

The background of the slide features a complex network diagram. It consists of numerous nodes, represented by circles of varying sizes, connected by a dense web of thin, light blue lines. The nodes are distributed across the frame, with a larger, more prominent node located in the upper left quadrant. The overall aesthetic is technical and scientific, suggesting a database or a complex system of interactions.

Reactome

A database of human biological pathways

Contact: help@reactome.org



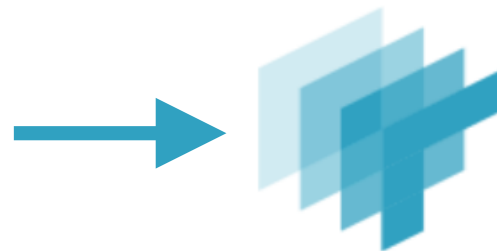
reactome

Rationale – Journal information

Nature 407(6805):770-6. The Biochemistry of Apoptosis.

“Caspase-8 is the key initiator caspase in the death-receptor pathway. Upon ligand binding, death receptors such as CD95 (Apo-1/Fas) aggregate and form membrane-bound signalling complexes (Box 3). These complexes then recruit, through adapter proteins, several molecules of procaspase-8, resulting in a high local concentration of zymogen. The induced proximity model posits that under these crowded conditions, the low intrinsic protease activity of procaspase-8 (ref. 20) is sufficient to allow the various proenzyme molecules to mutually cleave and activate each other (Box 2). A similar mechanism of action has been proposed to mediate the activation of several other caspases, including caspase-2 and the nematode caspase CED-3 (ref. 21).”

How can I access the pathway described here and reuse it?

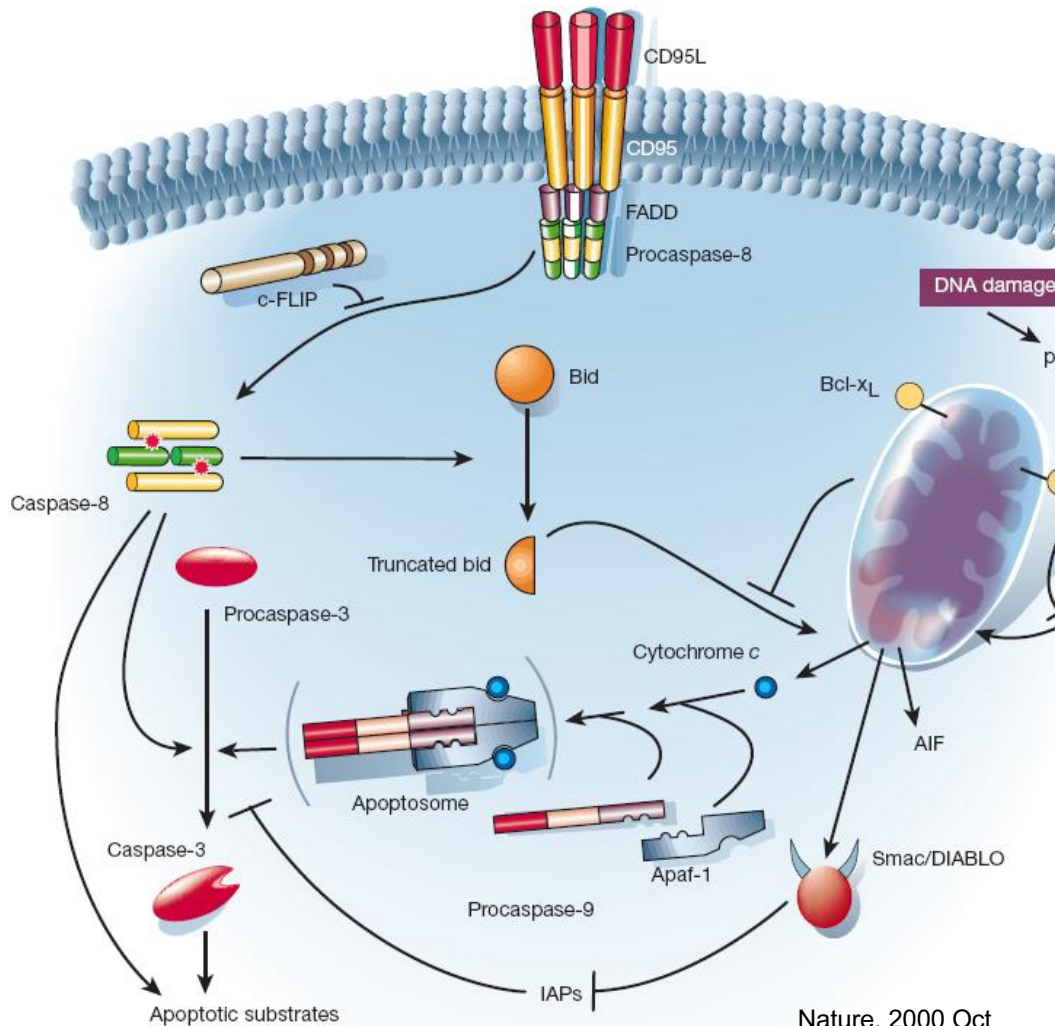


Rationale - Figures

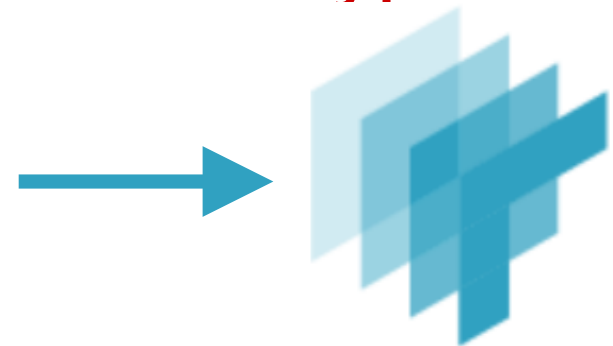
A picture paints a thousand words...

but....

- Just pixels
- Omits key details
- Assumes
- Fact or Hypothesis?



Nature. 2000 Oct
12;407(6805):770-6.
The biochemistry of apoptosis.

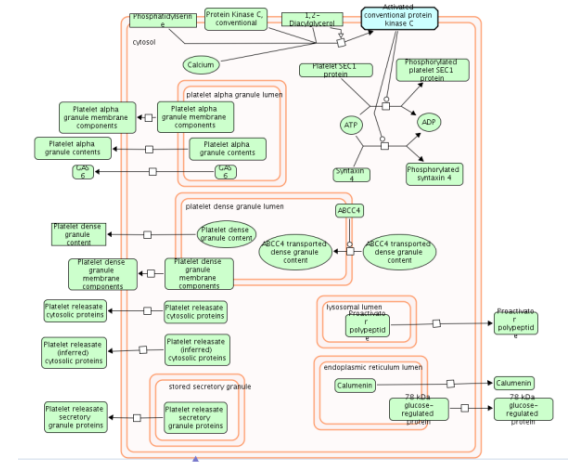


Reactome is...

Free, online, open-source curated database of pathways and reactions in human biology

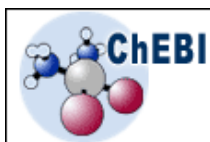
Authored by expert biologists, maintained by Reactome editorial staff (curators)

Mapped to cellular compartment



Reactome is...

Extensively **cross-referenced**

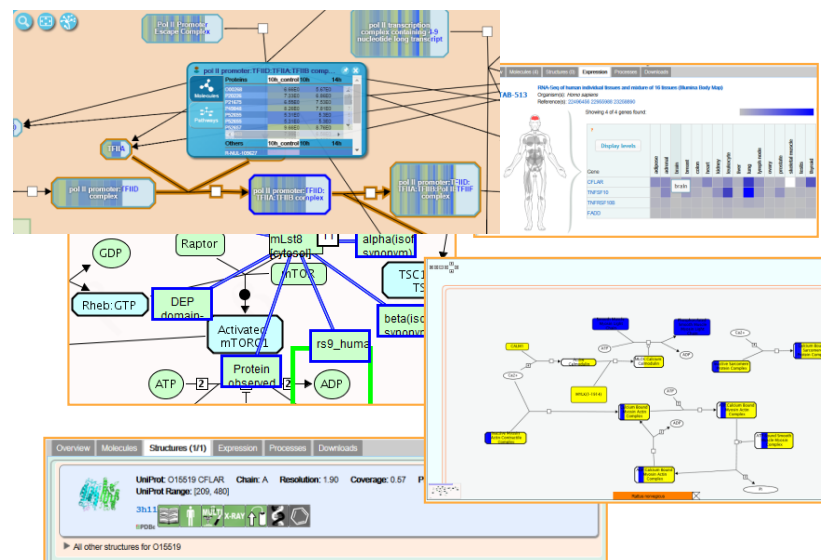


Entrez Gene



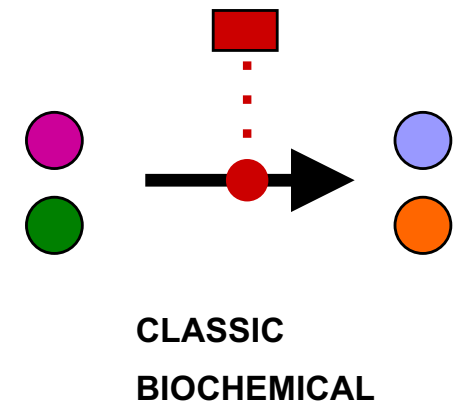
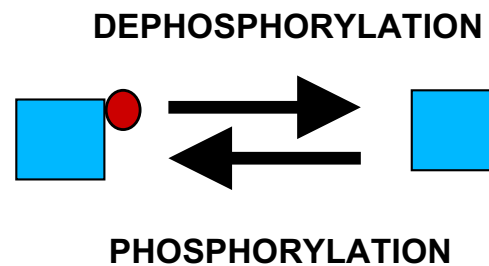
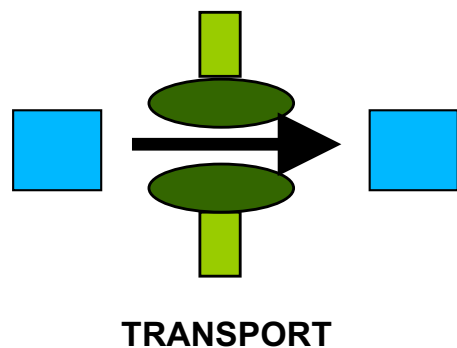
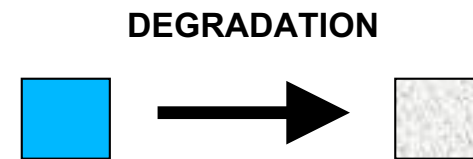
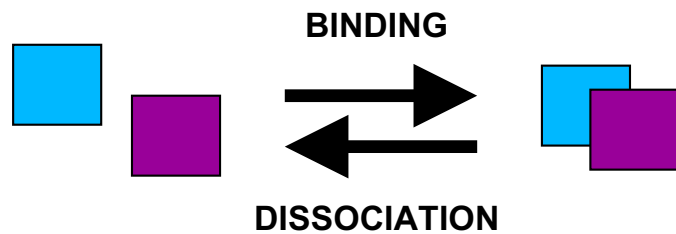
Tools for data analysis –
Pathway Analysis,
Expression Overlay, Species
Comparison

Used to infer **orthologous**
events in 17 other species

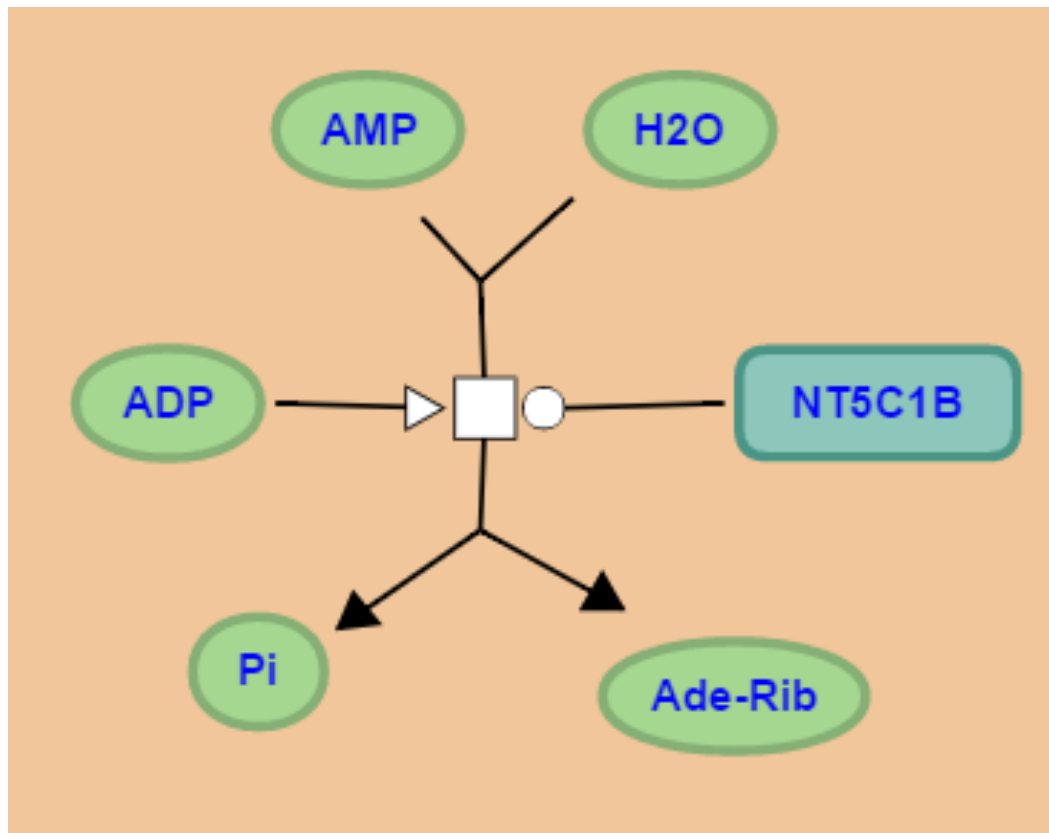


Theory - Reactions

Pathway steps = the “units” of Reactome
= events in biology



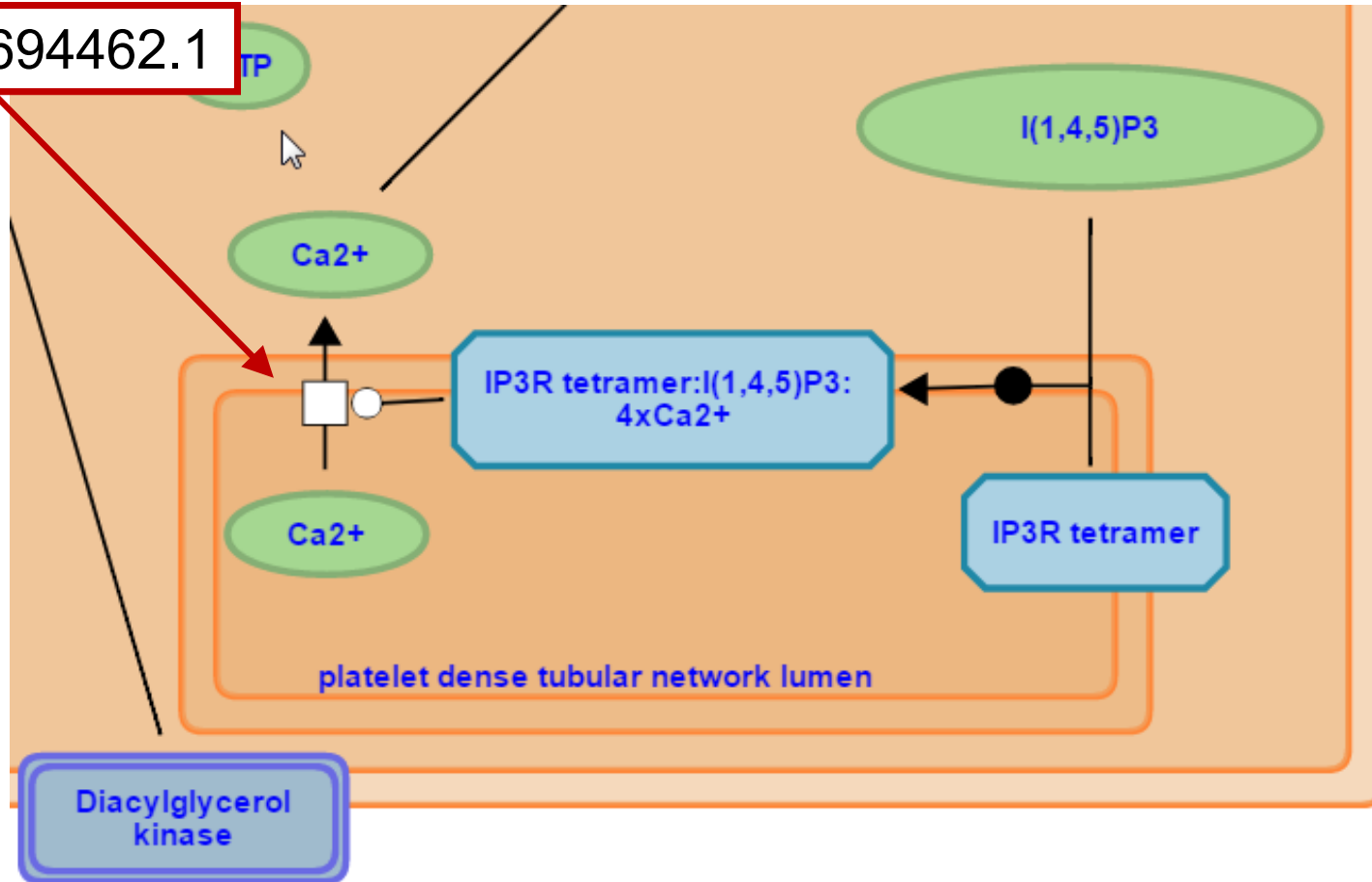
Reaction example 1: Enzymatic



Reaction example 2: Transport

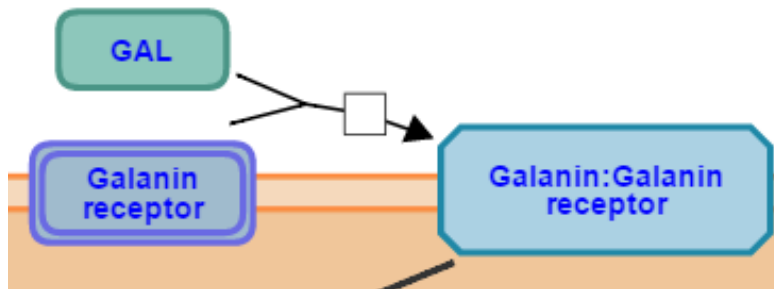
Transport of Ca^{++} from platelet dense tubular system to cytoplasm

R-HSA-5694462.1

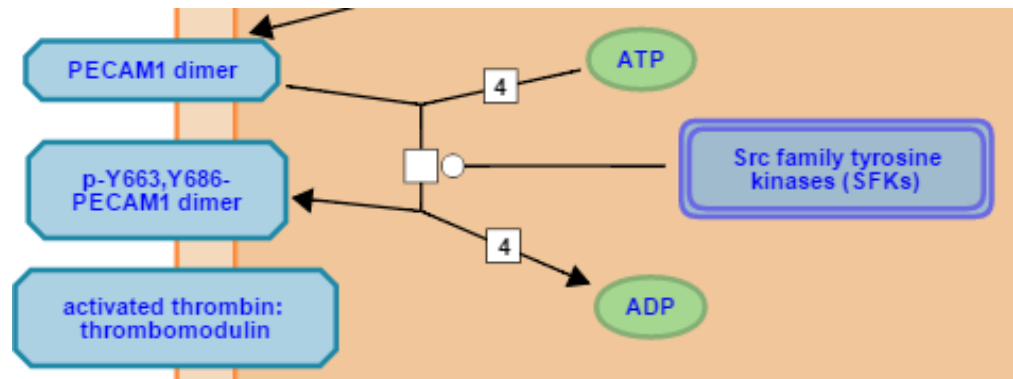
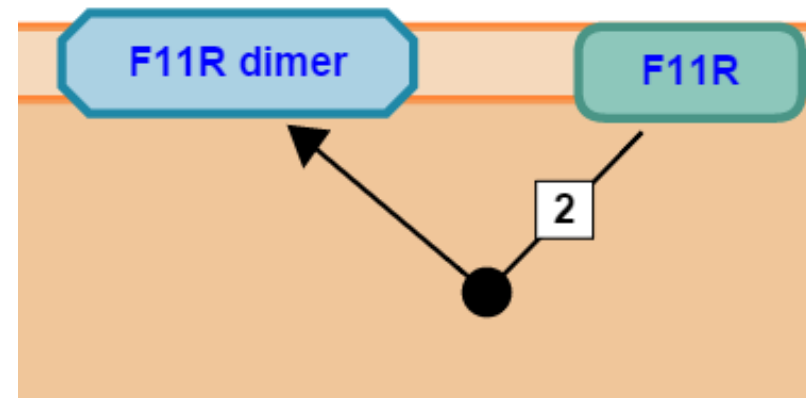


