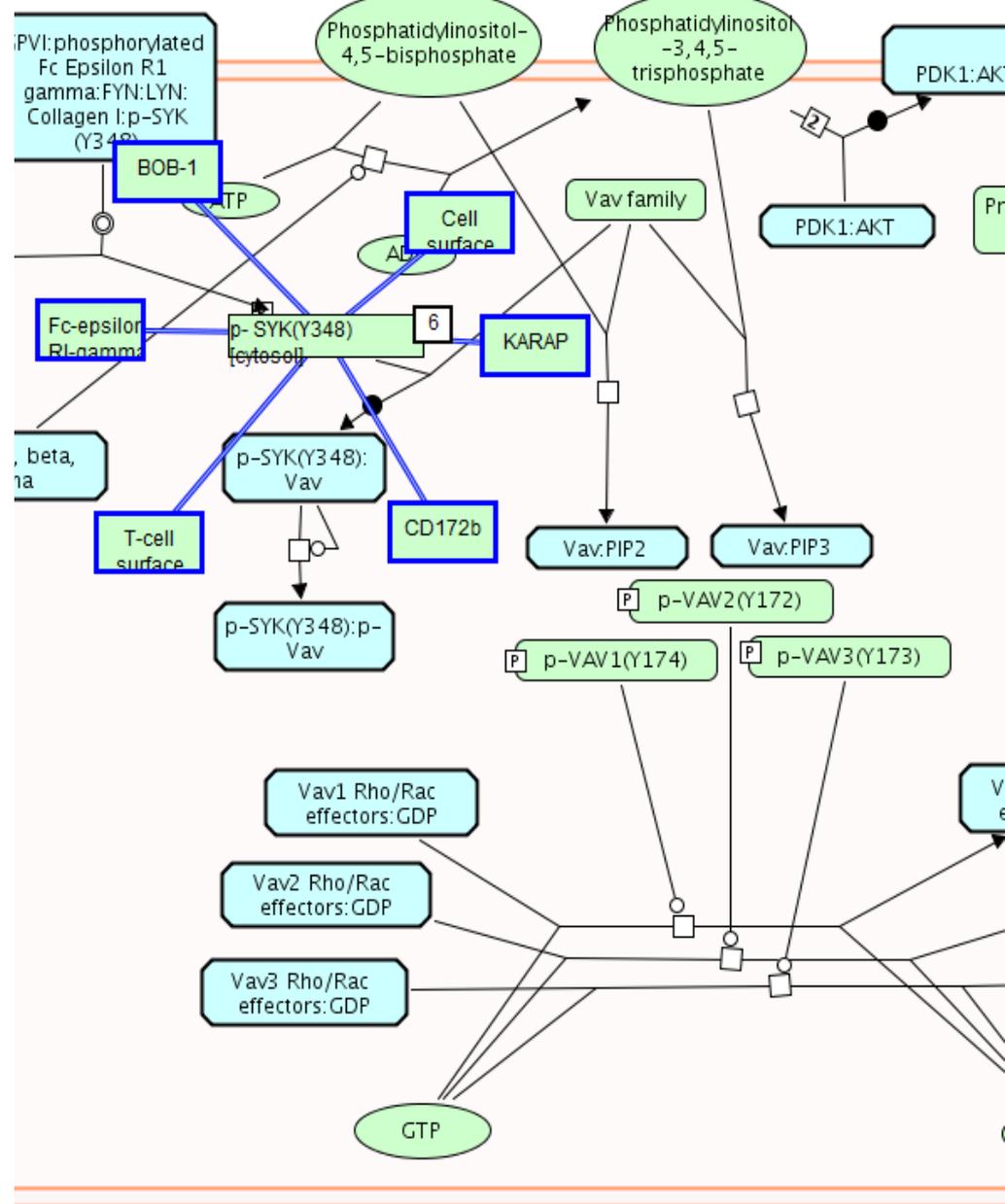




# A Database of human biological pathways

Steve Jupe - [sjupe@ebi.ac.uk](mailto:sjupe@ebi.ac.uk)

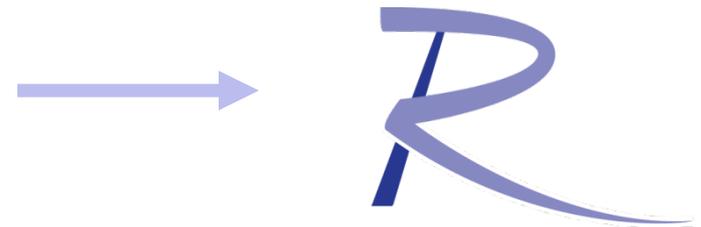


# Rationale – Journal information

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?

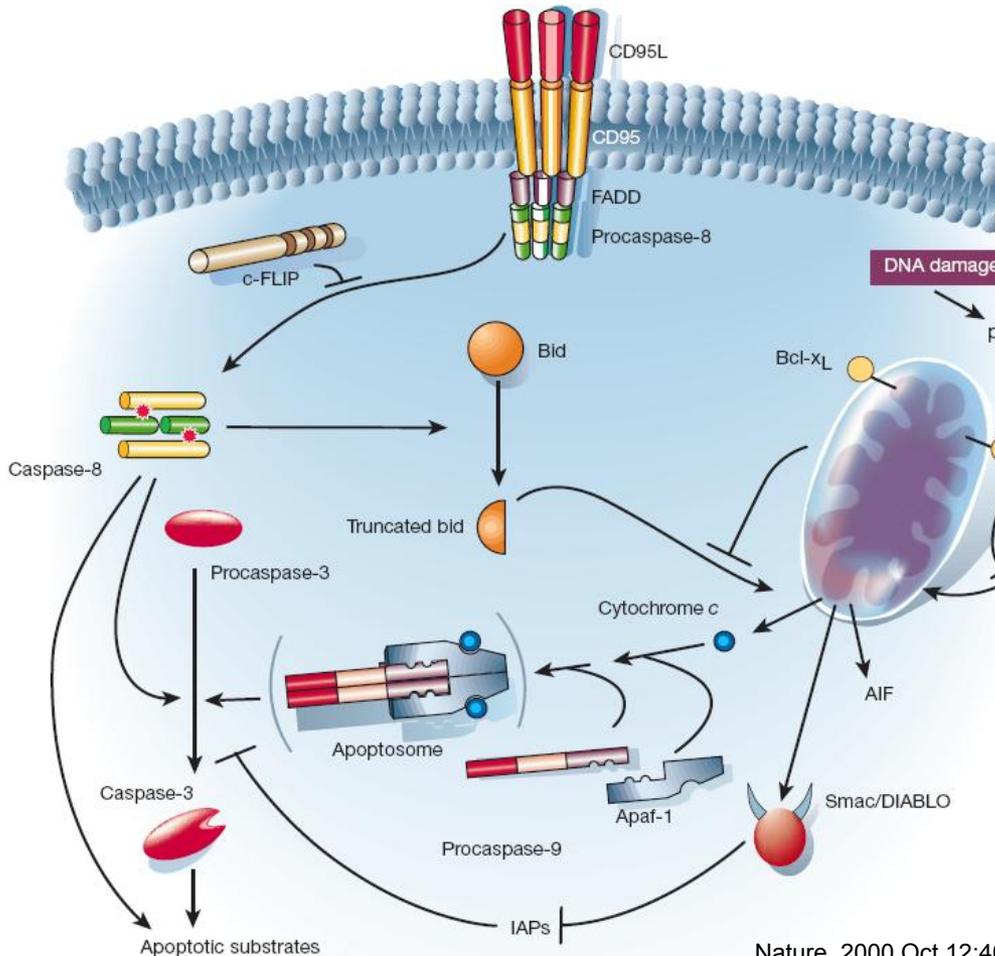


# Rationale - Figures

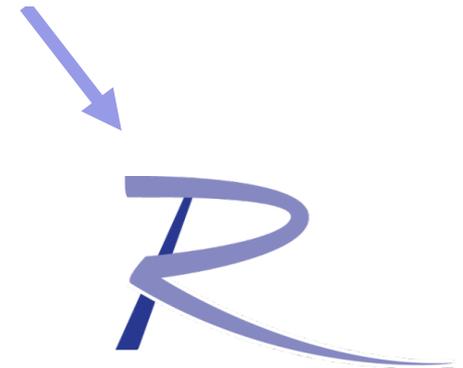
A picture paints a thousand words...

but....

