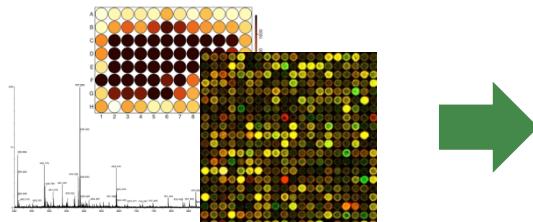
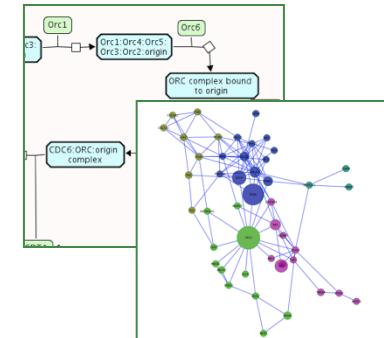


# What is Reactome?

- Open source and open access pathway database
  - 1400+ human pathways encompassing metabolism, signaling, gene regulation, and other biological processes
- Tools and datasets for browsing and visualizing pathway data, and interpreting your experimental data.

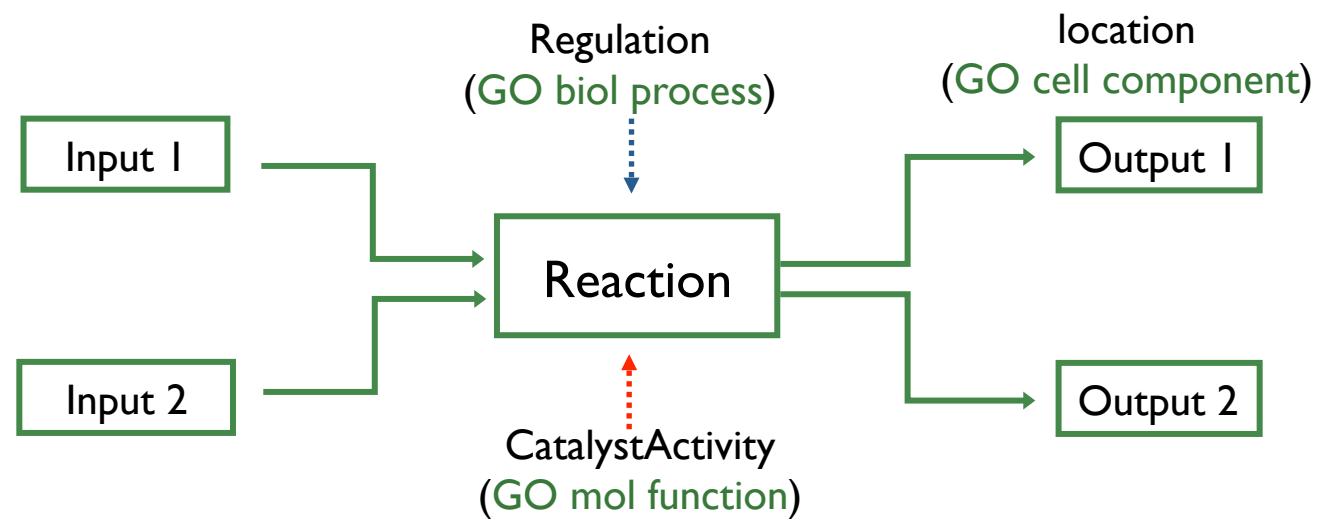
A screenshot of the Reactome Pathway Database. It shows a search results page with a table of pathways. The columns include Name, Description, Last Update, and Pathway ID. One row is highlighted in blue, showing the pathway 'ORC complex bound to origin'.

[www.reactome.org](http://www.reactome.org)

# Data model in a nutshell

- Reactome is a Reaction Network Database
- Explicitly describe biological processes as a series of biochemical reactions and events.
- Represents many events and states found in biology.
- PD (lite): represent mechanistic and temporal aspects of biological events

protein (UniProt) or  
molecule (ChEBI) or  
complex (GO/PRO) or  
ncRNA (miRBase) or  
disease variants (UniProt)  
therapeutics (ChEBI)



# Curator Tool

Untitled - Reactome Curator Tool

Schema View Event Hierarchical View Entity Level View

Tree View Show in All Binding of the influenza virion to the host cell

Graphic Display

Reaction Properties

Property Name	Value
catalystActivity	Cleaved HA Influenza A...
input	sialic acid [plasma mem...
output	Sialic Acid Bound Influen...
DB_ID	168272
_displayName	Binding of the influenza vi...
_doRelease	true
authored	
compartment	extracellular region plasma membrane
created	Gillespie, ME, 2005-11...
crossReference	
definition	
disease	
edited	
entityOnOtherCell	
evidenceType	
figure	/figures/influenza_bindi...
goBiologicalProcess	entry of virus into host cell
hasMember	
inferredFrom	
isChimeric	
literatureReference	Orthomyxoviridae: The... Gillespie, ME, 2005-11... Gillespie, ME, 2005-11... Gillespie, ME, 2005-11... Gillespie, ME, 2005-11... D'Eustachio, P, 2005-1... 2007-04-16 22:35:07 Gopinathrao, G, 2005-... D'Eustachio, P, 2006-0... Gillespie, ME, 2006-11... Gillespie, ME, 2009-10... Gillespie, ME, 2009-11...
modified	
name	Binding of the influenza vi...

Search Events

Choose Class: Event

Choose Attribute: DB\_ID

Attribute Value: Equals

Search Search More...

```
graph LR; A[Cleaved HA Influenza A Viral Particle  
[extracellular region]] --> B[sialic acid  
[plasma membrane]]; B --> C[Sialic Acid Bound Influenza A Viral Particle  
[plasma membrane]]
```

# Focus on Disease Topics

Pathways Help

- + Developmental Biology
- **UPDATED Disease**
  - + HIV Infection
  - + Influenza Infection
  - + Latent infection of Homo sapiens with Mycobacterium tuberculosis
  - + Signaling by EGFR in Cancer
  - + Amyloids
  - + Botulinum neurotoxicity
  - + Signaling by FGFR in disease
  - + Abnormal metabolism in phenylketonuria
  - + Mucopolysaccharidoses
  - + **NEW Diseases associated with visual transduction**
  - + PI3K/AKT Signaling in Cancer
  - **NEW Signaling by NOTCH1 in Cancer**
    - + **NEW Signaling by NOTCH1 t(7;9)(NOTCH1:M1580\_K2555) Translocation**
    - + Signaling by NOTCH1 HD Domain Mutants in Cancer
    - + Signaling by NOTCH1 PEST Domain Mutants in Cancer
    - + Signaling by NOTCH1 HD+PEST Domain Mutants in Cancer
    - + FBXW7 Mutants and NOTCH1 in Cancer
    - + Abnormal conversion of 2-oxoglutarate to 2-hydroxyglutarate
  - + DNA Repair
  - + DNA Replication
  - **UPDATED Extracellular matrix organization**
  - + Gene Expression
  - + Hemostasis
  - **UPDATED Immune System**

- Not new to Reactome!
- Reorganized the Pathway Hierarchy.
- Modified the Data Model.
- Updating the Pathway Browser.
- Annotate:
  - An infection introduces new proteins into the cell.
  - The amount of a normal protein is changed and this changes the function of the protein.
  - A mutation (somatic or germline) changes the function of a protein.
  - Mode of action of anti-cancer therapeutics.