Other reaction examples

Binding

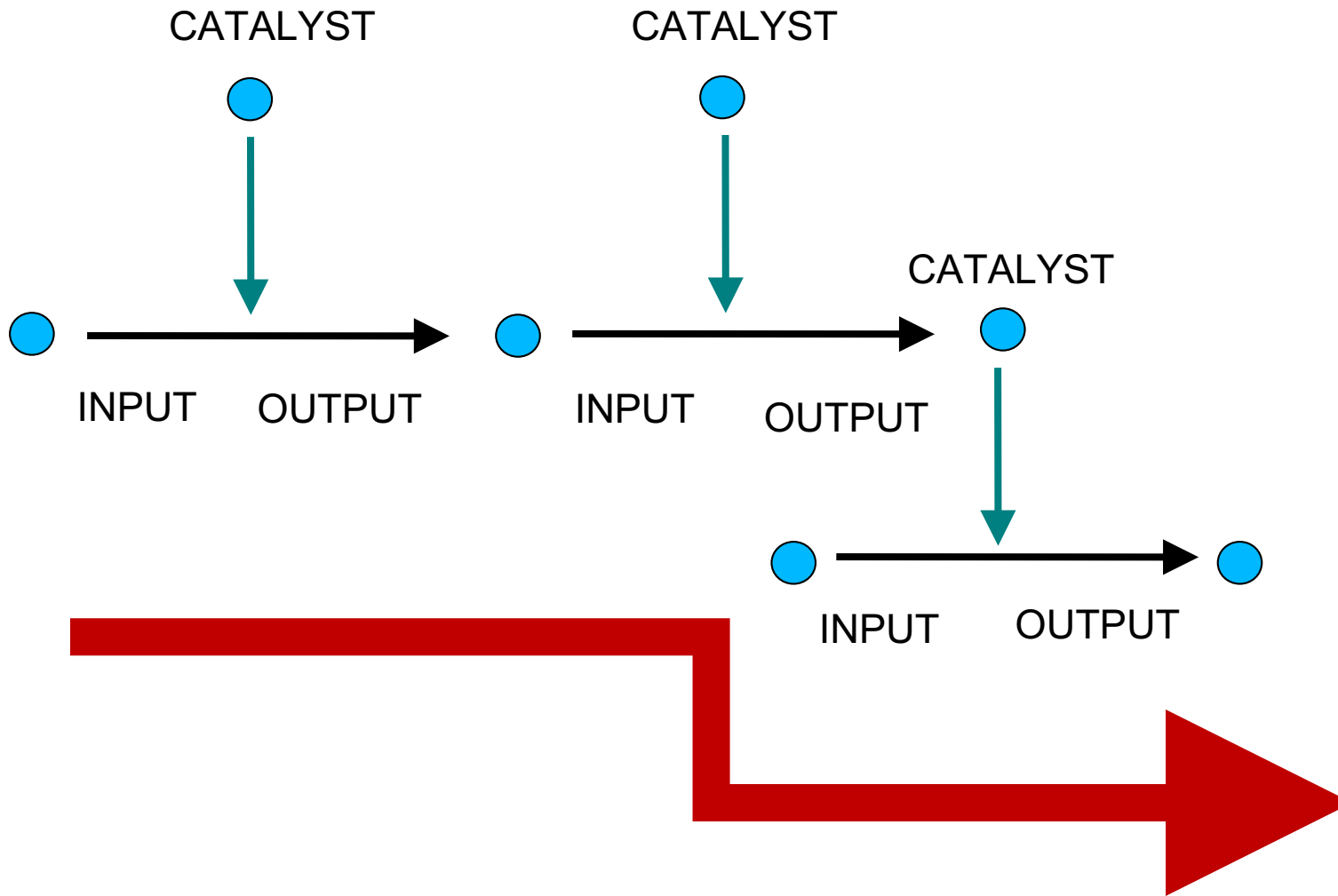


Dimerization

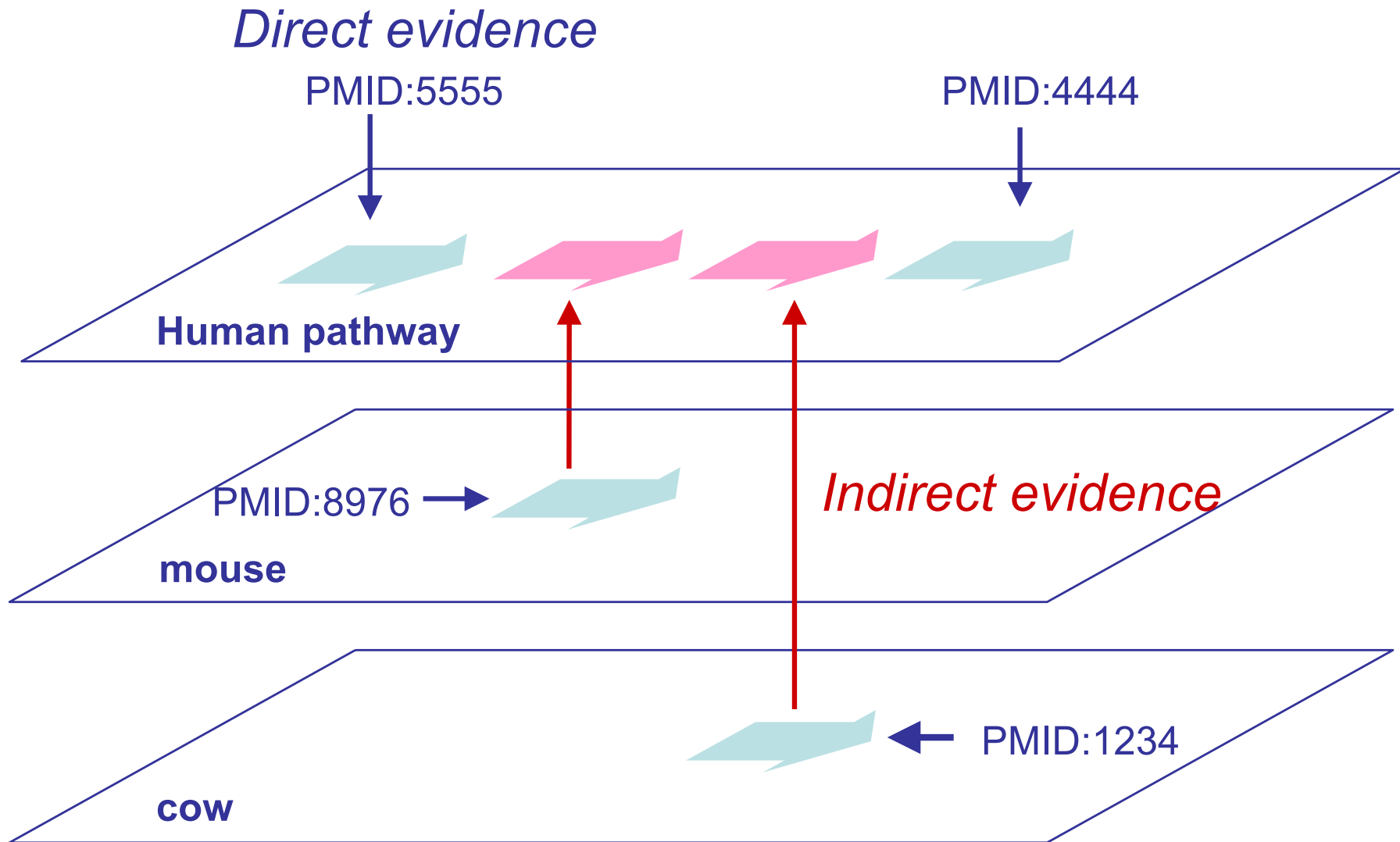


Phosphorylation

Reactions connect into Pathways



Evidence – Inferred Reactions



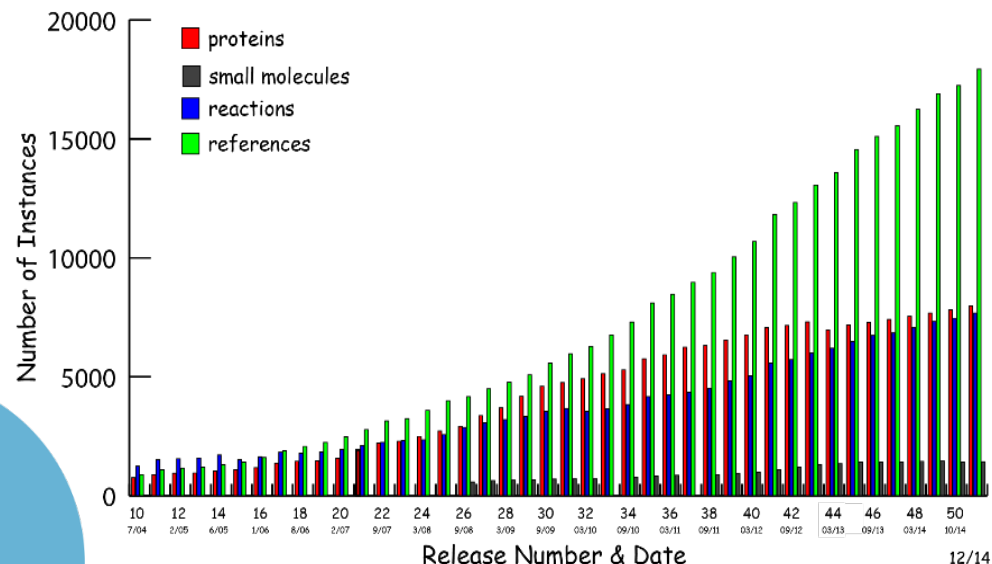
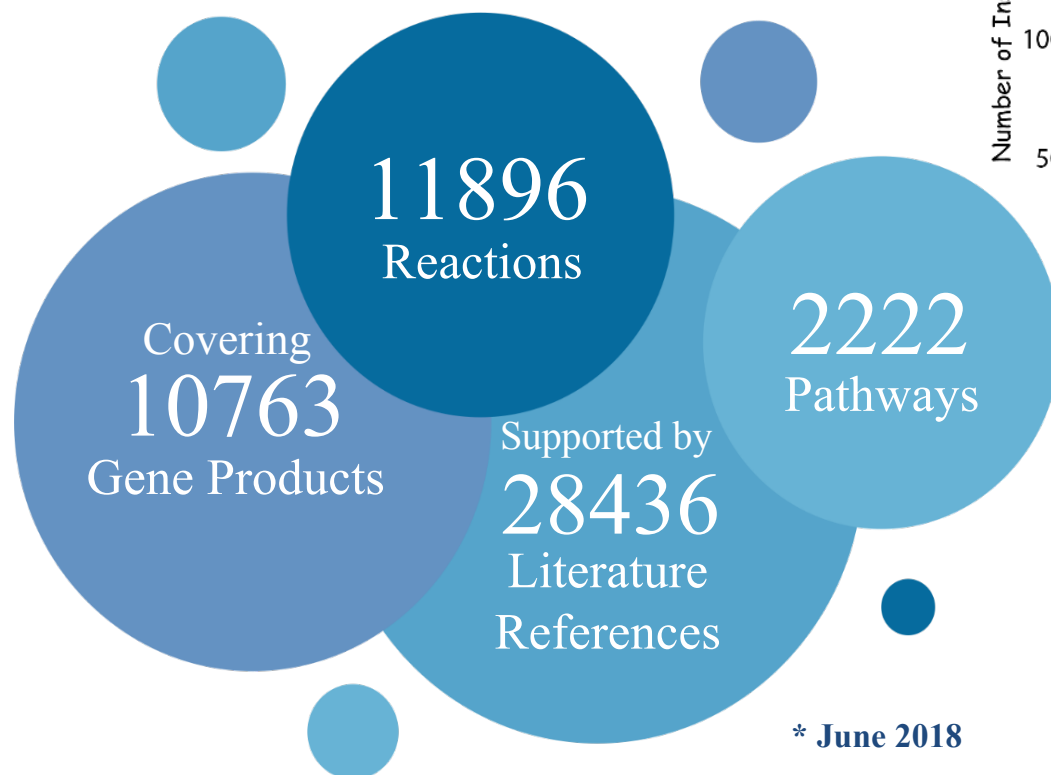
Primary external sources

- Gene Ontology
 - Molecular Function
 - Compartment
 - Biological Process
- ChEBI – small molecules
- UniProt – proteins
- Ensembl – genes and transcripts
- PubMed – literature evidence for events

Curation

- 52.6% of the 20,296 predicted human protein-coding genes

► Human content in numbers*



Data Curation Process



**Experts
(recruited)**



**Curators
(staff)**

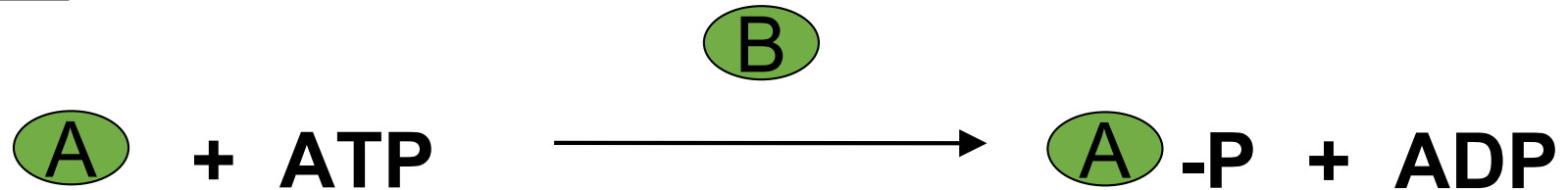


**Reviewers
(recruited)**

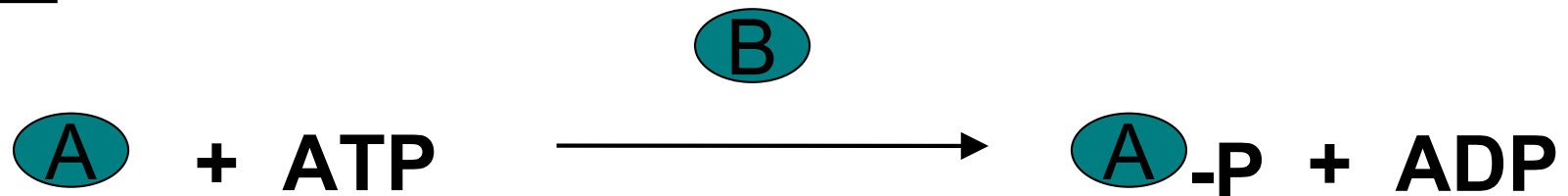
- Pathways authored and reviewed by expert biologists
- Curator works with Author to represent knowledge in Reactome data structure
- All new pathways are internally reviewed within Reactome
- New pathways sent for Review by another expert
- New data release every 3 months
- Regular Pathway updates.
- ORCID and doi[®] as attributions for Reactome content
 - For visibility of expert contributions (authors, reviewers and curators).

Data Expansion – Projecting to Other Species

Human



Mouse



Drosophila



Reaction not
projected

No orthologue - Protein not projected

Species Selection

The screenshot shows the Reactome website interface. At the top, the Reactome logo is on the left, and a version number '3.0' is on the right. Below the logo, the text 'Event Hierarchy:' is followed by a list of biological processes, each with a plus icon and a small 'u' icon. The 'Pathways for:' dropdown menu is open, displaying a list of species names. A mouse cursor is hovering over 'Rattus norvegicus', which is highlighted in blue. The background of the website shows a partial view of a metabolic pathway diagram with blue arrows and text like 'production' and 'mentalogy'.

REACTOME 3.0

Pathways for: Homo sapiens

Event Hierarchy:

- Cell Cycle
- Cell-Cell communication
- Cellular responses to stress
- Chromatin organization
- Circadian Clock
- Developmental Biology
- Disease
- DNA Repair
- DNA Replication
- Extracellular matrix organization
- Gene Expression
- Hemostasis
- Immune System

Species Selection List:

- Homo sapiens
- Arabidopsis thaliana
- Bos taurus
- Caenorhabditis elegans
- Canis familiaris
- Danio rerio
- Dictyostelium discoideum
- Drosophila melanogaster
- Gallus gallus
- Mus musculus
- Mycobacterium tuberculosis
- Oryza sativa
- Plasmodium falciparum
- Rattus norvegicus**
- Saccharomyces cerevisiae
- Schizosaccharomyces pombe
- Sus scrofa
- Taeniopygia guttata
- Xenopus tropicalis

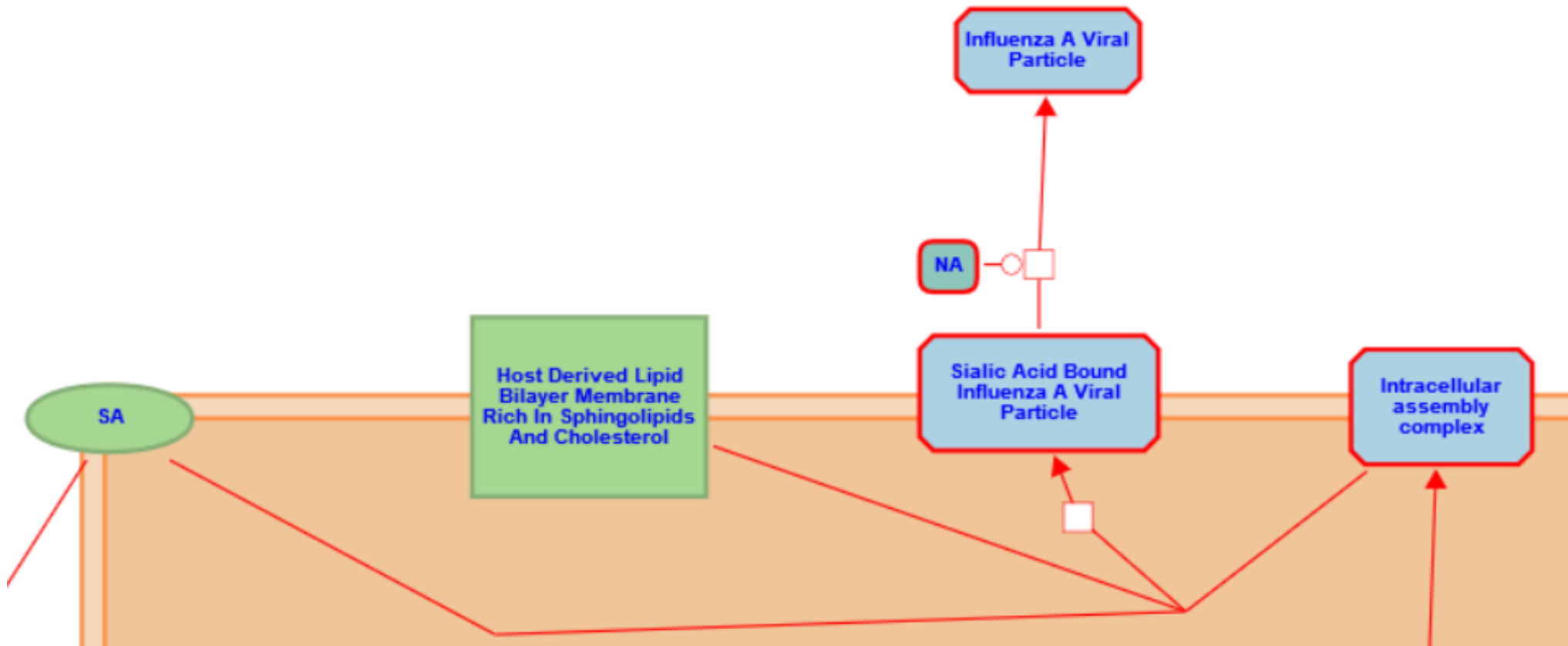
Disease annotation in Reactome

Three main areas:

- Infection (eg. HIV, influenza, botulism)
 - microbially-expressed proteins
- Cancer (eg. EGFR, FGFR and NOTCH signalling)
 - altered protein functions
- Metabolic diseases (eg. mucopolysaccharidoses, phenylketonuria, vitamin metabolism abnormalities)
 - altered expression of proteins