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



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

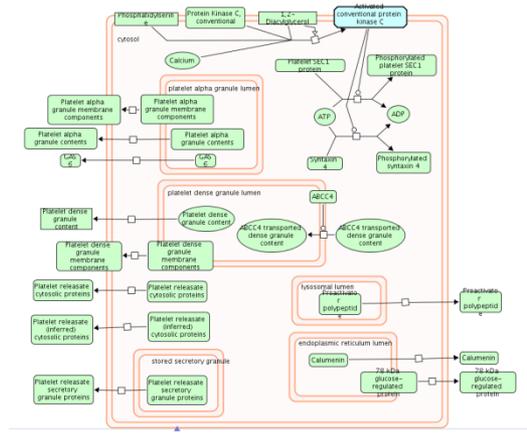
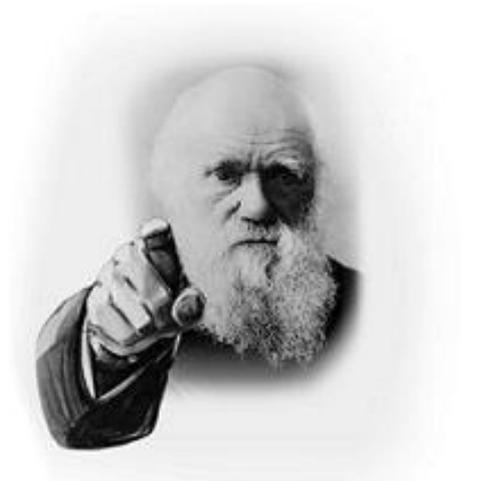


