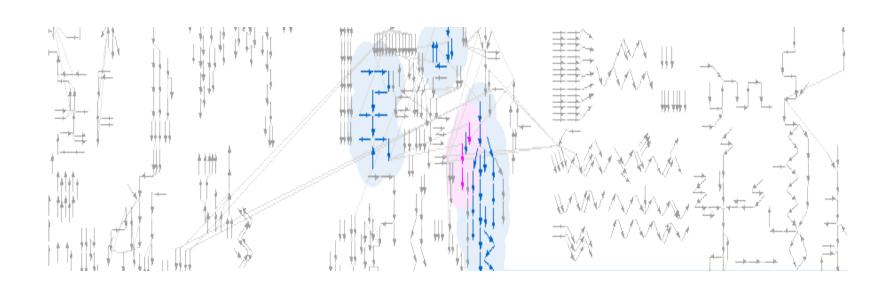
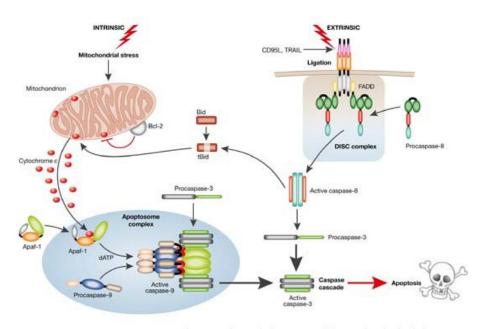
# REACTOME



Nayibe L. Buitrago Jorge Cortázar

## REACTOME

#### www.reactome.org



Apoptosis and disease: a life or death decision. EMBO Rep. 2004 Jul;5(7):674-8. Epub 2004 Jun 25.

Cold Spring Harbor Laboratory
The European Bioinformatics Institute
The Gene Ontology Consortium

Homo sapiens

Experimentally confirmed reaction-



Manually inferred reaction-

Apoptosis	Cell Cycle Checkpoints	Cell Cycle, Mitotic	DNA Repair
DNA Replication	Electron Transport Chain	Epidermal Growth Factor Receptor (EGFR) signaling	Fibroblast Growth Factor Receptor (FGFR) signaling
Gap junction trafficking and regulation	Gene Expression	HIV Infection	Hemostasis
Immune System signaling	Influenza Infection	Insulin receptor mediated signaling	Integration of pathways involved in energy metabolism
Maintonanco of Tolomoroe	Metabolism of amino acids and related nitrogen- containing molecules	Motaboliem of earbohydratee	Motaboliem of lipide and lipeprotoine
Metabolism of nucleotides	Metabolism of porphyrins	Notch Signaling Pathway	Oxidative decarboxylation of pyruvate and TCA cycle
Post-translational modification of proteins	Transforming Growth Factor (TGF) beta signaling	Transcription	Translation
mRNA Processing	Xenobiotic metabolism		

#### About Reactome

The Reactome project is a collaboration among Cold Spring Harbor Laboratory, The European Bioinformatics Institute, and The Gene Ontology Consortium to develop a curated receive of core pathways and reactions in human biology. The information in this database is authored by biological researchers with expertse in their fields, maintained by the Reactome editorial staff, and cross-referenced with the sequence databases at NCBI, Ensembl and UniProt, the UCSC Genome Browser, HapMap, KEGG (Gene and Compound ). ChEBI, PubMed and GC. In addition to curated human events inferred orthologous events in 22 non-human species including mouse, rat, chicken, zebra fish, worm, fy, yeast, two plants and Ecoli are also available.

Reactome is a free or-line resource, and Reactome software is open-scurce. However, please take note of our disclaimer.

More...

#### **News and Notes**

Linked reactions

· February 28, 2007: Version 20 Released

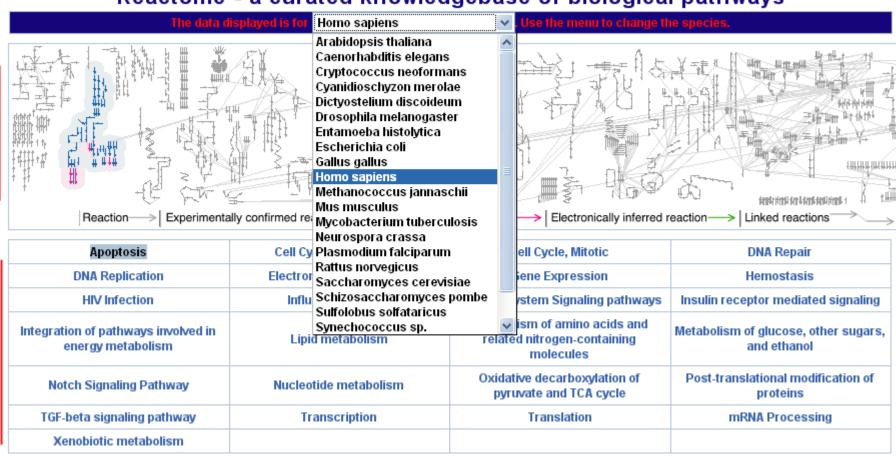
e the menu to change the species. Check  $\square$  for cross species comparison.

| Electronically inferred reaction-

- New topics released in Version 20 are Fibroblast Growth Factor Receptor (FGFR) signaling, Epidormal Growth Factor Receptor (EGFR) egnaling under eignaling pathways, Gap junction trafficking under cell biology, and Porphyrin metabolism, Digestion of dietary carbohydrate and lipid under metabolic pathways. Additional events for HIV REV protein interacticns, and Influenza virus RNP assembly have been added to corresponding infectious disease pathways. Updated release statistics and the Editorial Calendar are available. Click here to contact us.
- More...

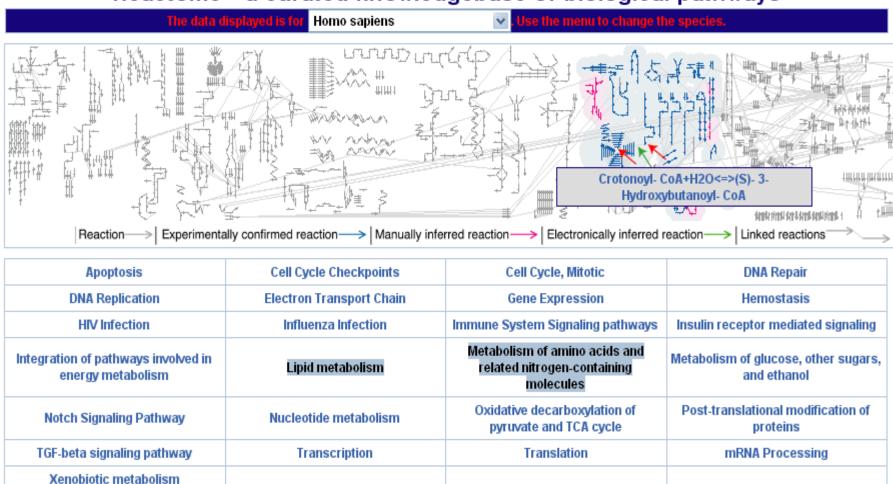
## REACTOME

Reactome - a curated knowledgebase of biological pathways

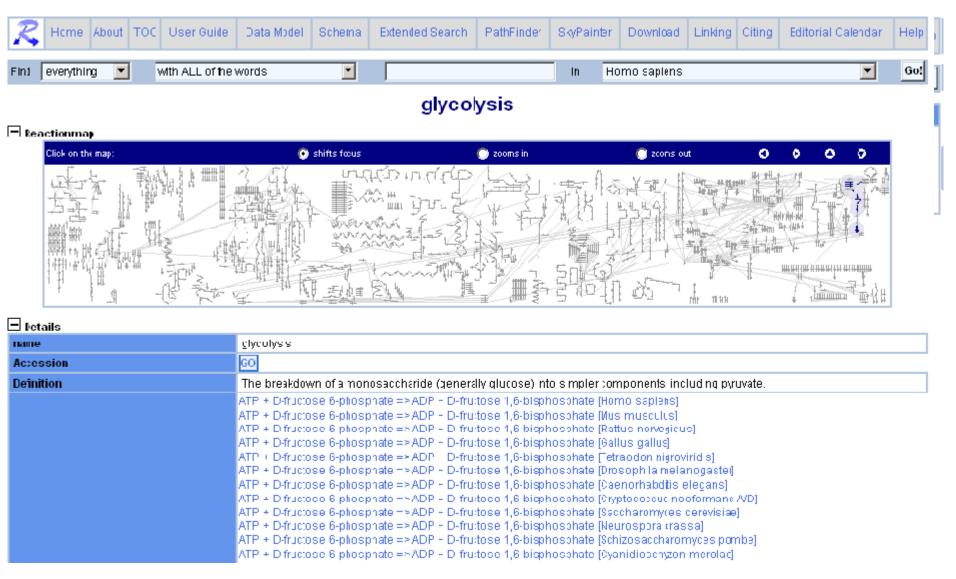


### CONVENCIONES

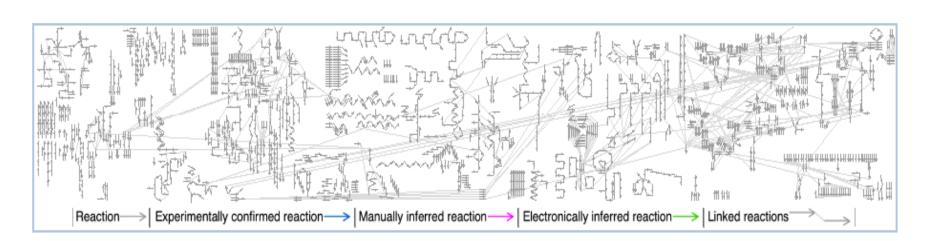
#### Reactome - a curated knowledgebase of biological pathways



## BUSQUEDAS



The data displayed is for Homo sapiens . Use the menu to change the species. Check for cross-species comparison.