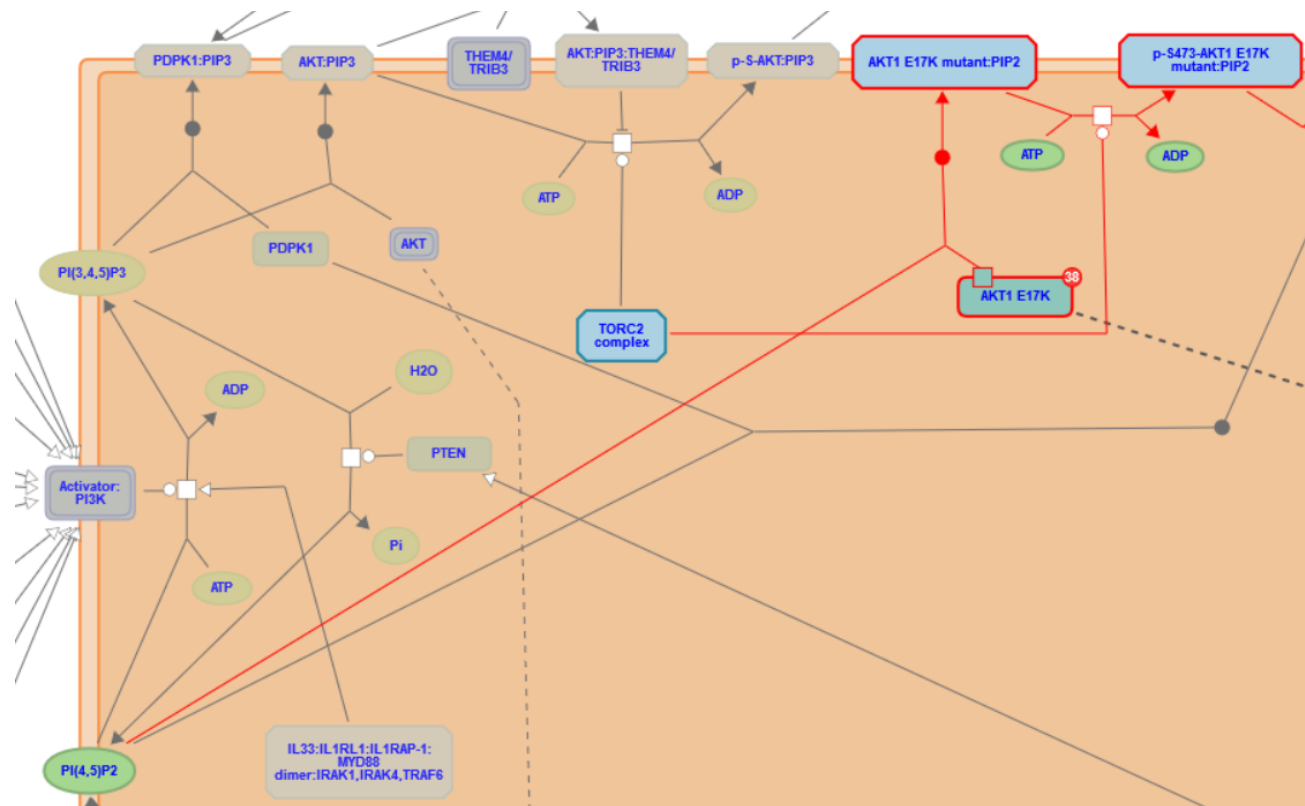
Disease display in Reactome - Infection

Influenza virus life cycle: budding



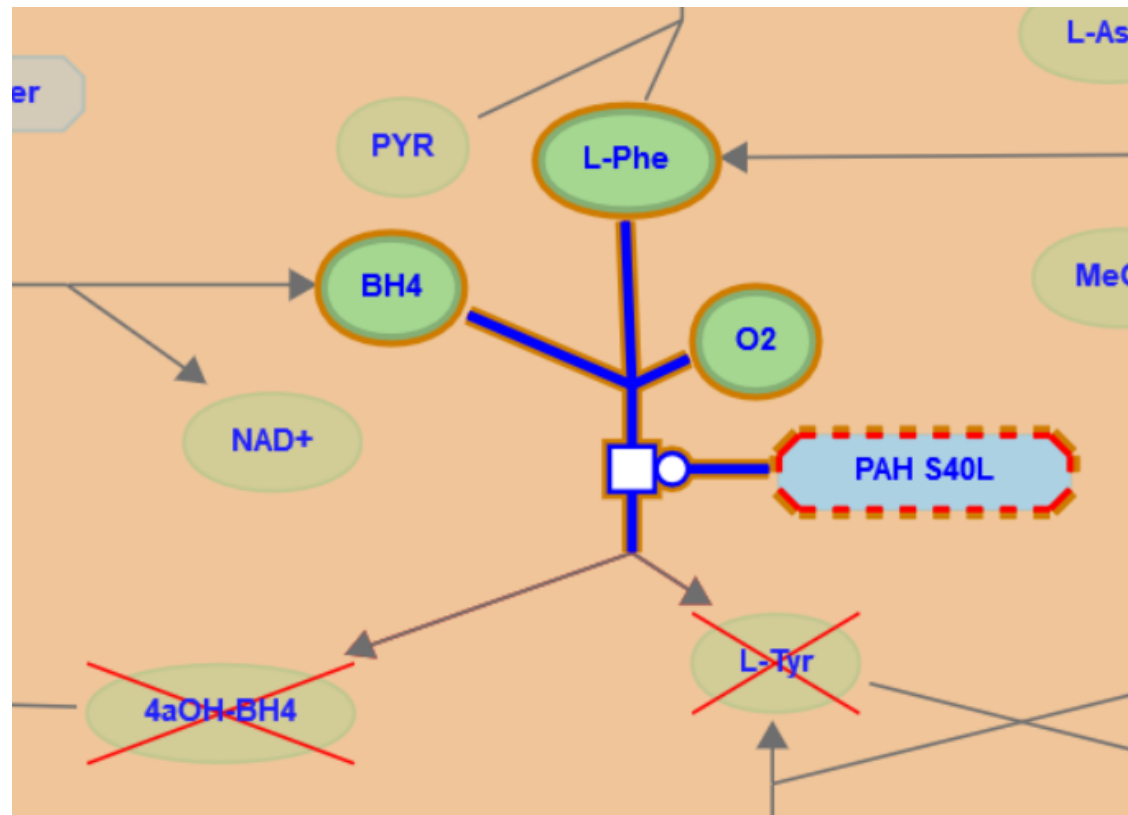
Altered protein function in Cancer

Constitutive Signaling by AKT1 E17K in Cancer



Disease display in Reactome – Loss of function in metabolism

Phenylketonuria



Downloads

- Small(ish) sections from Pathway Browser as text, PDF, etc.
- Entire database content (and software) from Downloads page (linked to Homepage).
- Reusable standard formats BioPAX & SBML
- Illustrations and icon library
- UniProt to Pathways
- GO annotations
- Protein-Protein interaction pairs - Interactions between proteins in the same complex, reaction, or adjoining reaction

Coverage – Content, TOC

And many more...

Topic	Authors	Released	Revised	Reviewers	Editors
Cell Cycle [Homo sapiens] • Cell Cycle Checkpoints • Cell Cycle, Mitotic • Chromosome Maintenance • Meiosis	Hoffmann, I, Khanna, KK, Walworth, N, Yen, TJ, O'Donnell, M, Bosco, G, Matthews, L, Orlic-Milacic, M, Gillespie, ME, May, B, Blackburn, EH, Seidel, J, D'Eustachio, P, Borowiec, JA, Pagano, M, Davey, MJ, Tye, BK, Lorca, T, Castro, A, Roger, PP, Gopinathrao, G, Tom, S, Bambara, RA, Lee, KS, Gallie, BL, Sanchez, Y, Nasi, S, Annibali, D, Joshi-Tope, G, Jupe, S, Watanabe, N, Hunter, T	2011-12-06 UPDATED		Sanchez, Y, Knudsen, E, Hardwick, KG, Manfredi, J, MacPherson, D, Grana, X, Bolcun-Filas, E, Cohen, PE, Holloway, JK, Lyndaker, A, Schimenti, JC, Strong, E, Price, C, Bird, AW, Peters, JM, Coqueret, O, Zhang, N, Watanabe, Y, Tanno, Y, Lorca, T, Almouzni-Pettinotti, G, Dunleavy, EM, Foltz, DR, Borowiec, JA, Zaccara, S, Inga, A, Weil, R, Bruinsma, W, Merdes, A, Chen, H, Maxwell, CA, Grant, R, Linton, C, Shah, K, Wang, Y, Colanzi, A, Malhotra, V, Longworth, MS, Mochida, S, Burgess, A, Gorjancic, M, Mattaj, JW, Cheeseman, IM, Bosco, G, Samarajiva, S, Roger, PP, D'Eustachio, P, Greene, LA, Pires, IM, Janssens, V, Avruch, J, Antonin, W, Dixit, VM, Herlihy, A	Matthews, L, Gopinathrao, G, Joshi-Tope, G, May, B, Orlic-Milacic, M, D'Eustachio, P, Gillespie, ME, Jupe, S, D'Eustachio, P
Cell-Cell communication [Homo sapiens] • Cell junction organization (DOI) • Signal regulatory protein family interactions (DOI) • Nephron family interactions (DOI)	Garapati, P V, de Bono, B, Matthews, L, Jassal, B	2011-09-20 UPDATED		Barclay, AN, Huber, TB, Grahmmer, Florian, Ebnert, K, Wu, C, Sonnenberg, A, Honig, B, Sanes, JR, D'Eustachio, P	Garapati, P V, Matthews, L, Jupe, S, Jassal, B, Wu, C
Cellular responses to external stimuli [Homo sapiens] • Response to metal ions (DOI) • Macroautophagy (DOI) • Cellular responses to stress	D'Eustachio, P, May, B, Jupe, S, Matthews, L, Shamovsky, V, Orlic-Milacic, M, Jassal, B, Vastrik, I, Stephan, R, Luo, F, Khanna, KK, Pagano, M, Nasi, S, Annibali, D	2017-03-27 NEW		Atrian, S, D'Eustachio, P, Kilonsky, DJ, Toote, SA, Ford, D, Wang, Q, Kavdia, M, Pani, B, Samarajiva, S, Rothfels, K, Echeverria, PC, Picard, D, Brown, DR, Rantanen, K, Inga, A, Zaccara, S, Warner, D, Roger, PP, Gillespie, ME, Gay, NJ, Borowiec, JA, Du, F, Sun, Y, Sanchez, Y, Coqueret, O, Greene, LA, Maltepe, E	D'Eustachio, P, May, B, Jupe, S, Matthews, L, Shamovsky, V, D'Eustachio, P, Jassal, B, Vastrik, I, Orlic-Milacic, M
Chromatin organization [Homo sapiens] • Chromatin modifying enzymes (DOI)	May, B, Jupe, S, Jassal, B, Orlic-Milacic, M, Walport, J, Hopkinson, J	2013-12-04		Karagiannis, T, Yang, XJ, Schofield, CJ, Walport, J, Hopkinson, J, Motamedi, M, Guccione, E, Fischle, W, Meldal, BH, D'Eustachio, P, Mandal, M, Cheng, X, Faines, PØ	May, B, Jupe, S, Jassal, B, Orlic-Milacic, M, Duenas, C, Shamovsky, V
Circadian Clock [Homo sapiens] (DOI) • BMAL1-CLOCK/NPAS2 activates circadian gene expression • RORA activates gene expression • NR1D1 (REV-ERBA) represses gene expression	May, B	2010-12-14		D'Eustachio, P, Albrecht, U, Kay, SA, Hirota, T, Delaunay, F, Kersten, S, Lezza, AM, Jain, MK	May, B
Developmental Biology [Homo sapiens] • Axon guidance (DOI) • Myogenesis (DOI) • Regulation of beta-cell development (DOI) • Signaling by NODAL (DOI) • Transcriptional regulation of white adipocyte differentiation • Transcriptional regulation of pluripotent stem cells (DOI) • Activation of HOX genes during	Garapati, P V, Ferrer, J, Tello-Ruiz, MK, May, B, Jupe, S, Orlic-Milacic, M, Jassal, B, Heldin, CH, Moustakas, A, Humnicki, L, Rezsohazy, R, Nasi, S, Annibali, D, Charalambous, M, Akkerman, JW	2011-09-20 UPDATED		Maness, PF, Krauss, RS, Walmod, PS, Jensen, J, Peng, C, D'Eustachio, P, Sethi, JK, Wang, J, Blasi, F, Rezsohazy, R, Meijer, D, Blumenberg, M, Kumanogoh, A, Kikutani, H, Cooper, HM, Kidd, T, Jaworski, A, Ip, NY, Morales, D, Luo, W, Heldin, CH, Huang, T, Chen, YG, May, B, Kersten, S	Matthews, L, Garapati, P V, D'Eustachio, P, May, B, Gopinathrao, G, Jupe, S, Orlic-Milacic, M, Jassal, B, Schmidt, EE

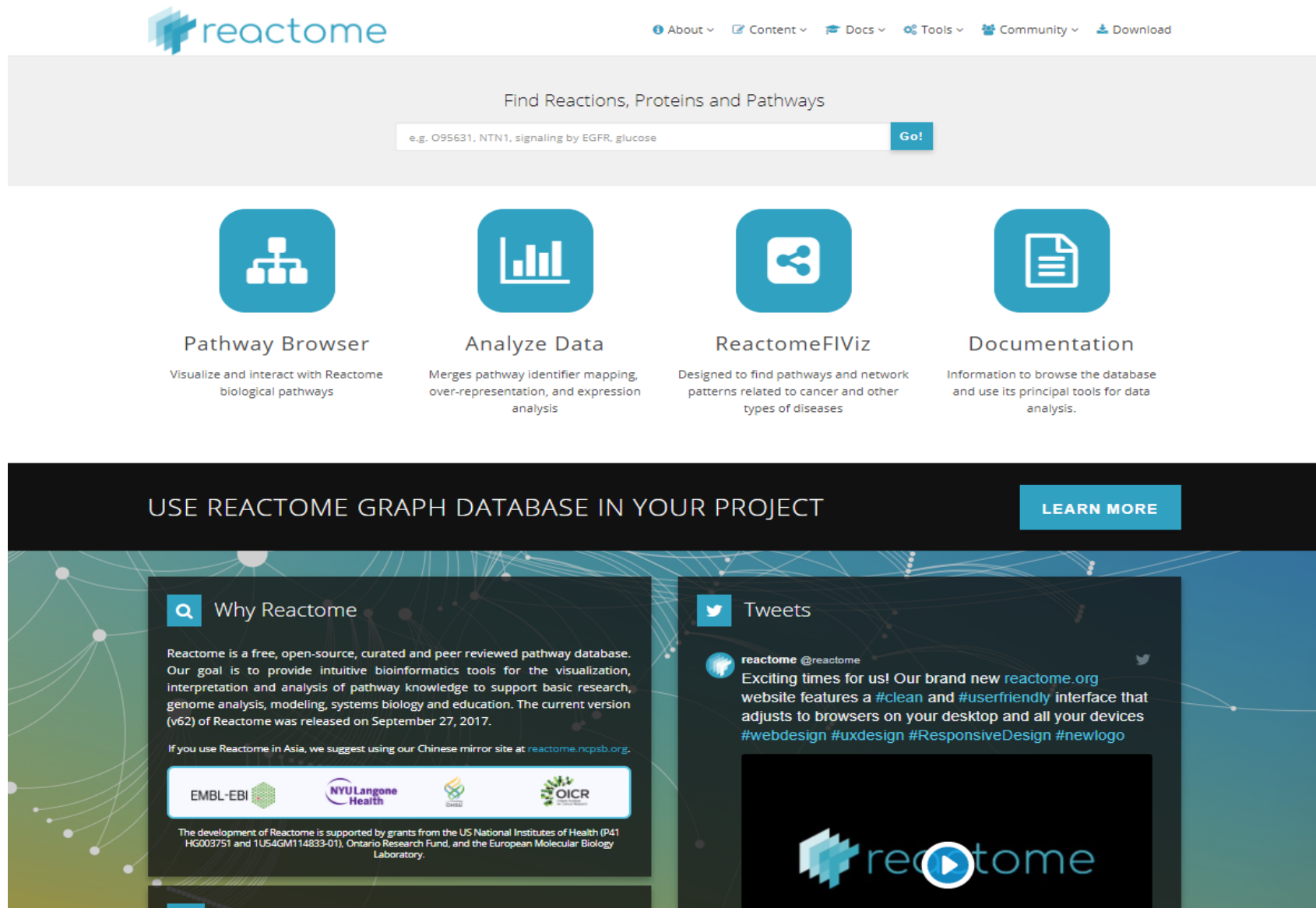
Digestion and absorption (Homo sapiens) • Digestion • Intestinal absorption	Jassal, B, D'Eustachio, P, Stephan, R	2017-03-27 NEW	D'Eustachio, P, Jassal, B, Nichols, BL, Wright, EM, Naim, HY, Anwar, M	D'Eustachio, P, Jassal, B				
			Molra, K, Spillmann, D, D'Eustachio, P, Anra, S, Jassal, B, Sauer, S, Klose, S					
			Raisz, M, Zhao, X, Wille, L, Cantatore, P, Karghori, F, Harrison, CJ, Matthews, L, Freedman, LS, Hernandez, N, Tomari, Y, Li, LC, Steynowski-Camacho, A, Sato, K, Di Croce, L, Pfeifer, GP, Mukherji, M					
Disease (Homo sapiens) • Diseases of signal transduction • Disorders of transmembrane transporters • Diseases of metabolism • Diseases of glycosylation • Infectious disease • Diseases of Immune System • Neurodegenerative Disease • Diseases of Mitochondrial Repar (DOI)	Gene expression (Transcription factors) • RNA Polymerase I Transcription • RNA Polymerase II Transcription • RNA Polymerase III Transcription • Transcription from mitochondrial promoters (DOI) • Gene silencing by RNA • Epigenetic regulation of gene expression	Komshim, AR, Proutfess, NG, Cuddy, M, D'Eustachio, P	Innate Immune System (Gallus gallus) • Complement Cascade • Toll-like receptors (TLR) cascades • RLR (RIG-like receptor) mediated induction of IFN alpha/beta	Shamovsky, V, Shamovsky, V	2012-12-04	D'Eustachio, P, Jupe, S, Garapati, P V, D'Eustachio, P	Shamovsky, V, Shamovsky, V	
DNA Repair (Homo sapiens) • Base Excision Repair (DOI) • DNA Damage Bypass (DOI) • DNA Damage Reversal (DOI) • DNA Double-Strand Break Repair • Nucleotide Excision Repair (DOI) • Mismatch Repair (DOI) • Fanconi Anemia Pathway (DOI)	Hemostasis (Homo sapiens) • Platelet homeostasis • Platelet Adhesion to exposed • Platelet activation, signaling & aggregation • Formation of Fibrin Clot (Clot Cascade) (DOI) • Dissolution of Fibrin Clot (Clot Cascade) (DOI) • Cell surface interactions at cell-cell (DOI) • Factors involved in megakaryocyte development and platelet production		Metabolism (Homo sapiens) • Metabolism of carbohydrates • Inositol phosphate metabolism • Metabolism of lipids • Integration of energy metabolism • Metabolism of nitric oxide • The citric acid (TCA) cycle and respiratory electron transport • Metabolism of nucleotides • Metabolism of vitamins and cofactors • Metabolism of amino acids and derivatives • Metabolism of porphyrins • Biological oxidations • Mitochondrial iron-sulfur cluster biogenesis (DOI) • Abacavir transport and metabolism (DOI) • Reversible hydration of carbon dioxide (DOI) • Cytosolic iron-sulfur cluster assembly (DOI) • Pyrophosphate hydrolysis	D'Eustachio, P, Schmidt, EE, Williams, MG, Jassal, B, Gillespie, ME, Gopinathrao, G, Hemish, J, Birney, E, Liu, R, May, B, Cameselle, JC, Ribeiro, JM, Orlic-Milacic, M, Stephan, R, Jupe, S, Garapati, P, Joshi-Tope, G, Le Novre, N, Vanuat, TM, Brand, MD, Esteves, TC, Barrientos, A, Vastrik, I, Mahajan, SS, Nasi, S, Annibali, D, Swann, P		2011-09-20 UPDATED	Wunderberg, T, Rush, MG, Enikolopov, G, Graves, L, Sessa, S, D'Eustachio, P, Rouault, TA, Tong, WH, Jassal, B, Silverman, DN, Uringa, EJ, Kersten, S, Gillespie, ME, Gopinathrao, G, Hannun, YA, Luberto, C, Ferguson, SJ, Ito, S, d'Iscia, M, Banci, L, Harris, RA, Inga, A, Zaccara, S, Wakelam, M, Stephan, R, Liang, G, Potolout, V, Kibede, M, Madiraju, MS, Akkerman, JW, Sevigny, J, Blauer, WS, Kawamuki, M, Neale, JK, Pederson, B, He, L, Lezza, AM, Sethi, JK, Delaunay, F, Ito, Y, Chuang, LS, Albrecht, U, Kay, SA, Hirota, T, Levy, BD, Sourley, SL, Calamita, G, Beitz, E, Castagnoli, L, Burmeister, T, Meldal, BH, Ito, R, Rosenblatt, DS, Drosaki, J, Restituto, S, Porteu, F, Greene, LA, Thorne, L, Yuzugulu, H, Zhao, JJ, Leslie, N, Kriplani, N, Divecha, N, May, B, Nakaki, T	D'Eustachio, P, Schmidt, EE, Williams, MG, Joshi-Tope, G, Jassal, B, Gillespie, ME, May, B, Gopinathrao, G, Jupe, S, Orlic-Milacic, M, Garapati, P V, Vastrik, I, Mahajan, SS
DNA Replication (Homo sapiens) • MMS1 Transition (DOI) • Synthesis of DNA • Regulation of DNA replication • DNA replication and repair (Gallus gallus) • DNA repair • Telomere maintenance	Drosophila signaling pathways (Drosophila melanogaster) • Circadian Clock pathway (DOI) • Hedgehog pathway (DOI) • Hippo/YAP pathway (DOI) • Imd pathway (DOI) • Insulin receptor-mediated signal • JAK/STAT pathway (DOI) • Ras/Raf Cell Proliferation pathway (DOI) • Toll pathway (DOI) • Wingless pathway (DOI)		Metabolism (Gallus gallus) • Carbohydrate metabolism • Pyruvate metabolism • Lipid metabolism • The tricarboxylic acid cycle • Amino acid metabolism • Nucleotide metabolism • Heme metabolism	D'Eustachio, P, D'Eustachio, P, Schmidt, C	2011-12-06	Harris, RA, D'Eustachio, P, D'Eustachio, P	D'Eustachio, P, D'Eustachio, P	
Extracellular matrix organization (Homo sapiens) • Collagen formation • Fibronectin matrix formation (DOI) • Elastic fiber formation (DOI) • Laminin interactions (DOI) • Non-integrin membrane-ECM interactions	Immune System (Homo sapiens) • Adaptive Immune System		Metabolism of proteins (Homo sapiens) • Translation • Protein folding (DOI) • Post-translational protein modification (DOI) • Mitochondrial protein import • Peptide hormone metabolism • Regulation of Insulin-like Growth Factor (IGF) transport and uptake by Insulin-like Growth Factor Binding Proteins (IGFBPs) • Unfolded Protein Response (UPR) • Protein repair (DOI) • Sulfuric acid metabolism • Amyloid fiber formation (DOI)	Matthews, L, Merrick, WC, Bedwell, DM, Gebauer, F, Anand, M, Balar, B, Gross, SR, Ortiz, PA, Ottuz, S, Pittman, VR, Ullouque, R, Hentze, MW, Kinzy, TG, D'Eustachio, P, May, B, Jupe, S, Jassal, B, Gopinathrao, G, Dai, CH, GM, Rothfels, K, Gillespie, ME, Orlic-Milacic, M, Johansson, HE, Williams, MG, Garapati, P V, Lu, J, Yang, WC	2009-04-01 UPDATED	Hartweg, JW, Sonnenberg, N, Hinnebusch, AG, Cowan, NE, Orian, P, Stafford, DW, D'Eustachio, P, Endo, T, May, B, Matthews, L, Gillespie, ME, Urano, F, Meldal, BH, Perry, JC, Antonellis, A, Chrzastowska-Kruglowicz, ZM, Spremull, LL, Gagneux, P, Garg, AK, Azevedo, JS, Patardedeal, CC, Parnes, PD, Jassal, B, Pick, E, Wiley, SE, Zhang, Weichen, Joseph, J, Bloom, SR, Schröder, M, He, L, Willardson, BM, Liu, S, Ferrar, A, Hansen, L, Joshi, H, Ferrar, S, Lu, J, Matsui, M, Yang, HC, Floss, G, Bach, A, Zhang, XD, Huang, T, Zaccara, S, Inga, A, Kawai, T, Akira, S, Rajakulendran, N, van Amerongen, R, Kluschn, A, Kufel, TA, Rittiger, K, Wong, E, Lin, WC, Deng, L, Pomerantz, JL, Yu, X, Zhu, B, Myung, K, Cimprich, KA, Lehner, B, van den Boomen, DJ, Medrano, JF	Matthews, L, Tello-Ruiz, MK, Gillespie, ME, Gopinathrao, G, Jassal, B, Rothfels, K, Orlic-Milacic, M, Garapati, P V, Yu, X, Zhu, B, Myung, K, Lehner, B, van den Boomen, DJ, Laprinco, D, Bee, J, Crispini, L, Thibault, P	