# Pathway Browser

Divide reaction space into ~170 canonical pathways

Home & Search Analyze, Annotate & Upload

Switch Species: Homo sapiens

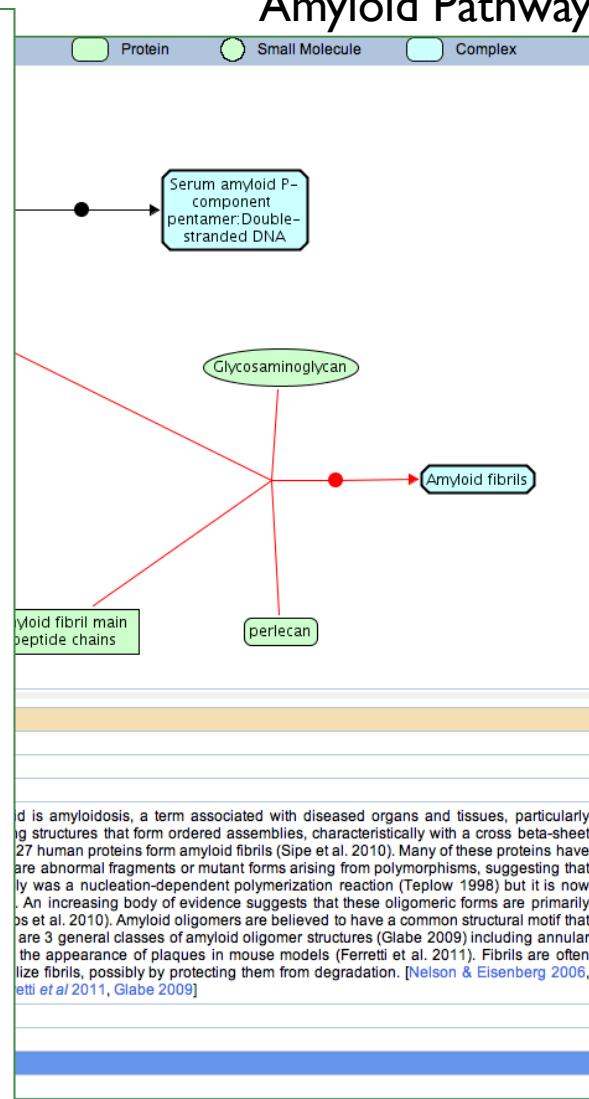
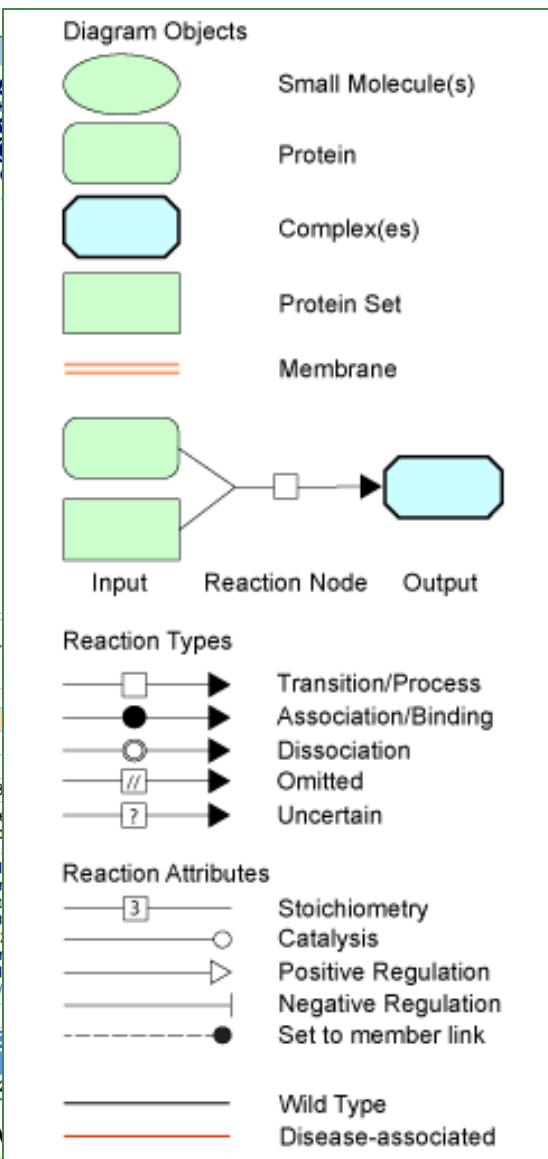
Pathways Help

- + Cell-Cell communication
- + NEW Cellular responses to stress
- + Circadian Clock
- + Developmental Biology
- UPDATED Disease
  - + HIV Infection
  - + Influenza infection
  - + NEW Latent infection of Homo sapiens with Mycobacterium
  - + Signaling by EGFR in Cancer
  - Amyloid
    - ↳ Serum amyloid P-component forms homopeptamers
    - ↳ Amyloid precursor proteins form ordered fibrils
    - ↳ Amyloid fibrils have additional components
    - ↳ Formation of serum amyloid P decamer
    - ↳ Serum amyloid P binds DNA and chromatin
  - + Botulinum neurotoxicity
  - + Diabetes pathways
  - + NEW Signaling by FGFR in disease
  - + NEW Abnormal metabolism in phenylketonuria
- + DNA Repair

Stable identifier REACT\_75925.1  
Authored Jupe, S, 2010-10-15  
Reviewed Perry, G, 2011-04-08

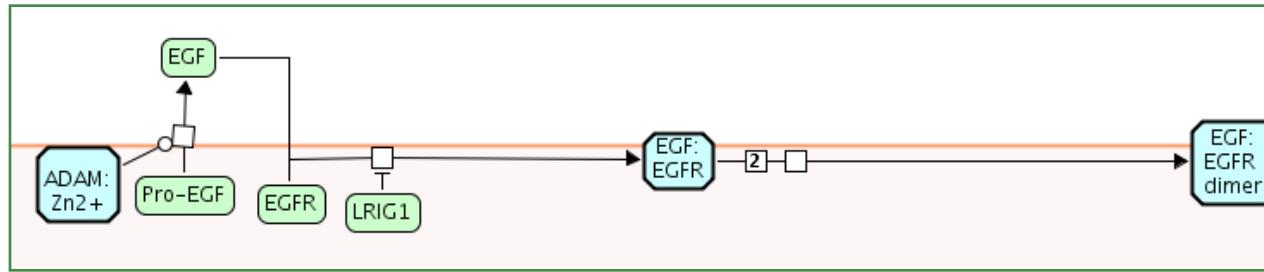
Amyloid is a term used to describe typically extracellular deposits of aggregated neurodegenerative diseases such as Alzheimer's, Parkinson's and Huntington's disease. It refers to a protein structure where the sheets run parallel to the direction of the fibril (Sawaya et al., 2007). Amyloid has non-pathological functions; the trigger that leads to abnormal aggregations during the initial event may be aggregation of misfolded or unfolded peptides. Early events are understood to be more complex, with multiple 'off-pathway' events leading to the formation of the fibril. Amyloid is responsible for the neurotoxic effects of Amyloid-beta (Roychaudhuri et al., 2009). Amyloid fibrils are independent of the protein involved and not present in fibrils (Kayed et al., 2008). Amyloid fibrils are associated with other molecules, notably heparan sulfate proteoglycans and perlecan (Sipe et al. 2010, Sawaya et al. 2007, Teplow 1998, Roychaudhuri et al. 2009, Vandevert et al. 2009).