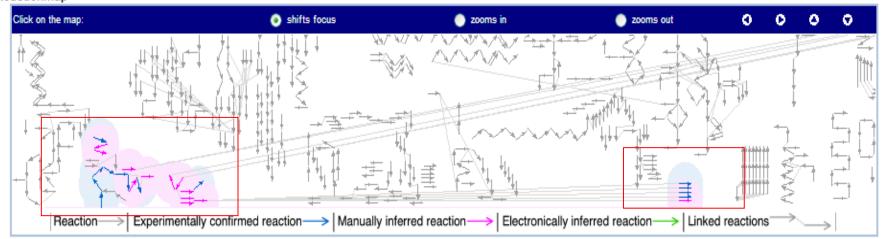


Apoptosis	Cell Cycle Checkpoints	Cell Cycle, Mitotic	DNA Repair
DNA Replication	Electron Transport Chain	Epidermal Growth Factor Receptor (EGFR) signaling	Fibroblast Growth Factor Receptor (FGFR) signaling
Gap junction trafficking and regulation	Gene Expression	HIV Infection	Hemostasis
Immune System signaling	Influenza Infection	Insulin receptor mediated signaling	Integration of pathways involved in energy metabolism
Maintenance of Telomeres	Metabolism of amino acids and related nitrogen-containing molecules	Metabolism of carbohydrates	Metabolism of lipids and lipoproteins
Metabolism of nucleotides	Metabolism of porphyrins	Notch Signaling Pathway	Oxidative decarboxylation of pyruvate and TCA cycle
Post-translational modification of proteins	Transforming Growth Factor (TGF) beta signaling	Transcription	Translation
mRNA Processing	Xenobiotic metabolism		

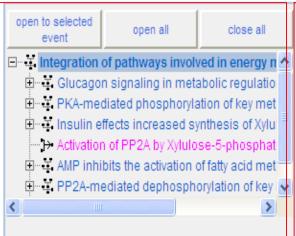


#### Integration of pathways involved in energy metabolism [Homo sapiens]









Stable identifier	REACT_1505.1	
Authored	Conjugatoran G D'Eustachin P 2005-05-11	

Authored Gopinathrao, G, D'Eustachio, P, 2005-05-11

Reviewed Rush, MG, 2005-09-10

Many hormones that affect individual physiological processes including the regulation of appetite, absorption, transport, and oxidation of foodstuffs influence energy metabolism pathways. While **insulin** mediates the storage of excess nutrients, **glucagon** is involved in the mobilization of energy resources in response to low blood glucose levels, principally by stimulating hepatic glucose output. Small doses of glucagon are sufficient to induce significant glucose elevations. These hormone-driven regulatory pathways enable the body to sense and respond to changed amounts of nutrients in the blood and demands for energy.

Integration of pathways involved in energy metabolism

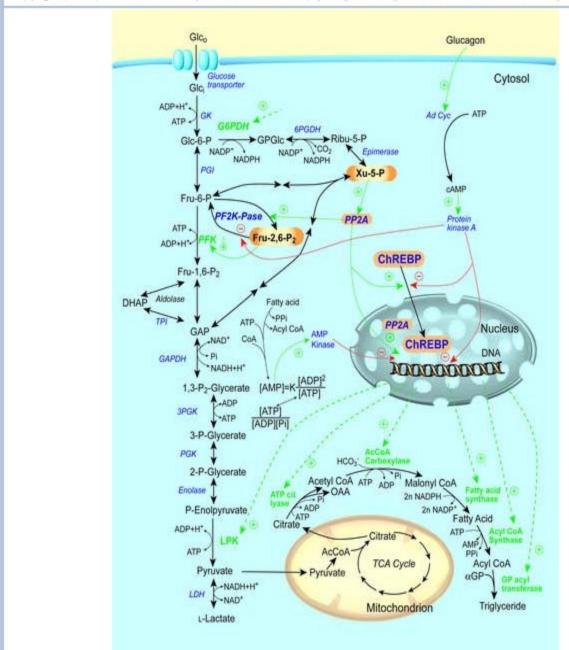
Glucagon and Insulin act through various metabolites and enzymes that target specific steps in metabolic pathways for sugar and fatty acids. The processes responsible for the long-term control of fat synthesis and short term control of glycolysis by key metabolic products and enzymes are annotated in this module as six specific pathways:

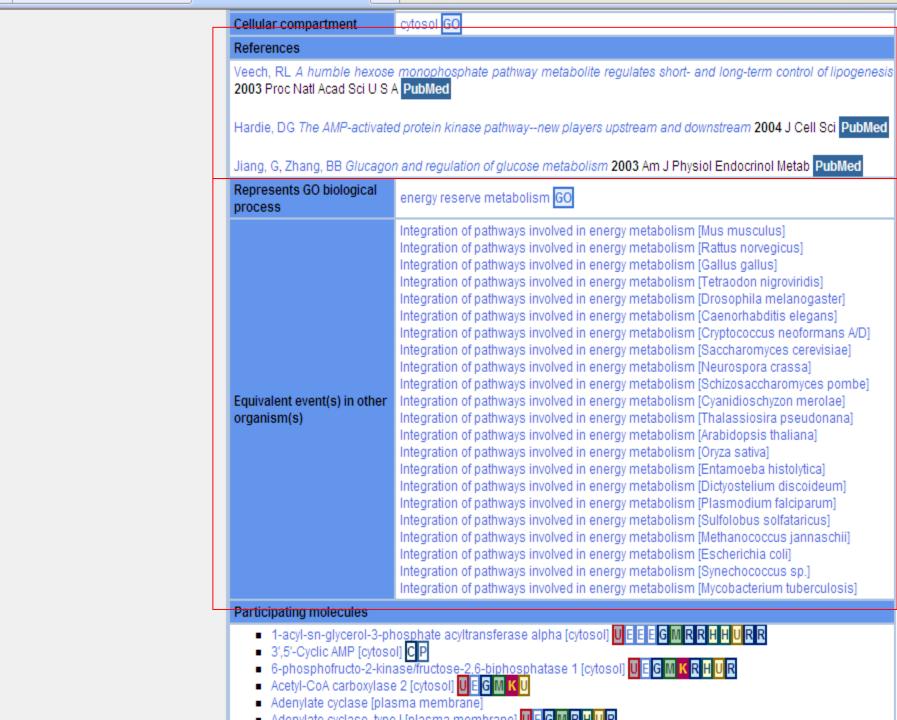
Pathway 1. Glucagon signalling in metabolic pathways: In response to low blood glucose, pancreatic alpha-cells

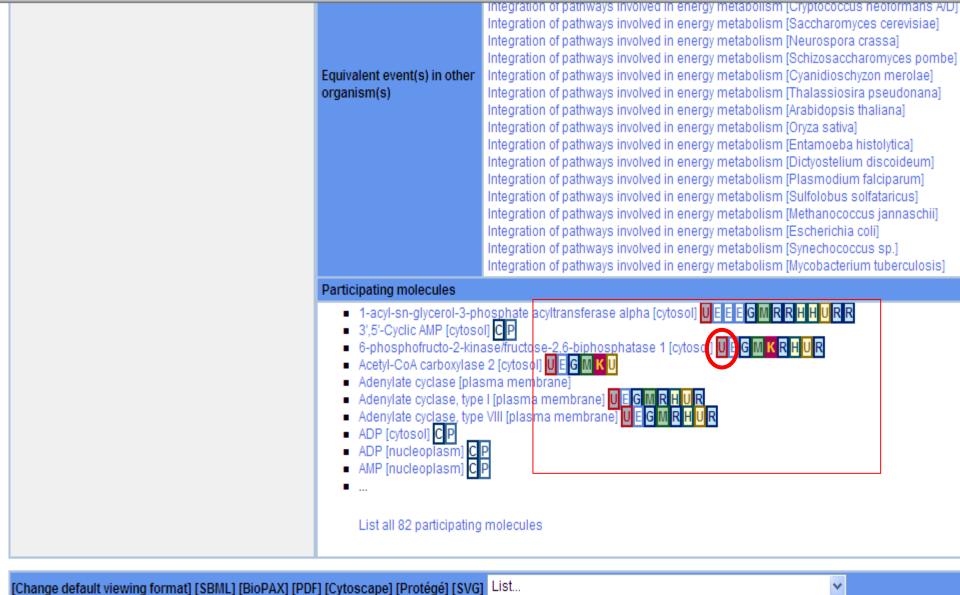
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event	open all	close all	Stable identifier	REACT_1505.1
□··  ☐ Integration	of pathways invol	lved in energy n 🛆	Authored	Gopinathrao, G, D'Eustachio, P, 2005-05-11
	n signaling in met	_	Reviewed	Rush, MG, 2005-09-10
⊞ - ¥ Insulin e 	diated phosphoryl effects increased s n of PP2A by Xylulo ibits the activation ediated dephosph	ynthesis of Xylu see-5-phosphat	and oxidation of foodstuffs nutrients, glucagon is involve principally by stimulating her elevations. These hormone-contrients in the blood and der Glucagon and Insulin act throsugar and fatty acids. The public glucagon and Insulin act throsugar and fatty acids. The public glucagon signal release glucagon. The bindin (PKA) activation.  Pathway 2. PKA mediate kinase /Fructose-2,6-bisphose Element Binding Protein (Chell Insulin mediated responses of insulin to its receptor lease of insulin to	dividual physiological processes including the regulation of appetite, absorption, transport, influence energy metabolism pathways. While insulin mediates the storage of excess yed in the mobilization of energy resources in response to low blood glucose levels, patic glucose output. Small doses of glucagon are sufficient to induce significant glucose triven regulatory pathways enable the body to sense and respond to changed amounts of nands for energy.  Jough various metabolites and enzymes that target specific steps in metabolic pathways for processes responsible for the long-term control of fat synthesis and short term control of oducts and enzymes are annotated in this module as six specific pathways:  Illing in metabolic pathways: In response to low blood glucose, pancreatic alpha-cells and glucagon to its receptor results in increased cAMP synthesis, and Protein Kinase A sted phosphorylation:PKA phosphorylates key enzymes, e.g., G-Phosphofructo-2-phatase (PF2K-Pase) at serine 36, and regulatory proteins, e.g., Carbohydrate Response REBP) at serine 196 and threonine 666.  To high blood glucose will be annotated in future versions of Reactome. In brief, the binding leads to increased protein phosphatase activity and to hydrolysis of cAMP by cAMP in the regulatory effects of glucagon.  In creased synthesis of Xylulose-5-phosphate (Xy-5-P). Activation of the insulin receptor IXy-5-P synthesis from Glyceraldehyde-3-phosphate and Fructose-6-phosphate. Xy-5-P, a sphate pathway, stimulates protein phosphatase PP2A.  PK) mediated response to high AMP:ATP ratio: In response to diet with high fat content or ollic AMP:ATP ratio is increased. AMP triggers a complicated cascade of events. In this only the phosphorylation of ChREBP by AMPK at serine 568, which inactivates this only the phosphorylation of ChREBP by AMPK at serine 568, which inactivates this only the phosphorylation and nuclear ChREBP:  activation of metabolic genes by ChREBP: Dephosphorylated ChREBP activates the directors of events. Black lines are metab

carboxylase, fatty acid synthetase, acyl CoA synthase and glycerol phosphate acyl transferase.