Reactome Tools

- Interactive Pathway Browser
- Analysis
 - Over-representation
 - Pathway topology
 - Expression overlay
- Molecular Interaction overlay
- Species Comparison

Front Page

<http://www.reactome.org>



The image shows the front page of the Reactome website. At the top, the Reactome logo is on the left, and navigation links for About, Content, Docs, Tools, Community, and Download are on the right. Below the navigation bar is a search bar with the placeholder text "Find Reactions, Proteins and Pathways" and a "Go!" button. The search bar contains the example text "e.g. O95631, NTN1, signaling by EGFR, glucose". Below the search bar are four main sections, each with an icon and a title: "Pathway Browser" (tree icon), "Analyze Data" (bar chart icon), "ReactomeFIViz" (share icon), and "Documentation" (document icon). Each section has a brief description of its function. Below these sections is a large banner with the text "USE REACTOME GRAPH DATABASE IN YOUR PROJECT" and a "LEARN MORE" button. The banner features a background image of a network graph. On the left side of the banner, there is a "Why Reactome" section with a magnifying glass icon, a paragraph of text, and logos for EMBL-EBI, NYU Langone Health, and OICR. On the right side of the banner, there is a "Tweets" section with a Twitter icon and a tweet from @reactome. At the bottom right of the banner is a large Reactome logo with a play button icon.

reactome

About Content Docs Tools Community Download

Find Reactions, Proteins and Pathways

e.g. O95631, NTN1, signaling by EGFR, glucose Go!

Pathway Browser
Visualize and interact with Reactome biological pathways

Analyze Data
Merges pathway identifier mapping, over-representation, and expression analysis

ReactomeFIViz
Designed to find pathways and network patterns related to cancer and other types of diseases

Documentation
Information to browse the database and use its principal tools for data analysis.

USE REACTOME GRAPH DATABASE IN YOUR PROJECT [LEARN MORE](#)

Why Reactome

Reactome is a free, open-source, curated and peer reviewed pathway database. Our goal is to provide intuitive bioinformatics tools for the visualization, interpretation and analysis of pathway knowledge to support basic research, genome analysis, modeling, systems biology and education. The current version (v62) of Reactome was released on September 27, 2017.

If you use Reactome in Asia, we suggest using our Chinese mirror site at reactome.ncpsb.org.

EMBL-EBI NYU Langone Health OICR

The development of Reactome is supported by grants from the US National Institutes of Health (P41 HG003751 and 1U54GM114833-01), Ontario Research Fund, and the European Molecular Biology Laboratory.

Tweets

reactome @reactome
Exciting times for us! Our brand new reactome.org website features a [#clean](#) and [#userfriendly](#) interface that adjusts to browsers on your desktop and all your devices [#webdesign](#) [#uxdesign](#) [#ResponsiveDesign](#) [#newlogo](#)

reactome

The Pathway Browser

The image shows the Reactome Pathway Browser interface with several components labeled:

- Home**: A button in the top navigation bar.
- Species**: A button in the top navigation bar.
- Analyse Data**: A button in the top navigation bar.
- Video Tour**: A button in the top navigation bar.
- Layout**: A button in the top navigation bar.
- Search Diagram**: A button in the top navigation bar.
- Open Diagram**: A button in the top navigation bar.
- Fit to Page**: A button in the top navigation bar.
- Illustrations**: A button in the top navigation bar.
- Key**: A button in the top navigation bar.
- Export**: A button in the top navigation bar.
- Settings Sidebar**: A button in the top navigation bar.
- Hierarchy Panel**: A panel on the left side of the interface.
- Pathway Panel**: A panel in the center of the interface.
- Thumbnail**: A panel in the center of the interface.
- Detail Panel**: A panel at the bottom of the interface.
- Zoom/Move**: A button in the bottom right corner.

The interface also features a top navigation bar with buttons for Home, Species, Analyse Data, Video Tour, Layout, Search Diagram, Open Diagram, Fit to Page, Illustrations, Key, and Export. A left sidebar contains a Hierarchy Panel. The main area displays a Pathway Panel and a Thumbnail. A bottom section contains a Detail Panel with a description of the selected item.

reactome 3.5 62 Pathways for: Homo sapiens

Analysis: Tour: Layout:

Event Hierarchy:

- Cell Cycle
- Cell-Cell communication
- Cellular responses to external stimuli
- Chromatin organization
- Circadian Clock
- Developmental Biology
- Digestion and absorption
- Disease
- DNA Repair
- DNA Replication
- Extracellular matrix organization
- Gene
- Hemostasis
- Immune System
- Metabolism
- Metabolism
- Mitophagy
- Muscle contraction
- Neuronal System
- Organelle biogenesis and maintenance
- Programmed Cell Death
- Reproduction
- Signal Transduction
- Transport of small molecules
- Vesicle-mediated transport

Immune System

Metabolism of F

Chromatin organization

aplication

Cell Cycle

Programmed Cell Death

Muscle contraction

Reproduction

Cellular responses to external stimuli

Extracellular matrix organization

Transport of small molecules

Organelle biogenesis and maintenance

Mitophagy

Signal Transduction

Developmental Biology

Metabolism

Metabolism

Mitophagy

Muscle contraction

Neuronal System

Organelle biogenesis and maintenance

Programmed Cell Death

Reproduction

Signal Transduction

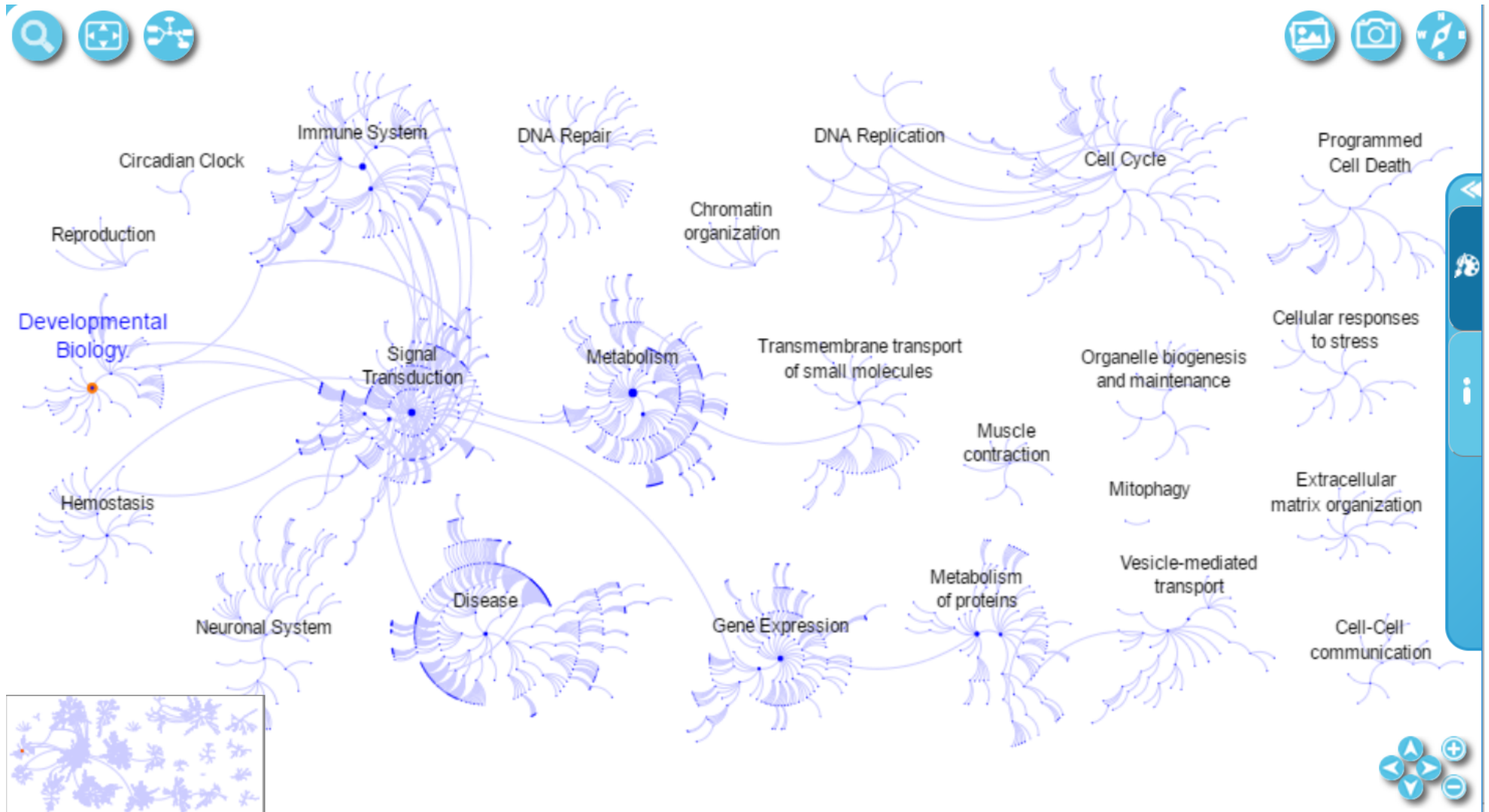
Transport of small molecules

Vesicle-mediated transport

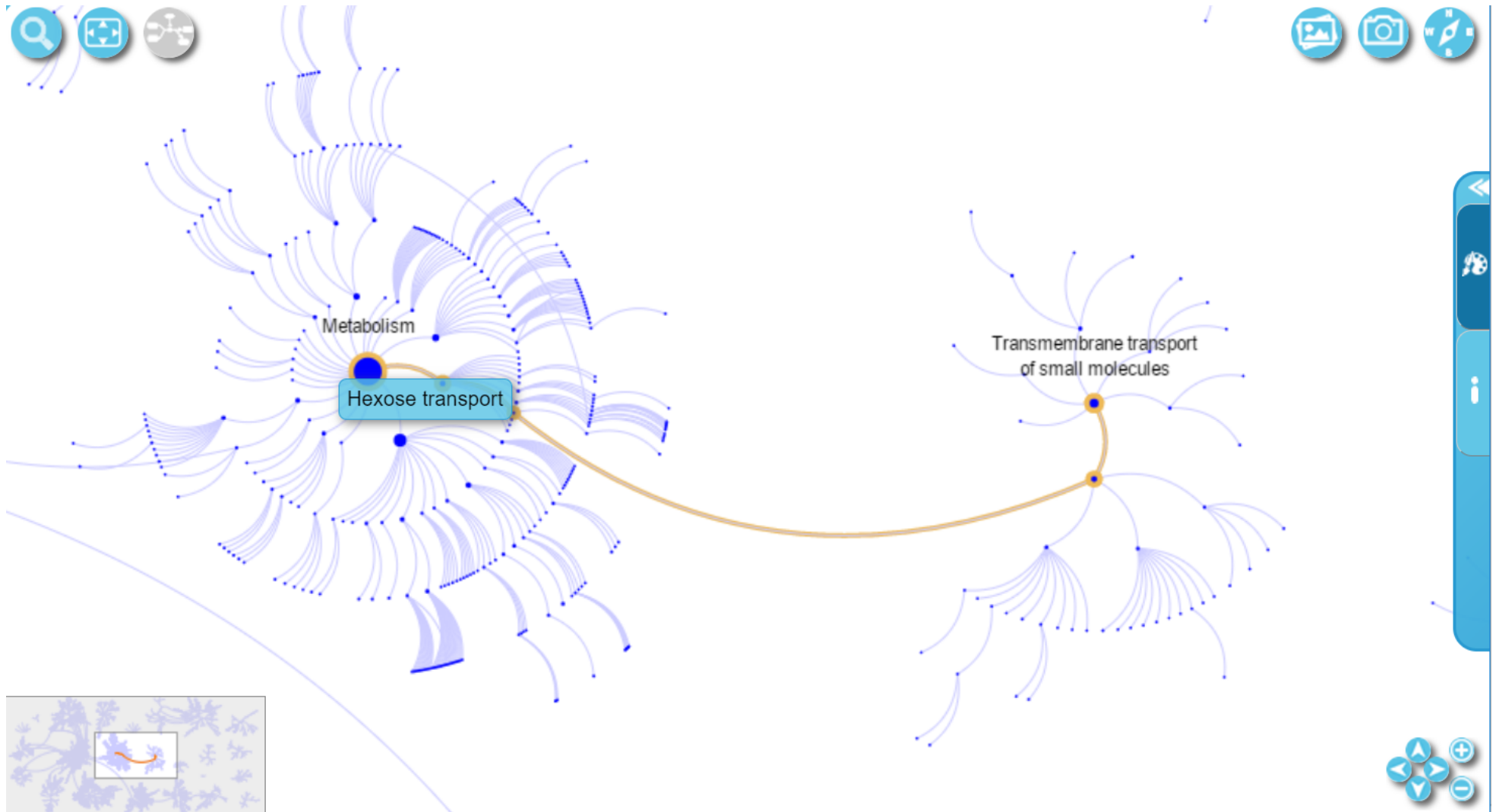
Description Molecules Structures Expression Analysis Downloads

Displays details when you select an item in the Pathway Browser. For example, when a reaction is selected, shows details including the input and output molecules, summary and references containing supporting evidence. When relevant, shows details of the catalyst, regulators, preceding and following events.