Organism Homo sapiens  
Cellular compartment extracellular region  
References Westerman, P Aspects on human amyloid forms and their fibril polypeptides

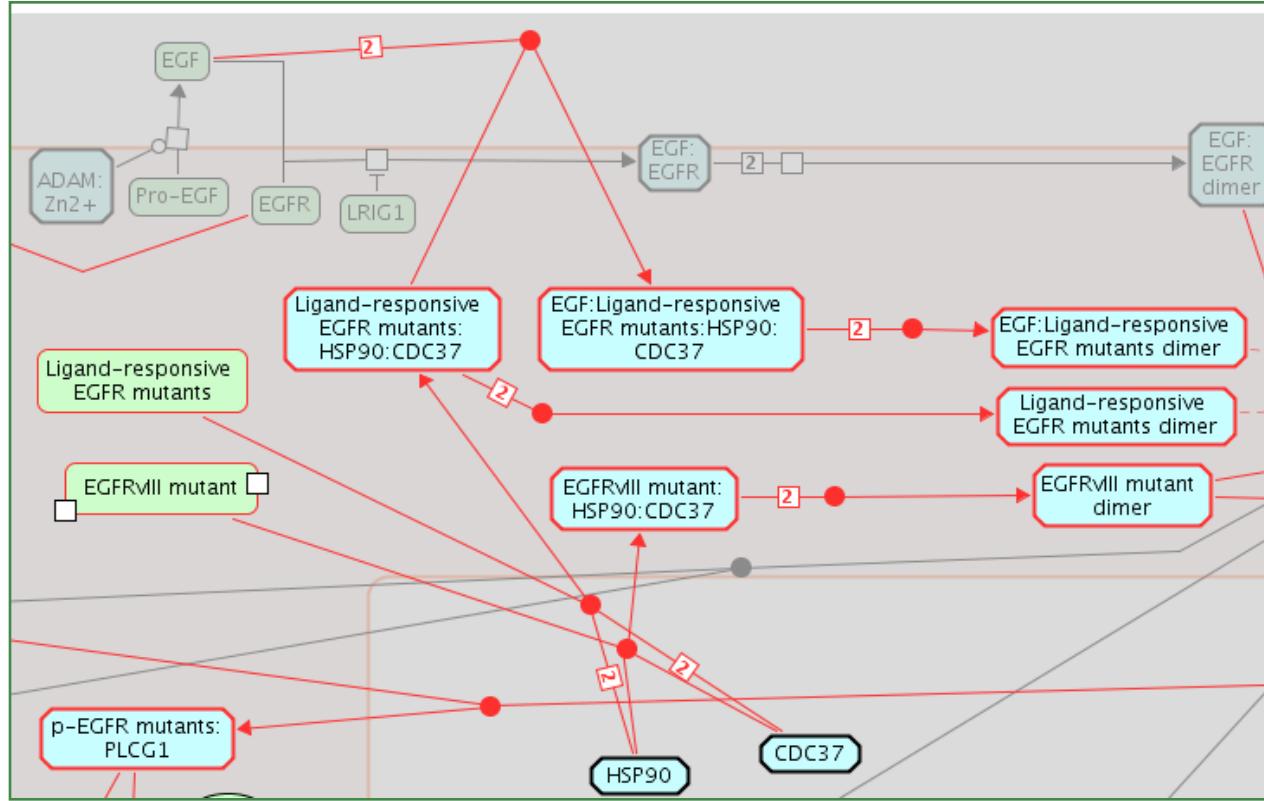


Google-map style pathway

# Browsing Normal & Disease Pathways

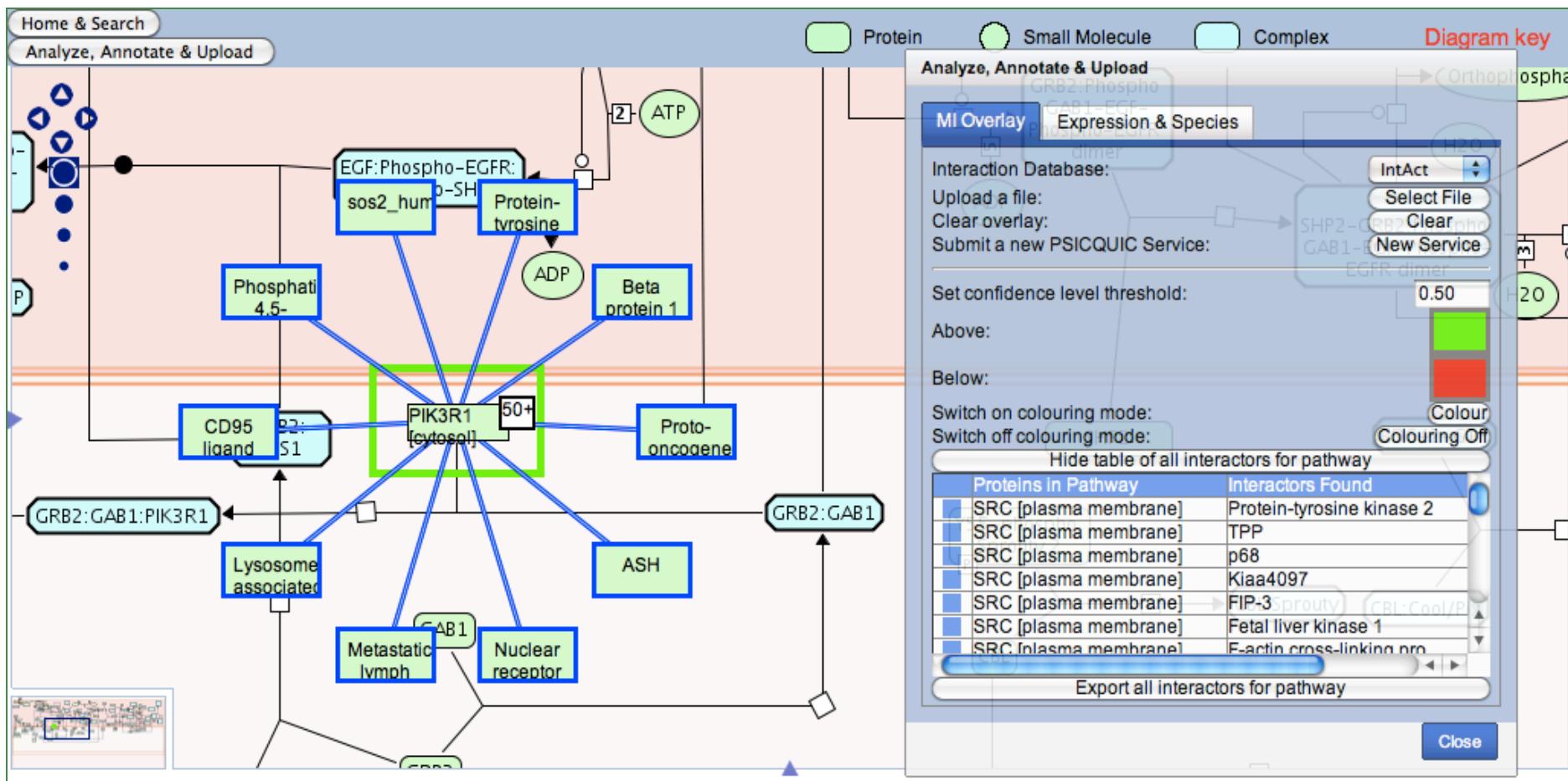


Signaling by EGFR Pathway

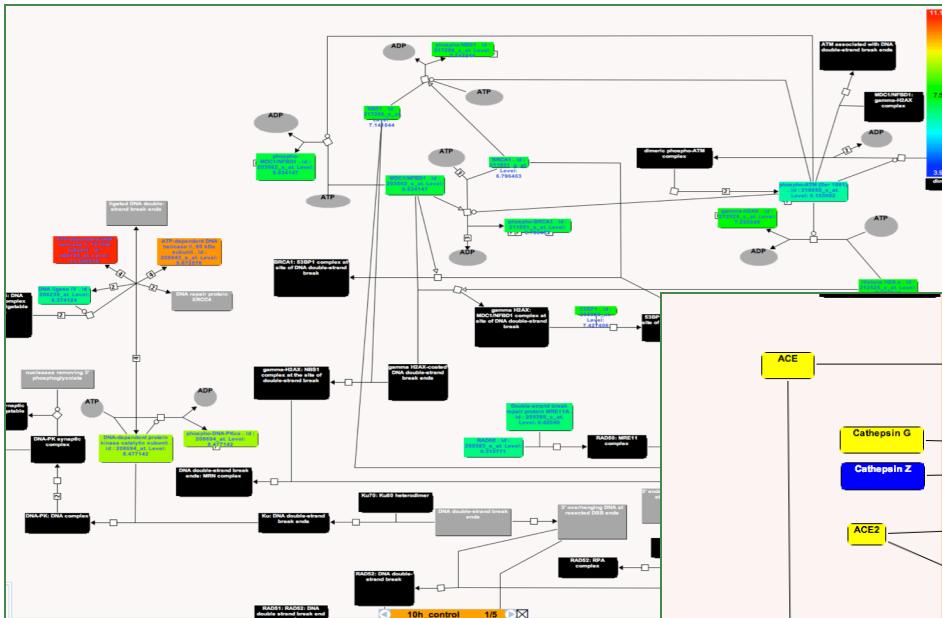


Signaling by EGFR Pathway in Cancer

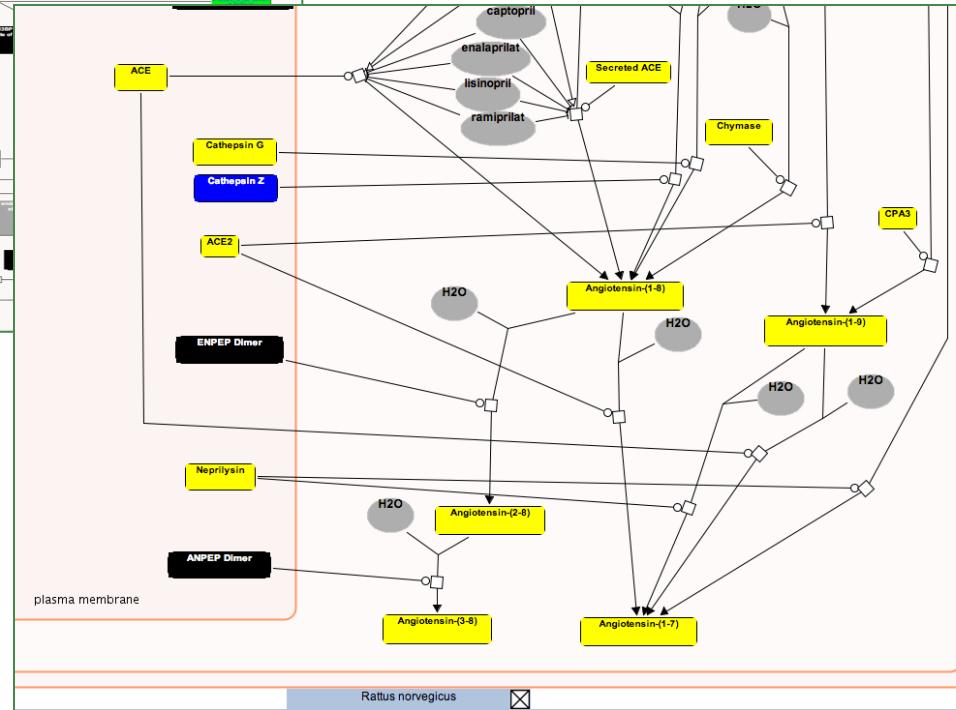
# Molecular Interaction Overlay



# Analyses of Gene lists



Colorize pathway diagrams with



Compare human and M/O pathways

# New Pathway Browser

REACTOME

Pathways for: Homo sapiens

Events Hierarchy:

- Disease
- HIV Infection
- Influenza Infection
- Latent infection of Homo sapiens with Mycobacterium tuberculosis
- Signaling by EGFR in Cancer
- Amyloids
  - Serum amyloid P-component forms homopentamers
    - Amyloid precursor proteins form ordered fibrils
    - Amyloid fibrils have additional components
    - Formation of serum amyloid P decamer
    - Serum amyloid P binds DNA and chromatin
  - Botulinum neurotoxicity
  - Diabetes pathways
  - Signaling by FGFR in disease
  - Abnormal metabolism in phenylketonuria
  - PI3K/AKT Signaling in Cancer
  - Mucopolysaccharidoses
  - DNA Repair
  - DNA Replication
  - Extracellular matrix organization
  - Gene Expression
  - Hemostasis
  - Immune System
  - Meiosis

Double-stranded DNA and chromatin

Serum amyloid P component

Ca<sup>2+</sup>

Serum amyloid P component homopentamer

Serum amyloid P decamer

Glycosaminoglycan

Perlecan

Amyloid fibril monomers

Amyloid fibril main peptide chains

Amyloid fibrils

Overview Processes Molecules Structures Downloads

Amyloids

The download options below are for the selected pathway, not individual events or entities selected in it.

