ELSEVIER

QUICK REFERENCE

ENTITY TYPES

(mammal, mammal+CE+Dfx, and plant database)

	Cell Process * – biological processes, most coincide with Gene Ontology.
	Clinical Parameter – measured parameters of the human body used in clinical practice (mammal and mammal+CE+DFx only).
	Complex * – several polypeptides that form a complex via physical interactions.
	Disease – Mammal: health conditions and disease terms from MeSH; plant: Plant diseases.
	Functional Class * – most functional classes coincide with Gene Ontology.
	Protein – defined by Entrez Gene - represents both genes and the gene products, including proteins and miRNAs.
	Small Molecule – Mammal: naturally occurring metabolites and small molecules found in cells; ChemEffect® adds drugs (including some biologically active polypeptides that work as drugs such as monoclonal antibodies) and non-naturally occurring small molecules to the mammal database. Plant: naturally occurring metabolites and small molecules and other plant related chemicals (ex. herbicides or research related chemicals).
	Treatment – non-chemical treatments and environmental conditions, such as cold shock.

**Container Entities – these are valid entities but also can have proteins mapped to them. You can see the proteins for the container entities in the "child concepts" in the property records for the specific entity.*

PROTEIN SUB-TYPES

(mammal, mammal+CE+Dfx, and plant database)

Complexes are also "protein" entities but represent a group of proteins functioning together. In the Pathway Studio® database they function as a complex entity type so are considered separately.

Protein (no class assigned)

Protein kinase

Transcription factor

Phosphatase

Receptor

miRNA

Ligands

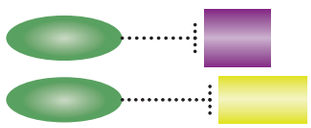
RELATION TYPES

(both mammal and plant database)

Binding	direct physical interaction between two molecules.
ChemicalReaction	enzyme catalyzed reaction involving small molecules.
DirectRegulation	influences target activity by direct physical interaction (excluding promoter binding interactions).
Expression	regulator changes protein abundance by affecting levels of transcript or protein stability.
miRNAEffect	the inhibitory effect of a miRNA on its mRNA target.
Regulation	changes the activity of the target by an unknown mechanism (may be direct or indirect). This is a less specific relation type than others provided.
MolSynthesis	regulator changes the concentrations of the target (usually a small molecule target).
MolTransport	regulator changes the localization of the target (molecular translocation, export, import etc.).
PromoterBinding	regulator binds to the promoter of a gene.
ProtModification	regulator changes the modification of the target molecule, usually by a direct interaction. **Filtering Field Name:** Mechanism **Sub-Categories:** acetylation, cleavage, deacetylation, demethylation, dephosphorylation, direct interaction, methylation, phosphorylation, posttrascriptional inhibition, proteolysis, ubiquitination.

ADDITIONAL DATA IN THE CHEMEFFECT® DATABASE

(added to Mammal)



- Relations between small molecules and diseases/cell processes.
- Relations between non-naturally occurring metabolites (small molecules), such as drugs, which are not included in the Mammal database.

ADDITIONAL DATA IN THE DISEASEFX™ DATABASE

(added to Mammal)

Additional relation types in DiseaseFx™:

Quantitative Change	Changes in abundance/activity/expression of a gene/protein/small molecule in a disease state (between disease-protein/complex/functional class/small molecules). **Filtering Field name:** Quantitative Change **Sub-Categories:** Expression, Abundance, Activity
Genetic Change	Genetic changes in a gene in a disease state such as gene deletions, amplifications, mutations or epigenetic changes (between disease-protein/complex/functional class). **Filtering Field Name:** Change Type **Sub-Categories:** Gene Deletion, Mutation, Gene Amplification, Epigenic methylation
Biomarkers	Identification of proteins/complexes/functional classes/metabolites that are prognostic or diagnostic biomarkers for a disease (between disease-protein/complex/functional class/naturally occurring small molecules). **Filtering Field Name:** Biomarker Type **Sub-Categories:** Diagnostic, Prognostic
State Change	Changes in a protein's post-translational modification status or alternative splicing events associated with a disease (between disease-protein/complex/functional class). **Filtering Field Name:** Change Type **Sub-Categories:** Alternate Splicing, Phosphorylation
Functional Association	Different types of functional associations between a disease and a cellular process or another disease (between Disease – Cell Process) (no sub-types).
Clinical Trials	Disease/cell process relation representing clinical trials conducted for a drug against a disease (from ClinicalTrials.gov) (between Disease/Cell Process – Small Molecule) (no sub-types).

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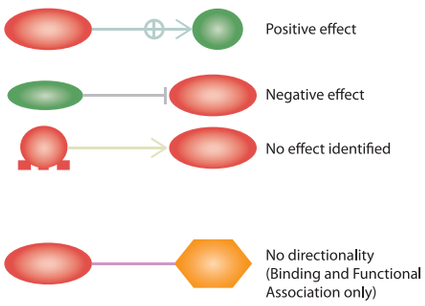
ADDITIONAL INFORMATION ABOUT RELATIONS

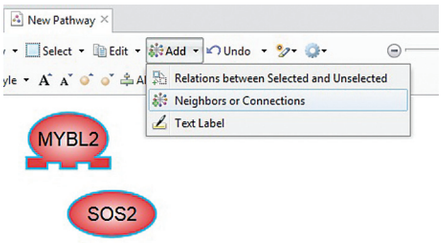
Each relation type is assigned a distinct color

Positive or negative effect for the relation are indicated by arrow head. Relations have arrows to indicate directionality (except Binding).