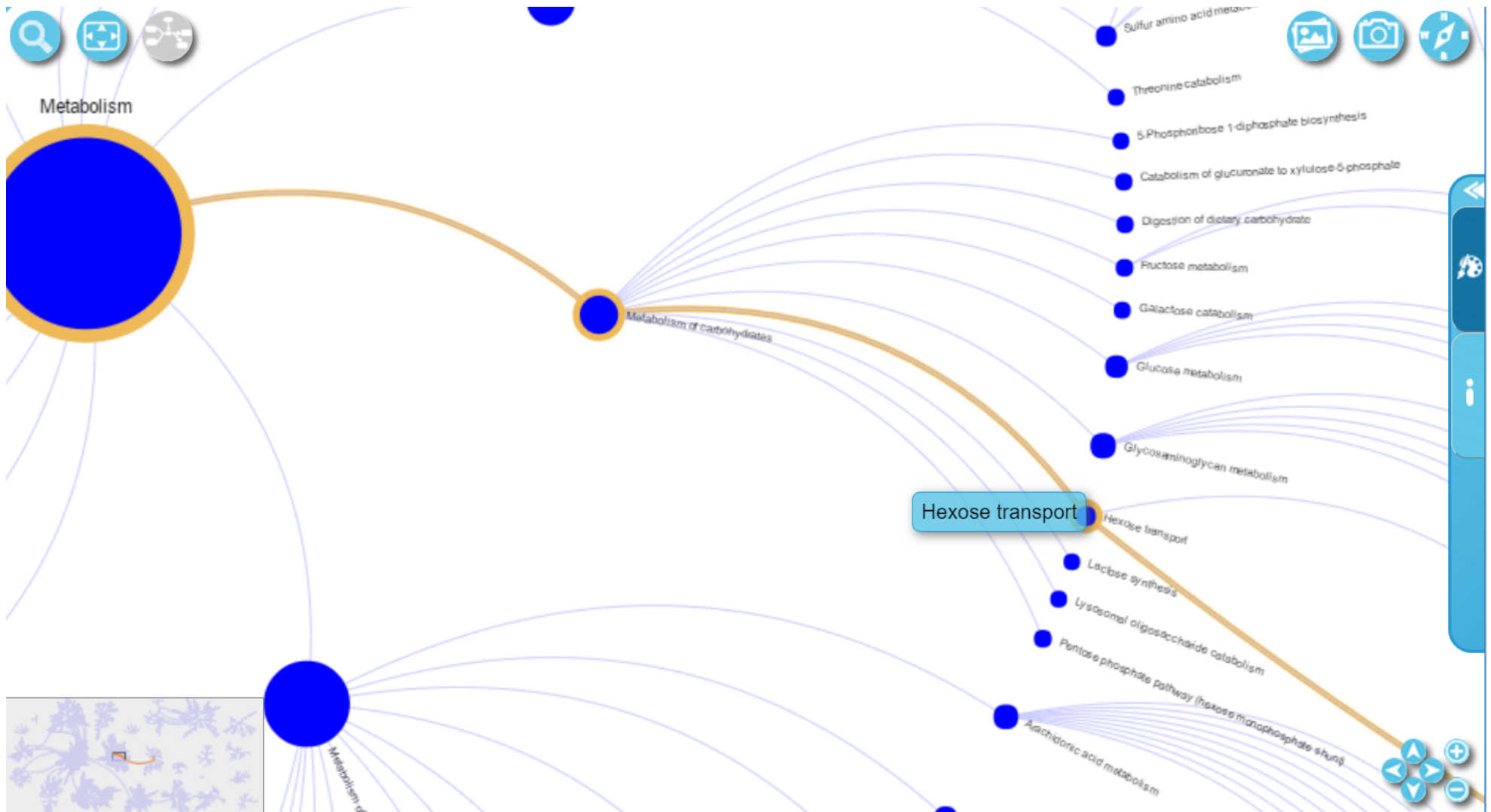
Pathway Overview



Edges = shared pathways



Zoom in for pathway names



Hierarchy Panel

REACTOME 3.0
54 Pathways for: Homo sapiens

Event Hierarchy:

- Cell Cycle
- Cell-Cell communication
 - Cell junction organization
 - Signal regulatory protein (SIRP) family interactions
 - DSCAM interactions
 - Nephrin interactions
- Cellular responses to stress
- Chromatin organization
- Circadian Clock
- Developmental Biology
- Disease
- DNA Repair
- DNA Replication
- Extracellular matrix organization
- Gene Expression
- Hemostasis
- Immune System
- Mitophagy
- Metabolism
- Metabolism of proteins
- Muscle contraction
- Neuronal System
- Organelle biogenesis and maintenance
- Programmed Cell Death
- Reproduction
- Signal Transduction
- Transmembrane transport of small molecules
- Vesicle-mediated transport



Pathway



Reaction



Black-box



Inferred from



New



Updated



Disease

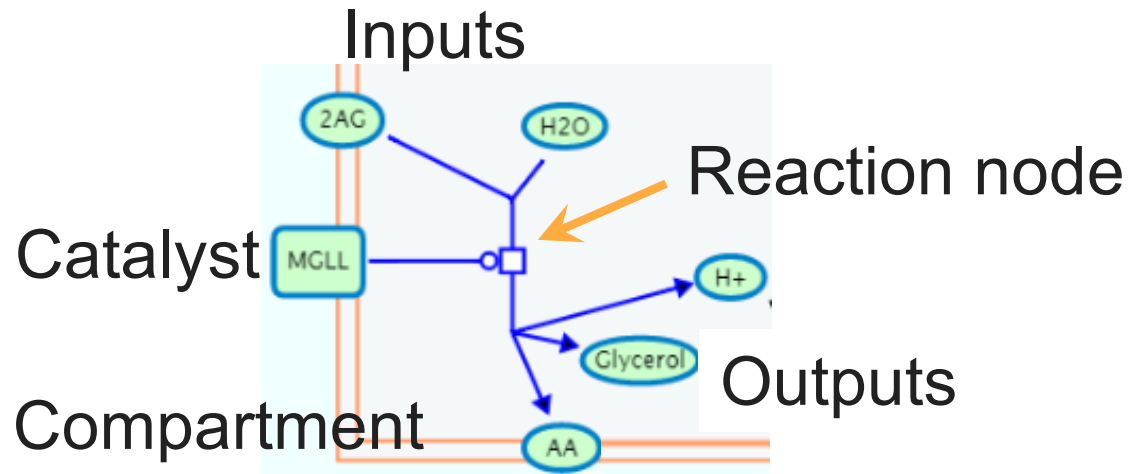
The Pathway Browser - Pathway Diagrams

Ovals are small molecules (or sets of)

Green boxes are proteins,

Blue are complexes,

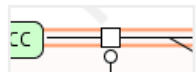
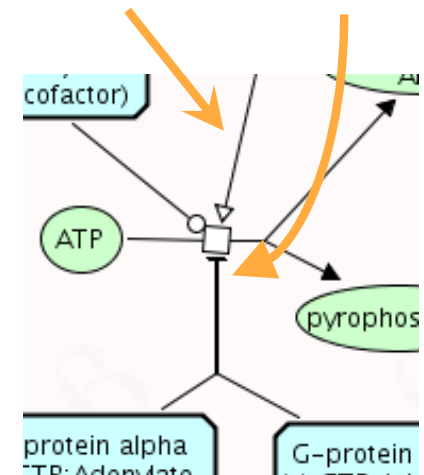
Blue with double-boundary are sets



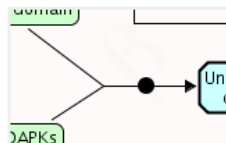
Regulation

+ve

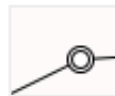
-ve



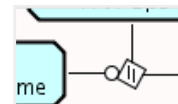
Transition



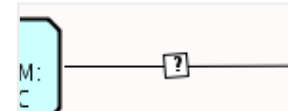
Binding



Dissociation

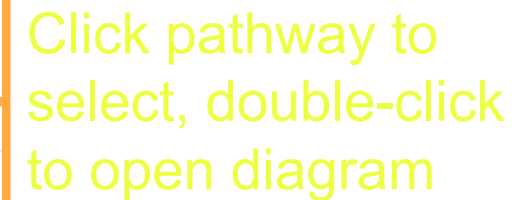


Omitted



Uncertain

Home button



Navigating in the Pathway Browser

Selected

Highlights

Details don't update until selection

Hover mouse

Event Hierarchy:

- Cell Cycle
- Cell-Cell communication
- Cellular responses to external stimuli
- Chromatin organization
- Circadian Clock
- Developmental Biology
- Digestion and absorption
- Disease
- DNA Repair
- DNA Replication
- Extracellular matrix organization
- Gene expression (Transcription)
- Hemostasis
- Immune System
- Metabolism
- Metabolism of proteins
- Metabolism of RNA
- Mitophagy
- Muscle contraction
- Neuronal System
- Organelle biogenesis and maintenance
- Programmed Cell Death
- Reproduction
- Signal Transduction**
 - Signaling by Receptor Tyrosine Kinases
 - Signaling by TGF-beta family members
 - Signaling by GPCR
 - Signaling by NOTCH**
 - Pre-NOTCH Expression and Processing
 - Signaling by NOTCH1**
 - Activated NOTCH1 Transmits Signal to the Nucleus**
 - NOTCH1 Intracellular Domain Regulates Transcription
 - Signaling by NOTCH2
 - Signaling by NOTCH3
 - Signaling by NOTCH4
 - Signaling by WNT
 - Signaling by Hippo
 - Signaling by Hedgehog
 - Signaling by Leptin
 - Integrin signaling
 - Signaling by Nuclear Receptors
 - MAPK family signaling cascades

Description | **Molecules** | **Structures** | **Expression** | **Analysis** | **Downloads**

Activated NOTCH1 Transmits Signal to the Nucleus | **Id: R-HSA-2122948** | **Species: Homo sapiens**

Summary

Mature NOTCH1 heterodimer on the cell surface is activated by one of its ligands: DLL1 (Cordle et al. 2008, Jarriault et al. 1998), DLL4 (Benedito et al. 2009), JAG1 (Li et al. 1998, Benedito et al. 2009) or JAG2 (Luo et al. 1997, Shimizu et al. 2000), expressed in trans on a neighboring cell. Thus, a ligand-expressing cell is a signal-sending cell, while the NOTCH1-expressing cell is a signal-receiving cell. If NOTCH1 has undergone Fringe modification in the Golgi, it is preferentially activated by Delta ligands (Yang et al. 2005), DLL1 and DLL4.

Upon binding to NOTCH1 on a neighboring cell, the ligand is internalized and the bound NOTCH1 receptor is endocytosed (Koo et al. 2007, Koo et al. 2002, Pan et al. 1997). S2 cleavage of the NOTCH1 intracellular domain releases the active NOTCH1 intracellular domain, which then translocates to the nucleus and activates transcription of target genes.

signaling can also be activated by ligands other than DLL1, DLL4, JAG1 and JAG2. CNTN1 (Contactin-1), transiently expressed during central and peripheral nervous system

Pathway Diagram Viewer

Zoomed-out view

- Subpathway boxes
- No glyph labels, No trivial molecules

Close view

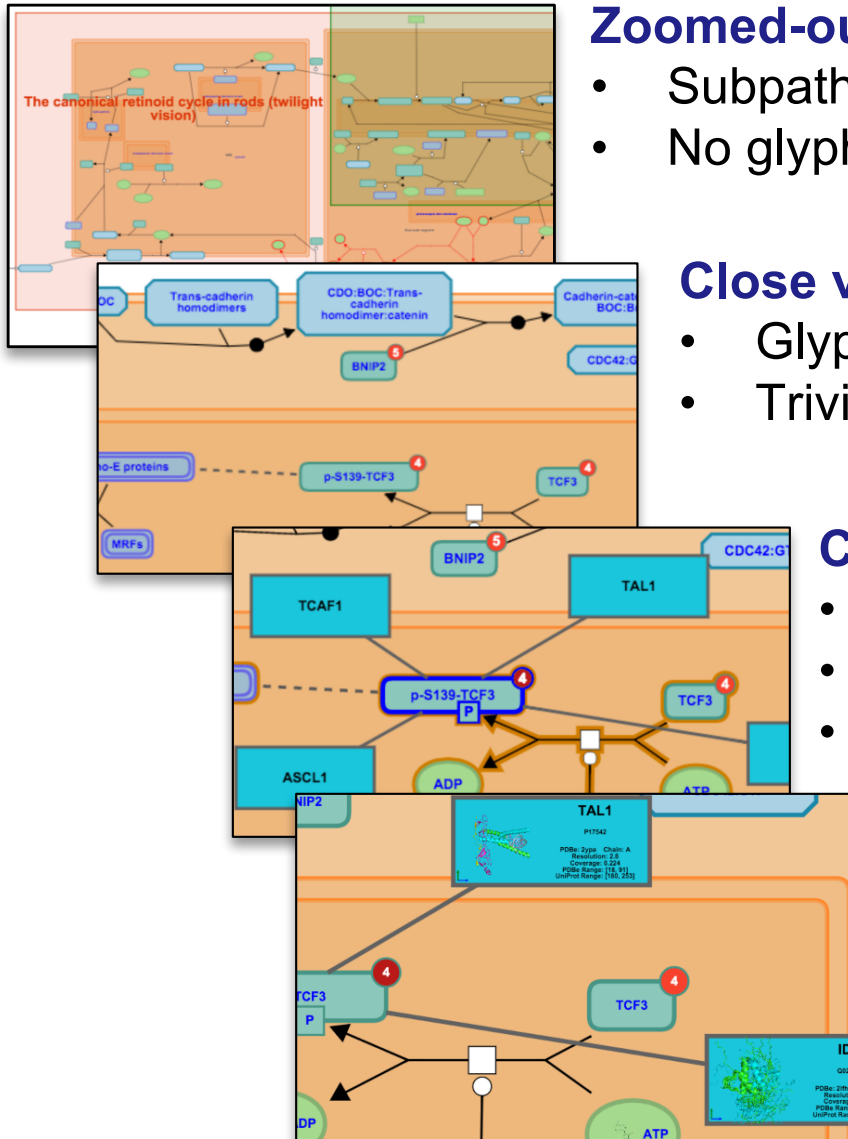
- Glyph labels
- Trivial molecules and interactor summary appear

Closer view

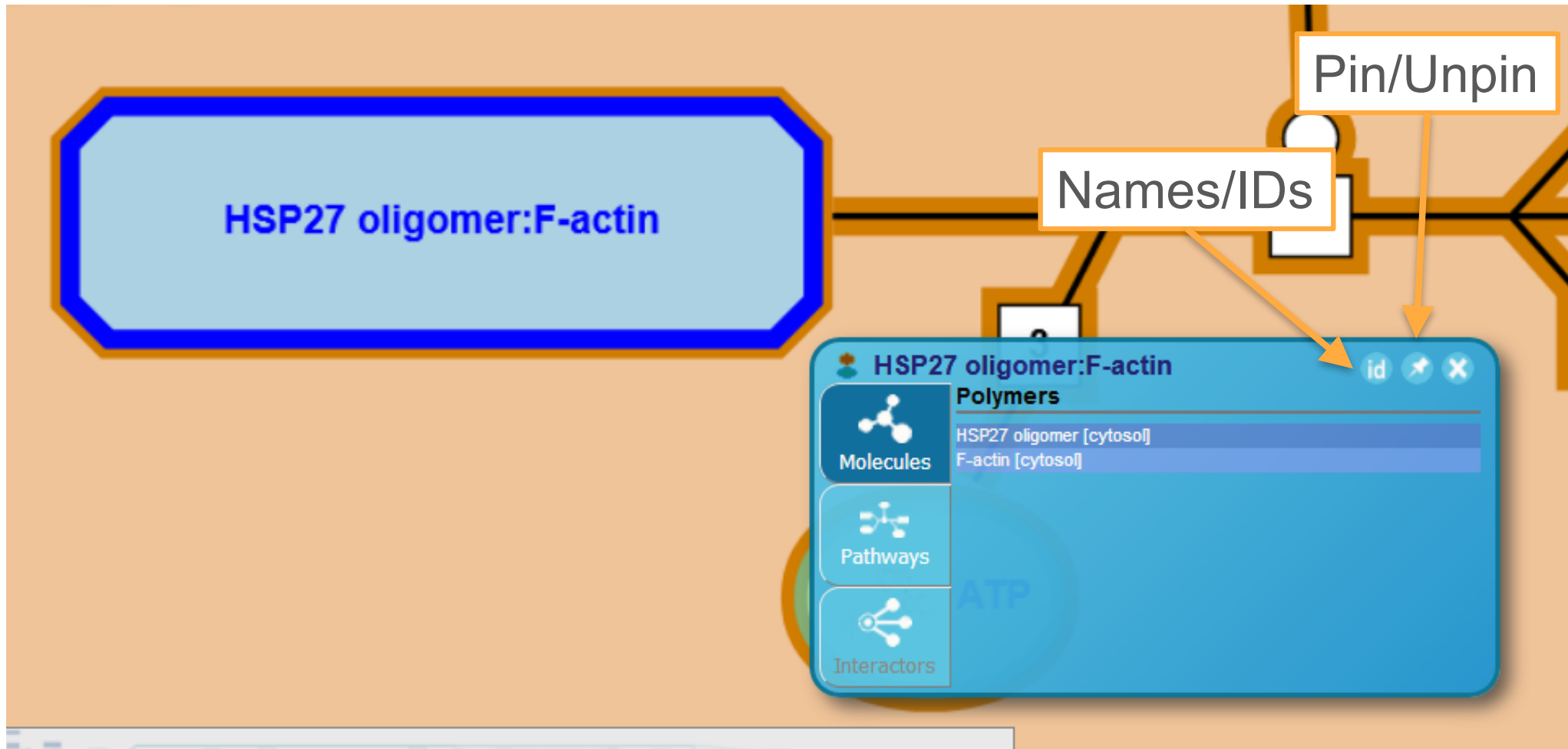
- Stoichiometry shown
- Node attachments appear
- Interactors show gene or chemical name

Zoomed-in view

- Interactors show structures and details
- Diagram proteins, chemicals extra info