SBML

SBGN

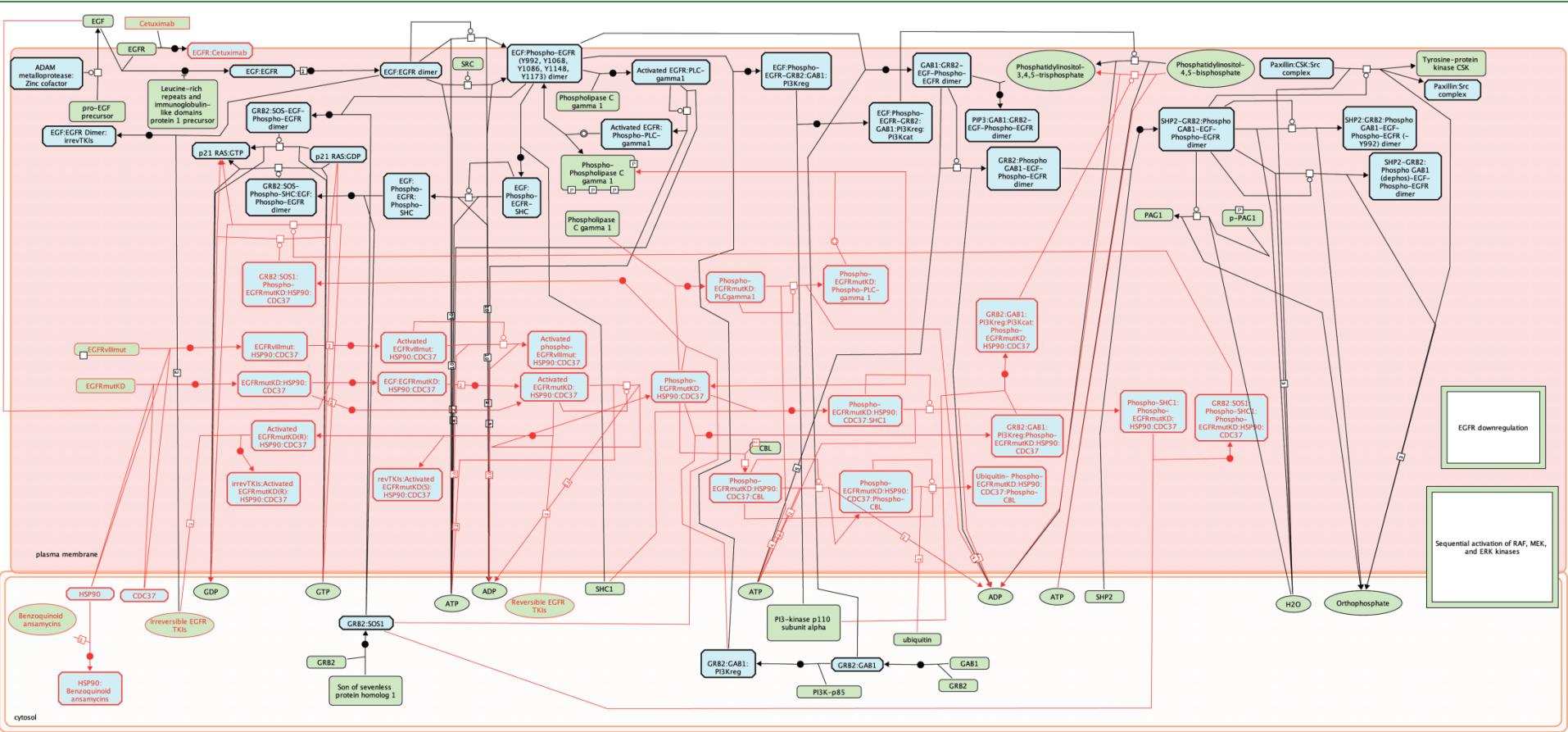
BIOPAX 2

BIOPAX 3

PDF

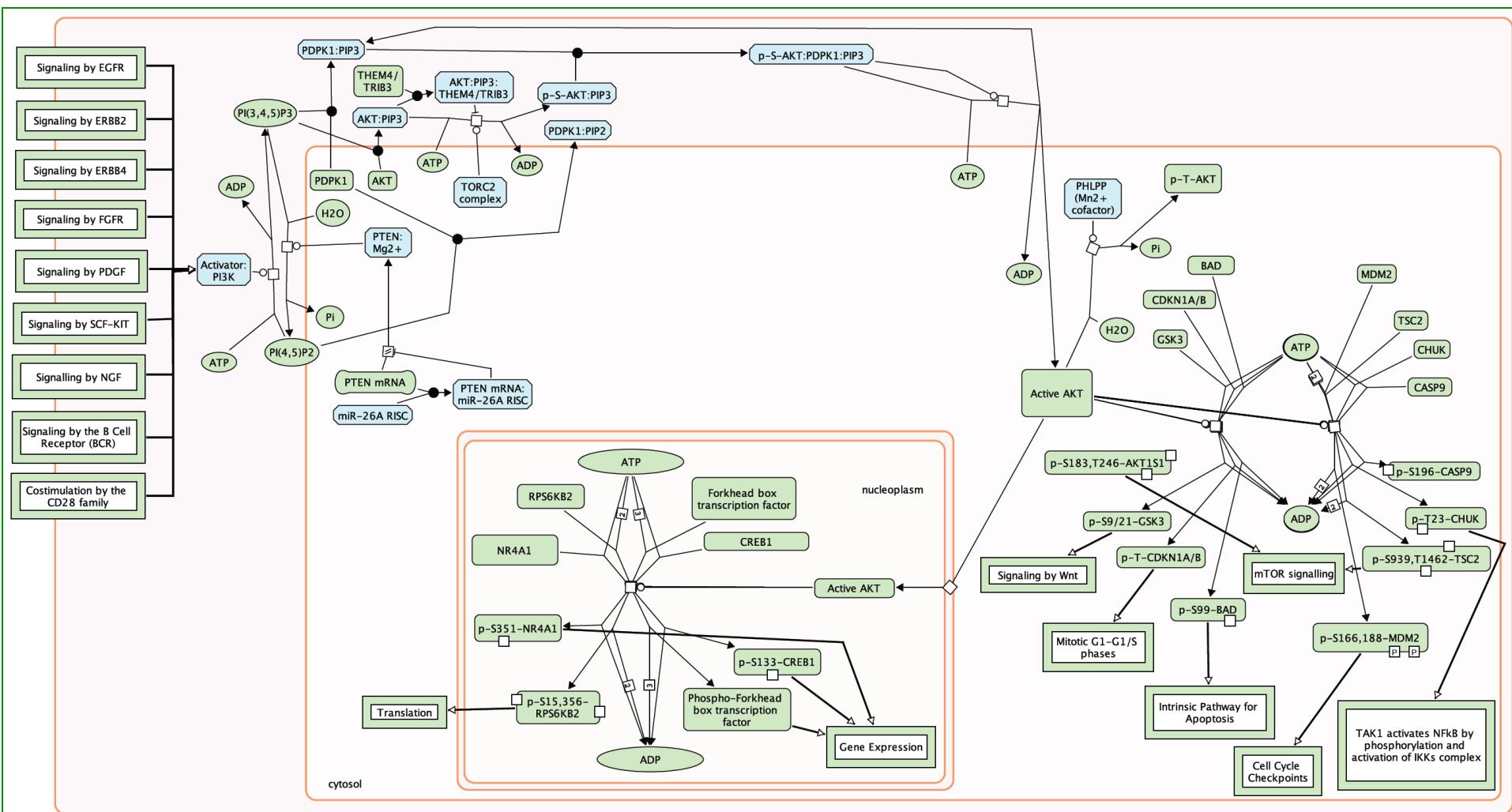