# Reactome is...

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

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

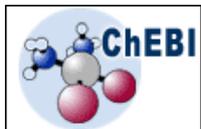
Mapped to cellular compartment



# Reactome is...

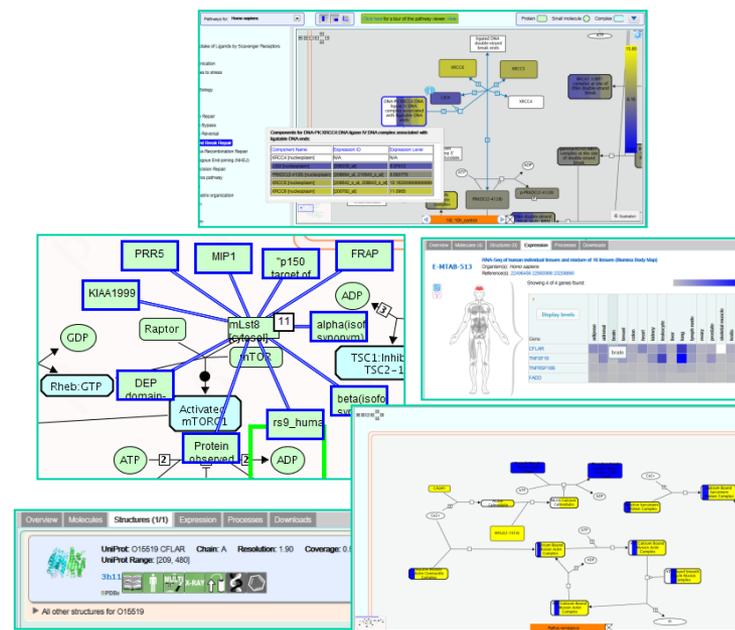
Extensively **cross-referenced**

Entrez Gene

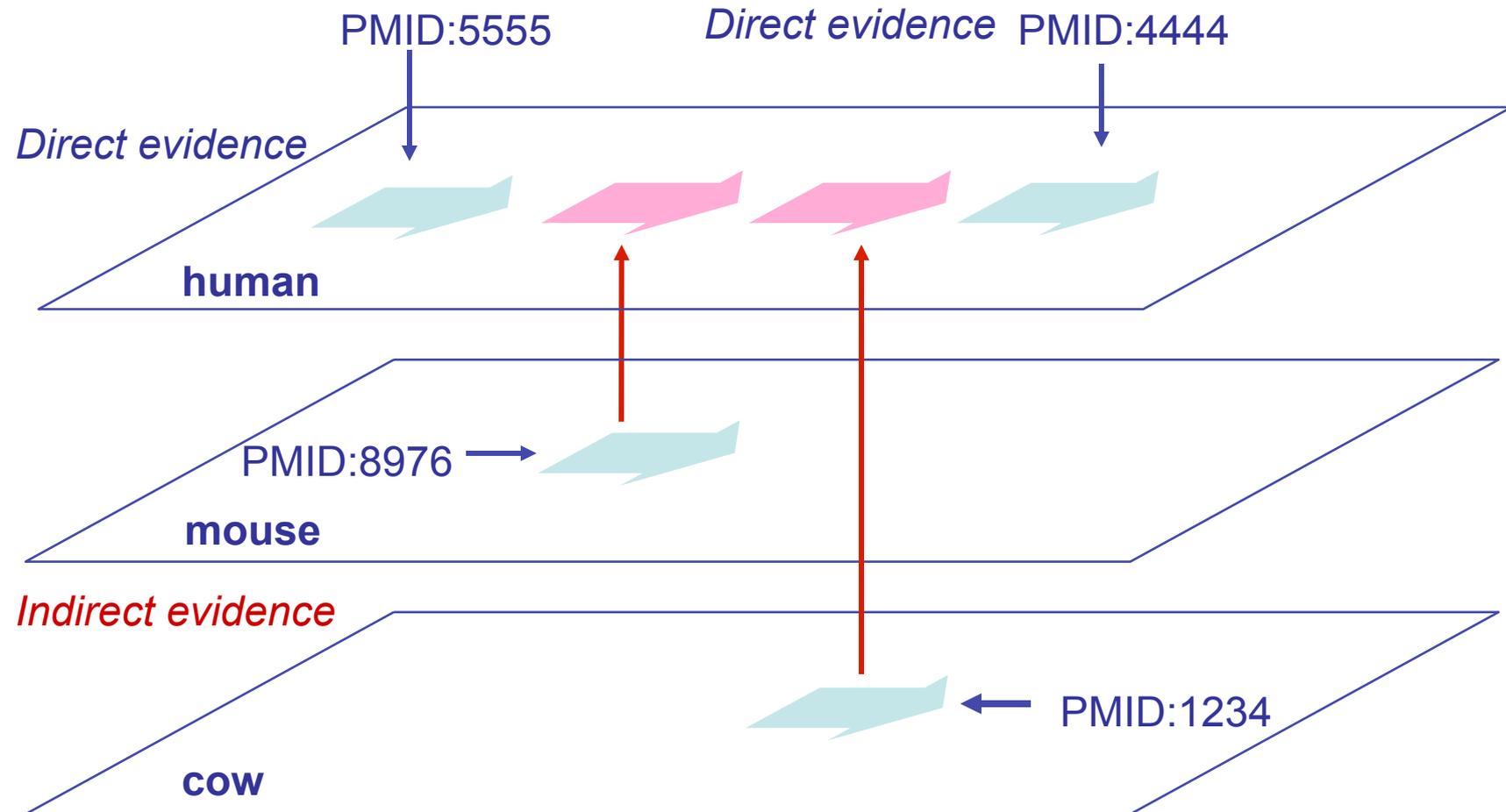


**Tools** for data analysis –  
**Pathway Analysis,**  
**Expression Overlay, Species**  
**Comparison, Biomat...**

Used to infer **orthologous**  
**events** in 20 other species

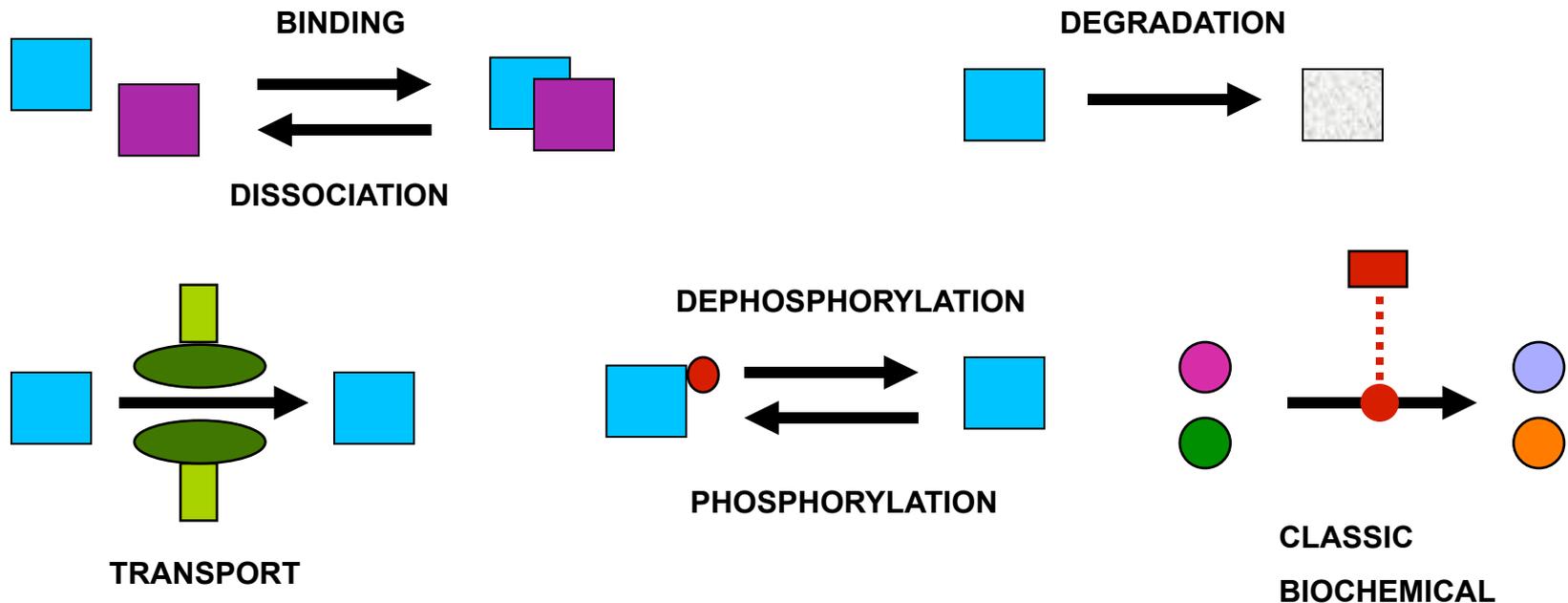


# Using model organism data to build pathways – Inferred pathway events

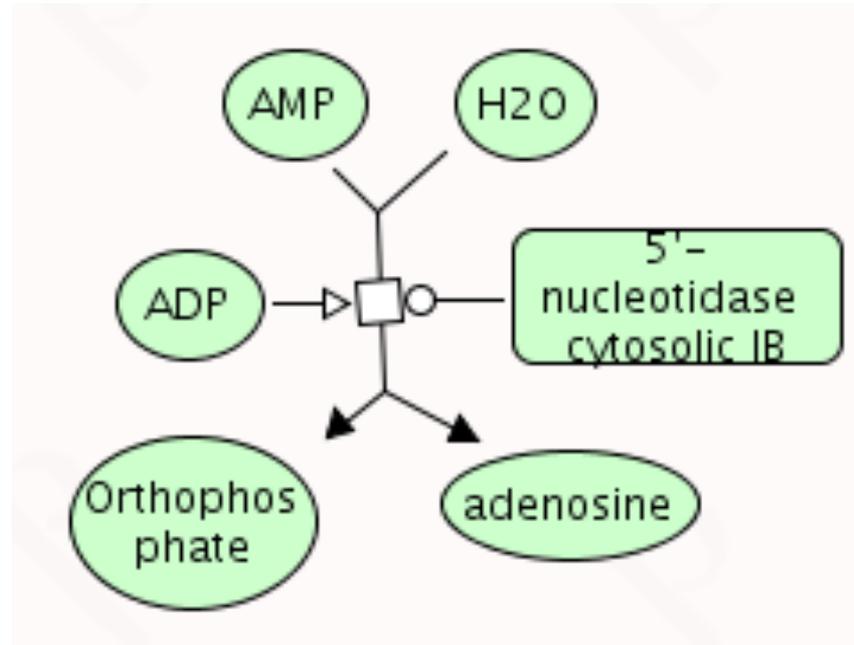


# Theory - Reactions

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



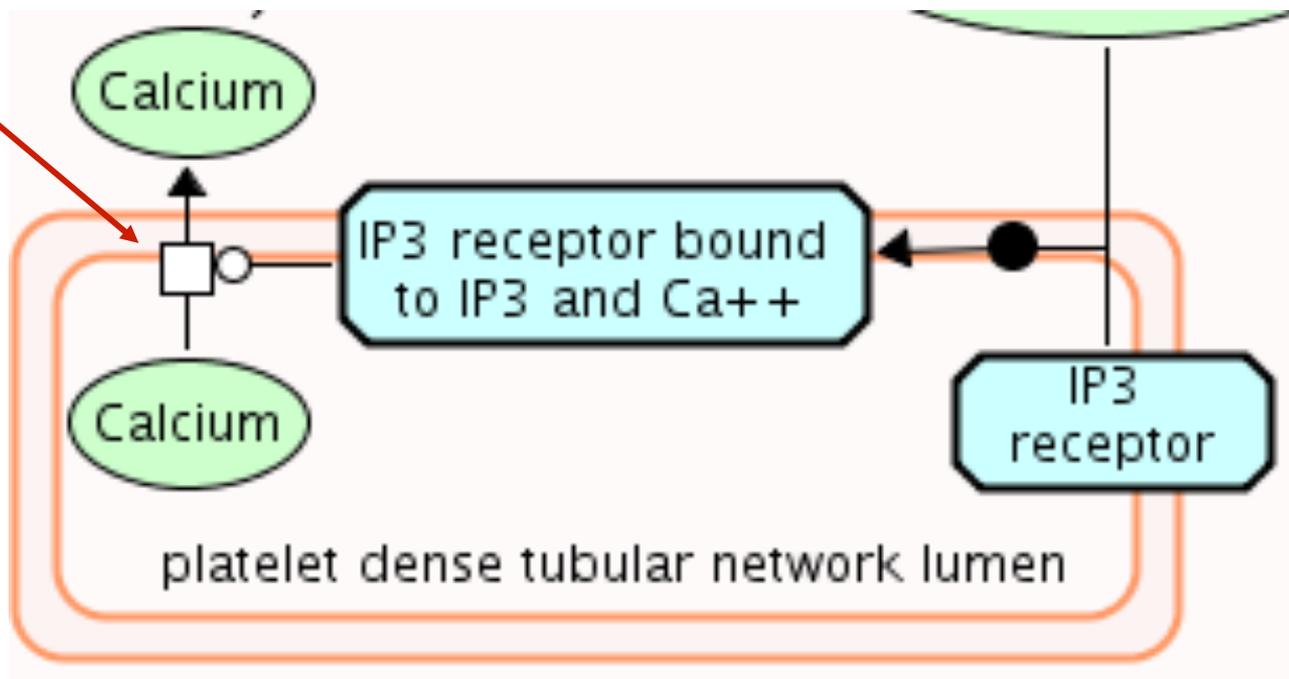
# Reaction Example 1: Enzymatic



# Reaction Example 2: Transport

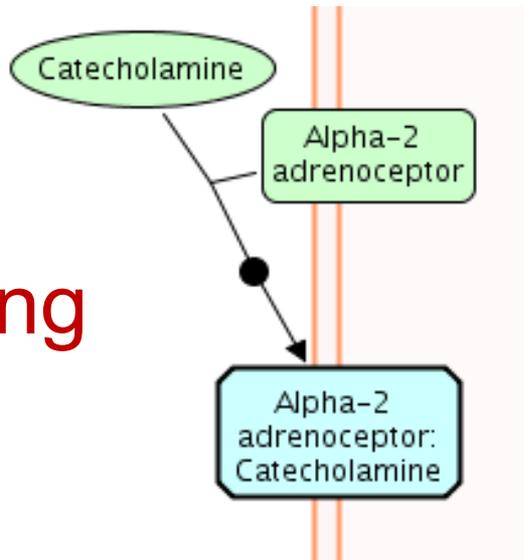
Transport of  $\text{Ca}^{++}$  from platelet dense tubular system to cytoplasm