Contextual Information Panel



Colour Profiles

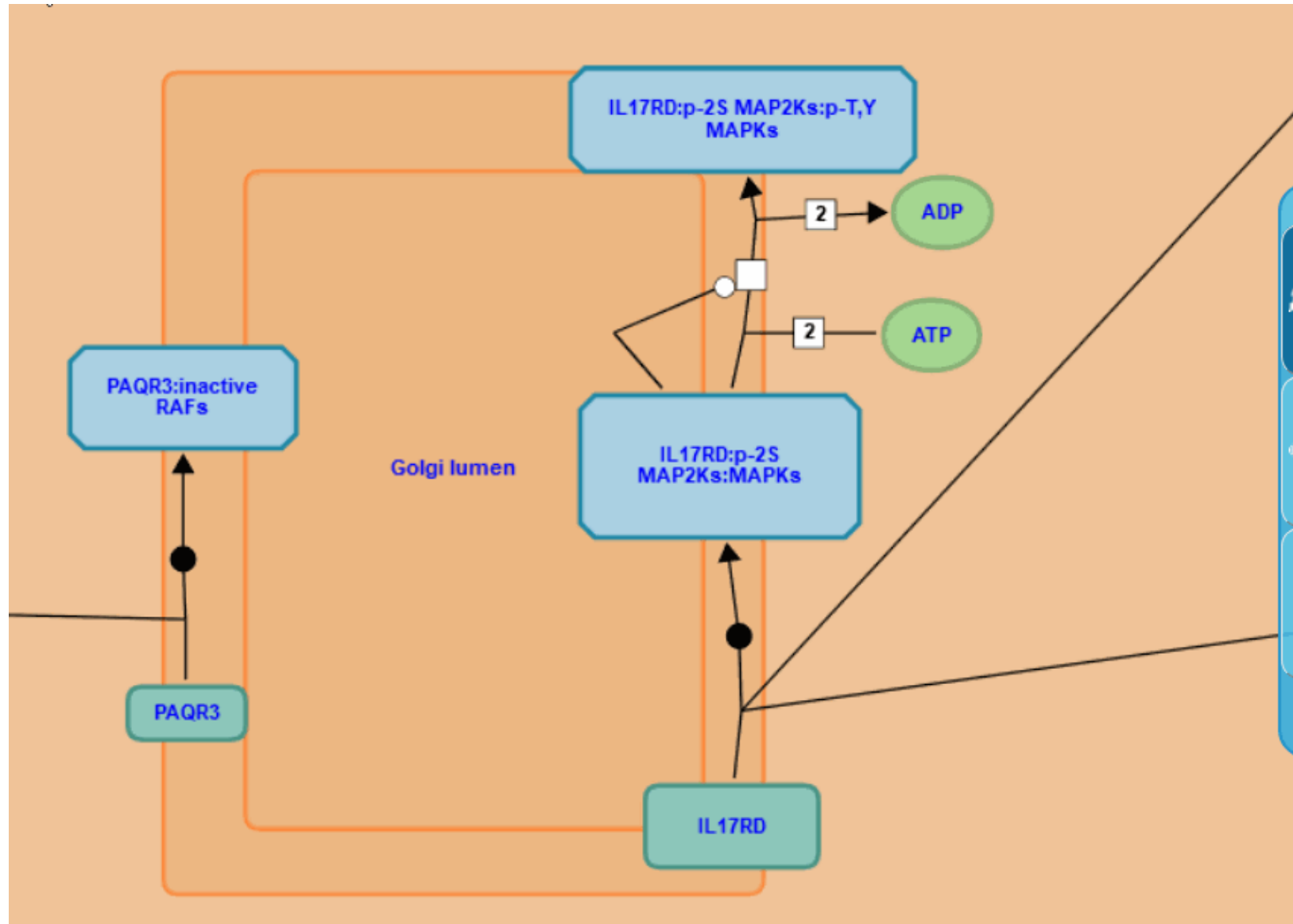
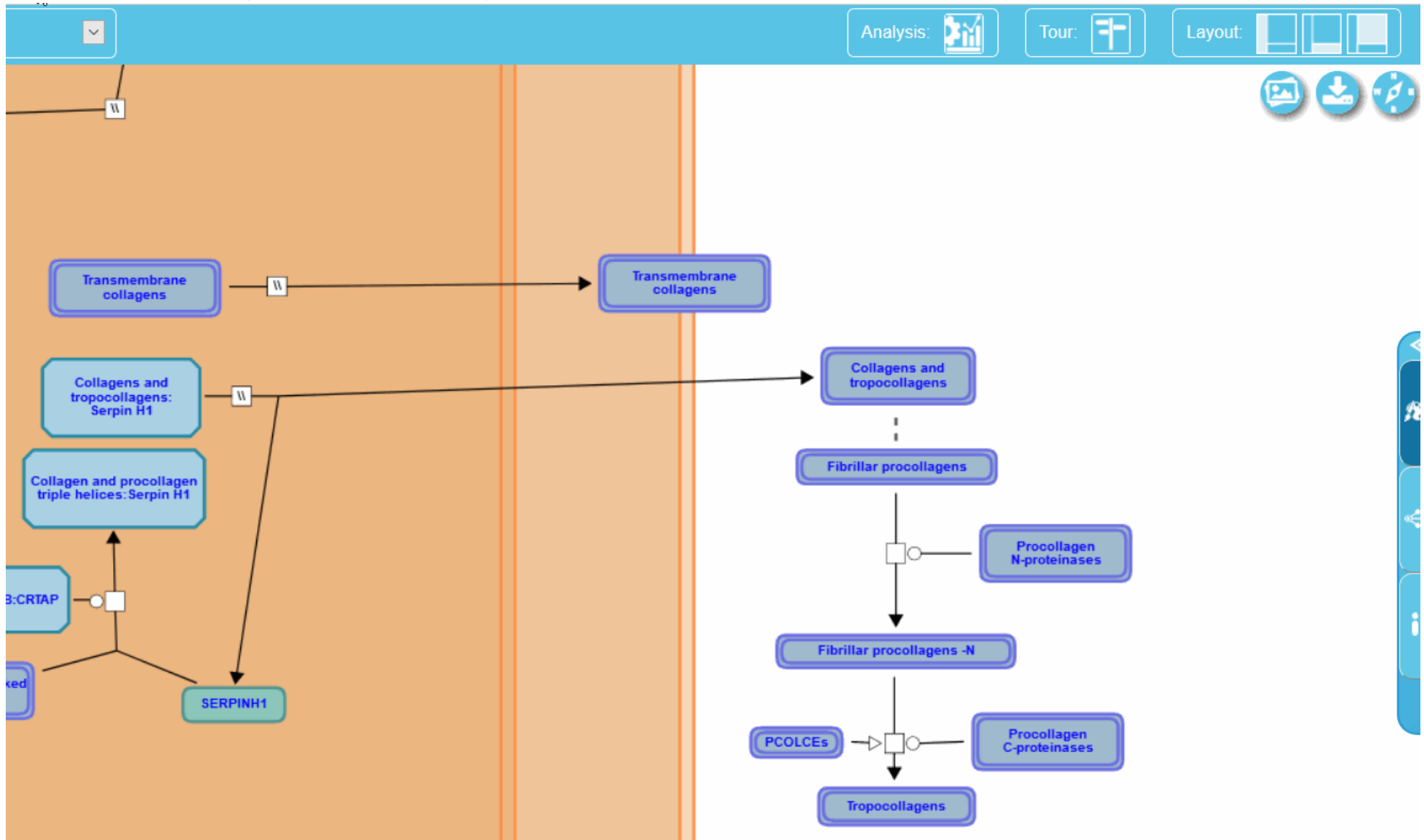
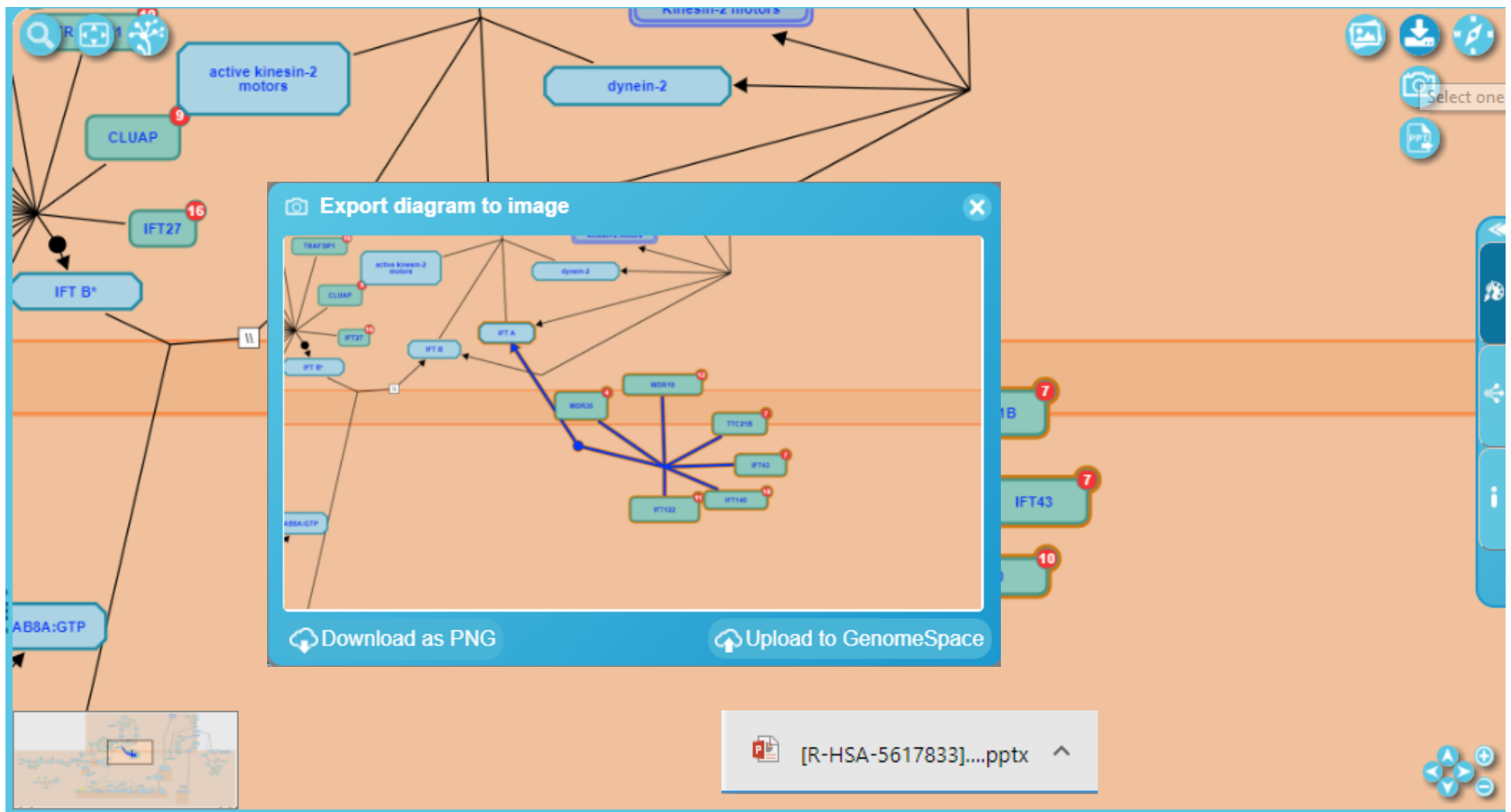


Diagram Key



Export Diagram



Show Illustration

3.2

Pathways for: Homo sapiens

Analysis:
Tour:
Layout:

Event Hierarchy:

- Effects of PIP2 hydrolysis
- Response to elevated platelet cytosolic Ca²⁺
- Formation of Fibrin Clot (Clotting Cascade)
- Dissolution of Fibrin Clot
- Cell surface interactions at the vascular wall
- Factors involved in megakaryocyte development
- Immune System
- Mitophagy
- Metabolism
- Metabolism of proteins
- Muscle contraction
- Neuronal System
- Organelle biogenesis and maintenance**
 - Mitochondrial biogenesis
 - Mitochondrial translation
- Assembly of the primary cilium**
 - Anchoring of the basal body to the plasma membrane
 - Cargo trafficking to the periciliary membrane
 - Intraflagellar transport
 - ATAT acetylates microtubules
 - HDAC6 deacetylates microtubules
- Programmed Cell Death
 - Apoptosis
 - Regulated Necrosis
- Reproduction
- Signal Transduction

CILIOGENESIS

ASSEMBLY OF THE PRIMARY CILIUM INTRAFLAGELLAR TRANSPORT AND CARGO TRAFFICKING

Description
 Molecules
 Structures
 Expression
 Analysis
 Downloads

Analysis results are shown here when an analysis has been run. To start an analysis, click on the Analyse Data button in the top bar.

The Details Panel - Overview

Background

Select

Orthologues

Key literature

DescriptionMoleculesStructuresExpressionAnalysisDownloads

Collagen type I binds integrin alpha1beta1, alpha2beta1, alpha10beta1Id: R-HSA-114563Species: Homo sapiens

Summation

Integrin alpha1beta1 binds to collagen type IV and VI with higher affinity than to types I-III, whereas alpha2beta1 has a higher affinity for collagen types I-III than for type IV. Integrin alpha10beta1 binds collagen types I, IV, and VI with similar affinities (Tulla et al. 2001). Integrin alpha11beta1 binds preferentially to the fibril-forming collagen types I and II, binding to type III is weaker and collagens IV and VI are poor ligands (Zhang et al. 2003).

Binding to collagen type I occurs at sites corresponding to the six-residue sequence G(F/L)OGER (Knight et al. 1998, 2000, Xu et al. 2000).

Integrin alpha2beta1 is the major platelet collagen receptor (Kunicki et al. 1988). It requires Mg2+ to interact with collagen and may require initiation mediated by the activation of Integrin alphaIIbBeta3 (van de Walle 2007).

► Background literature references...

Input

Collagen type I fibril [extracellular region]

Mg2+ [extracellular region]

Integrin alpha1beta1, alpha2beta1, alpha10beta1 [plasma membrane]

Output

Integrins alpha1beta1, alpha2beta1:Collagen type I fibril:Mg2+ [plasma membrane]

Cellular compartment

extracellular region

plasma membrane

Inferred from another species

Collagen type I binds integrin alpha1beta1, alpha2beta1, alpha10beta1 [Homo sapiens, Rattus norvegicus]

Authored

Geiger, B, Horwitz, R, 2008-05-07 08:30:32

Reviewed

Yamada, K, Humphries, MJ, Hynes, R, 2008-05-07 08:53:37

Ricard-Blum, Sylvie, 2013-08-13

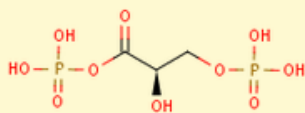
Revised

Jupe, S, 2013-08-13

Reveal
Details



► All other struct



Secondary ChEBI IDs CHEBI:1658, CHEBI:11881, CHEBI:20189

Download

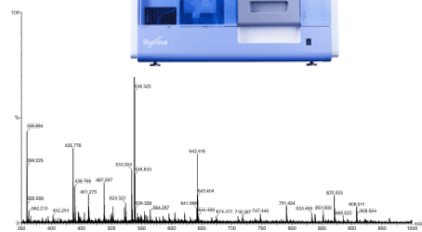
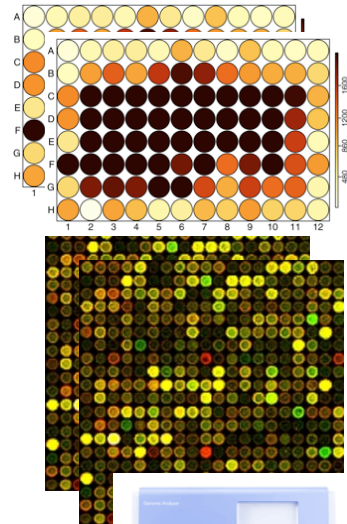


Expression level in FPKM

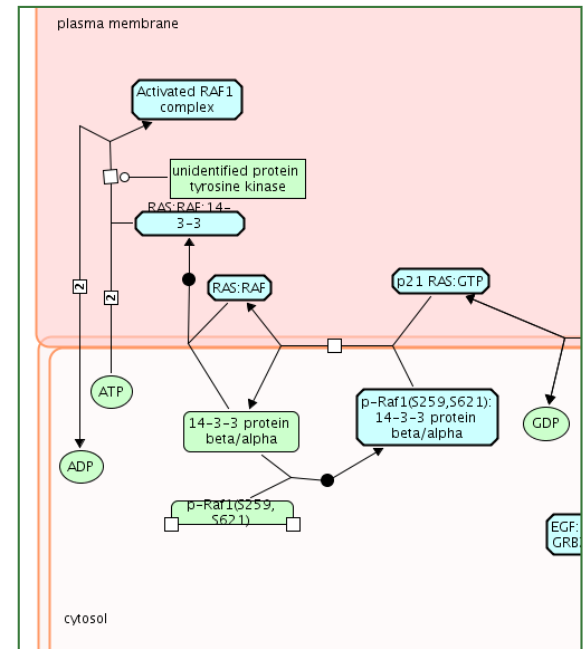
	adipose tissue	bone marrow	colon	endometrium	fallopian tube	heart	liver	lymph node	pancreas	prostate gland	saliva-secreting gland	small intestine	spleen	testis	tonsil	vermiform appendix
GUCY1A2	Low	Low	High	Low	Low	Low	Low	Low	High	Low	Low	High	High	Low	Low	Low
GUCY1B3	High	High	Low	High	High	High	Low	Low	High	Low	Low	High	High	Low	High	High
STRN4	High	High	High	High	High	High	Low	High	High	Low	Low	High	High	High	Low	High
GUCY1A3	High	Low	High	Low	High	High	Low	Low	High	Low	Low	High	High	High	High	Low

Please send any queries or feedback to arrayexpress-atlas@ebi.ac.uk.