The illustration below summarizes this network of events. Black lines are metabolic reactions, red lines are negative regulatory events, and green lines are positive regulatory events (figure reused with permission from Veech (2003) - Copyright (2003) National Academy of Sciences, U.S.A.). [Jiang & Zhang 2003, Kabashima et al 2003]



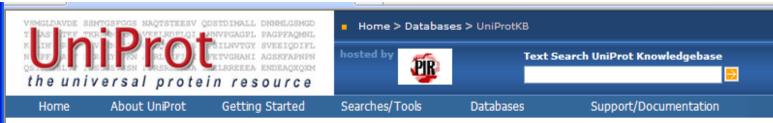




#### Stable link for this page

Date: 2007-03-02 07:26:41 help@reactome

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#### UniProtKB Entry

#### **PIR View**

UniProtKB Entry: P16118

ENTRY THEORMATION

ENTRY INFORMATION	
ENTRY NAME	F261 HUMAN
ACCESSION NUMBERS	P16118; Q5JXS5; Q99951
Integrated into Swiss-Prot on	1990-04-01
Sequence was last modified on	1997-11-01 (Sequence version 3)
Annotations were last modified on	2007-02-20 (Entry version 83)

	nodified on	2007-02-20 (Entry version 83)		
N	NAME AND ORIGIN OF THE PROTEIN			
P	PROTEIN NAME	6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 1		
S	ynonyms	6PF-2-K/Fru-2,6-P2ASE liver isozyme		
1	ncludes	6-phosphofructo-2-kinase (EC 2.7.1.105) Fructose-2,6-bisphosphatase (EC 3.1.3.46)		
G	SENE NAME	Name: PFKFB1		

### Link a las siguientes Bases de Datos

U UniProt

E Ensembl

G Entrez Gene

M OMIM

K KEGG (Kyoto Enciclopedia of Genes and Genomes)

R Entrez Nucleotide

H International HapMap Project

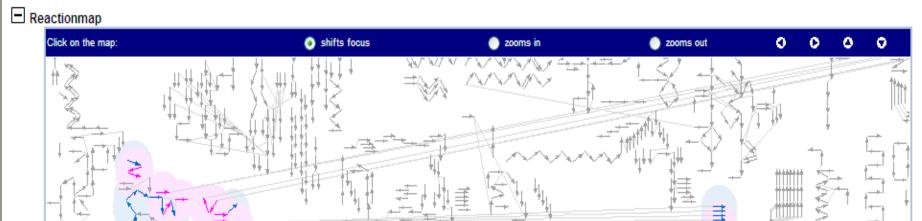
C ChEBI

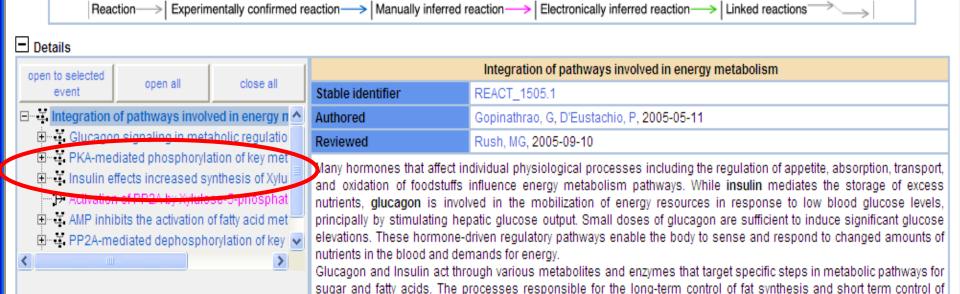
P PubChem

GO Gene Ontology



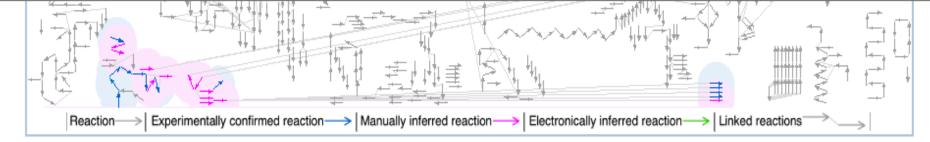
#### Integration of pathways involved in energy metabolism [Homo sapiens]





glycolysis by key metabolic products and enzymes are annotated in this module as six specific pathways:

Pathway 1. Glucagon signalling in metabolic pathways: In response to low blood glucose, pancreatic alpha-cells



#### Details

open to selected event	open all	close all
□ Integration	of pathways involv	ed in energy n
⊞ I Glucago	n signaling in meta	abolic regulatio
□ ∓ PKA-me	diated phosphoryla	ation of key met
> PKA (	catalytic subunit tra	nslocates to th
> Phos	phorylation of ChR	EBP at Thr(666
> Phos	phoChREBP (Thr	666) is exported
> Phos	phorylation of pCh	REBP (Thr 666
→ Nucle	ear transport of pCl	nREBP (Thr 66)
> Phos	phorylation of PF2I	K-Pase by PKA
	ctose 2,6-bisphosp	ohate + H20 =>
□ ∓ Insulin e	ffects increased sy	nthesis of Xylu
···· → D-fru	ctose 6-phosphate	+ D-erythrose
	ceraldehyde 3-pho	
	ceraldehyde 3-pho	sphate + sedol
	n of PP2A by Xylulo	
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□ ¥ PP2A-me	ediated dephosph	orylation of key 🔻
ab IIII		4

#### Integration of pathways involved in energy metabolism

REACT 1505.1 Authored Gopinathrao, G. D'Eustachio, P. 2005-05-11

#### Reviewed Rush, MG, 2005-09-10

Stable identifier

and oxidation of foodstuffs influence energy metabolism pathways. While insulin mediates the storage of excess nutrients, qlucagon is involved in the mobilization of energy resources in response to low blood glucose levels, principally by stimulating hepatic glucose output. Small doses of glucagon are sufficient to induce significant glucose elevations. These hormone-driven regulatory pathways enable the body to sense and respond to changed amounts of nutrients in the blood and demands for energy. Glucagon and Insulin act through various metabolites and enzymes that target specific steps in metabolic pathways for sugar and fatty acids. The processes responsible for the long-term control of fat synthesis and short term control of

Many hormones that affect individual physiological processes including the regulation of appetite, absorption, transport,

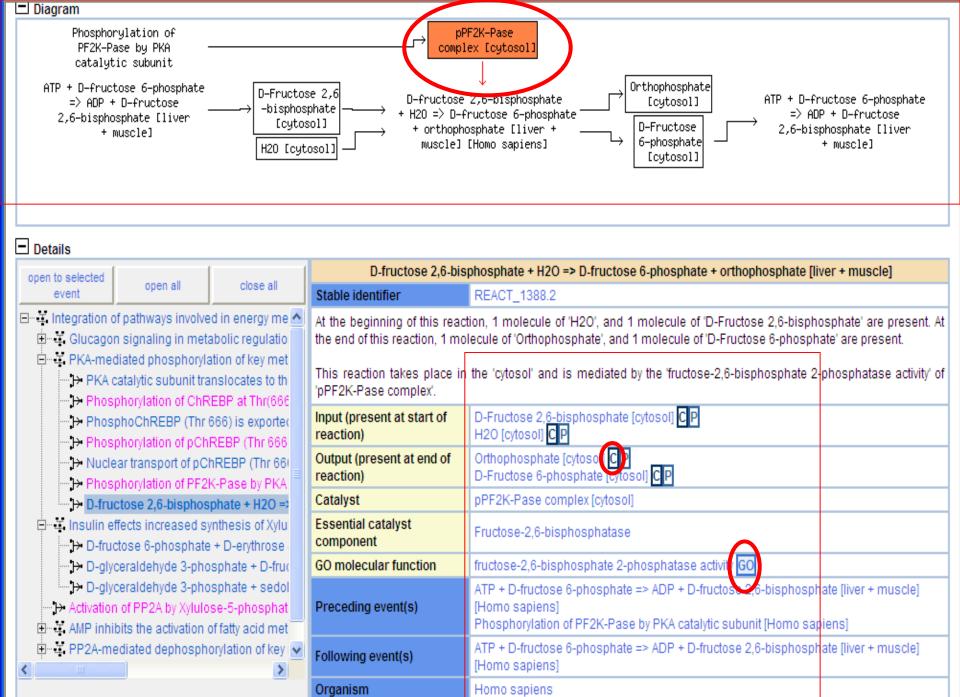
glycolysis by key metabolic products and enzymes are annotated in this module as six specific pathways: Pathway 1. Glucagon signalling in metabolic pathways: In response to low blood glucose, pancreatic alpha-cells release glucagon. The binding of glucagon to its receptor results in increased cAMP synthesis, and Protein Kinase A (PKA) activation.

Pathway 2. PKA mediated phosphorylation:PKA phosphorylates key enzymes, e.g., 6-Phosphofructo-2kinase /Fructose-2,6-bisphosphatase (PF2K-Pase) at serine 36, and regulatory proteins, e.g., Carbohydrate Response Element Binding Protein (ChREBP) at serine 196 and threonine 666.

Insulin mediated responses to high blood glucose will be annotated in future versions of Reactome. In brief, the binding of insulin to its receptor leads to increased protein phosphatase activity and to hydrolysis of cAMP by cAMP phosphodiesterase. These events counteract the regulatory effects of glucagon.

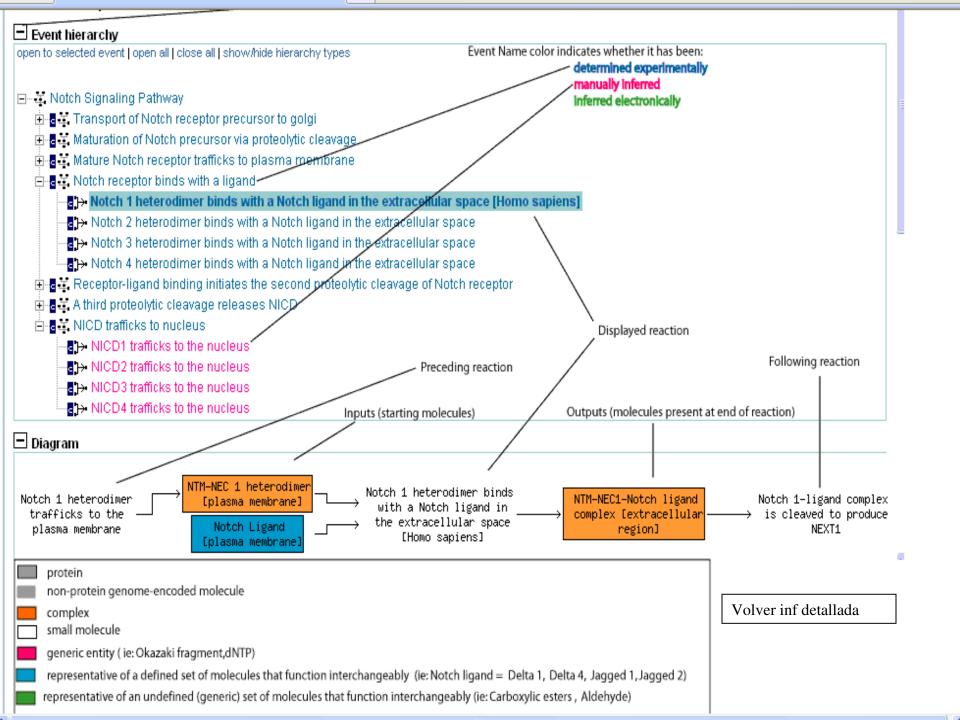
Pathway 3: Insulin stimulates increased synthesis of Xylulose-5-phosphate (Xy-5-P). Activation of the insulin receptor results indirectly in increased Xy-5-P synthesis from Glyceraldehyde-3-phosphate and Fructose-6-phosphate. Xy-5-P, a metabolite of the pentose phosphate pathway, stimulates protein phosphatase PP2A.