REACT\_945.4

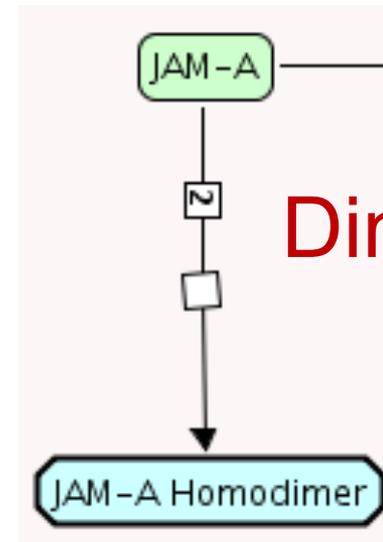


# Other Reaction Types

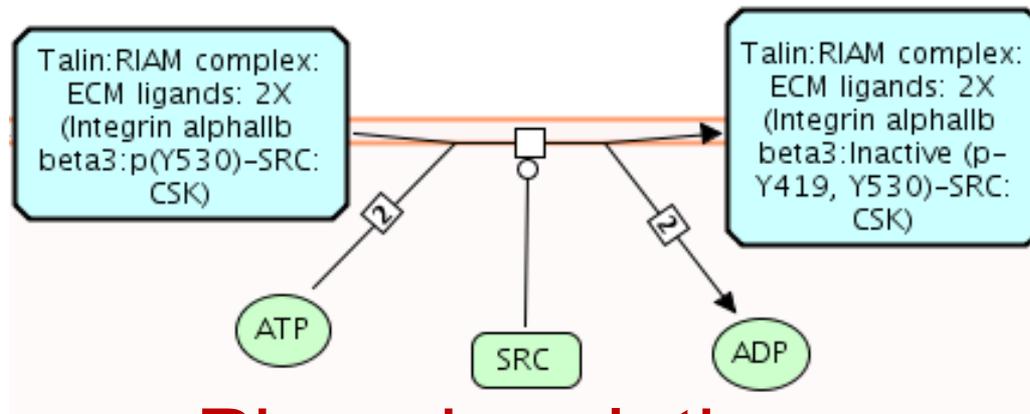
Binding



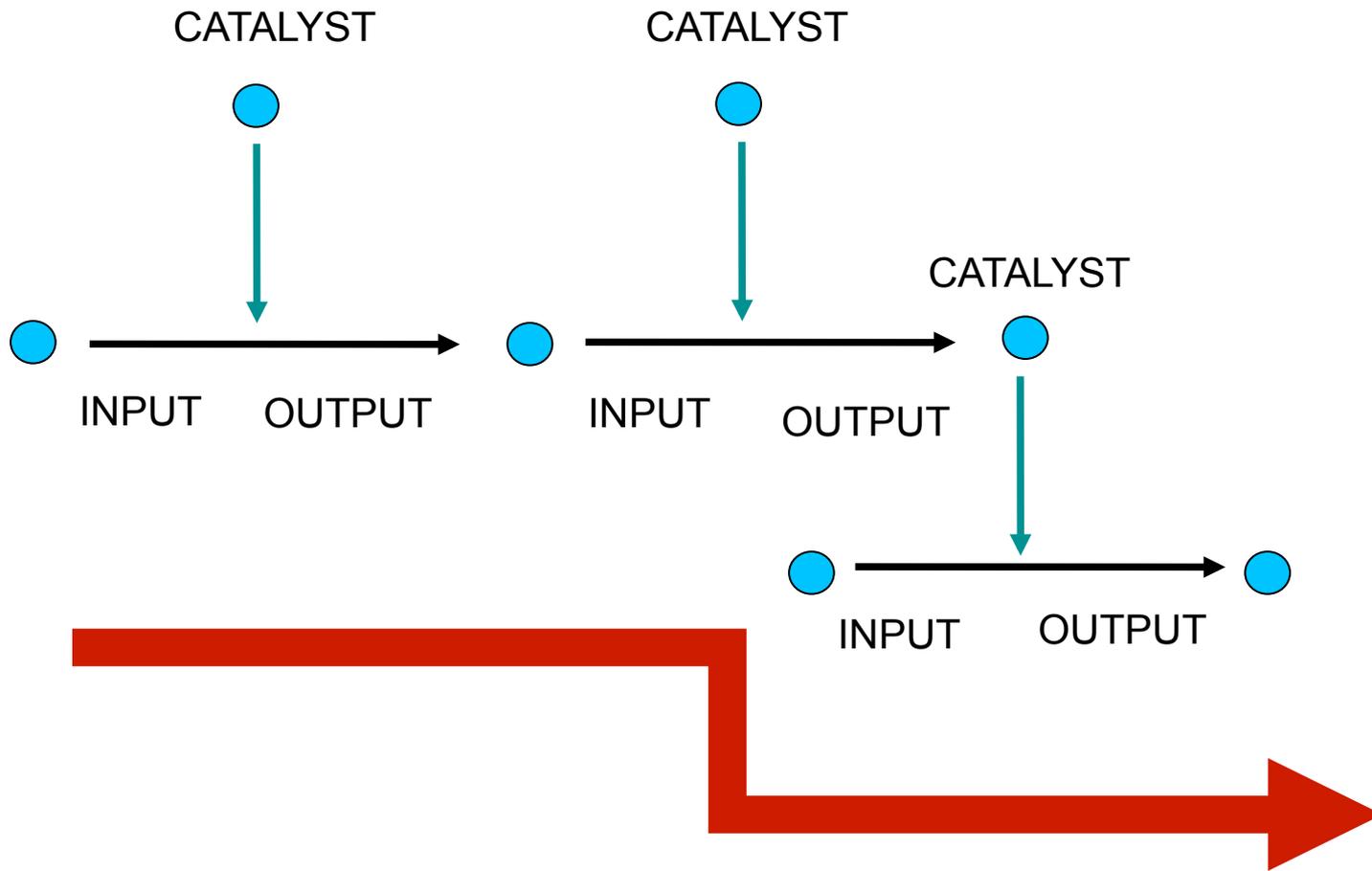
Dimerization



Phosphorylation



# Reactions Connect into Pathways



# Evidence Tracking – Inferred Reactions

*Direct evidence*

PMID:5555

PMID:4444

**Human pathway**

PMID:8976

**mouse**

*Indirect evidence*

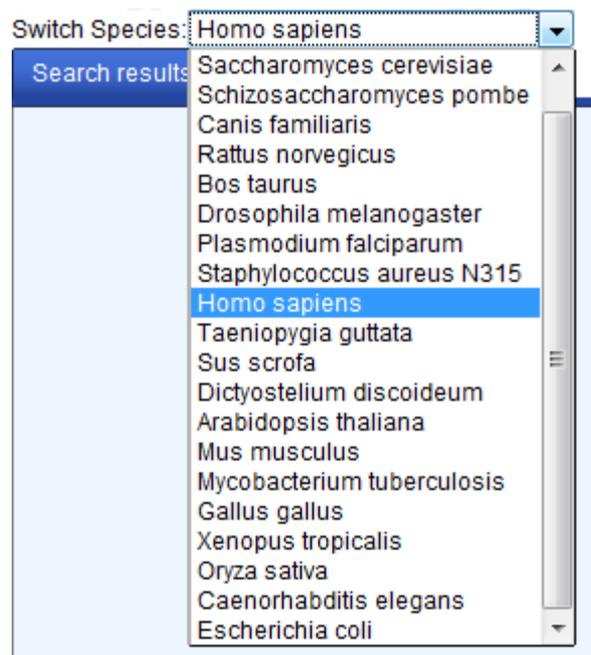
**cow**

PMID:1234

# Data Expansion - Link-outs From Reactome

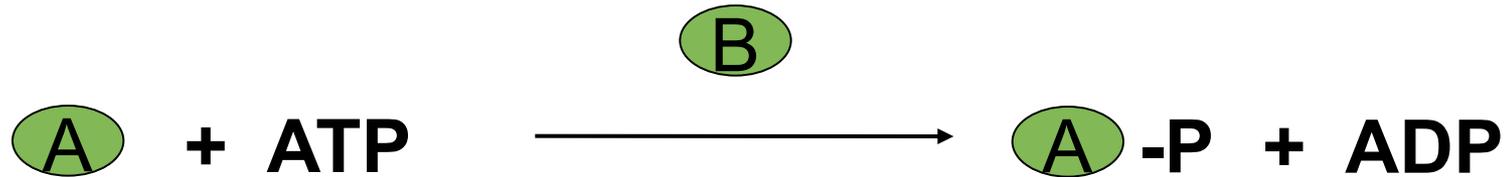
- GO
  - Molecular Function
  - Compartment
  - Biological process
- KEGG, ChEBI – small molecules
- UniProt – proteins
- Sequence dbs – Ensembl, OMIM, Entrez Gene, RefSeq, HapMap, UCSC, KEGG Gene
- PubMed references – literature evidence for events

# Species Selection

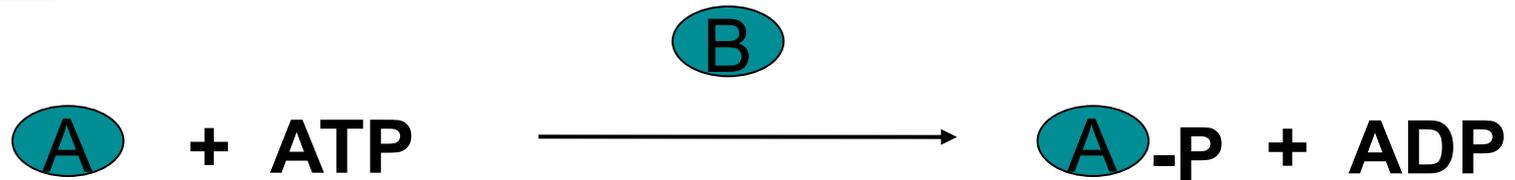


# Data Expansion – Projecting to Other Species

Human



Mouse



Drosophila



Reaction not  
inferred

No orthologue - Protein not inferred

# Exportable Protein-Protein Interactions

Inferred from complexes and reactions  
(more on this later)

Interactions between proteins in the same  
complex, reaction, or adjoining reaction

Lists available from Downloads

See Readme document for more details



# Planned Coverage – Editorial Calendar

Next Release - Ver 47 : December 2013 [Reactome](#)

Curator	Pathway Topic	Author	Reviewer
Karen Rothfels	Beta-catenin independent WNT signaling	Karen Rothfels	TBA
Veronica Shamovsky	Cell surface interaction at the vascular wall	Veronica Shamovsky	TBA
Steve Jupe	Chromatin modifying enzymes	TBA	TBA
Veronica Shamovsky	Complement cascade (Gallus)	Veronica Shamovsky	TBA
Marija Milacic	Condensation of Prophase Chromosomes	Brenda Gallie	TBA
Bruce May	Detoxification of reactive oxygen species	Bruce May	TBA
Bijay Jassal	Diseases associated with glycosaminoglycan metabolism	Bijay Jassal	TBA
Bijay Jassal	Diseases associated with glycosaminoglycan metabolism	Bijay Jassal	TBA
Phani Garapati	Ephrin signalin	Phani Vijay Garapati	TBA
Bruce May	Epigenetics	Bruce May	TBA
Peter D'Eustachio	Glycogen storage diseases	Peter D'Eustachio	TBA
Veronica Shamovsky	Heat shock response	Veronica Shamovsky	TBA
Veronica Shamovsky	HSP90 protein folding machinery	Veronica Shamovsky	TBA
Bruce May	Mitochondrial Biogenesis	Bruce May	TBA
Marc Gillespie	Mitophagy	Charleen T Chu	TBA
Marija Milacic	Nuclear Envelope Breakdown: Clearance of Nuclear Envelope from Chromatin - revision	Marija Milacic	Matyas Gorjanacz
Marija Milacic	Nuclear Envelope Reformation-revision	Marija Milacic	Matyas Gorjanacz
Marija Milacic	Cellular Senescence-revision	Marija Milacic	Shamith Samarajiwa
Bruce May	Organelle Biogenesis	Bruce May	TBA
Bijay Jassal	Sialic acid metabolism	Bijay Jassal	TBA
Bruce May	SUMO E3 ligases sumoylate target proteins	Bruce May	TBA
Karen Rothfels	TCF-dependent signaling in response to WNT	Karen Rothfels	TBA
Bruce May	Transcriptional Regulation of Pluripotent Stem Cell	Bruce May	TBA
Phani Garapati	VEGFA-VEGFR2 signaling	Phani Vijay Garapati	TBA
Karen Rothfels	WNT in cancer	Karen Rothfels	TBA

# Reactome Tools

- Interactive Pathway Browser
- Analysis
  - Pathway Mapping
  - Over-representation
  - Expression overlay
- Molecular Interaction overlay
- Biomart

# Front Page

http://www.reactome.org

**REACTOME**  
A CURATED PATHWAY DATABASE

About Content Documentation Tools Community Download Contact

**Browse Pathways** **Analyze Data** **Reactome FI Network**

**User Guide** **Data Download** **Contact Us**

**Reactome News**

**reactome** @reactome 23 Sep  
Version 46 Released: Topics with new or revised events include Disease (Defects in biotin metabolism, Defects ... [tinyurl.com/n2e9z4z](http://tinyurl.com/n2e9z4z)  
Expand

**reactome** @reactome 22 Sep  
Manteia database and data mining tools related to embryonic development is using Reactome data, [manteia.igbmc.fr](http://manteia.igbmc.fr), #useractome

**reactome** @reactome 22 Sep  
Michael Yaffe - how dynamic re-wiring of DDR signaling could be used to treat cancer #EMBOmtg

**About 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 (v45) of Reactome was released on June 11, 2013.

OICR NYU Langone MEDICAL CENTER CSH Cold Spring Harbor Laboratory EMBL-EBI

The development of Reactome is supported by a grant from the US National Institutes of Health (P41 HG003751), Ontario Research Fund, and the European Molecular Biology Laboratory.