- Regulation
- ChemicalReaction
- PromoterBinding
- MolSynthesis
- MolTransport
- DirectRegulation
- Expression
- Binding
- ProtModification
- miRNAEffect
- QuantitativeChange
- GeneticChange
- Biomarker
- StateChange
- FunctionalAssociation
- ClinicalTrial



BUILD PATHWAY WIZARD



Build Pathway Algorithms

Find Direct Links: find the relation between two or more selected entities on the network diagram.

Find Shortest Path for a Pair of Entities: find relations between two selected entities on the network diagram, adding intermediate entities as needed to form the connection.

Expand Pathway: find entities directly connected to the entity / entities selected on the network diagram from the database.

Find Common Targets: find target(s) that are regulated by at least two or more of the selected entities on the network diagram.

Find Common Regulators: find regulator(s) that regulate two or more of the selected entities on the network.

EXPERIMENTAL DATA ANALYSIS

GSEA	Gene Set Enrichment Analysis ranks experiment results by the absolute value of the fold change and identifies known gene sets (pathways and ontologies) that are statistically enriched. **Tool name:** Gene Set Enrichment Analysis.
SNEA	Sub-Network Enrichment Analysis is an extension of GSEA where the "gene sets" used in the enrichment analysis are small regulatory networks calculated de novo from the database by the algorithm. Identifies major regulators (proteins, miRNAs or small molecules), binding networks, metabolomics targets, enriched diseases and cell processes. **Tool name:** Sub-Network Enrichment Analysis.
Fisher's Exact Test	Enrichment analysis that does NOT include experimental values when calculating enrichment from a list. **Tool names:** Find Pathways/Groups Enriched; Find Enriched Genomic positions; Find Sub-Networks Enriched.

EXPERIMENTAL DATA

Name	60d SOD1 ...	60d SOD1 ...
Class: strain		
Class: age		
COPG1	-0.6807087	4.45907E-2
ATP6V0D1	0.17985488	6.78479E-1
GOLGA7	1.6789091	3.90912E-2
PSPH	1.7981919	1.90234E-1
TRAPPC4	0.989017	4.96238E-1
DPM2	0.020824222	9.59420E-1
PSMB5	-0.12114056	7.96351E-1
DHRS1	-1.1399802	1.43216E-1
PPM1A	0.33342692	5.00242E-1
Gm12396	-0.5927564	5.25581E-2
ANAPC1	0.2177488	6.59616E-1
MRPL43	0.72504836	1.08986E-1
XPO7	0.29989532	3.79844E-1
NMT1	1.5160563	2.34582E-2
ATG5	0.18824257	7.19968E-1
MTIF2	-0.43101956	1.36343E-1
RAB14	1.020479	5.56361E-1
PSAP	-0.16931395	6.76258E-1
UBE2G1	0.7851216	9.71774E-2
Zkscan4	-0.13540155	6.71391E-1
MRPL27	-0.827616	1.72493E-1
DLG1	0.2558937	6.24275E-1
CANX	0.8878748	9.47253E-2
DERL1	1.3268365	4.64684E-1
WARS	-0.40968728	3.86426E-1
PSMA1	0.57471424	2.28067E-1
SAR1A	0.37190115	3.56095E-1
G3BP2	0.163685	6.47731E-1
GOLM1	0.49954703	2.13203E-1

Name
AKT1
MYF5
IGF1
HDAC1
MYD88
TNF
SNCA
ATP2A1
DRD2
PPARGC1A
CAMKK2
AGT
TLR4
HIF1A
INS
ITGA2
TGFB1
DYSF
BGN
MTOR
NR3C1
CDKN2A
TP53
MDM2
IL10
MAPK3
SIK2
LEP
TP73
THRA
BCL2L1
EDNRA

ALGORITHM

GSEA

SNEA

Fisher's

Fisher's

ENRICHED GENE SETS RESULTS

Known Gene Sets:

Mammal: Cell Process Pathways, Disease Collections (pathways and groups), Expression Targets Pathways, Immunological Pathways, Metabolic Pathways, Nociception Pathways, Signaling Pathways, Gene Ontology, Pathway Studio® Ontology, Chromosomal localization enrichment.

Plant: AraCyc Pathways, Arabidopsis Signaling Pathways, MaizeCyc Pathways, RiceCyc Pathways, Plant Ontology, Pathway Studio® Ontology, Gene Ontology.

De novo user-defined sub-networks: expression regulators, miRNA regulators, binding networks, metabolomics targets, disease and cell process enrichment.

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PATHWAY STUDIO®

http://help.elsevier.com/app/pathway_select/p/9048