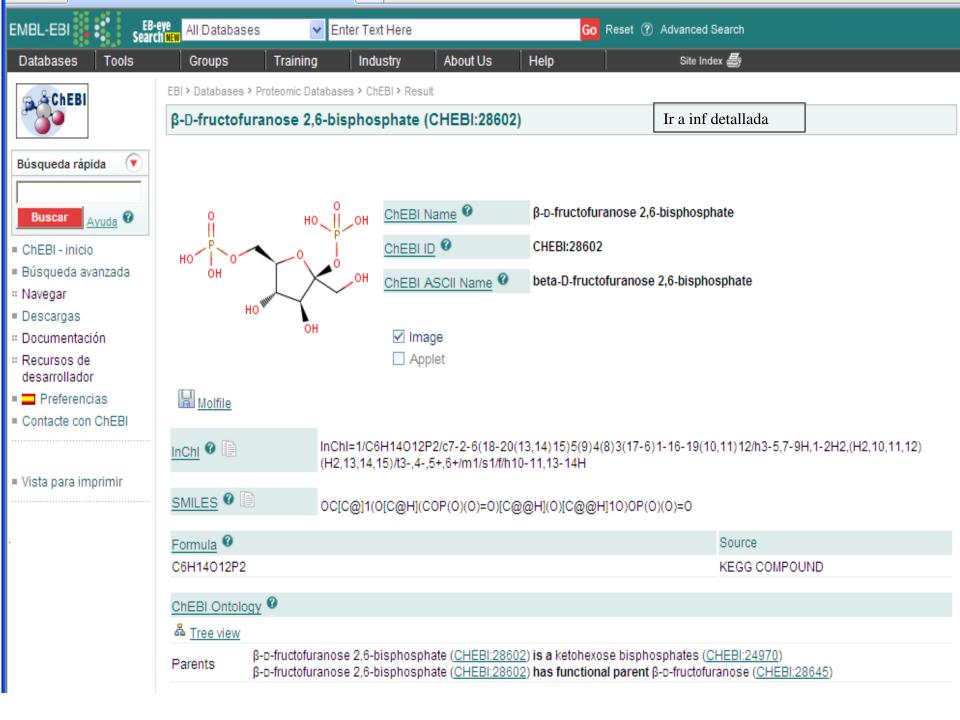
Pathway 4: AMP Kinase (AMPK) mediated response to high AMP:ATP ratio: In response to diet with high fat content or low energy levels, the cytosolic AMP:ATP ratio is increased. AMP triggers a complicated cascade of events. In this module we have annotated only the phosphorylation of ChREBP by AMPK at serine 568, which inactivates this transcription factor. Pathway 5: Dephosphorylation of key metabolic factors by PP2A: Xy-5-P activated PP2A efficiently dephosphorylates

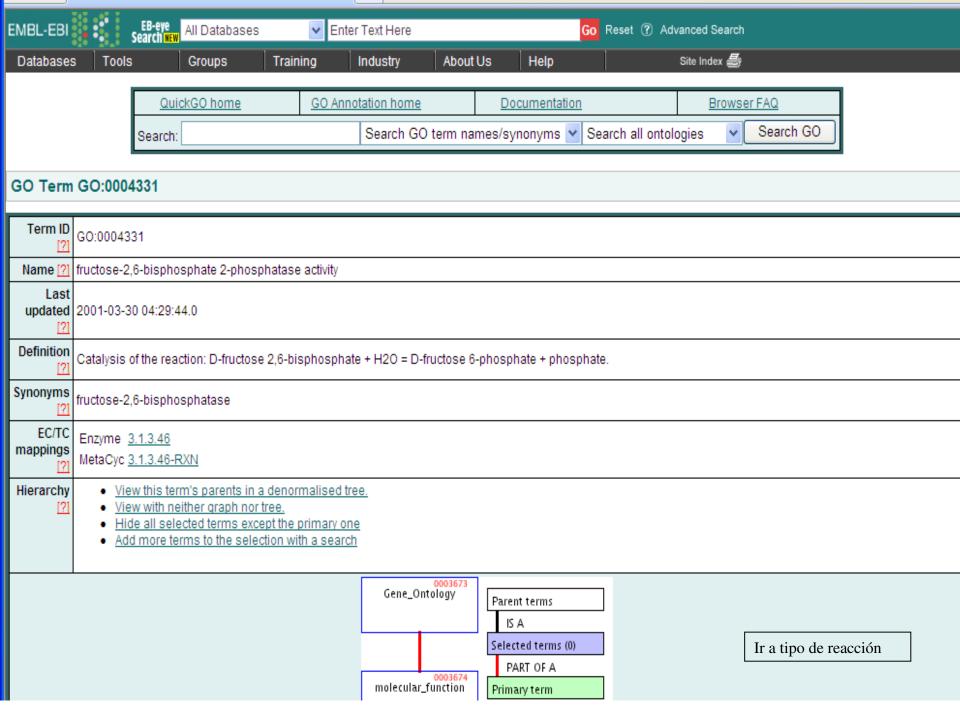


cytosol GO

Cellular compartment

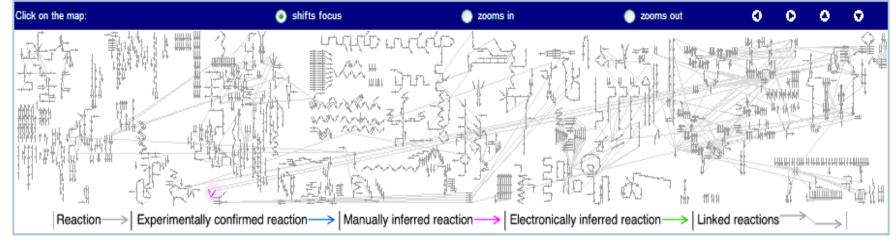


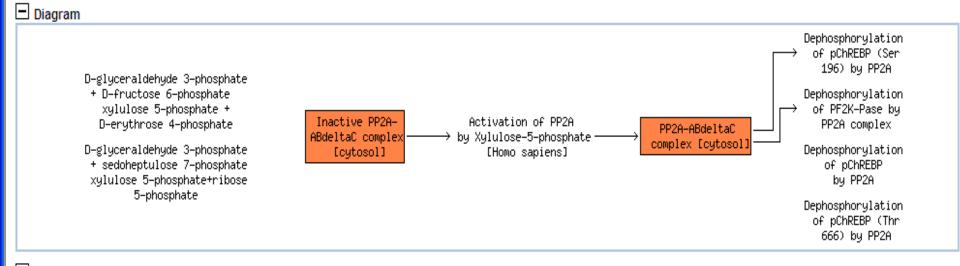


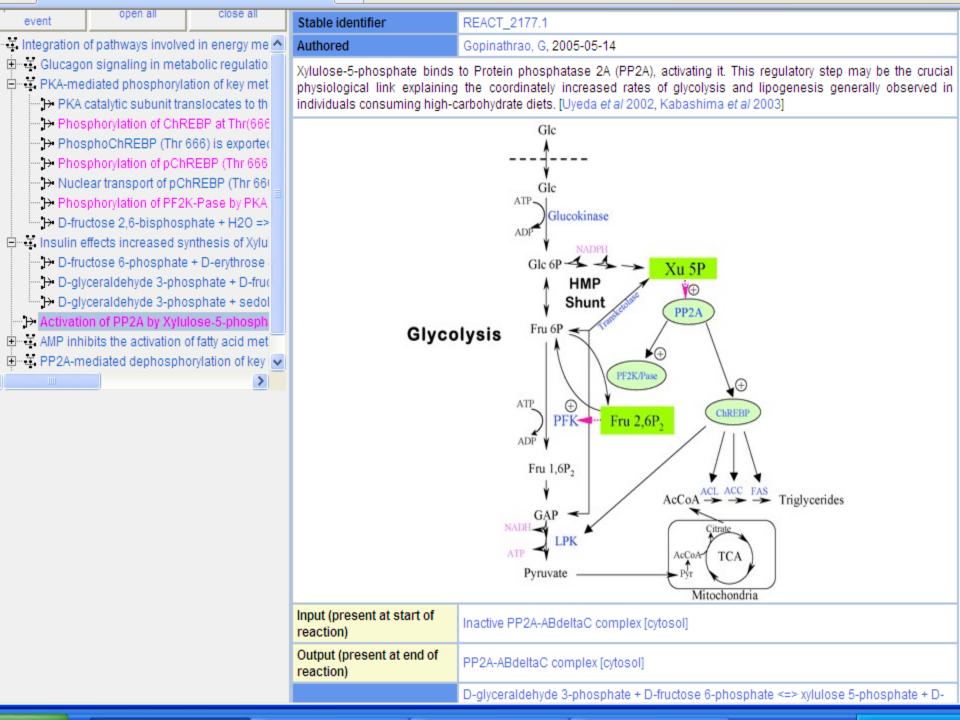








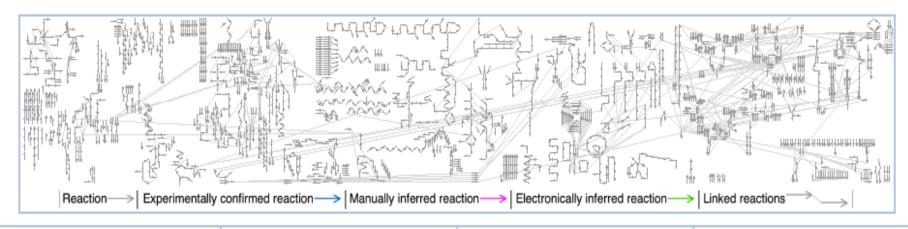




The data displayed is for Homo sapiens

💟 . Use the menu to change the species. Check 💟 🔭 cross-species comparison.





Apoptosis Hs Mm Rn Gg Tn Dm Ce Cn Sc Nc Sp Cm Tp At Os Dd Pf	Cell Cycle Checkpoints Hs Mm Rn Gg Tn Dm Ce Cn Sc Nc Sp Cm Tp At Os Eh Dd	Cell Cycle, Mitotic  Hs Mm Rn Gg Tn Dm Ce Cn Sc Nc Sp Cm Tp At Os Eh Dd Pf Ss Mj Ec Mt	DNA Repair Hs Mm Rn Gg Tn Dm Ce Cn Sc Nc Sp Cm Tp At Os Eh Dd Pf Ss Mj Ec Ss Mt
DNA Replication Hs Mm Rn Gg Tn Dm Ce Cn Sc Nc Sp Cm Tp At Os Eh Dd Pf Ss Mj	Electron Transport Chain Hs Mm Rn Tn Dm Ce Cn Sc Nc Sp Cm Tp At Os Dd Ss Ec Mt	Epidermal Growth Factor Receptor (EGFR) signaling Hs Mm Rn Gg Tn	Fibroblast Growth Factor Receptor (FGFR) signaling Hs Mm Rn Gg Tn Ce
Gap junction trafficking and regulation Hs Mm Rn Gg Tn	Gene Expression  Hs Mm Rn Gg Tn Dm Ce Cn Sc Nc Sp Cm Tp At Os Eh Dd Pf Ss Mj Ec Mt	HIV Infection Hs	Hemostasis Hs Mm Rn Gg Tn Dm Ce Nc Tp At Dd
Immune System signaling Hs Mm Rn Gg Tn Dm Nc Sp At Os	Influenza Infection Hs	Insulin receptor mediated signaling Hs Dm Mm Rn Gg Tn Dm Ce Cn Sc Nc Sp Cm Tp At Os Eh Dd Pf	Integration of pathways involved in energy metabolism Hs Mm Rn Gg Tn Dm Ce Cn Sc Nc Sp Cm Tp At Os Eh Dd Pf Ss Mj Ec Ss Mt
Maintenance of Telomeres Hs Mm Rn Gg Tn Dm Ce Cn Sc Nc Sp Cm Tp At Os Eh Dd Pf	Metabolism of amino acids and related nitrogen-containing molecules Hs Mm Rn Gg Tn Dm Ce Cn Sc Nc Sp Cm Tp At Os Eh Dd Pf Ss Mj Ec Ss Mt	Metabolism of carbohydrates Hs Mm Rn Gg Tn Dm Ce Cn Sc Nc Sp Cm Tp At Os Eh Dd Pf Ss Mj Ec Ss Mt	Metabolism of lipids and lipoproteins Hs Mm Rn Gg Tn Dm Ce Cn Sc Nc Sp Cm Tp At Os Eh Dd Pf Ss Mj Ec Ss Mt
			Ovidative decarbovulation of purposts