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**Content** Table of Contents DOIs Data Schema Editorial Calendar Statistics

**Documentation** User Guide Data Model Orthology Prediction Object/Relational Mapping Wiki Linking to Reactome Referencing Reactome

**Tools** Pathway Browser Analyze Data Species Comparison Reactome FI Network Advanced Search Small Molecule Search BioMart

**Community** Reactome Outreach Reactome Events Reactome Training Reactome Publications Papers Citing Reactome Resources Guide Mailing List

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# The Pathway Browser

Home button

Species Selector

Show/Hide

Quick Tour

Diagram Key

The screenshot displays the Reactome Pathway Browser interface. At the top, navigation buttons include 'Home button', 'Species Selector' (set to 'Homo sapiens'), 'Show/Hide', 'Quick Tour', and 'Diagram Key'. A search bar on the right contains 'Protein', 'Small molecule', and 'Complex' filters. On the left, the 'Event Hierarchy' panel lists various biological processes, with 'Muscle contraction' and 'Smooth Muscle Contraction' expanded. The central 'Pathway Diagram Panel' shows a detailed metabolic pathway with a 'Zoom/Move Toolbar' and a 'Thumbnail' in the bottom-left corner. A 'Search & Tools' icon is in the top-right. Below the diagram, a 'Details Panel' for 'MLCK Active Calmodulin Binding' (REACT\_20521.1) provides a summation and input list, including 'MYLK(1-1914) [cytosol]' and 'Active Calmodulin [cytosol]'. The bottom of the interface features tabs for 'Overview', 'Molecules', 'Structures', 'Expression', 'Processes', and 'Downloads'.

Hierarchy Panel

Zoom/Move Toolbar

Pathway Diagram Panel

Search & Tools

Thumbnail

Details Panel

# Pathway Hierarchy Panel

 REACTOME

Event Hierarchy:

Pathways for: **Homo sapiens** ▼

- Apoptosis
- Binding and Uptake of Ligands by Scavenger Receptors
- Cell Cycle
- Cell-Cell communication
- Cellular responses to stress
- Circadian Clock
- Developmental Biology
- Disease
- DNA Repair
- DNA Replication
- Extracellular matrix organization
- Gene Expression
- Hemostasis
- Immune System
- Meiosis
- Membrane Trafficking
- Metabolism
- Metabolism of proteins
- Muscle contraction
- Neuronal System
- Reproduction
- Signal Transduction
- SUMOylation
- Transmembrane transport of small molecules



Pathway



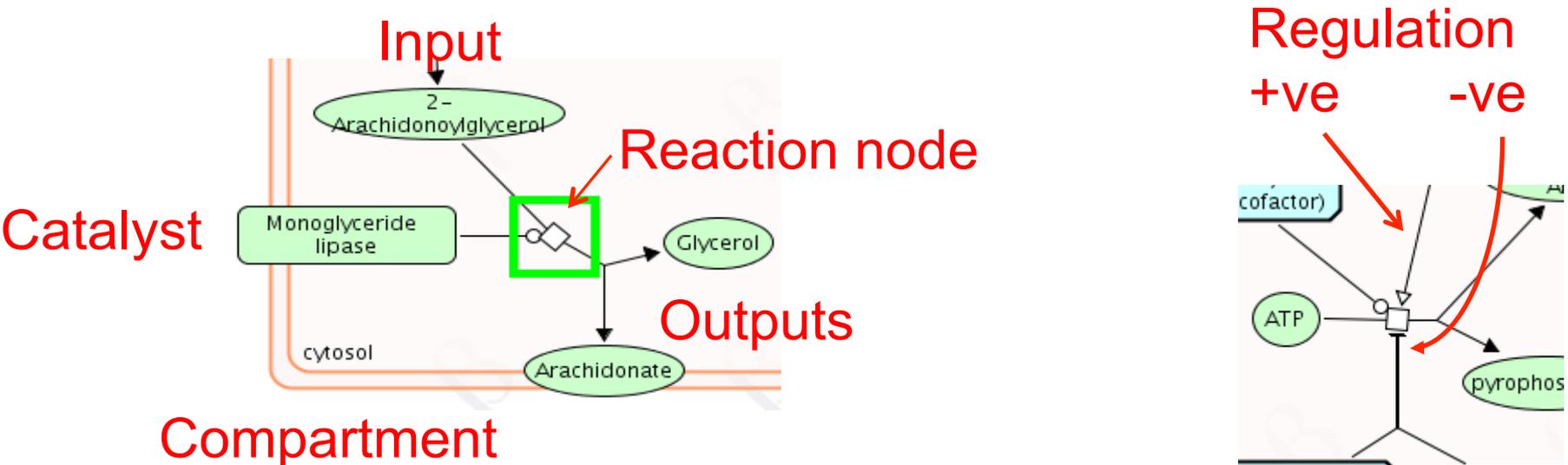
Reaction



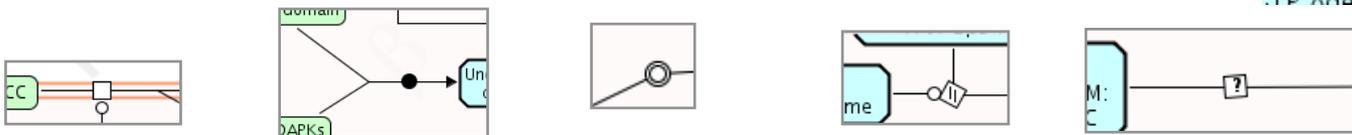
Black-box

# The Pathway Browser - Pathway Diagrams

Boxes are proteins, protein sets, mixed sets or complexes.  
 Ovals are small molecules (or sets of)  
 Green boxes are proteins or sets, blue are complexes.



Compartment



Transition Binding Dissociation Omitted Uncertain

# The Details Panel

**Overview** Molecules Structures Expression Processes Downloads

TRAIL:TRAIL receptor-2 Trimer Binds FADD Species: Homo sapiens

**Stable Identifier**  
REACT\_1721.2

**Summation**  
The trimeric complex of TRAIL and TRAIL receptor-2 (TRAIL:TRAIL receptor-2) binds FADD (Sprick et al. 2000).

**Input**

- TRAIL receptor-2:TRAIL Trimer [plasma membrane] +
- 2 x FADD [cytosol] +

**Output**

- TRAIL:TRAIL receptor-2:FADD [plasma membrane] +

**Preceding Event(s)**

- TRAIL Binds TRAIL-Receptor2 [Homo sapiens] +

**Following Event(s)**

- TRAIL:TRAIL-Receptor2 Trimer:FADD complex binds Caspase-10 [Homo sapiens] +
- TRAIL:TRAIL-Receptor2 Trimer:FADD complex binds Caspase-8 [Homo sapiens] +

**Computationally inferred to**  
Select a species to go to...

**Negatively regulated by**

- CFLAR(1-376) [cytosol] +

Overview Molecules **Structures (1/1)** Expression Processes Downloads



UniProt: O15519 CFLAR Chain: A Resolution: 1.90 Coverage: 0.57 PDB Range: [1, 272]  
 UniProt Range: [209, 480]

3h11        

► All other structures for O15519

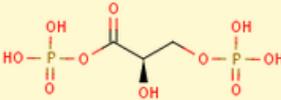
ChEBI Name 3-phospho-D-glyceroyl dihydrogen phosphate

ChEBI ID [CHEBI:16001](#)

Definition The (R)-enantiomer of 3-phosphoglyceroyl dihydrogen phosphate.