Understanding gene lists...Reactome Tools



Gene	Description	Accession ID	NCBI RefSeq	Ensembl
CDKN2A	cyclin dependent kinase 2	U05393.1	U05393.1	U05393.1
CDKN2B	cyclin dependent kinase 2	U05394.1	U05394.1	U05394.1
CDKN2C	cyclin dependent kinase 2	U05395.1	U05395.1	U05395.1
CDKN2D	cyclin dependent kinase 2	U05396.1	U05396.1	U05396.1
CDKN2E	cyclin dependent kinase 2	U05397.1	U05397.1	U05397.1
CDKN2F	cyclin dependent kinase 2	U05398.1	U05398.1	U05398.1
CDKN2G	cyclin dependent kinase 2	U05399.1	U05399.1	U05399.1
CDKN2H	cyclin dependent kinase 2	U05400.1	U05400.1	U05400.1
CDKN2I	cyclin dependent kinase 2	U05401.1	U05401.1	U05401.1
CDKN2J	cyclin dependent kinase 2	U05402.1	U05402.1	U05402.1
CDKN2K	cyclin dependent kinase 2	U05403.1	U05403.1	U05403.1
CDKN2L	cyclin dependent kinase 2	U05404.1	U05404.1	U05404.1
CDKN2M	cyclin dependent kinase 2	U05405.1	U05405.1	U05405.1
CDKN2N	cyclin dependent kinase 2	U05406.1	U05406.1	U05406.1
CDKN2O	cyclin dependent kinase 2	U05407.1	U05407.1	U05407.1
CDKN2P	cyclin dependent kinase 2	U05408.1	U05408.1	U05408.1
CDKN2Q	cyclin dependent kinase 2	U05409.1	U05409.1	U05409.1
CDKN2R	cyclin dependent kinase 2	U05410.1	U05410.1	U05410.1
CDKN2S	cyclin dependent kinase 2	U05411.1	U05411.1	U05411.1
CDKN2T	cyclin dependent kinase 2	U05412.1	U05412.1	U05412.1
CDKN2U	cyclin dependent kinase 2	U05413.1	U05413.1	U05413.1
CDKN2V	cyclin dependent kinase 2	U05414.1	U05414.1	U05414.1
CDKN2W	cyclin dependent kinase 2	U05415.1	U05415.1	U05415.1
CDKN2X	cyclin dependent kinase 2	U05416.1	U05416.1	U05416.1
CDKN2Y	cyclin dependent kinase 2	U05417.1	U05417.1	U05417.1
CDKN2Z	cyclin dependent kinase 2	U05418.1	U05418.1	U05418.1
CDKN2AA	cyclin dependent kinase 2	U05419.1	U05419.1	U05419.1
CDKN2AB	cyclin dependent kinase 2	U05420.1	U05420.1	U05420.1
CDKN2AC	cyclin dependent kinase 2	U05421.1	U05421.1	U05421.1
CDKN2AD	cyclin dependent kinase 2	U05422.1	U05422.1	U05422.1
CDKN2AE	cyclin dependent kinase 2	U05423.1	U05423.1	U05423.1
CDKN2AF	cyclin dependent kinase 2	U05424.1	U05424.1	U05424.1
CDKN2AG	cyclin dependent kinase 2	U05425.1	U05425.1	U05425.1
CDKN2AH	cyclin dependent kinase 2	U05426.1	U05426.1	U05426.1
CDKN2AI	cyclin dependent kinase 2	U05427.1	U05427.1	U05427.1
CDKN2AJ	cyclin dependent kinase 2	U05428.1	U05428.1	U05428.1
CDKN2AK	cyclin dependent kinase 2	U05429.1	U05429.1	U05429.1
CDKN2AL	cyclin dependent kinase 2	U05430.1	U05430.1	U05430.1
CDKN2AM	cyclin dependent kinase 2	U05431.1	U05431.1	U05431.1
CDKN2AN	cyclin dependent kinase 2	U05432.1	U05432.1	U05432.1
CDKN2AO	cyclin dependent kinase 2	U05433.1	U05433.1	U05433.1
CDKN2AP	cyclin dependent kinase 2	U05434.1	U05434.1	U05434.1
CDKN2AQ	cyclin dependent kinase 2	U05435.1	U05435.1	U05435.1
CDKN2AR	cyclin dependent kinase 2	U05436.1	U05436.1	U05436.1
CDKN2AS	cyclin dependent kinase 2	U05437.1	U05437.1	U05437.1
CDKN2AT	cyclin dependent kinase 2	U05438.1	U05438.1	U05438.1
CDKN2AU	cyclin dependent kinase 2	U05439.1	U05439.1	U05439.1
CDKN2AV	cyclin dependent kinase 2	U05440.1	U05440.1	U05440.1
CDKN2AW	cyclin dependent kinase 2	U05441.1	U05441.1	U05441.1
CDKN2AX	cyclin dependent kinase 2	U05442.1	U05442.1	U05442.1
CDKN2AY	cyclin dependent kinase 2	U05443.1	U05443.1	U05443.1
CDKN2AZ	cyclin dependent kinase 2	U05444.1	U05444.1	U05444.1
CDKN2BA	cyclin dependent kinase 2	U05445.1	U05445.1	U05445.1
CDKN2BB	cyclin dependent kinase 2	U05446.1	U05446.1	U05446.1
CDKN2BC	cyclin dependent kinase 2	U05447.1	U05447.1	U05447.1
CDKN2BD	cyclin dependent kinase 2	U05448.1	U05448.1	U05448.1
CDKN2BE	cyclin dependent kinase 2	U05449.1	U05449.1	U05449.1
CDKN2BF	cyclin dependent kinase 2	U05450.1	U05450.1	U05450.1
CDKN2BG	cyclin dependent kinase 2	U05451.1	U05451.1	U05451.1
CDKN2BH	cyclin dependent kinase 2	U05452.1	U05452.1	U05452.1
CDKN2BI	cyclin dependent kinase 2	U05453.1	U05453.1	U05453.1
CDKN2BJ	cyclin dependent kinase 2	U05454.1	U05454.1	U05454.1
CDKN2BK	cyclin dependent kinase 2	U05455.1	U05455.1	U05455.1
CDKN2BL	cyclin dependent kinase 2	U05456.1	U05456.1	U05456.1
CDKN2BM	cyclin dependent kinase 2	U05457.1	U05457.1	U05457.1
CDKN2BN	cyclin dependent kinase 2	U05458.1	U05458.1	U05458.1
CDKN2BO	cyclin dependent kinase 2	U05459.1	U05459.1	U05459.1
CDKN2BP	cyclin dependent kinase 2	U05460.1	U05460.1	U05460.1
CDKN2BQ	cyclin dependent kinase 2	U05461.1	U05461.1	U05461.1
CDKN2BR	cyclin dependent kinase 2	U05462.1	U05462.1	U05462.1
CDKN2BS	cyclin dependent kinase 2	U05463.1	U05463.1	U05463.1
CDKN2BT	cyclin dependent kinase 2	U05464.1	U05464.1	U05464.1
CDKN2BU	cyclin dependent kinase 2	U05465.1	U05465.1	U05465.1
CDKN2BV	cyclin dependent kinase 2	U05466.1	U05466.1	U05466.1
CDKN2BW	cyclin dependent kinase 2	U05467.1	U05467.1	U05467.1
CDKN2BX	cyclin dependent kinase 2	U05468.1	U05468.1	U05468.1
CDKN2BY	cyclin dependent kinase 2	U05469.1	U05469.1	U05469.1
CDKN2BZ	cyclin dependent kinase 2	U05470.1	U05470.1	U05470.1
CDKN2CA	cyclin dependent kinase 2	U05471.1	U05471.1	U05471.1
CDKN2CB	cyclin dependent kinase 2	U05472.1	U05472.1	U05472.1
CDKN2CC	cyclin dependent kinase 2	U05473.1	U05473.1	U05473.1
CDKN2CD	cyclin dependent kinase 2	U05474.1	U05474.1	U05474.1
CDKN2CE	cyclin dependent kinase 2	U05475.1	U05475.1	U05475.1
CDKN2CF	cyclin dependent kinase 2	U05476.1	U05476.1	U05476.1
CDKN2CG	cyclin dependent kinase 2	U05477.1	U05477.1	U05477.1
CDKN2CH	cyclin dependent kinase 2	U05478.1	U05478.1	U05478.1
CDKN2CI	cyclin dependent kinase 2	U05479.1	U05479.1	U05479.1
CDKN2CJ	cyclin dependent kinase 2	U05480.1	U05480.1	U05480.1
CDKN2CK	cyclin dependent kinase 2	U05481.1	U05481.1	U05481.1
CDKN2CL	cyclin dependent kinase 2	U05482.1	U05482.1	U05482.1
CDKN2CM	cyclin dependent kinase 2	U05483.1	U05483.1	U05483.1
CDKN2CN	cyclin dependent kinase 2	U05484.1	U05484.1	U05484.1
CDKN2CO	cyclin dependent kinase 2	U05485.1	U05485.1	U05485.1
CDKN2CP	cyclin dependent kinase 2	U05486.1	U05486.1	U05486.1
CDKN2CQ	cyclin dependent kinase 2	U05487.1	U05487.1	U05487.1
CDKN2CR	cyclin dependent kinase 2	U05488.1	U05488.1	U05488.1
CDKN2CS	cyclin dependent kinase 2	U05489.1	U05489.1	U05489.1
CDKN2CT	cyclin dependent kinase 2	U05490.1	U05490.1	U05490.1
CDKN2CU	cyclin dependent kinase 2	U05491.1	U05491.1	U05491.1
CDKN2CV	cyclin dependent kinase 2	U05492.1	U05492.1	U05492.1
CDKN2CW	cyclin dependent kinase 2	U05493.1	U05493.1	U05493.1
CDKN2CX	cyclin dependent kinase 2	U05494.1	U05494.1	U05494.1
CDKN2CY	cyclin dependent kinase 2	U05495.1	U05495.1	U05495.1
CDKN2CZ	cyclin dependent kinase 2	U05496.1	U05496.1	U05496.1
CDKN2DA	cyclin dependent kinase 2	U05497.1	U05497.1	U05497.1
CDKN2DB	cyclin dependent kinase 2	U05498.1	U05498.1	U05498.1
CDKN2DC	cyclin dependent kinase 2	U05499.1	U05499.1	U05499.1
CDKN2DD	cyclin dependent kinase 2	U05500.1	U05500.1	U05500.1
CDKN2DE	cyclin dependent kinase 2	U05501.1	U05501.1	U05501.1
CDKN2DF	cyclin dependent kinase 2	U05502.1	U05502.1	U05502.1
CDKN2DG	cyclin dependent kinase 2	U05503.1	U05503.1	U05503.1
CDKN2DH	cyclin dependent kinase 2	U05504.1	U05504.1	U05504.1
CDKN2DI	cyclin dependent kinase 2	U05505.1	U05505.1	U05505.1
CDKN2DJ	cyclin dependent kinase 2	U05506.1	U05506.1	U05506.1
CDKN2DK	cyclin dependent kinase 2	U05507.1	U05507.1	U05507.1
CDKN2DL	cyclin dependent kinase 2	U05508.1	U05508.1	U05508.1
CDKN2DM	cyclin dependent kinase 2	U05509.1	U05509.1	U05509.1
CDKN2DN	cyclin dependent kinase 2	U05510.1	U05510.1	U05510.1
CDKN2DO	cyclin dependent kinase 2	U05511.1	U05511.1	U05511.1
CDKN2DP	cyclin dependent kinase 2	U05512.1	U05512.1	U05512.1
CDKN2DQ	cyclin dependent kinase 2	U05513.1	U05513.1	U05513.1
CDKN2DR	cyclin dependent kinase 2	U05514.1	U05514.1	U05514.1
CDKN2DS	cyclin dependent kinase 2	U05515.1	U05515.1	U05515.1
CDKN2DT	cyclin dependent kinase 2	U05516.1	U05516.1	U05516.1
CDKN2DU	cyclin dependent kinase 2	U05517.1	U05517.1	U05517.1
CDKN2DV	cyclin dependent kinase 2	U05518.1	U05518.1	U05518.1
CDKN2DW	cyclin dependent kinase 2	U05519.1	U05519.1	U05519.1
CDKN2DX	cyclin dependent kinase 2	U05520.1	U05520.1	U05520.1
CDKN2DY	cyclin dependent kinase 2	U05521.1	U05521.1	U05521.1
CDKN2DZ	cyclin dependent kinase 2	U05522.1	U05522.1	U05522.1
CDKN2EA	cyclin dependent kinase 2	U05523.1	U05523.1	U05523.1
CDKN2EB	cyclin dependent kinase 2	U05524.1	U05524.1	U05524.1
CDKN2EC	cyclin dependent kinase 2	U05525.1	U05525.1	U05525.1
CDKN2ED	cyclin dependent kinase 2	U05526.1	U05526.1	U05526.1
CDKN2EE	cyclin dependent kinase 2	U05527.1	U05527.1	U05527.1
CDKN2EF	cyclin dependent kinase 2	U05528.1	U05528.1	U05528.1
CDKN2EG	cyclin dependent kinase 2	U05529.1	U05529.1	U05529.1
CDKN2EH	cyclin dependent kinase 2	U05530.1	U05530.1	U05530.1
CDKN2EI	cyclin dependent kinase 2	U05531.1	U05531.1	U05531.1
CDKN2EJ	cyclin dependent kinase 2	U05532.1	U05532.1	U05532.1
CDKN2EK	cyclin dependent kinase 2	U05533.1	U05533.1	U05533.1
CDKN2EL	cyclin dependent kinase 2	U05534.1	U05534.1	U05534.1
CDKN2EM	cyclin dependent kinase 2	U05535.1	U05535.1	U05535.1
CDKN2EN	cyclin dependent kinase 2	U05536.1	U05536.1	U05536.1
CDKN2EO	cyclin dependent kinase 2	U05537.1	U05537.1	U05537.1
CDKN2EP	cyclin dependent kinase 2	U05538.1	U05538.1	U05538.1
CDKN2EQ	cyclin dependent kinase 2	U05539.1	U05539.1	U05539.1
CDKN2ER	cyclin dependent kinase 2	U05540.1	U05540.1	U05540.1
CDKN2ES	cyclin dependent kinase 2	U05541.1	U05541.1	U05541.1
CDKN2ET	cyclin dependent kinase 2	U05542.1	U05542.1	U05542.1
CDKN2EU	cyclin dependent kinase 2	U05543.1	U05543.1	U05543.1
CDKN2EV	cyclin dependent kinase 2	U05544.1	U05544.1	U05544.1
CDKN2EW	cyclin dependent kinase 2	U05545.1	U05545.1	U05545.1
CDKN2EX	cyclin dependent kinase 2	U05546.1	U05546.1	U05546.1
CDKN2EY	cyclin dependent kinase 2	U05547.1	U05547.1	U05547.1
CDKN2EZ	cyclin dependent kinase 2	U05548.1	U05548.1	U05548.1
CDKN2FA	cyclin dependent kinase 2	U05549.1	U05549.1	U05549.1
CDKN2FB	cyclin dependent kinase 2	U05550.1	U05550.1	U05550.1
CDKN2FC	cyclin dependent kinase 2	U05551.1	U05551.1	U05551.1
CDKN2FD	cyclin dependent kinase 2	U05552.1	U05552.1	U05552.1
CDKN2FE	cyclin dependent kinase 2	U05553.1	U05553.1	U05553.1
CDKN2FF	cyclin dependent kinase 2	U05554.1	U05554.1	U05554.1
CDKN2FG	cyclin dependent kinase 2	U05555.1	U05555.1	U05555.1
CDKN2FH	cyclin dependent kinase 2	U05556.1	U05556.1	U05556.1
CDKN2FI	cyclin dependent kinase 2	U05557.1	U05557.1	U05557.1
CDKN2FJ	cyclin dependent kinase 2	U05558.1	U05558.1	U05558.1
CDKN2FK	cyclin dependent kinase 2	U05559.1	U05559.1	U05559.1
CDKN2FL	cyclin dependent kinase 2	U05560.1	U05560.1	U05560.1
CDKN2FM	cyclin dependent kinase 2	U05561.1	U05561.1	U05561.1
CDKN2FN	cyclin dependent kinase 2	U05562.1	U05562.1	U05562.1
CDKN2FO	cyclin dependent kinase 2	U05563.1	U05563.1	U05563.1
CDKN2FP	cyclin dependent kinase 2	U05564.1	U05564.1	U05564.1
CDKN2FQ	cyclin dependent kinase 2	U05565.1	U05565.1	U05565.1
CDKN2FR	cyclin dependent kinase 2	U05566.1	U05566.1	U05566.1
CDKN2FS	cyclin dependent kinase 2	U05567.1	U05567.1	U05567.1
CDKN2FT	cyclin dependent kinase 2	U05568.1	U05568.1	U05568.1
CDKN2FU	cyclin dependent kinase 2	U05569.1	U05569.1	U05569.1
CDKN2FV	cyclin dependent kinase 2	U05570.1	U05570.1	U05570.1
CDKN2FW	cyclin dependent kinase 2	U05571.1	U05571.1	U05571.1
CDKN2FX	cyclin dependent kinase 2	U05572.1	U05572.1	U05572.1
CDKN2FY	cyclin dependent kinase 2	U05573.1	U05573.1	U05573.1
CDKN2FZ	cyclin dependent kinase 2	U05574.1	U05574.1	U05574.1
CDKN2GA	cyclin dependent kinase 2	U05575.1	U05575.1	U05575.1
CDKN2GB	cyclin dependent kinase 2	U05576.1	U05576.1	U05576.1
CDKN2GC	cyclin dependent kinase 2	U05577.1	U05577.1	U05577.1
CDKN2GD	cyclin dependent kinase 2	U05578.1	U05578.1	U05578.1
CDKN2GE	cyclin dependent kinase 2	U05579.1	U05579.1	U05579.1
CDKN2GF	cyclin dependent kinase 2	U05580.1	U05580.1	U05580.1
CDKN2GG	cyclin dependent kinase 2	U05581.1	U05581.1	U05581.1
CDKN2GH	cyclin dependent kinase 2	U05582.1	U05582.1	U05582.1
CDKN2GI	cyclin dependent kinase 2	U05583.1	U05583.1	U05583.1
CDKN2GJ	cyclin dependent kinase 2	U05584.1	U05584.1	U05584.1
CDKN2GK	cyclin dependent kinase 2	U05585.1	U05585.1	U05585.1
CDKN2GL	cyclin dependent kinase 2	U05586.1	U05586.1	U05586.1
CDKN2GM	cyclin dependent kinase 2	U05587.1	U05587.1	U05587.1
CDKN2GN	cyclin dependent kinase 2	U05588.1	U05588	

[illegible]

Analysis

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Find Reactions, Proteins and Pathways

e.g. O95631, NTN1, signaling by EGFR, glucose



Pathway Browser
Visualize and interact with Reactome biological pathways



Analyze Data
Merges pathway viewer mapping, over-representation, and expression analysis



ReactomeFIViz
Designed to find pathways and network patterns relevant to your study






Documentation
Information to browse the database

USE REACTOME GRAPH DATABASE IN YOUR PROJECT


Why Reactome

Reactome is a free, open-source, curated and peer reviewed pathway database. Our goal is to provide intuitive bioinformatics tools for the visualization, interpretation and analysis of pathway knowledge to support basic research, genome analysis, modeling, systems biology and education. The current version (v62) of Reactome was released on September 27, 2017.

If you use Reactome in Asia, we suggest using our Chinese mirror site at reactome.ncpsb.org.

The development of Reactome is supported by grants from the US National Institutes of Health (P41 HG003751 and 1U54GM114833-01), Ontario Research Fund, and the European Molecular Biology Laboratory.

 **Pathways for: Homo sapiens**

Analysis **Tour** **Layout**

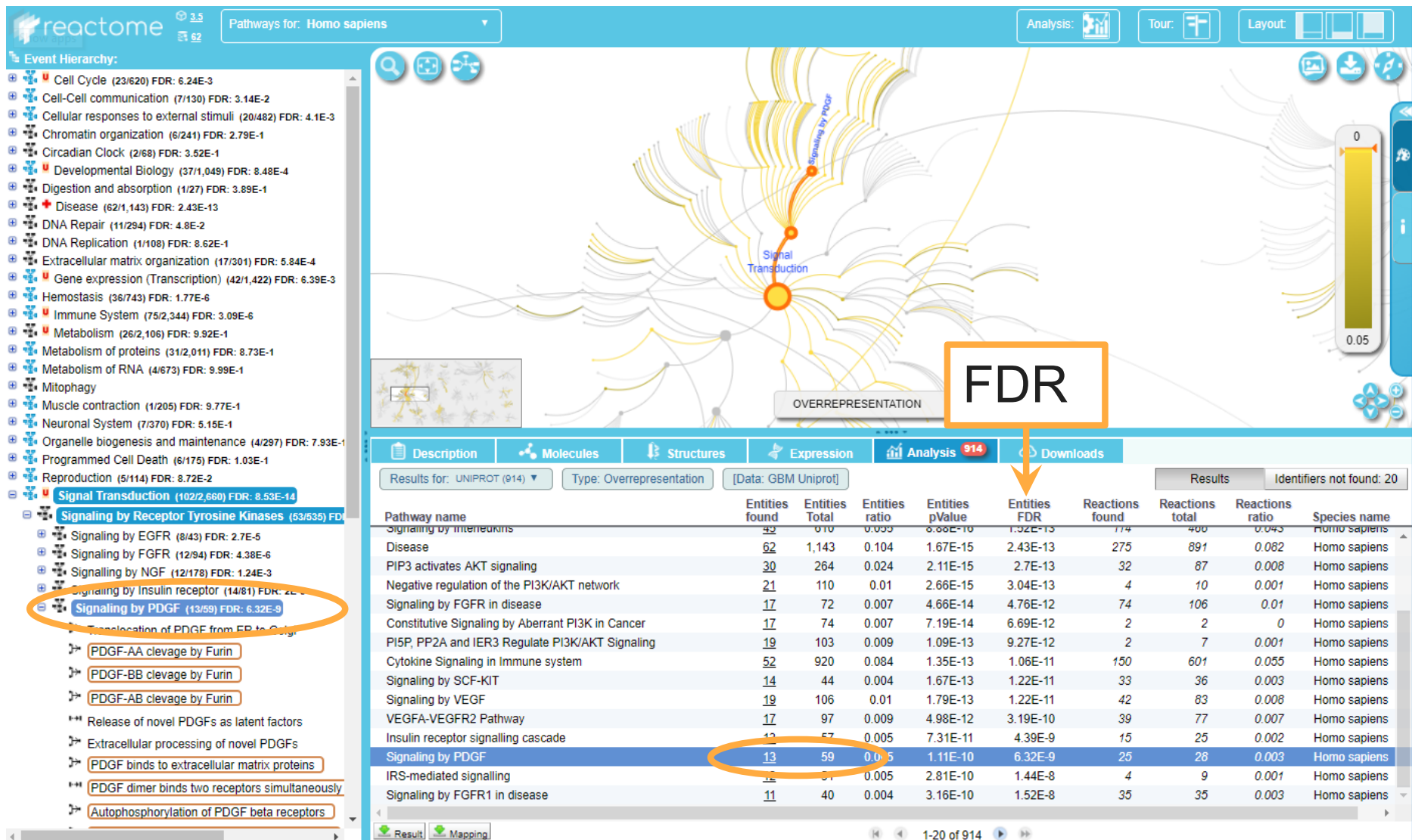
Event Hierarchy:

- Cell Cycle
- Cell-Cell communication
- Cellular responses to external stimuli
- Chromatin organization
- Circadian Clock
- Developmental Biology
- Digestion and absorption
- Disease
- DNA Repair
- DNA Replication
- Extracellular matrix organization
- Gene expression (Transcription)
- Hemostasis
- Immune System
- Metabolism
- Metabolism of proteins
- Metabolism of RNA
- Mitophagy
- Muscle contraction
- Neuronal System
- Organelle biogenesis and maintenance
- Programmed Cell Death
- Reproduction
- Signal Transduction
- Transport of small molecules
- Vesicle-mediated transport

Description **Molecules** **Structures** **Expression** **Analysis** **Downloads**

Displays details when you select an item in the Pathway Browser. For example, when a reaction is selected, shows details including the input and output molecules, summary and references containing supporting evidence. When relevant, shows details of the catalyst, regulators, preceding and following events.

Analysis Result – Over-representation



Analysis - Pathway topology matching

reactome 3.5 62 Pathways for: Homo sapiens Analysis: Tour: Layout:

Event Hierarchy:

- Signaling by Insulin receptor (14/81) FDR: 2E-8
- Signaling by PDGF (13/59) FDR: 6.32E-9
- Translocation of PDGFR from ER to Golgi
- PDGF-AA cleavage by Furin
- PDGF-BB cleavage by Furin
- PDGF-AB cleavage by Furin
- Release of novel PDGFs as latent factors
- Extracellular processing of novel PDGFs
- PDGF binds to extracellular matrix proteins
- PDGF dimer binds two receptors simultaneously
- Autophosphorylation of PDGF beta receptors
- Autophosphorylation of PDGF alpha receptors
- Autophosphorylation of PDGF alpha/beta receptors
- Downstream signal transduction (10/30) FDR: 1.52
- PI3-kinase binds to the active receptor
- PI3K catalyses the phosphorylation of PIP2 to PIP3
- PLC-gamma binds to the active receptor
- Phosphorylation of PLCgamma by PDGFR
- Activated PLC gamma dissociates from the G12/G13 complex
- SH2 domain of Src binds to the active receptor
- Activation of Src
- SHP2 binds to the active receptor
- GAP binds to PDGF-beta receptors only
- Grb2/Sos1 complex binds to the active receptor
- Sos-mediated nucleotide exchange of Ras (F)
- STAT binds to the active receptor
- Crk binds to the active PDGF receptor
- p130Cas and C3G bind PDGFR bound Crk
- Nck binds to the active PDGF receptor
- Grb7 binds to the active PDGF receptor

Downstream signal transduction

OVERREPRESENTATION

Results for: UNIPROT (914) Type: Overrepresentation [Data: GBM Uniprot]

Pathway name

Negative regulation of the PI3K/AKT network

Signaling by FGFR in disease

Constitutive Signaling by Ab

PI5P, PP2A and IER3 Regul

Cytokine Signaling in Immun

Signaling by SCF-KIT

Signaling by VEGF

VEGFA-VEGFR2 Pathway

Insulin receptor signalling ca

Signaling by PDGF

IRS-mediated signalling

Signaling by FGFR1 in disea

Entities found Entities Total Entities ratio Entities pValue Entities FDR Reactions found Reactions total Reactions ratio Species name