The data displayed is for Homo sapiens

| See the minute change the species. Check | for cross-species comparison.

| Peaction | Experimentally confirmed reaction | Manually inferred reaction | Electronically inferred reaction | Linked reactions | Linked react

Apoptosis	Cell Cycle Checkpoints	Cell Cyde, Mitotic	DNA Repair
DNA Replication	Electron Transport Chain	Epidermal Growth Factor Receptor (EGFR) signaling	Fibroblast Growth Factor Receptor (FGFR) signaling
Gap junction trafficking and regulation	Gene Expression	HIV Irfection	Hemostasis
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Pos:-translational modification of proteins	Transforming Growth Factor (TGF) beta signaling	Transcription	Translation
mRNA Processing	Xenobiotic metabolism		

Home About TOC User Guide Data Mod	del Schema Extended Searc	ch PathFinde	er SkyPair	nter Download Linking	Citing Editorial Calendar He	lp
Find everything with ALL of the words	v		in	Homo sapiens	<b>✓</b> Go	0!
Topic	Authors	Released	Revised	Reviewers	Editors	
Apoptosis [Homo sapiens]  - Extrinsic Pathway for Apoptosis  - Activation, myristolyation of BID and translocation to mitochondria  - Intrinsic Pathway for Apoptosis  - Activation of Effector Caspases  - Apoptotic execution phase	Alnemri, E, Hengartner, M, Tschopp, J, Tsujimoto, Y, Hardwick, JM, Gillespie, ME, Gopinathrao, G, Matthews, L	2004-09-20		Vaux, D, Hengartner, M	Gopinathrao, G, Matthews, L, Gillespie, ME, Joshi-Tope, G	
Cell Cycle Checkpoints [Homo sapiens] - G1/S DNA Damage Checkpoints - G2/M Checkpoints - Mitotic Spindle Checkpoint	Hoffmann, I, Khanna, K, O'Connell, M, Walworth, N, Yen, TJ, Yen, T, Borowiec, JA, Matthews, L, Matthews, L	2005-01-24		Sanchez, Y, Knudsen, E, Hardwick, KG, Peters, JM, Manfredi, J, Coqueret, O	Matthews, L, Joshi-Tope, G, D'Eustachio, P, Matthews, L	
Cell Cycle, Mitotic [Homo sapiens]  - G1 Phase  - G1/S Transition  - S Phase  - G2 Phase  - G2/M Transition  - M Phase  - M/G1 Transition  - APC/C-mediated degradation of cell cycle proteins	O'Connell, M, Walworth, N, Bosco, G, Lorca, T, Castro, A, Gopinathrao, G, Pagano, M, Lee, KS, Davey, MJ, O'Donnell, M, Tye, BK, Matthews, L, Tom, S, Bambara, RA, Yen, T	2004-07-06		Manfredi, J, Lorca, T, Pete JM, Coqueret, O	rs, Matthews, L, Gopinathrao, G, Matthews, L, Gillespie, ME	
DNA Repair [Homo sapiens]  - Base Excision Repair  - DNA Damage Bypass  - DNA Damage Reversal  - Double-Strand Break Repair  - Nucleotide Excision Repair	Hoeijmakers, JH, Lees-Miller, S, Thompson, L, Gopinathrao, G, Matthews, L, Schultz, R, Pegg, A, Joshi-Tope, G	2004-07-06		Khanna, KK, Lindahl, T, W SC, Wood, RD	/est, Matthews, L, Gopinathrao, G, Joshi-Tope, G	
DNA Replication [Homo sapiens]	Bambara, RA, Catlett, M, Davey,	2003-01-06	2005-09-	Mendez, J, Aladjem, M	D'Eustachio, P, Joshi-Tope, (	G,

The data displayed is for Homo sapiens

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| Possible | Possib

Apoptosis	Cell Cycle Checkpoints	Cell Cyde, Mitotic	ONA Repair
DNA Replication	Electron Transport Chain	Epidermal Growth Factor Receptor (EGFR) signaling	Fibroblast Growth Factor Receptor (FGFR) signaling
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Pos:-translational modification of proteins	Transforming Growth Factor (TGF) beta signaling	Transcription	Translation
mRNA Processing	Xenobiotic metabolism		

#### Data model

properates or are motanices (e.g., are rachaacs or are morecales and paracipate as impais and outputs in a reaction)

#### Key data classes

#### PhysicalEntity

PhysicalEntities include individual molecules, multi-molecular complexes, and sets of molecules or complexes grouped together on the basis of shared characteristics. Molecules are further classified as genome encoded (DNA, RNA, and proteins) or not (all others). Attributes of a PhysicalEntity instance capture the chemical structure of an entity, including any covalent modifications in the case of a macromolecule, and its subcellular localization.

PhysicalEntity instances that represent, e.g., the same chemical in different compartments, or different post-translationally modified forms of a single protein, share numerous invariant features such as names, molecular structure and links to external databases like UniProt or ChEBI. To enable storage of this shared information in a single place, and to create an explicit link among all the variant forms of what can also be seen as a single chemical entity, Reactome creates instances of the separate ReferenceEntity class. A ReferenceEntity instance captures the invariant features of a molecule. A PhysicalEntity instance is then the combination of a ReferenceEntity attribute (e.g., Glycogen phosphorylase UniProt:P06737) and attributes giving specific conditional information (e.g., localization to the cytosol and phosphorylation on serine residue 14).

The PhysicalEntity class has subclasses to distinguish between different kinds of entities and to ensure data integrity while enabling different handling rules for different categories:

EntityWithAccessionedSequence - proteins and nucleic acids with known sequences.

GenomeEncodedEntity - a species-specific protein or nucleic acid whose sequence is unknown, such as an enzyme that has been characterized functionally but not yet

purified and sequenced, e.g., cytosolic triokinase

SimpleEntity - other fully characterized molecules, e.g., nucleoplasmic ATP or cytosolic glutathione

Complex- a complex of two or more PhysicalEntities, e.g., FASL:FAS Receptor Trimer:FADD complex associated with the plasma membrane

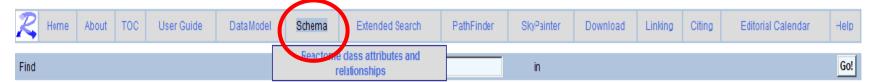
EntitySet - a set of PhysicalEntities (molecules or complexes) which function interchangeably in a given situation, e.g., Notch ligand associated with the plasma membrane. This notation allows collective properties of multiple individual entities to be described explicitly.

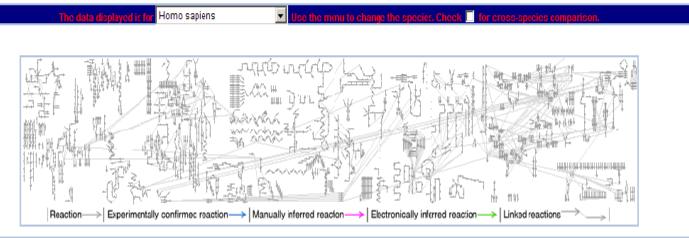
#### CatalystActivity

PhysicalEntities are paired with molecular functions taken from the Gene Ontology molecular function controlled vocabulary to describe instances of biological catalysis. An optional ActiveUnit attribute indicates the specific domain of a protein or subunit of a complex that mediates the catalysis. If a PhysicalEntity has multiple catalytic activities, a separate CatalystActivity is created for each. This strategy allows the association of specific activities with specific variant forms of a protein or complex, and also enables easy retrieval of all activities of a protein, or all proteins capable of mediating a specific molecular function.

#### Event

Events - the conversion of input PhysicalEntities to output PhysicalEntities - are the building blocks used in Reactome to represent all biological processes. At present, only two subclasses of Event are recognized, *Reaction* and *Pathway*. A Reaction is an event that converts inputs to outputs in a single step. A pathway is any grouping of related events. An event may be a member of more than one pathway.





Apoptosis	Cell Cycle Checkpoints	Cell Cyde, Mitotic	DNA Repair
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Gap junction trafficking and regulation	Gene Expression	HIV Irfection	Hemostasis
Immune System signaling	Influenza Infection	Insulin receptor mediated signaling	Integration of pathways involved in enercy metabolism
Maintenance of Telomeres	Metabolism of amino acids and related nilrogen- containing molecules	Metabolism of carbohydrates	Metabolism of lipids and lipoproteins
Metabolism of nucleotides	Metabolism of porphyrins	Notch Signaling Pathway	Oxidative decarboxylation of pyruvate and TCA cycle
Pos:-translational modification of proteins	Transforming Growth Factor (TGF) beta signaling	Transcription	Translation
mRNA Processing	Xenobiotic metabolism		



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ReferenceSequence [29485] ReferenceDNASequence [8025] ReferencePeptideSequence [19700] ReferenceRNASequence [1760]

#### Attributes of class 'DatabaseObject'

Attribute name	Cardinality	Value type	Allowed classes	Attribute origin	Value defines instance	Db column type
DB_ID	1	INTERNAL_ID	N/A	DatabaseObject		NTEGER(10) UNSIGNED
is_ghost	1	OTHER	N/A	DatabaseObject		ENUM('TRUE')
_displayName	1	TEXT	N/A	DatabaseObject		TEXT
_timestamp	1	OTHER	N/A	DatabaseObject		TIMESTAMF
created	1	INSTANCE	InstanceEdit	DatabaseObject		NTEGER(10) UNSIGNED
modified	+	INSTANCE	InstanceEdit	DatabaseObject		NTEGER(10) UNSIGNED
stableldentifier	1	INSTANCE	StableIdentifier	DatabaseObject		NTEGER(10) UNSIGNED

Sidebar on the left shows the hierarchy of Reactome classes. The number of instances of this class is shown in square brackets and is hyperlinked to a page listing all instances in this class.

The main panel shows attributes of the selected class. Own attributes, i.e. the ones which are not inherited from a parent class are indicated in colour.

Value defines instance' column indicates the attributes the values of which determine instance identity and are used to check if an identical instance has been stored in the database already. 'ALL' indicates that that all of the values of a civen attribute must be identical while 'ANY' shows that identity of any single value of a given attribute is enough. Of course, if the identity is defined by multiple attributes each of them has to match.

<sup>&#</sup>x27;+' in 'Cardinality' column indicates that this is a multi-value attribute.