Stars ★★

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



Overview Molecules (4) Structures (0) **Expression** Processes Downloads

**E-MTAB-513** RNA-Seq of human individual tissues and mixture of 16 tissues (Illumina Body Map)  
 Organism(s): *Homo sapiens*  
 Reference(s): 22496456 22955988 23258890

Showing 4 of 4 genes found: 



Display levels

Gene	adipose	adrenal	brain	breast	colon	heart	kidney	leukocyte	liver	lung	lymph node	ovary	prostate	skeletal muscle	testis	thyroid
CFLAR			brain													
TNFSF10																
TNFRSF10B																
FADD																

# Analysis – identifier list

**REACTOME**  
A CURATED PATHWAY DATABASE

About Content Documentation Tools Community Download Contact e.g. 095631, NTN1, signaling Search

Submit analysis data Analysis results Identifier results Summary results

## Submit your data for analysis

Takes gene expression data (and also numerical proteomics data) and shows how expression levels affect reactions and pathways in living organisms. May be time-consuming, depending on the number of identifiers you are submitting; less than 5000: a few seconds, 5000 - 10000: a few minutes, 10000 or more: 10 minutes or longer. Your data should be formatted as a tab-delimited file, where the first column contains identifiers and subsequent columns contain numerical expression data. You may paste your data into the supplied text area, or you can also upload it from a file. Click on the "Analyse" button to perform this analysis.

Browse... No file selected. Clear Load example data: Protein UniProt ID list

000139  
000186  
000187  
000204  
000217  
000231  
000232  
000233  
000254  
000267  
000268  
000273  
000303

Analyse

# Overrepresentation

Submit analysis data **Analysis results** Identifier results Summary results

## Analysis results, per pathway

This table provides an overview of your expression data in a pathway context. For each Reactome pathway, the total number of proteins is shown, plus the number of genes/proteins in your dataset that match. By clicking on a pathway name, you will be taken to an interactive graphical representation of the pathway, where your expression levels are represented as coloration of proteins.

P-val

Select format to download this table:

Pathway ▼▲	Species ▼▲	IDs in pathway (%) ▼▲	Enrichment (pval) ▼▲	FDR ▼▲
<i>Not assigned</i>	<i>Not known</i>	76 (0%)		
<a href="#">Apoptosis</a>	<a href="#">Homo sapiens</a>	73 (48%)	1.21E-05	8.45E-05
<a href="#">Binding and Uptake of Ligands by Scaveng</a>	<a href="#">Homo sapiens</a>	5 (2%)	0.5	0.5
<a href="#">Cell Cycle</a>	<a href="#">Homo sapiens</a>	162 (36%)	6.90E-10	1.52E-08
<a href="#">Cell-Cell communication</a>	<a href="#">Homo sapiens</a>	18 (14%)	6.94E-02	6.94E-02
<a href="#">Cellular responses to stress</a>	<a href="#">Homo sapiens</a>	23 (15%)	0.4	0.4
<a href="#">Circadian Clock</a>	<a href="#">Homo sapiens</a>	4 (11%)	0.2	0.2
<a href="#">Developmental Biology</a>	<a href="#">Homo sapiens</a>	62 (17%)	1.10E-02	2.21E-02
<a href="#">Disease</a>	<a href="#">Homo sapiens</a>	232 (22%)	4.96E-03	1.49E-02
<a href="#">DNA Repair</a>	<a href="#">Homo sapiens</a>	58 (54%)	5.07E-02	5.88E-02
<a href="#">DNA Replication</a>	<a href="#">Homo sapiens</a>	57 (56%)	1.03E-06	1.13E-05
<a href="#">Extracellular matrix organization</a>	<a href="#">Homo sapiens</a>	53 (21%)	0.2	0.2
<a href="#">Gene Expression</a>	<a href="#">Homo sapiens</a>	229 (32%)	5.88E-02	5.88E-02
<a href="#">Hemostasis</a>	<a href="#">Homo sapiens</a>	116 (27%)	7.01E-04	3.51E-03
<a href="#">Immune System</a>	<a href="#">Homo sapiens</a>	233 (19%)	3.05E-03	1.22E-02
<a href="#">Meiosis</a>	<a href="#">Homo sapiens</a>	18 (31%)	3.29E-02	5.88E-02
<a href="#">Membrane Trafficking</a>	<a href="#">Homo sapiens</a>	13 (9%)	0.5	0.5
<a href="#">Metabolism</a>	<a href="#">Homo sapiens</a>	353 (24%)	7.11E-03	2.13E-02
<a href="#">Metabolism of proteins</a>	<a href="#">Homo sapiens</a>	64 (12%)	0.9	0.9
<a href="#">Muscle contraction</a>	<a href="#">Homo sapiens</a>	1 (1%)	0.2	0.2
<a href="#">Neuronal System</a>	<a href="#">Homo sapiens</a>	22 (8%)	0.6	0.6
<a href="#">Reproduction</a>	<a href="#">Homo sapiens</a>	0 (0%)		
<a href="#">Signal Transduction</a>	<a href="#">Homo sapiens</a>	226 (13%)	3.19E-02	5.88E-02
<a href="#">SUMOylation</a>	<a href="#">Homo sapiens</a>	0 (0%)		
<a href="#">Transmembrane transport of small molecu</a>	<a href="#">Homo sapiens</a>	43 (8%)	0.5	0.5

25 rows

# Expression overlay I



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e.g. O95631, NTN1, signaling

[Submit analysis data](#)

[Analysis results](#)

[Identifier results](#)

[Summary results](#)

## Submit your data for analysis

Takes gene expression data (and also numerical proteomics data) and shows how expression levels affect reactions and pathways in living organisms. May be time-consuming, depending on the number of identifiers you are submitting; less than 5000: a few seconds, 5000 - 10000: a few minutes, 10000 or more: 10 minutes or longer. Your data should be formatted as a tab-delimited file, where the first column contains identifiers and subsequent columns contain numerical expression data. You may paste your data into the supplied text area, or you can also upload it from a file. Click on the "Analyse" button to perform this analysis.

No file selected.  Load example data:

#Probeset	10h_control	10h	14h	18h	24h	
1053_at	8.040078	7.147358	6.706705	7.112222	6.794622	7.475157
1729_at	6.869688	6.99104	7.129922	7.112222	7.04721	
1861_at	6.437999	6.620092	6.20117	6.407735	5.717815	
200000_s_at	9.381569	9.710802	9.874874	9.934639	9.495911	
200002_at	12.555275	12.511045	12.564419	12.538642	12.439174	
200003_s_at	12.401259	12.054083	12.275169	12.206342	12.015476	
200005_at	9.609852	9.099299	9.73072	9.530097	9.194303	
200012_x_at	12.486269	12.402275	12.302666	12.256543	12.282444	
200014_s_at	10.371458	9.548578	9.978313	9.871472	8.753136	
200016_x_at	12.110468	11.913288	11.938524	11.899243	11.458105	
200022_at	12.205038	11.927471	12.064725	12.031422	11.932256	
200023_s_at	10.377248	9.902753	9.990862	10.248412	9.513486	

# Expression overlay II

Submit analysis data

**Analysis results**

Identifier results

Summary results

## Analysis results, per pathway

This table provides an overview of your expression data in a pathway context. For each Reactome pathway, the total number of proteins is shown, plus the number of genes/proteins in your dataset that match. By clicking on a pathway name, you will be taken to an interactive graphical representation of the pathway, where your expression levels are represented as coloration of proteins.

Select format to download this table:

Microsoft Xcel (TSV)

