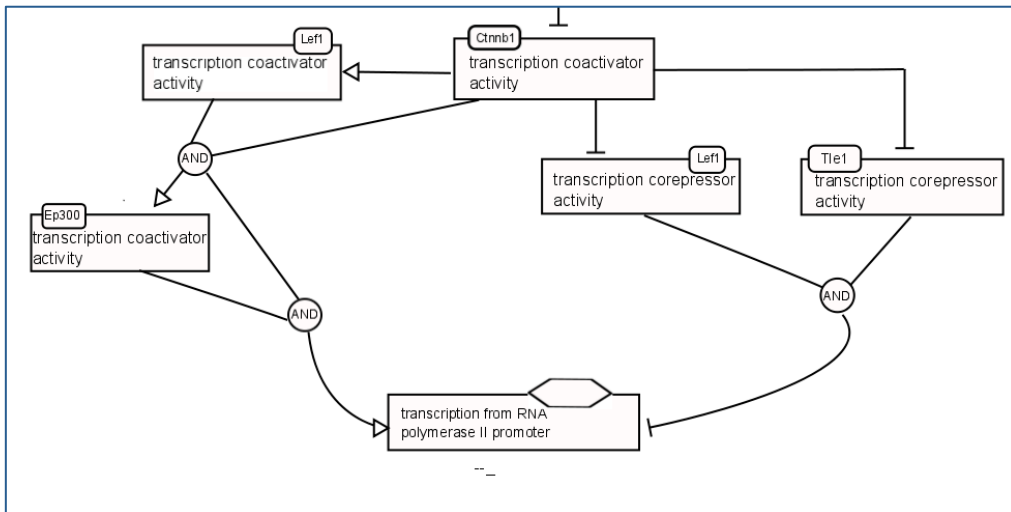
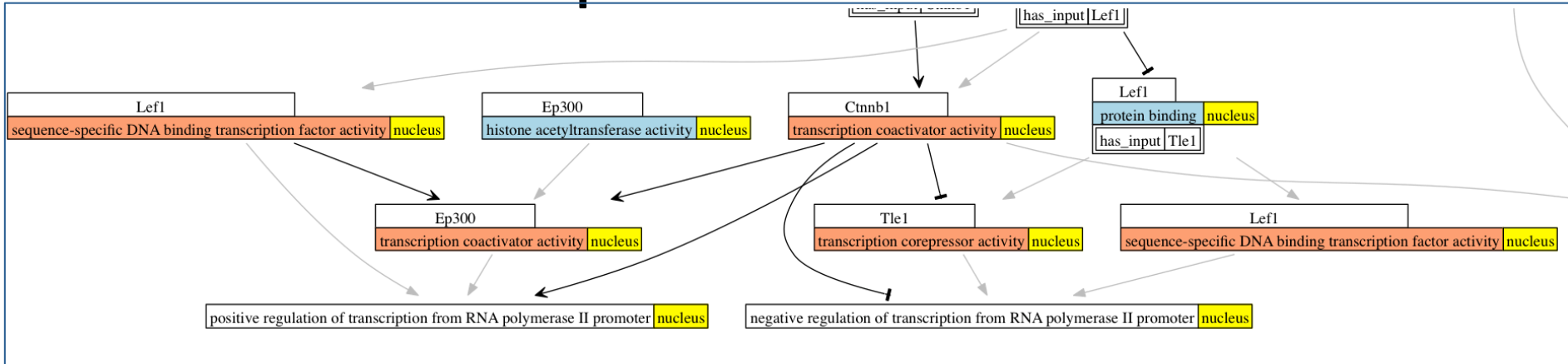
Mapping LEGO to SBGN-AF