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	-	ventSet [3				Attribute n	name	Cardinality	Value type	All	lowed classes	Attribute original	gin Valu	ie defines ii	nstance	Db column ty	/ре
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	ntPage [1]	•				evidenceTyp	е	1	INSTANCE		denceType	Event				INTEGER(10) U	
		alProcess				figure		+	INSTANCE	Figu		Event				INTEGER(10) U	
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#### Attributes of class 'DatabaseObject'

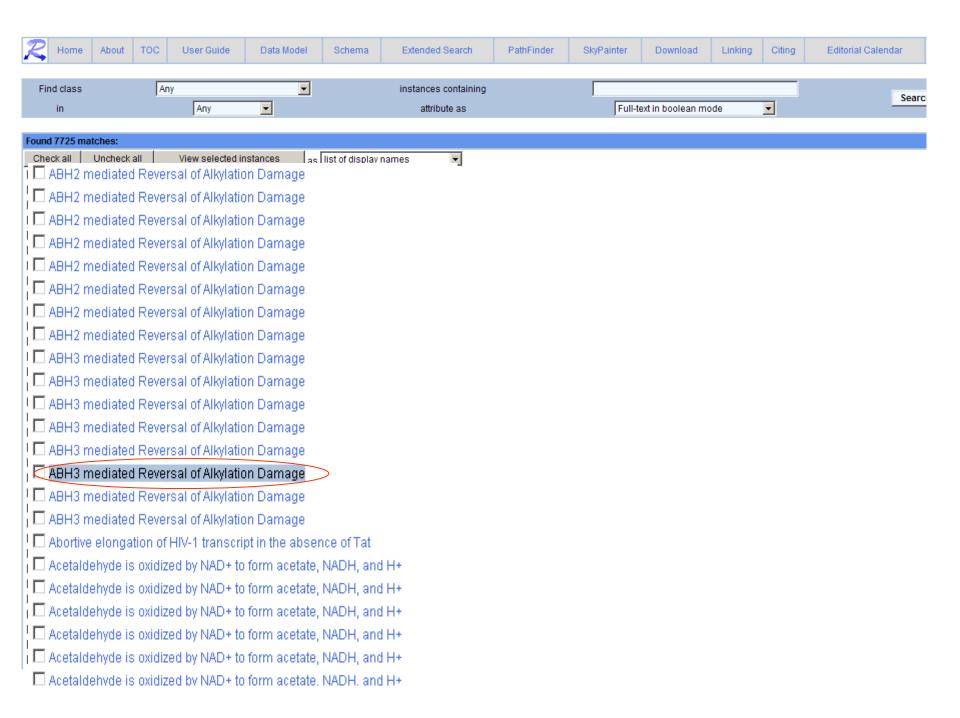
Attribute name	Cardinality	Value type	Allowed classes	Attribute origin	Value defines instance	Db column type
DB_ID	1	INTERNAL_ID	N/A	DatabaseObject		NTEGER(10) UNSIGNED
is_ghost	1	OTHER	N/A	DatabaseObject		ENUM('TRUE')
_displayName	1	TEXT	N/A	DatabaseObject		TEXT
_timestamp	1	OTHER	N/A	DatabaseObject		TIMESTAMP
created	1	INSTANCE	InstanceEdil	DatabaseObject		NTEGER(10) UNSIGNED
modified	+	INSTANCE	InstanceEdit	DatabaseObject		NTEGER(10) UNSIGNED
stableldentifier	1	INSTANCE	StableIdentifier	DatabaseObject		NTEGER(10) UNSIGNED

Sidebar on the left shows the hierarchy of Reactome classes. The number of instances of this class is shown in square brackets and is hyperlinked to a page listing all instances in this class.

The main panel shows attributes of the selected class. Own attributes, i.e. the ones which are not inherited from a parent class are indicated in colour.

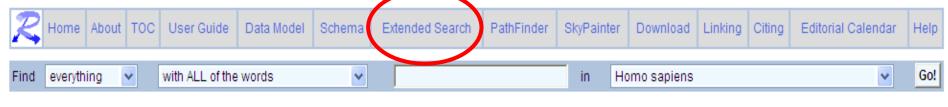
'+' in 'Cardinality' column indicates that this is a multi-value attribute.

Value defines instance' column indicates the attributes the values of which determine instance identity and are used to check if an identical instance has been stored in the database already. 'ALL' indicates that that all of the values of a given attribute must be identical while 'ANY' shows that identity of any single value of a given attribute is enough. Of course, if the identity is defined by multiple attributes each of them has to match.



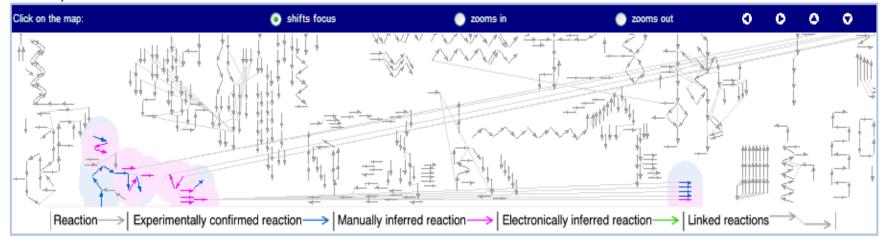
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Class:ld	Pathway:259057
_displayName	ABH3 mediated Reversal of Alkylaton Damage
_timestamp	20070222130753
ompartment	[Compartment:352] nucleus
reated	[InstanceEdit:255821] Schmidt, EE
videnceType	[EvidenceType:203113] inferred by electronic annotation
oBiologicalProcess	[GO_BiologicalProcess:17672] DNA dealkylation
nasComponent	<ul> <li>■ [Reaction:258262] Oxidative demethylation of 1-MeA damaged DNA By ABH3 [Neurospora crassa]</li> <li>■ [Reaction:258263] Oxidative demethylation of 3-MeC damaged DNA By ABH3 [Neurospora crassa]</li> <li>■ [Reaction:258261] Oxidative demethylation of 1-EtA damaged DNA By ABH3 [Neurospora crassa]</li> </ul>
nferredFrom	■ [Pathway:112126] ABH3 mediated Reversal of Alkylation Damage [Homo sapiens]
name	ABH3 mediated Reversal of Alkylaton Damage
orthologousEvent	<ul> <li>■ [Pathway:112126] ABH3 mediated Reversal of Alkylation Damage [Homo sapiens]</li> <li>■ [Pathway:211877] ABH3 mediated Reversal of Alkylation Damage [Mus musculus]</li> <li>■ [Pathway:221642] ABH3 mediated Reversal of Alkylation Damage [Rattus norvegicus]</li> <li>■ [Pathway:230235] ABH3 mediated Reversal of Alkylation Damage [Gallus gallus]</li> <li>■ [Pathway:238273] ABH3 mediated Reversal of Alkylation Damage [Neurospora crassa]</li> <li>■ [Pathway:259057] ABH3 mediated Reversal of Alkylation Damage [Muscobacterium tuberculosis]</li> <li>■ [Pathway:293716] ABH3 mediated Reversal of Alkylation Damage [Mycobacterium tuberculosis]</li> </ul>
species	[Species:176745] Neurospora crassa
summation	[Summation:203111] This event has been computationally inferred from an event t
hasComponent)	[Pathway:259169] Reversal of Alkylation Damage By DNA Dioxygenases [Neurospora crassa]
orthologousEvent)	[Pathway:112126] ABH3 mediated Reversal of Alkylation Damage [Homo sapiens]

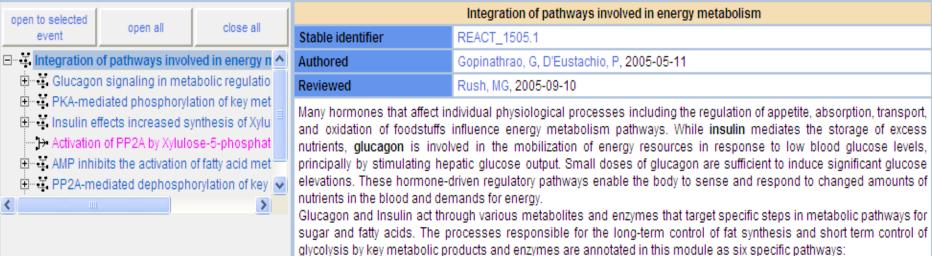


#### Integration of pathways involved in energy metabolism [Homo sapiens]



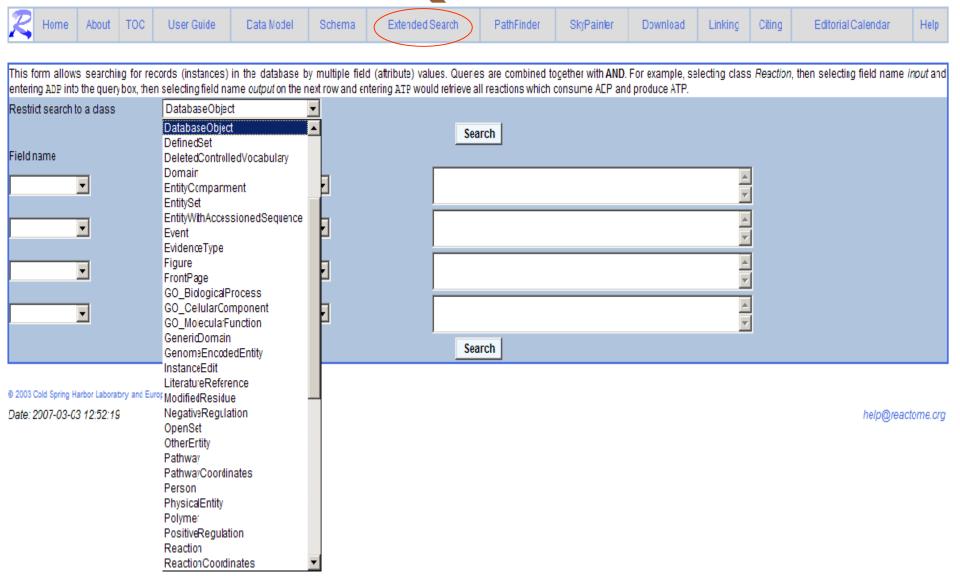






Pathway 1. Glucagon signalling in metabolic pathways: In response to low blood glucose, pancreatic alpha-cells