# Too many lines, where do I start & stop?



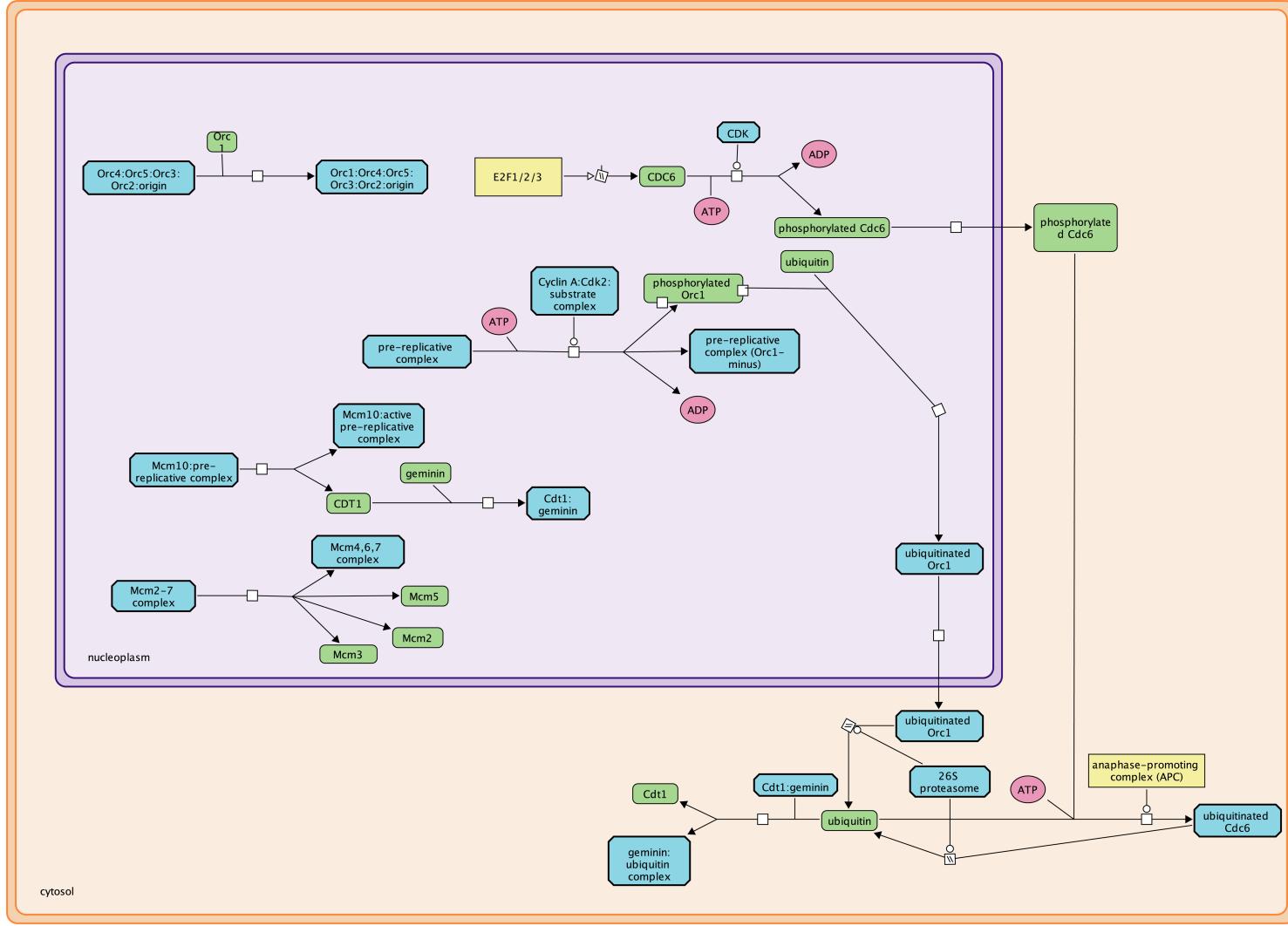
Prototype: Signaling by EGFR Pathway in Cancer