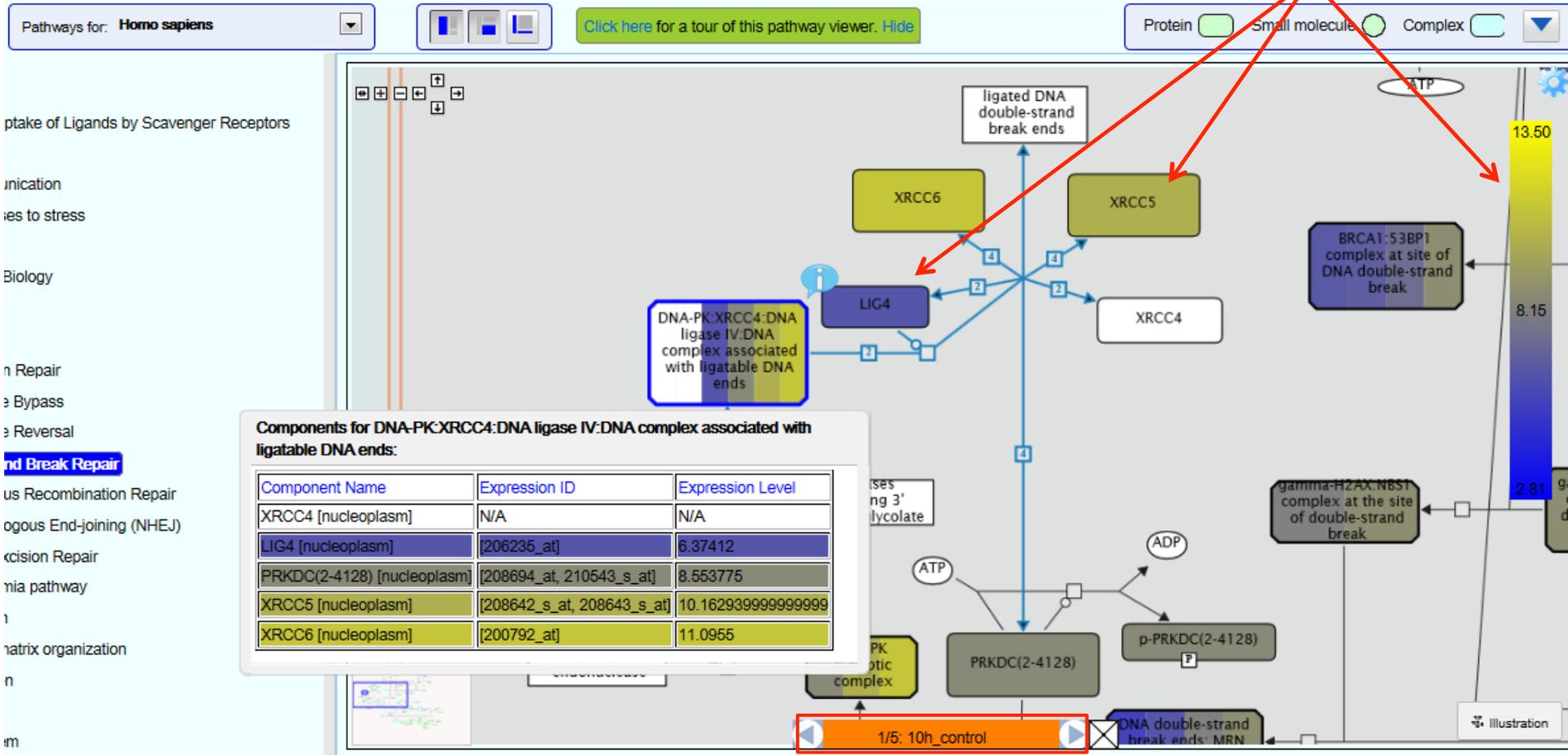
Download

Pathway ▼▲	Species ▼▲	IDs in pathway (%) ▼▲	10h_control ▼▲	10h ▼▲	14h ▼▲	18h ▼▲	24h ▼▲
<i>Not assigned</i>	<i>Not known</i>	21	7.3	6.8	7.0	6.9	6.5
<a href="#">Apoptosis</a>	<a href="#">Homo sapiens</a>	71 (48%)	7.9	7.7	7.8	7.7	7.4
<a href="#">Binding and Uptake of Ligands by Scaveng</a>	<a href="#">Homo sapiens</a>	6 (3%)	4.8	5.2	5.2	5.0	5.4
<a href="#">Cell Cycle</a>	<a href="#">Homo sapiens</a>	114 (26%)	8.4	7.8	8.0	8.0	7.5
<a href="#">Cell-Cell communication</a>	<a href="#">Homo sapiens</a>	4 (3%)	7.8	7.8	7.9	7.7	7.8
<a href="#">Cellular responses to stress</a>	<a href="#">Homo sapiens</a>	3 (11%)	8.2	7.5	7.8	7.7	7.2
<a href="#">Circadian Clock</a>	<a href="#">Homo sapiens</a>	1 (2%)	10.3	10.1	10.1	10.2	9.3
<a href="#">Developmental Biology</a>	<a href="#">Homo sapiens</a>	19 (5%)	6.5	6.5	6.6	6.5	6.6
<a href="#">Disease</a>	<a href="#">Homo sapiens</a>	165 (18%)	9.2	8.9	9.0	9.0	8.7
<a href="#">DNA Repair</a>	<a href="#">Homo sapiens</a>	74 (69%)	7.6	7.1	7.2	7.3	6.9
<a href="#">DNA Replication</a>	<a href="#">Homo sapiens</a>	77 (77%)	8.8	8.1	8.3	8.3	7.7
<a href="#">Extracellular matrix organization</a>	<a href="#">Homo sapiens</a>	16 (7%)	5.8	6.0	6.0	6.0	6.1
<a href="#">Gene Expression</a>	<a href="#">Homo sapiens</a>	272 (39%)	9.0	8.6	8.8	8.8	8.4
<a href="#">Hemostasis</a>	<a href="#">Homo sapiens</a>	76 (17%)	6.0	6.0	6.0	6.0	6.1
<a href="#">Immune System</a>	<a href="#">Homo sapiens</a>	95 (8%)	8.0	7.7	7.8	7.8	7.5
<a href="#">Meiosis</a>	<a href="#">Homo sapiens</a>	14 (24%)	7.4	6.9	6.9	7.0	6.6
<a href="#">Membrane Trafficking</a>	<a href="#">Homo sapiens</a>	7 (5%)	7.6	7.4	7.3	7.3	7.0
<a href="#">Metabolism</a>	<a href="#">Homo sapiens</a>	292 (20%)	7.7	7.5	7.6	7.6	7.4
<a href="#">Metabolism of proteins</a>	<a href="#">Homo sapiens</a>	81 (15%)	10.3	10.1	10.3	10.3	10.0
<a href="#">Muscle contraction</a>							
<a href="#">Neuronal System</a>	<a href="#">Homo sapiens</a>	10 (3%)	6.1	5.9	6.0	5.9	5.9
<a href="#">Reproduction</a>	<a href="#">Homo sapiens</a>	1 (4%)	9.7	8.9	9.2	9.0	8.8
<a href="#">Signal Transduction</a>	<a href="#">Homo sapiens</a>	116 (6%)	7.2	7.1	7.1	7.1	6.9
<a href="#">SUMOylation</a>							
<a href="#">Transmembrane transport of small molecu</a>	<a href="#">Homo sapiens</a>	16 (3%)	6.2	6.2	6.2	6.1	6.4

25 rows

# Expression overlay III

Yellow = high  
Blue = low



Step through  
Data columns

# Species Comparison I

Compare species    Compare species results

## Compare pathways between species

This tool allows you to compare pathways between human and any of the other species inferred from Reactome by orthology. Use the species selector to choose the other species; the table which appears will provide you with a summary of the differences for all pathways.

Compare all **human** pathways with:

- Arabidopsis thaliana
- Bos taurus
- Caenorhabditis elegans
- Canis familiaris
- Chlamydia trachomatis
- Clostridium botulinum
- Danio rerio
- Dictyostelium discoideum
- Drosophila melanogaster
- Escherichia coli
- Gallus gallus
- Human immunodeficiency virus 1
- Influenza A virus
- Mus musculus
- Mycobacterium tuberculosis
- Neisseria meningitidis serogroup B
- Oryza sativa
- Plasmodium falciparum
- Rattus norvegicus**
- Saccharomyces cerevisiae

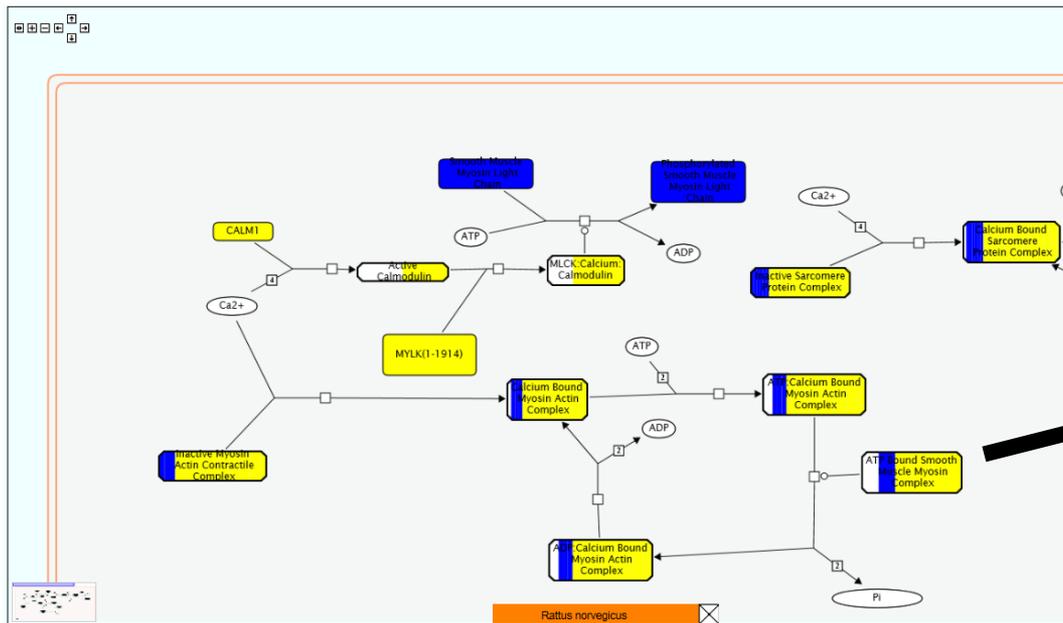
<b>About</b> <ul style="list-style-type: none"><li>About Reactome</li><li>News</li><li>Reactome Team</li><li>Scientific Advisory Board</li><li>Other Reactomes</li><li>License Agreement</li><li>Creative Commons License</li><li>Reactome Disclaimer</li></ul>	<b>Content</b> <ul style="list-style-type: none"><li>Table of Contents</li><li>DOIs</li><li>Data Schema</li><li>Editorial Calendar</li><li>Statistics</li></ul>	<b>Tools</b> <ul style="list-style-type: none"><li>Pathway Browser</li><li>Analyze Data</li><li>Pathway Overview</li><li>Compare Species</li><li>Reactome FI Network</li><li>Advanced Search</li><li>Small Molecule Search</li><li>BioMart</li></ul>	<b>Community</b> <ul style="list-style-type: none"><li>Reactome Community</li><li>Events Calendar</li><li>Training</li><li>Reactome Publications</li><li>Papers Citing Reactome</li><li>Resource Guide</li><li>Mailing List</li></ul>
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**Contact**      **Download**