## BUSQUEDAS

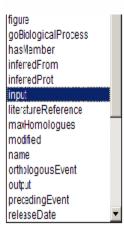




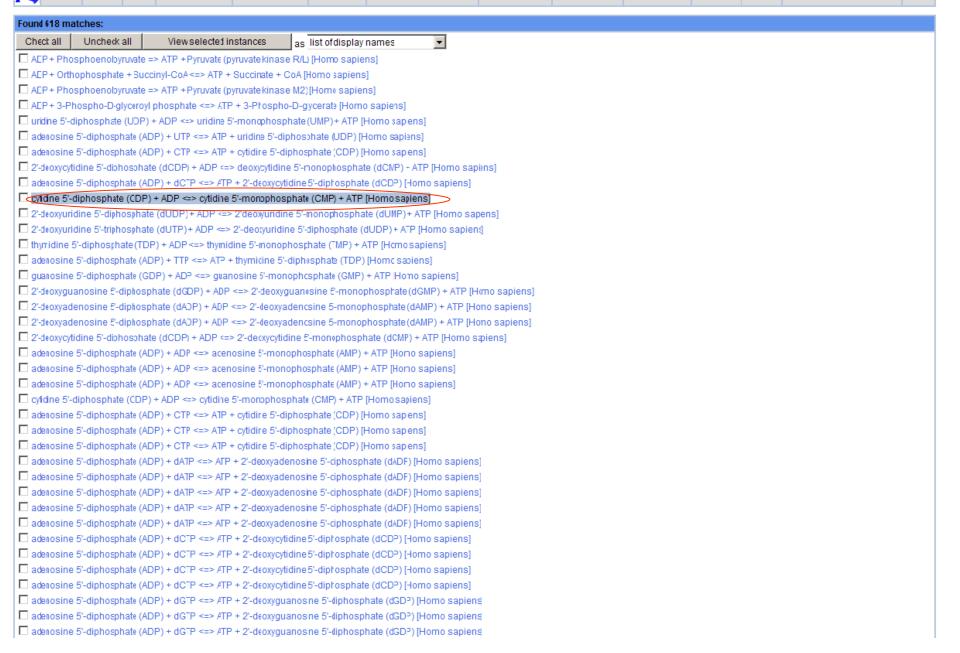
This form allows searching for records (instances) in the database by multiple field (attribute) values. Queries are combined together with AND. For example, selecting class Reaction, then selecting field name input and entering ADP into the query bix, then selecting field name output on the next rowand entering ADP would retrieve all reactions which consume ADP and produce ATP. Restrict search to a class Reaction Search Field nane ADP ▼ with the EXACT PHRASE ONLY input ATP with the EXACT PHRASE ONLY output with the EXACT PHRASE ONLY • with the EXACT PHRASE ONLY Search

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Date: 20(7-03-03 13:03:54

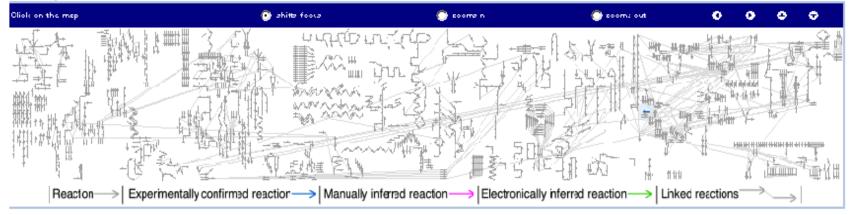


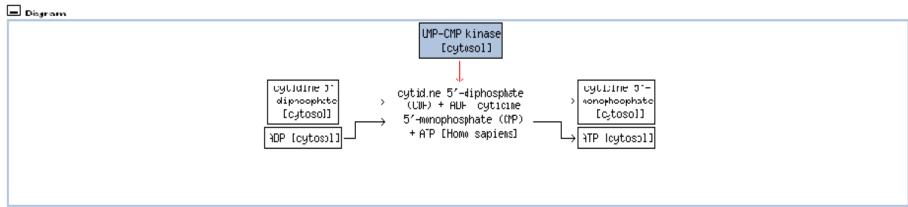




# cytidine 5'-diphosphate (CDP) + ADP <=> cytidine 5'-monophosphate (CMP) + ATP [Homo sapiens]

# ☐ Reactionmap







cytidine 5'-diphosphate(CDP) + ADP <=> cytidine 5'-nonophosphate(CMP) + ATP

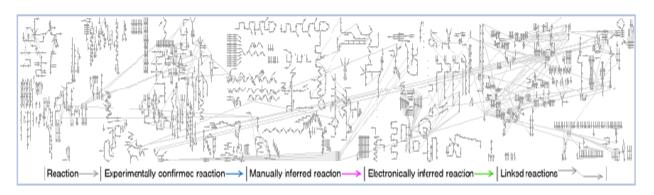
Stable identifier REACT\_24\*.2

At the beginning of this reaction, 1 molecule of 'cytidine 5-diphosphate', and 1 molecule of 'ADP' are present. At the end of this reaction, 1 molecule of 'cytidine 5'-monophosphate', and 1 molecule of 'ATP' are present.

This reaction takes place in the 'cypsol' and is mediated by the 'nucleoside kinase activity' of 'UMP-CMP kinase'.

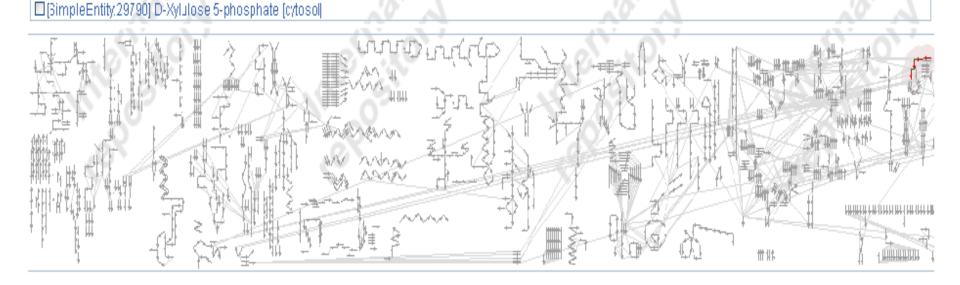


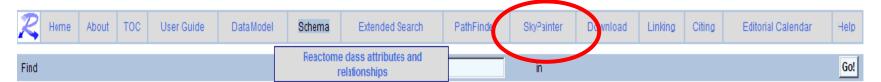
The data displayed is for Homo sapiens Use the monu to change the species, Check 🔲 for cross-species comparison.

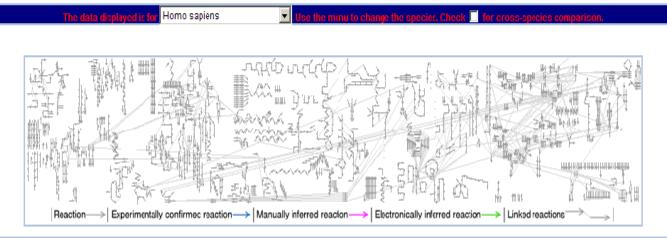


Apoptosis	Cell Cycle Checkpoints	Cell Cyde, Mitotic	DNA Repair
DNA Replication	Electron Transport Chain	Epidermal Growth Factor Receptor (EGFR) signaling	Fibroblast Growth Factor Receptor (FGFR) signaling
Gap junction trafficking and regulation	Gene Expression	HIV Irfection	Hemostasis
Immune System signaling	Influenza Infection	Insulin receptor mediated signaling	Integration of pathways involved in enercy metabolism
Maintenance of Telomeres	Metabolism of amino acids and related nilrogen- containing molecules	Metabolism oʻ carbohydrates	Metabolism of lipids and lipoproteins
Metabolism of nucleotides	Metabolism of porphyrins	Notch Signaling Pathway	Oxidative decarboxylation of pyruvate and TCA cycle
Pos:-translational modification of proteins	Transforming Growth Factor (TGF) beta signaling	Transcription	Translation
mRNA Processing	Xenobiotic metabolism		

# Found path: | Complex:70373] G6PD dimer [cytosol] [Homo sapiens] | CatalystActivity:70374] glucose-3-phosphate 1-dehydrogenase activity of G6PD dimer [cytosol] | Reaction:70377] alpha-D-glucose 6-phosphate + NADP+ => D-glucono-1,5-lactone 6-phosphate + NADPH + H+ [G6PD dimer] [Homo sapiens] | GimpleEntity:31467] D-Glucono-1,5-lactone 6-phosphate [cytosol] | Reaction:71296] D-glucoro-1,5-lactone 6-phosphate + H2O => 6-phospho-D-gluconate [Homo sapiens] | GimpleEntity:29396] 6-Phospho-D-gluconate | Cytosol] | Reaction:71299] 8-phospho-D-gluconate + NADP+ => D-ribulose 5-phosphate - CO2 + NADP+ + H+ [Homo sapiens] | Reaction:71303] D-ribulose 5-phosphate (cytosol]

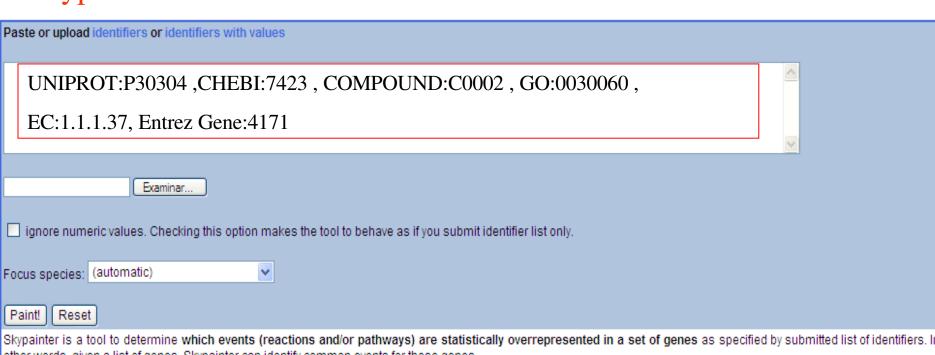






Apoptosis	Cell Cycle Checkpoints	Cell Cyde, Mitotic	DNA Repair
DNA Replication	Electron Transport Chain	Epidermal Growth Factor Receptor (EGFR) signaling	Fibroblast Growth Factor Receptor (FGFR) signaling
Gap junction trafficking and regulation	Gene Expression	HIV Irfection	Hemostasis
Immune System signaling	Influenza Infection	Insulin receptor mediated signaling	Integration of pathways involved in enercy metabolism
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Pos:-translational modification of proteins	Transforming Growth Factor (TGF) beta signaling	Transcription	Translation
mRNA Processing	Xenobiotic metabolism		

# Skypainter



Skypainter is a tool to determine which events (reactions and/or pathways) are statistically overrepresented in a set of genes as specified by submitted list of identifiers. In other words, given a list of genes, Skypainter can identify common events for these genes.

Given a set of M genes which participate in an event, the total of X genes (for the given species) that Reactome is aware of, and given the submitted list of K genes of which N genes participate in the given event, skypainter calculates (by performing the hypergeometric test) the probability of picking N or more genes involved in the given event purely by chance. Hence a low probability suggests that participation in a given event is what the genes in the submitted list have in common. Note, however, that the probabilities as reported by Skypainter are not corrected for multiple testing arising from evaluating the submitted list of genes against every event for the given species.

Identifiers which can be used are UniProt accession numbers and ids, GenBank/EMBL/DDBJ protein ids, RefPep, RefSeq, EntrezGene, MIM, InterPro, Affymetrix, Agilent and Ensembliprotein, transcript and gene identifiers. All purely numeric identifiers, such as from MIM and EntrezGene have to have the abbreviated database name and colon prepended to them, i.e. MIM:602544, EntrezGene:55718.

The colour of each reaction arrow on the reaction map indicates the the number of genes in the submitted list that participates in the reaction.