# Ideal Reactome Pathway?

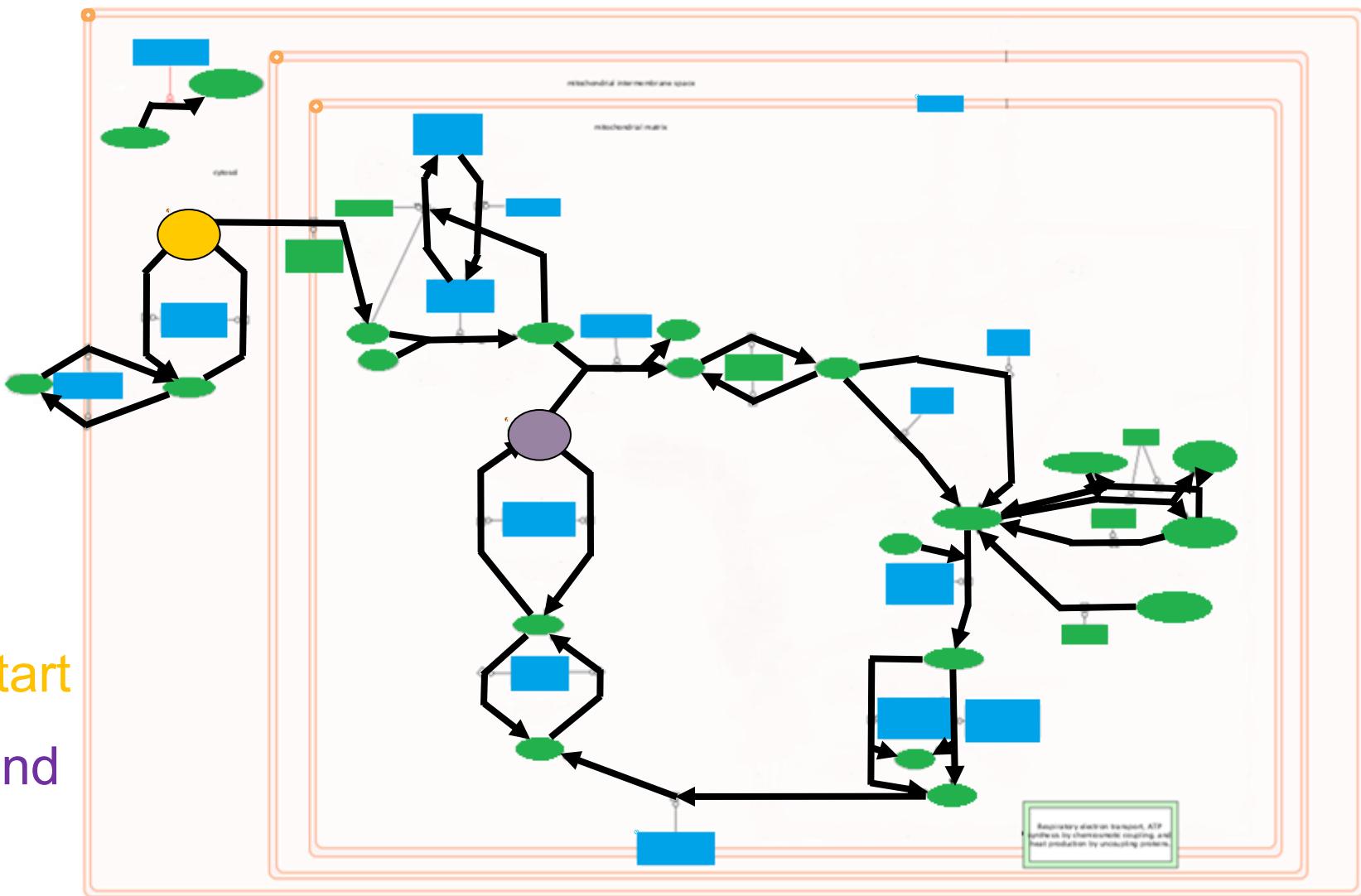


Akt Signaling

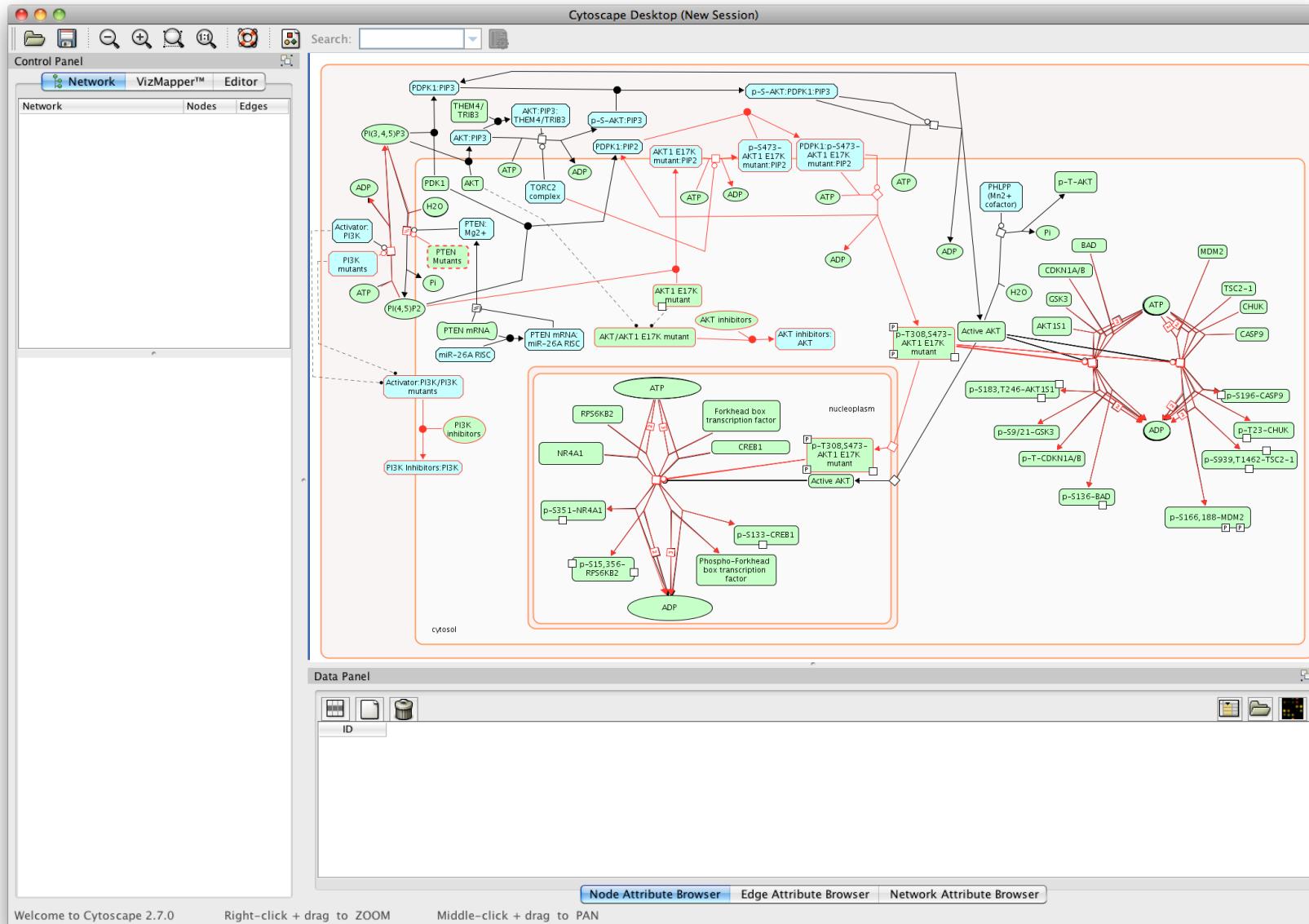
# Entity Colour Scheme



# Simplified Pathway View



# Reactome Pathways in Cytoscape

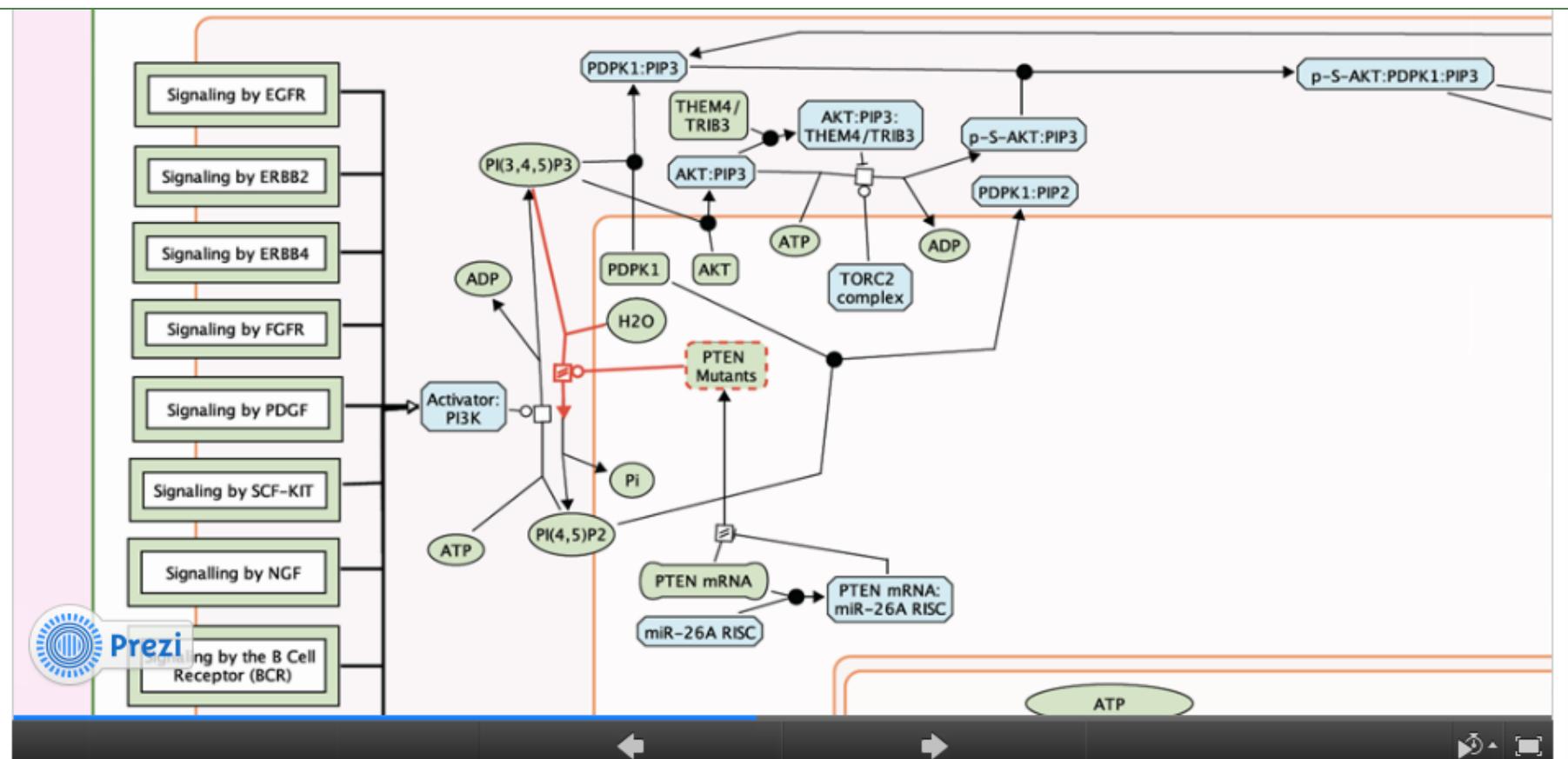


Welcome to Cytoscape 2.7.0

Right-click + drag to ZOOM

Middle-click + drag to PAN

# Community Outreach



Share

Like

## Reactome: An Exploration of Biological Pathways

Reactome is a curated knowledgebase of human biological pathways. It also offers many analytic and comparative tools for research applications.

More presentations by Clare Moffatt

# Continuing Priorities

## General

- Increase the number of curated proteins and other functional entities.
- Supplement normal pathways with variant reactions representing disease states.
- Improve annotation consistency and enrich the data model.