Entities not found

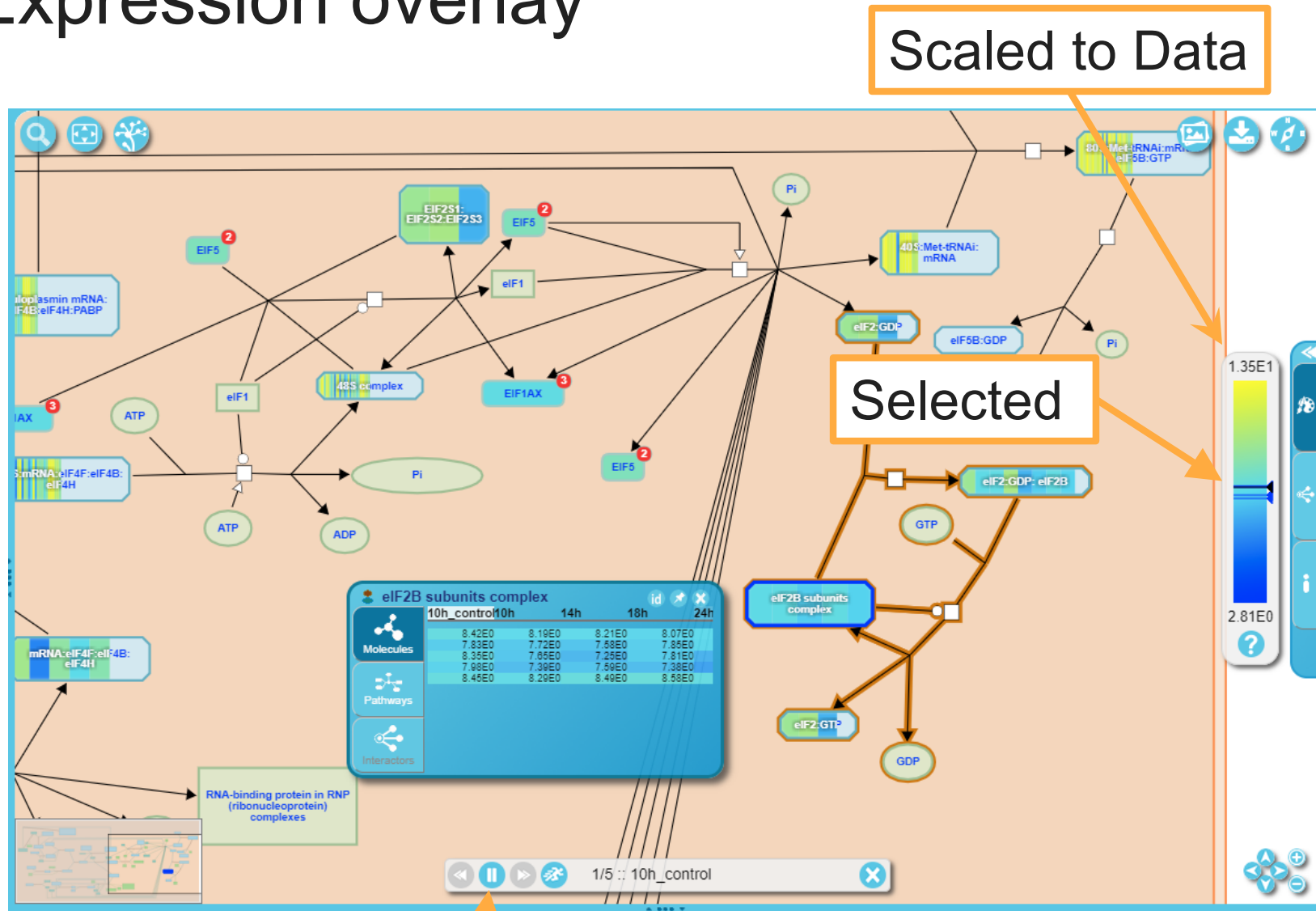
Pathway identifier	Pathway name	Entities found	Entities total	Entities ratio	Entities pValue	Entities FDR	Reactions found	Reactions total	Reactions ratio	Species name
1 R-HSA-5663202	Diseases of sig	10	30	0.002724	3.31E-10	1.52E-08	16	16	0.001472	
2 R-HSA-9006934	Signaling by Re	16	111	0.010078	3.59E-10	1.58E-08	24	46	0.004231	
3 R-HSA-2219528	PI3K/AKT Sign	14	81	0.007354	4.75E-10	2.00E-08	23	34	0.003127	
4 R-HSA-162582	Signal Transdu	12	55	0.004994	6.54E-10	2.68E-08	6	12	0.001104	
5 R-HSA-9006925	Intracellular si	12	58	0.005266	1.18E-09	4.60E-08	7	17	0.001564	
6 R-HSA-449147	Signaling by In	12	59	0.005357	1.42E-09	5.41E-08	7	19	0.001747	
7 R-HSA-1643685	Disease									
8 R-HSA-1257604	PIP3 activates									
9 R-HSA-199418	Negative regu									
10 R-HSA-1226099	Signaling by FG									
11 R-HSA-2219530	Constitutive S									
12 R-HSA-6811558	PI5P, PP2A and									
13 R-HSA-1280215	Cytokine Signe									
14 R-HSA-1433557	Signaling by SC									
15 R-HSA-194138	Signaling by V									
16 R-HSA-4420097	VEGFA-VEGFR									
17 R-HSA-74751	Insulin recept									
18 R-HSA-186797	Signaling by IR									
19 R-HSA-112399	IRS-mediated									
20 R-HSA-5655302	Signaling by FG									
21 R-HSA-186763	Downstream signal transduction									
22 R-HSA-6785807	Interleukin-4 and 13 signaling									
23 R-HSA-74752	Signaling by Insulin receptor									
24 R-HSA-2428928	IRS-related events triggered by IGF1R									
25 R-HSA-2428924	IGF1R signaling cascade									
26 R-HSA-2404192	Signaling by Type 1 Insulin-like Growt									

Result Mapping

Identifiers not found: 20



Identifiers not found: 20


Expression overlay




Step through Data columns

Species Comparison I

 Analysis tools 



Analyse your data


Species Comparison

Species Comparison

This tool allows you to compare human pathways with those in any of the other species inferred from Reactome by orthology.

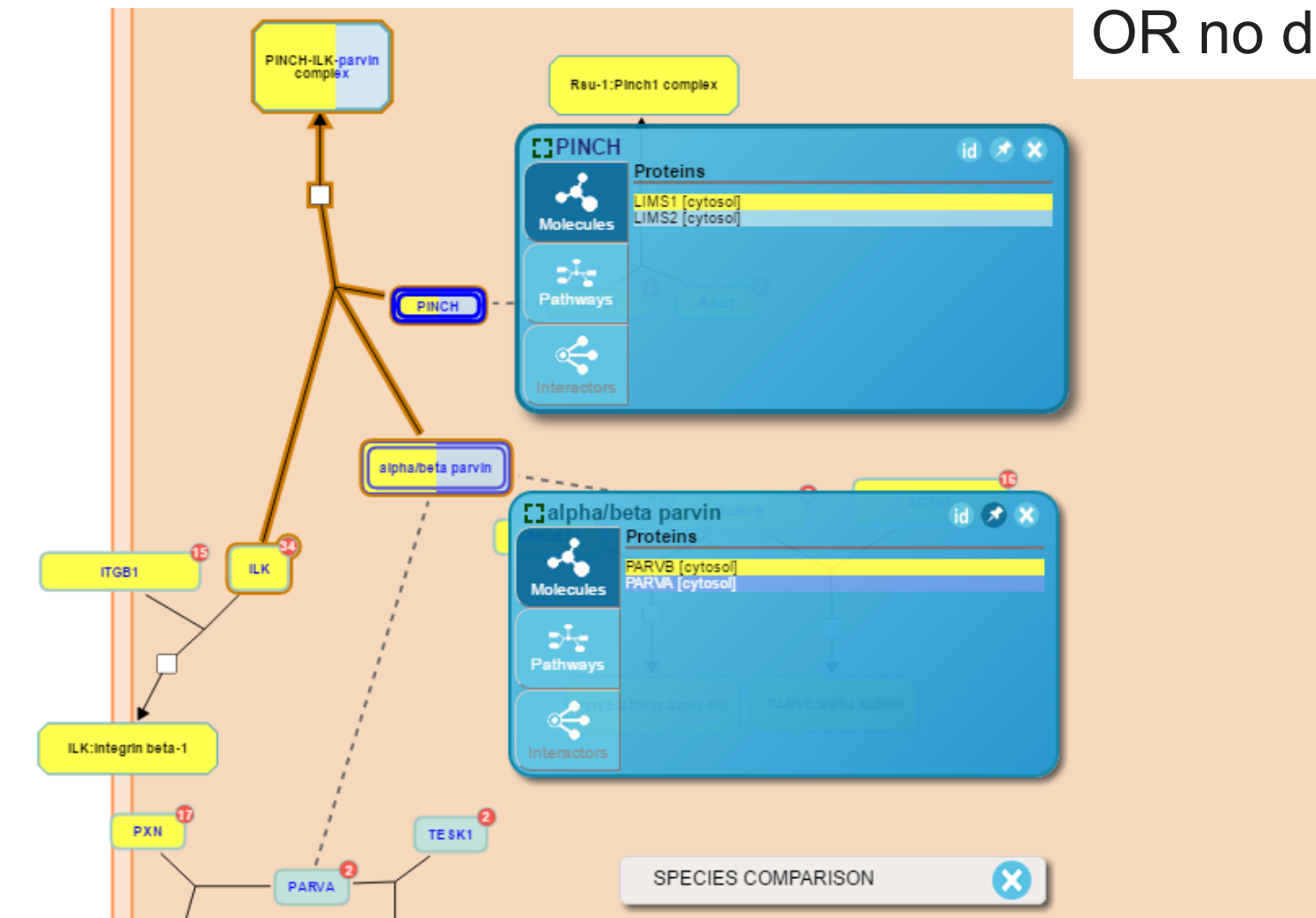
Use the species selector to choose the other species and click on the "GO" button to perform the comparison.

Compare **Homo sapiens** with 

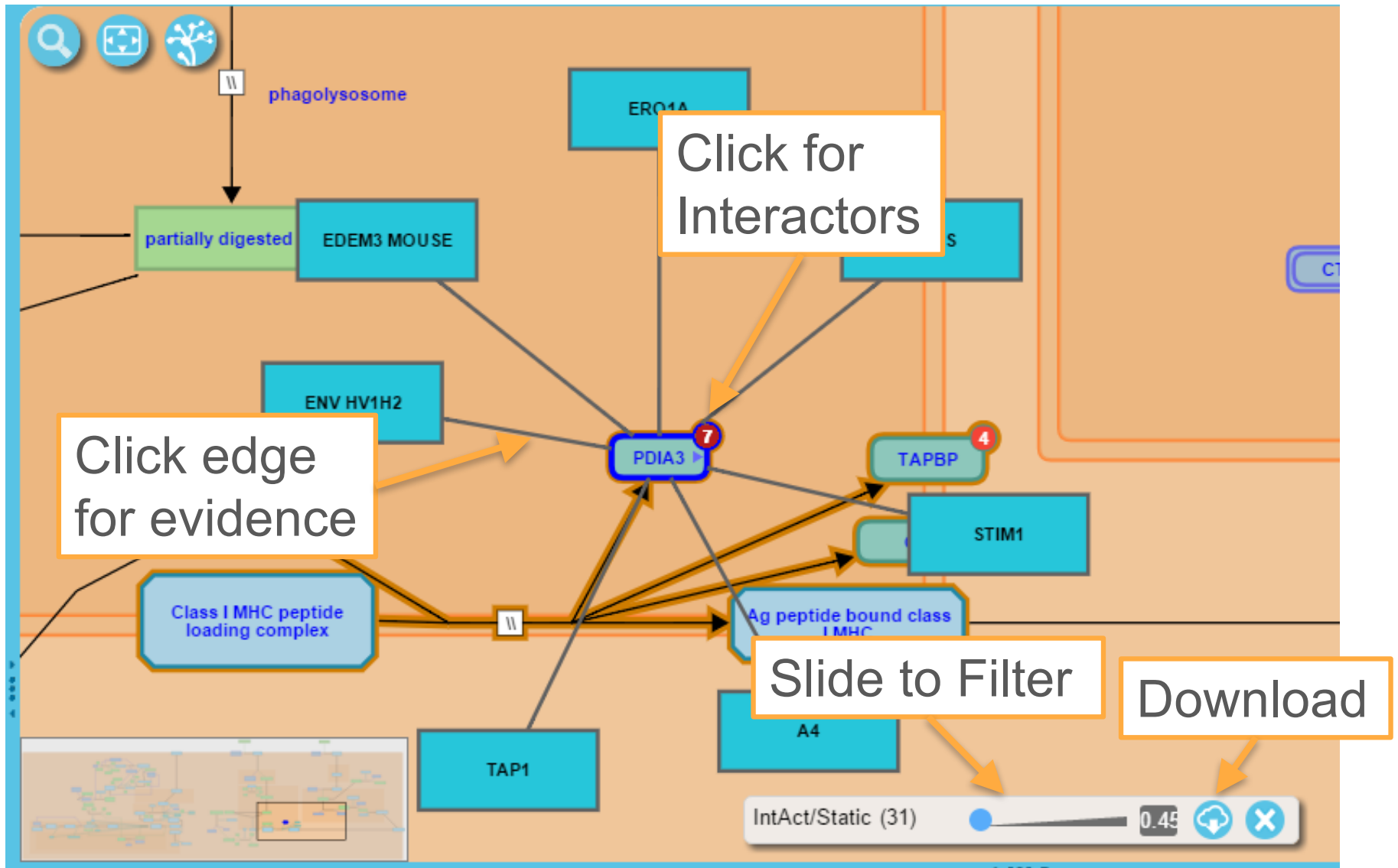
Go!

Species Comparison II

Yellow = orthologue
No colour = not found
OR no data



Interactors



Molecular Interaction Overlay - Data

EMBL-EBI

Services
Research
Training
About us

IntAct

EBI-8686389 OR EBI-8686371 OR EBI-7209397
Examples: BRCA2, Q06809, dmc1, 10831811

Search
Advanced

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Resources
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Feedback

IntAct > IntAct Search Results

Show more data from EMBL-EBI

7 binary interactions found for search term
EBI-8686389 OR EBI-8686371 OR EBI-7209397 OR EBI-8686317 OR EBI-8623527 OR EBI-7209415

Interactions (7)
Interactors
Interaction Details
Graph

No results in other databases.

What is this view?

Customize view
Select format to Download
Download

Dts	Molecule 'A'	Links 'A'	Molecule 'B'	Links 'B'	Interaction Detection Method	Interaction AC	Source Database
	PECAM1	P16284 EBI-716404	PTPN11	Q06124 EBI-297779	pull down	EBI-8623527 MINT-8033235	MINT
					pull down	EBI-8686299 MINT-8031324	MINT
					pull down	EBI-8686371 MINT-8033280	MINT
					surface plasmon resonance	EBI-8686317 MINT-8031339	MINT
					surface plasmon resonance	EBI-8686389 MINT-8033295	MINT
					lambda phage display	EBI-7209397 MINT-8031354	MINT
					lambda phage display	EBI-7209415 MINT-8033310	MINT

IntAct View version: 4.2.3.2

Molecular Interaction Overlay – Set source

The interface displays a central node labeled **FAK1** (highlighted with a blue border and a red circle with the number 8) connected to several chemical entities in light blue ovals:

- CHEMBL201511**: Chemical structure not available
- CHEMBL535**: Chemical structure shown
- CHEMBL205098**: Chemical structure shown

A settings panel titled **Settings** is open on the right, showing the **Interactor Overlays** section. It lists existing resources and PSICQUIC sources:

Existing resources:

- ☐ IntAct (Static)

PSICQUIC:

- ☐ BIND
- ☐ BindingDB
- ☐ BioGrid
- ☒ ChEMBL
- ☐ DIP
- ☐ DrugBank
- ☐ EBI-GOA-nonIntAct

A **ChEMBL** button is at the bottom of the settings panel. The bottom status bar shows **ChEMBL**, a slider set to **0.65**, and a close button.

Developer's Zone



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e.g. O95631, NTN1, signaling by EGFR, glucose

Go!

Developer's Zone

Explore our tools and web services and learn how to include them in your applications



Analysis Service

Use the Analysis Service to analyse your data against Reactome's content



Content Service

Use the Content Service to access all our knowledgebase content from your client



Graph Database

Access to the Reactome knowledgebase content as an interconnected graph database



Pathways Overview

Use this widget to include our pathways overview in your web application



Pathway Diagrams

Use this widget to include our pathway diagrams in your web application



Reactome Partners

Check out who is currently using Reactome web services and widgets

Extracting participating molecules using the Graph Database and Cypher

Breaking down complexes and sets to get their participants

The components of a complex, which are also physical entities, are stored in the “hasComponent” slot. Let’s use the complex “Ag-substrate:E3:E2:Ub” with identifier R-HSA-983126 as example in this case:

```
//First level components for the complex with stable identifier R-HSA-983126
MATCH (Complex{stId:"R-HSA-983126"})-[:hasComponent]->(pe:PhysicalEntity)
RETURN pe.stId AS component_stId, pe.displayName AS component
```

The result of the query is

component_stId	component
R-NUL-983035	antigenic substrate [cytosol]
R-HSA-976075	E3 ligases in proteasomal degradation [cytosol]
R-HSA-976165	Ubiquitin:E2 conjugating enzymes [cytosol]

Partners

 <p>The BLUEPRINT consortium has been formed with the aim to further the understanding of how genes are activated or repressed in both healthy and diseased human cells.</p> <p> <input checked="" type="checkbox"/> Analysis Service <input type="checkbox"/> Widgets <input type="checkbox"/> Graph Database </p> <p>BLUEPRINT</p>	 <p>Contains information for a large majority of all human protein-coding genes regarding the expression and localization of the corresponding proteins based on both RNA and protein data.</p> <p> <input checked="" type="checkbox"/> Analysis Service <input type="checkbox"/> Widgets <input type="checkbox"/> Graph Database </p> <p>The Human Protein Atlas</p>	 <p>compliant, public data repository for proteomics data, including protein and peptide identifications, post-translational modifications and supporting spectral evidence.</p> <p> <input checked="" type="checkbox"/> Analysis Service <input type="checkbox"/> Widgets <input type="checkbox"/> Graph Database </p> <p>PRIDE</p>	 <p>Integrative LINC is an integrative web platform for analysis of LINC data and signatures. The BD2K-LINC Data Coordination and Integration Center is part of the Big Data to Knowledge</p> <p> <input checked="" type="checkbox"/> Analysis Service <input type="checkbox"/> Widgets <input type="checkbox"/> Graph Database </p> <p>iLINC</p>
 <p>The COPa Knowledgebase (COPaKB) has been created as a unique resource to facilitate the discovery of novel biological insights from proteomic datasets. COPaKB was developed under the</p> <p> <input checked="" type="checkbox"/> Analysis Service <input type="checkbox"/> Widgets <input type="checkbox"/> Graph Database </p> <p>COPaKB</p>	 <p>For biomedical researchers who need to identify a biological target for a new therapy, Open Targets is a public-private initiative to generate evidence on the validity of therapeutic targets</p> <p> <input type="checkbox"/> Analysis Service <input checked="" type="checkbox"/> Widgets <input type="checkbox"/> Graph Database </p> <p>Open Targets</p>	 <p>Chemical Entities of Biological Interest (ChEBI) is a freely available dictionary of molecular entities focused on 'small' chemical compounds. The term 'molecular entity' refers to any constitutionally</p> <p> <input type="checkbox"/> Analysis Service <input checked="" type="checkbox"/> Widgets <input type="checkbox"/> Graph Database </p> <p>ChEBI</p>	 <p>PINT, the Proteomics INTEGRator, is an online experiment repository for final results coming from different qualitative and/or quantitative proteomics assays. PINT is a new</p> <p> <input checked="" type="checkbox"/> Analysis Service <input checked="" type="checkbox"/> Widgets <input type="checkbox"/> Graph Database </p> <p>PINT</p>
 <p>Integrated Proteomics Applications provides a comprehensive proteomic data analysis solution, the Integrated Proteomics Pipeline (IP2), which allows researchers to identify,</p> <p> <input type="checkbox"/> Analysis Service <input checked="" type="checkbox"/> Widgets <input type="checkbox"/> Graph Database </p>	 <p>Tabloid Proteome is a database of protein association network generated using publicly available mass spectrometry based experiments in PRIDE. These associations represent</p> <p> <input type="checkbox"/> Analysis Service <input type="checkbox"/> Widgets <input checked="" type="checkbox"/> Graph Database </p>		

Schema



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e.g. O95631, NTN1, signaling by EGFR, glucose

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ORCID Integration Project

Graph Database :: Data Schema

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 - FragmentInsertionModification [64]
 - FragmentReplacedModification [89]
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- TranslationalModification [67203]
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Attribute name	Cardinality	Value Type	Attribute Origin
authored	+	InstanceEdit	Event
compartment	+	Compartment	Event
created	1	InstanceEdit	DatabaseObject
crossReference	+	DatabaseIdentifier	Event
dbId	1	Long	DatabaseObject
definition	1	String	Event
disease	+	Disease	Event
displayName	1	String	DatabaseObject
doi	1	String	Pathway
edited	+	InstanceEdit	Event
eventOf	+	Pathway	Event
evidenceType	1	EvidenceType	Event
figure	+	Figure	Event
followingEvent	+	Event	Event
goBiologicalProcess	1	GO_BiologicalProcess	Event
hasDiagram	1	Boolean	Pathway
hasEvent	+	Event	Pathway
inferredFrom	+	Event	Event

More Information

- From the Reactome Homepage

- Reactome User Guide



- help@reactome.org

- Tour



- Train Online - <https://www.ebi.ac.uk/training/online/>

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