Similar functionality, i.e colouring reactions according to the number of times the reaction is hit by the identifiers in the submitted list, is also available for small molecule identifiers from ChEBI and KEGG COMPOUND identifiers (e.g. ChEBI:2359, C00002), Enzyme Commission (EC) numbers (e.g. 1.1.1.1) and Gene Ontology (GO) accession numbers (e.g. GO:0004672). GO cellular component accession numbers can be used to highlight reactions involving molecules localized to that compartment or which themselves correspond to the given GO cellular component term. GO molecular function accession numbers highlight reactions which are catalysed by the activities they specify. GO biological process accession numbers highlight reactions which either correspond or are components of pathways corresponding to the given GO biological processes. Please note that the overrepresentation analysis is not performed for those identifiers.

The data displayed is for Homo sapiens

| Use the menu to change the species. Check | Torcross species comparison.

| Reaction | Experimentally confirmed reaction | Manually inferred reaction | Electronically inferred reaction | Linked reaction |

Apcptosis	Cell Cycle Checkpoints	Cell Cycle, Witotic	DNA Repair
DNA Replication	Electron Transport Chain	Epidermal Growth Factor Receptor (EGFR) signaling	Fibroblast Growth Factor Receptor (FGFR) signaling
Gap junction trafficking and regulation	Gene Expression	HIV Infection	Hemostasis
Immune System signaling	Influenza infection	Insulin receptor mediated signaling	Integration of pathways involved in energy metabolism
Maintenance of Telomeres	Metabolism of amino acids and related nitrogen- containing molecules	Metabolism of carbohydrates	Metabolism of lipids and lipoproteins
Metabolism of nucleotides	Metabolism of porphyrins	Notch Signaling Pathway	Oxidative decarboxylation of pyruvate and TCA cycle
Post-translational modification of proteins	Transforming Growth Factor (TGF) beta signaling	Transcription	Translation
mRNA Processing	Xenobiotic metabolism		

# Download Reactome data and code

### The whole content of the Reactome can be downloaded as:

MySQL database dump (To use skypainter you also need this database)

### Several narrower datasets and download formats are also available:

- Human reactions in SBML (level 2, version 1) format.
- Human protein-protein interaction pairs in tab-delimited format.
- Events in the BioPAX level 2 format

### The complete Reactome textbook of biological pathways and processes can be downloaded in:

- PDF format.
- RTF format.

### The Reactome website can be installed locally:

- Instructions for local installation of Reactome database and website. Please note that you need to have root privileges on the computer onto which you plan to install the copy of Reactome.
- Download Reactome website contents and perlicode (requires additional non-Reactome software).

Two Java tools are available for Reactome data entry. The Author tool is designed for biologists to input data into Reactome, while the Curator tool is meant for use by curators to annotate biological pathways based on the Reactome schema.

- Author Tool (version 2.1, build 25, September 29, 2006)
- Curator Tool (version 2.0, build 33, December 5, 2008)

A SOAP based Web Services API is available to access the Reactome data. For details about this API, please follow the following links:

- . Simple Description for the Reactome Web Services API
- . Training Materials for the Reactome Web Services API
  - User's Guide in PDF (1M)
  - o Tutorial in Power Point Slides (2M)
  - Tutorial in Flash Movie (640 x 480) (11M)
  - Tutorial in Flash Movie (800 x 600) (12M)
- XML Schema for the data model
- WSDL file for the Reactome Web Servies API.

Date: 2007-03-04 22:26:29 help@reactome.org

Homo sapiens

Use the menu to change the species. Check for cross species comparison.

Reaction | Experimentally confirmed reaction | Manually inferred reaction | Electronically inferred reaction | Linked react

Apcptosis	Cell Cycle Checkpoints	Cell Cycle, Mitotic	DNA Repair
DNA Replication	Electron Transport Chain	Epidermal Growth Factor Receptor (EGFR) signaling	Fibroblast Growth Factor Receptor (FGFR) signaling
Gap junction trafficking and regulation	Gene Expression	HIV Infection	Hemostasis
Immune System signaling	Influenza infection	Insulin receptor mediated signaling	Integration of pathways involved in energy metabolism
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Post-translational modification of proteins	Transforming Growth Factor (TGF) beta signaling	Transcription	Translation
mRNA Processing	Xenobiotic metabolism		

# Linking to Reactome

Linking to Reactome can be achieved by creating URLs containing the name of and an identifier from an "external" database in the following format:

http://www.reactome.org/cgi-bin/link?SOURCE=Database name&ID=identifier



Below are few concrete examples

- UniProt accession numbers (the 'AC' line, preferred) and identifiers (the 'ID' line), e.g. UNIPROT:P30304 http://www.reactome.org/cgi-bin/link?SOURCE=UNIPROT&ID=P30304
- ChEBI identifiers, e.g. CHEBI:7423 http://www.reactome.org/cgi-bin/link?SOURCE=CHEBI&ID=7423
- identifiers, e.g. COMPOUND:C00002 http://www.reactome.org/cgi-bin/link?SOURCE=COMPOUND&ID=C00002
- Gene Ontology (GO) accession numbers, e.g. GO:0030060 http://www.reactome.org/cgi-bin/link?SOURCE=GO&ID=0030060
- Enzyme Classification (EC) numbers, e.g. EC:1.1.1.37
   http://www.reactome.org/cgi-bin/link?SOURCE=EC&ID=1.1.1.37
- Entrez Gene, e.g. Entrez Gene:4171 http://www.reactome.org/cgi-bin/link?SOURCE=Entrez+Gene&ID=4171

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Date: 2007-03-02 07:59:30 help@reactome.org



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Date: 2007-03-02 08:08:20 help@reactome.org

The data displayed is to

| Homo sapiens | Use the menu to charge the species. Check | for cross species comparison.

| Reaction | Experimentally confirmed reaction | Manually inferred reaction | Electronically inferred reaction | Linked reaction

Apcptosis	Cell Cycle Checkpoints	Cell Cycle, Witotic	DNA Repair
DNA Replication	Electron Transport Chain	Epidermal Growth Factor Receptor (EGFR) signaling	Fibroblast Growth Factor Receptor (FGFR) signaling
Gap junction trafficking and regulation	Gene Expression	HIV Infection	Hemostasis
Immune System signaling	Influenza infection	Insulin receptor mediated signaling	Integration of pathways involved in energy metabolism
Maintenance of Telomeres	Metabolism of amino acids and related nitrogen- containing molecules	Metabolism of carbohydrates	Metabolism of lipids and lipoproteins
Metabolism of nucleotides	Metabolism cf porphyrins	Notch Signaling Pathway	Oxidative decarboxylation of pyruvate and TCA cycle
Post-translational modification of proteins	Transforming Growth Factor (TGF) beta signaling	Transcription	Translation
mRNA Processing	Xenobiotic metabolism		

# Citing Reactome

### Publication to cite Reactome:

Joshi-Tope G, Gillespie M, Vastrik I, D'Eustachio P, Schmidt E, de Bono B, Jassal B, Gopinath GR, Wu GR, Matthews L, Lewis S, Birney E, Stein L. 2005. Reactome: a knowledgebase of biological pathways. Nucleic Acids Res. 2005 Jan 1;33 Database Issue:D428-32. PMID: 15608231

Joshi-Tope G., Vastrik I., Gopinathrao G., Matthews L., Schmidt E., Gillespie M., D'Eustachio P., Jassal B., Lewis S., Wu G., Birney E., and Stein L. The Genome Knowledgebase: A Resource for Biologists and Bioinformaticists. Cold Spring Harb Symp Quant Biol. 2003;68:237-43. PMID: 15338623

### Citing your contribution to Reactome:

### Citing a module in Reactome

[Module Author Names]. [Year of Publication]. [Module Name] in [Summation Title]. Reactome. World Wide Web URL - http://www.reactome.org

### Citing a summation in Reactome

[Summation Author names]. [Year of Publication]. Reactome. World Wide Web URL - http://www.reactome.org

## Citing Reactome (all of it)

Reactome. Cold Spring Harbor Laboratory, European Bioinformatics Institute, and GO Consortium. World Wide Web URL - http://www.reactome.org

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Date: 2007-03-02 08:00:05 help@reactome.org

The data displayed is for Homp sapiens

Use the menu to charge the species. Check for cross-species comparison.

Apcptosis	Cell Cycle Checkpoints	Cell Cycle, Witotic	DNA Repair
DNA Replication	Electron Transport Chain	Epidermal Growth Factor Receptor (EGFR) signaling	Fibroblast Growth Factor Receptor (FGFR) signaling
Gap junction trafficking and regulation	Gene Expression	HIV Infection	Hemostasis
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mRNA Frocessing	Xenobiotic metabolism		

→ Experimentally confirmed reaction → Manually inferred reaction → Electronically inferred reaction Linked reactions

# **Reactome Editorial Calendar**

The Editorial Calendar shows work now under way to expand the Reactome knowledgebase, organized by planned date of public release on this web site. The Calendar also shows the Reactome curator who is managing the work on each topic. For more information, including information about how you can participate in the Reactome editorial process, e-mail the curator.

Click here for an internal version of editorial calendar with status updates from Reactome curators.

Font color key: central dogma, cell cycle metabolism signaling, transport, cell motility immune function, host-virus interaction neural function

Pathway Modules	Curator	Release Date
adirius modulos	Curator	Nordade Bate
Porphyrin metabolism	Bijay Jassal	Current Release
Digestion of dietary lipids	Peter D'eustachio	Current Release
Digestion of carbohydrates	Peter D'eustachio	Current Release
Signaling pathways -EGFR signaling	Bijay Jassal	Current Release
Signaling pathways -FGFR signaling	Bernard de Bono	Current Release
Influenza virus life cycle- Regulation of RNPs	Marc Gillespie	Current Release
HIV life cycle - Rev protein interactions	Marc Gillespie	Current Release
Formation of gap junctions - trafficking	Lisa Matthews	Current Release
Lipoproteins - HDL and VLDL	Peter D'eustachio	mid-2007
Signaling pathways -PDGF signaling	Bijay Jassal	mid-2007
Interactions and signaling of immune synapses	Bernard de Bono	mid-2007
Neurotoxicity of Botulinum toxins	Gopal Gopinathrao	mid-2007
Influenza virus life cycle -M1 ion channel and neuraminidase	Marc Gillespie	mid-2007
Influenza virus life cycle -NS1 Pathway	Marc Gillespie	mid-2007
HIV - budding and release	Peter D'Eustachio	mid-2007
HIV life cycle - viral Assembly & Maturation	Gopal Gopinathrao	mid-2007
Signaling pathways -Rho GTPases	Gopal Gopinathrao	mid-2007
Epigenetic pathways I	Gopal Gopinathrao	mid-2007
Kinetochores	Lisa Matthews	late 2007
	Peter D'Eustachio	late 2007
Obesity pathways		
Cholesterol metabolism	Bijay Jassal	late 2007
HIV life cycle - Nef protein	Marc Gillespie	late 2007
Mitochondrial protein import	Marcela Tello-Ruiz	late 2007
Signaling pathways in beta cell differentiation	Marcela Tello-Ruiz	late 2007
Cell cycle, mitotic + checkpoints	Lisa Matthews	late 2007
Transcription, Pol II -revision	Marc Gillespie	future release
Cell motility: integrins, ECM attachment	Lisa Matthews	future release