- Continued support for SBML, BioPAX and PSI.
- Enhance the web site and other resources to meet the needs of a growing and diverse user community.

## SBGN

- Continue to support SBGN
- Provide feedback to the SBGN group (and vice versa)
- Improve Reactome compliance with SBGN
- Should Reactome adopt AF?
- Anything else?

# Acknowledgements



- Marija Orlic-Milacic
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- Steve Jupe
- Bruce May
- Antonio Fabregat Mundo
- Veronica Shamovsky
- Heeyeon Song
- Joel Weiser
- Mark Williams
- Henning Hermjakob
- Peter D'Eustachio
- **Lincoln Stein**

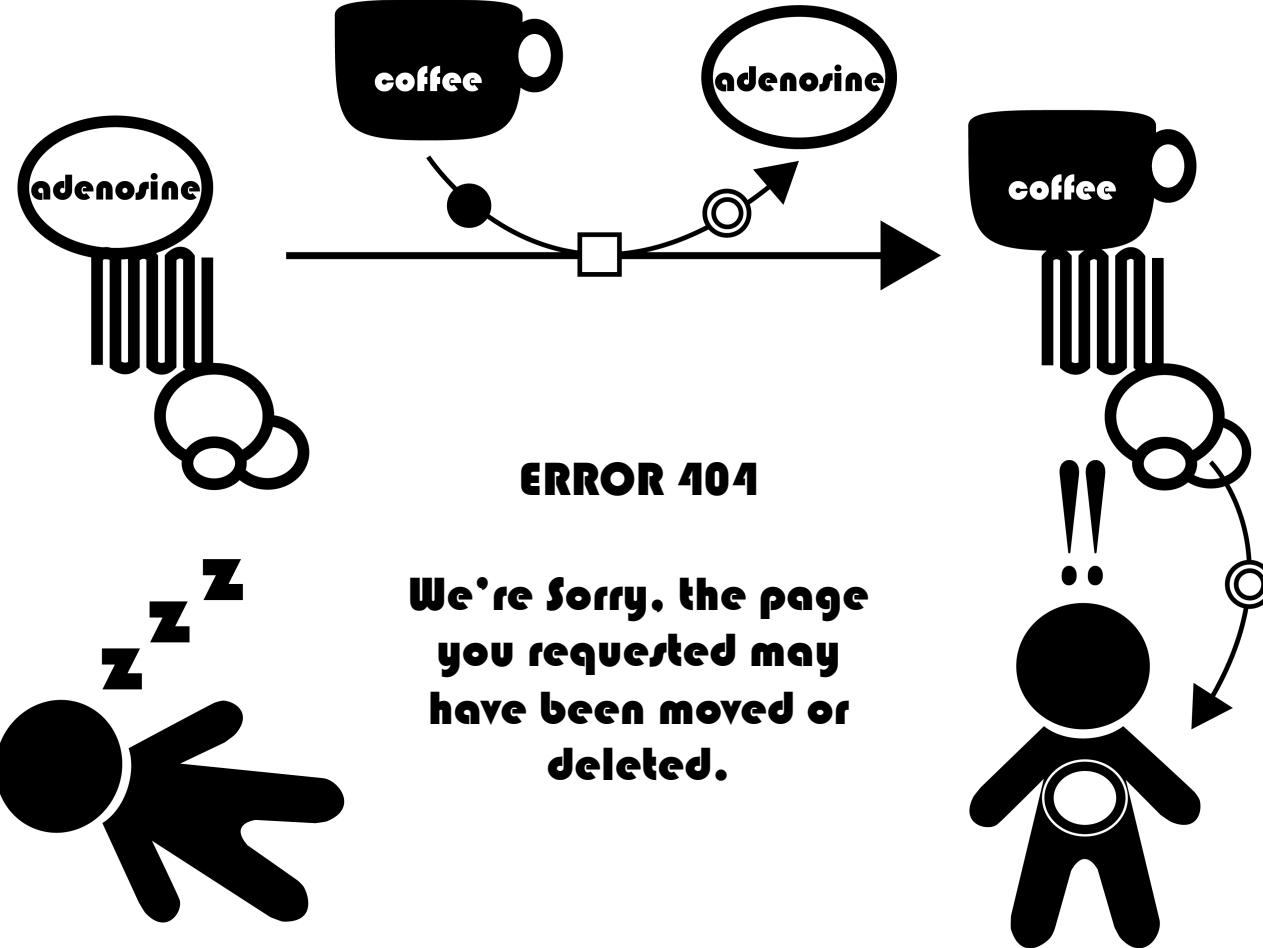


National Human  
Genome Research  
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Ministry of Economic  
Development and Innovation





If the caffeine hasn't worked, let's try one of the following remedies to get you back on track.....