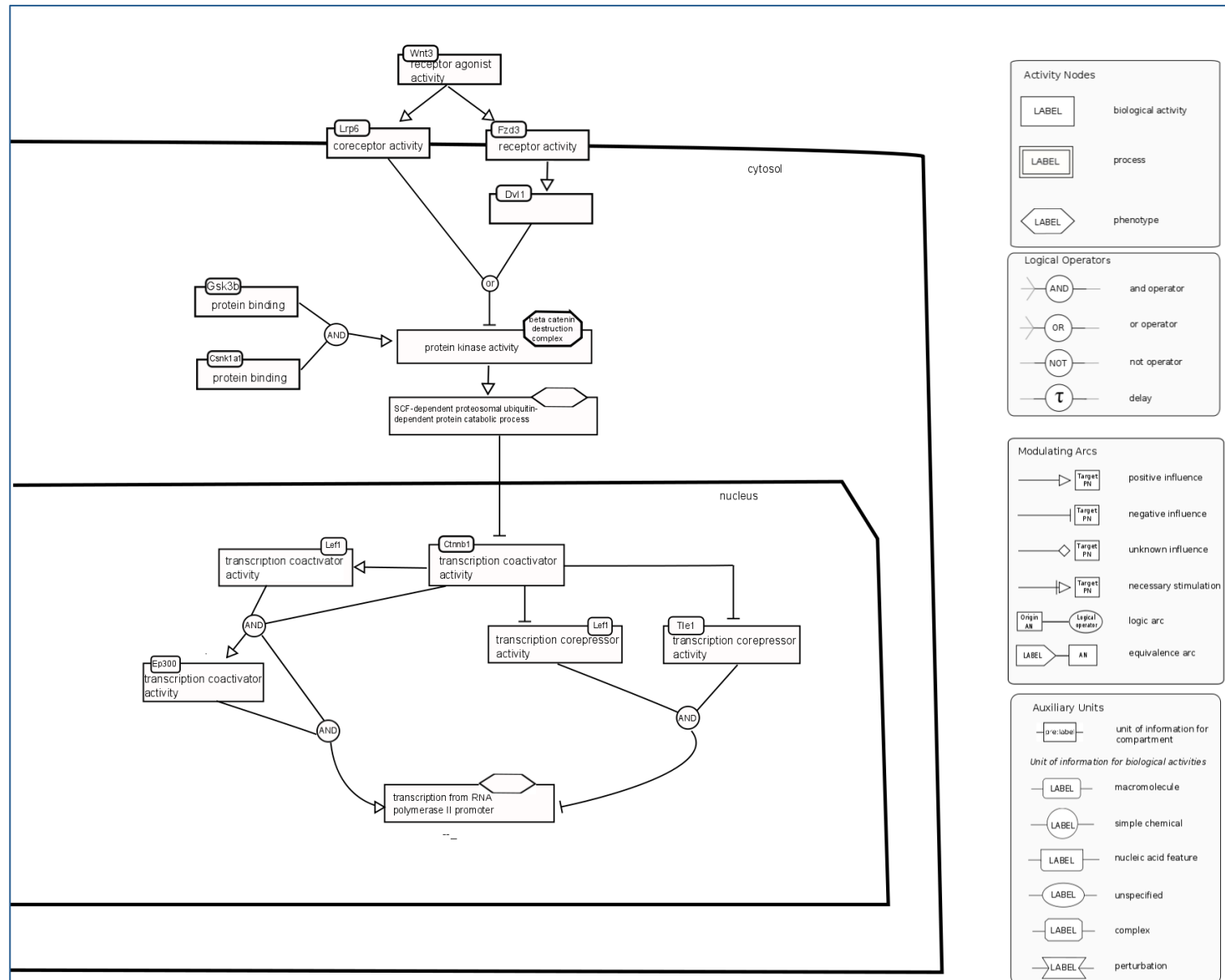
Mapping LEGO to SBGN-AF



Some part of pathway is easier to represent in PD



Wnt pathway in SBGN-AF



How SBGN-AF Can Support LEGO

- A LEGO curation tool is being developed.
- SBGN-ML is used to store coordinates.
- LEGO is SBGN-AF in principle, with some exceptions, e.g., entities are used for small chemicals.
- LEGO captures GO specific relationships, such as `part_of...`

Acknowledgements

GO PIs

- Judy Blake (Jackson Laboratory)
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- Suzanna Lewis (LBL)

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USC

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Curation

Jackson Laboratory

- David Hill