# Species Comparison II

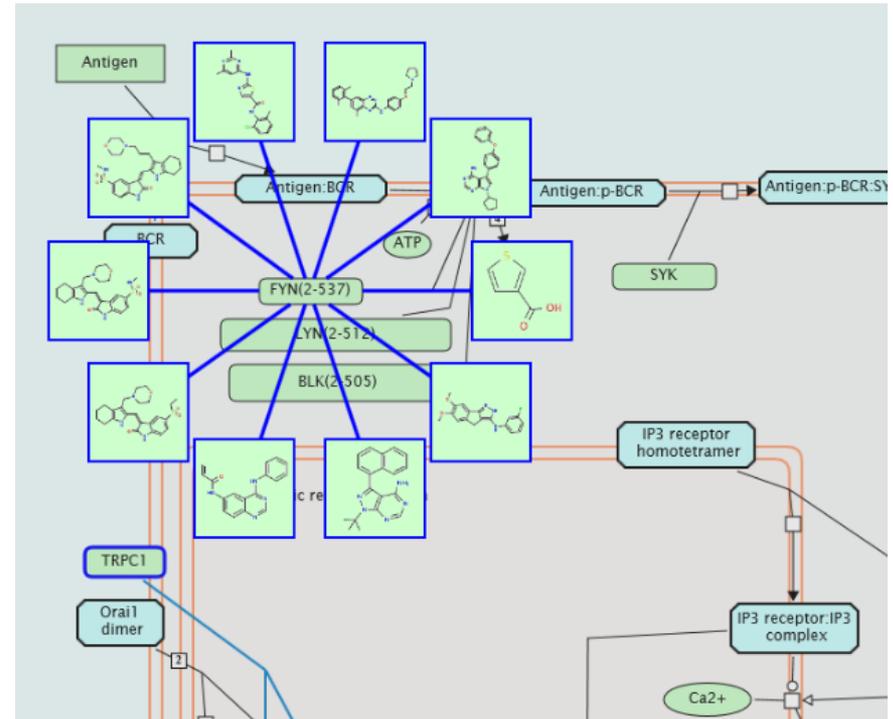
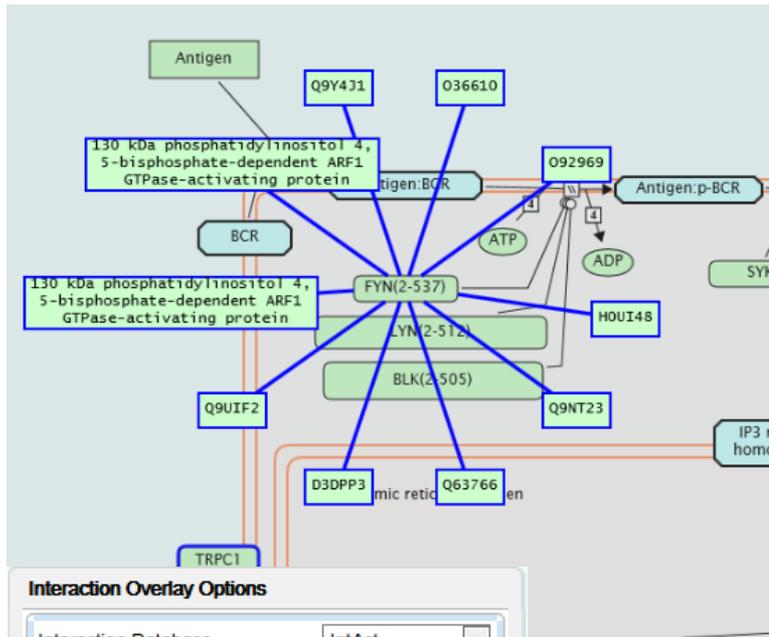
Yellow = human/rat  
 Blue = human only  
 No colour = no data



**Components for Calcium Bound Myosin Actin Complex**

Component Name
Calcium [ChEBI:29108]
UniProt:P60660 MYL6
UniProt:P06753 TPM3
UniProt:P62736 ACTA2
UniProt:O60504 SORBS3
UniProt:P14649 MYL6B
UniProt:Q9Y490 TLN1
UniProt:P56199 ITGA1
UniProt:P18206 VCL

# Molecular Interaction Overlay



**Interaction Overlay Options**

Interaction Database:

Upload a file:

Clear Overlay:

Submit a new PSICQUIC Service:

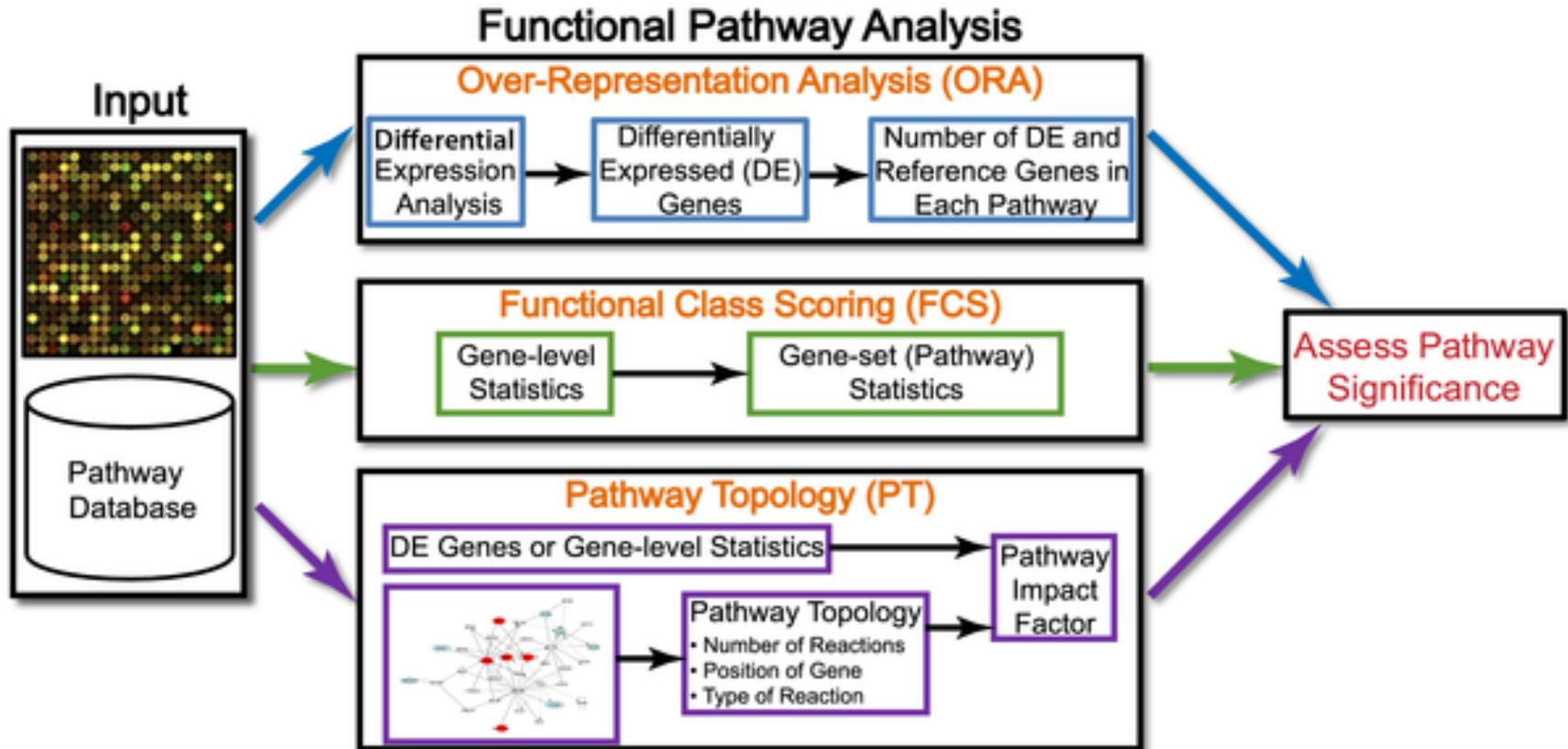
Set confidence level threshold:

Above Threshold: ■

Below Threshold: ■

Coloring Mode:  Turn on colouring

# Overview of existing pathway analysis methods



# Functional analysis methods - ORA

- Over-representation analysis (ORA) – statistically evaluate the fraction of genes in a particular pathway found among the set of genes showing changes in expression
- Limitations:
  - The statistical test used considers the number of genes alone and ignores any value associated with them, such as probe intensities
  - Each gene is treated equally and genes are considered independent
  - Only the most significant genes are used, the others are discarded
  - Pathways are considered independent
- Example: GO tools

# Functional analysis methods - FCS

- Functional class scoring (FCS) – based on the hypothesis that, although large changes in individual genes can have significant effects on pathways, weaker but coordinated changes in sets of functionally coordinated genes can also have significant effects.
- Pathway level statistics
- Limitations:
  - Pathways are considered independent
  - Changes in gene expressions are used to rank genes but then discarded from further analysis
- Example: GSEA (<http://www.broadinstitute.org/gsea/>), GSEABase (Bioconductor)

# Functional analysis methods - PT

- Pathway topology (PT)-based approaches – same as FCS but additionally using pathway topology to compute gene-level statistics. Include information about gene products that interact in a given pathway, how they interact and where they interact.
- Limitations:
  - Pathway topology is dependent on the type of cell due to cell-specific gene expression profiles and conditions being studied
  - Inability to model dynamic states
  - Inability to consider interactions between pathways
- Examples: SPIA (Bioconductor package)