

# **c-Mantic: a Cytoscape Semantic Web Plugin**

## **Tutorial: Reactome Pathways**

Version 1.1

December 2011

<http://www.epa.gov/ncct/v-liver/c-mantic>

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## Introduction - What is the c-Mantic Plugin?

c-Mantic (“seMantic”) is a [Cytoscape](#) plug-in that uses [Semantic Web](#) technologies to support the analysis of linked data networks.

The c-Mantic plug-in is useful for analyzing OWL/RDF data as Cytoscape networks. The OWL/RDF data can come from remote knowledgebases (SPARQL endpoints), imported from OWL/RDF data files, or from transforming the data in any Cytoscape network.

The work is part of the Virtual Liver (v-Liver™) project at the National Center for Computational Toxicology in the US Environmental Protection Agency (EPA). Visit <http://www.epa.gov/ncct/v-liver/> for more information. The c-Mantic plugin was implemented by Lockheed Martin under the guidance of the US EPA.

### Key Features

The c-Mantic plug-in can be used to,

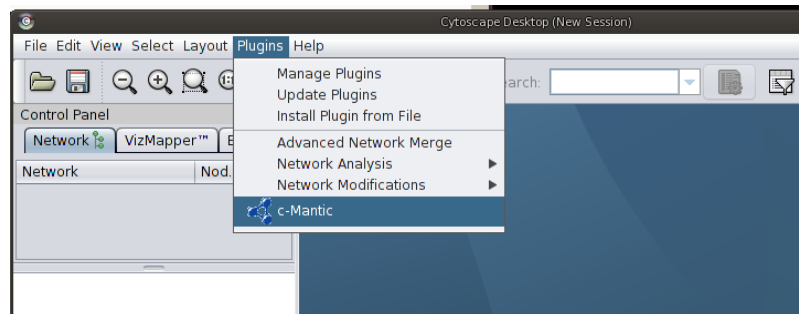
- Visualize OWL/RDF data as Cytoscape networks
- Query data from remote SPARQL endpoints and local knowledgebases
- Import OWL/RDF files (N3 or OWL/RDF/XML format)
- Export Cytoscape networks as OWL/RDF files
- Create local knowledge bases from Cytoscape networks

## Using c-Mantic to Analyze Reactome Pathways

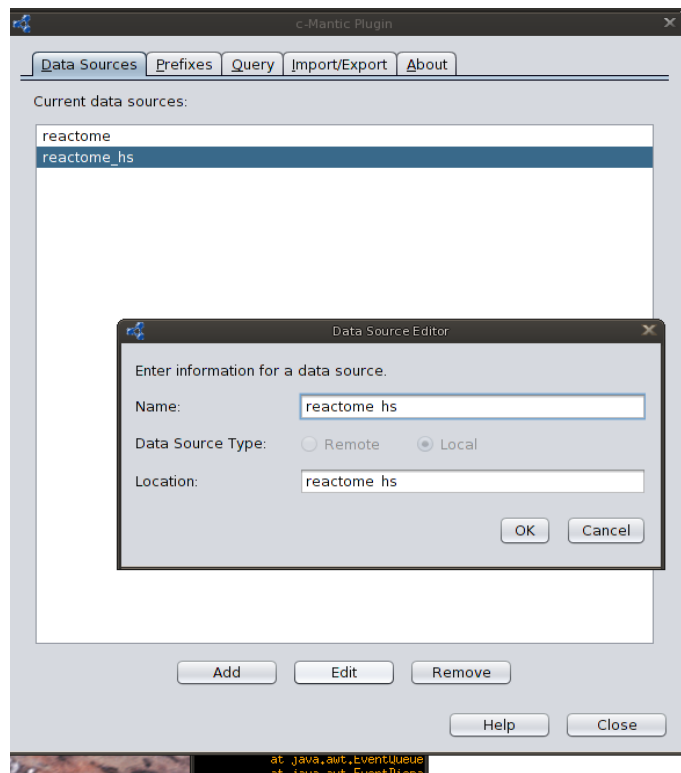
This tutorial provides steps by step instructions on using c-Mantic to analyze Reactome pathways. [Reactome](#) is an extensive resource of biological pathways which is available in OWL format. Additional information is available in the c-Mantic User Manual.

### Creating the KB

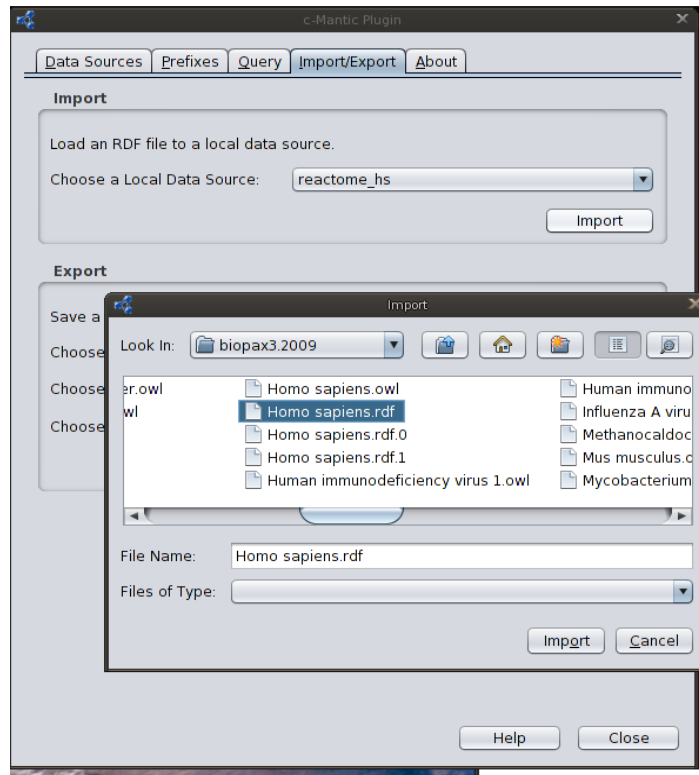
1. If you have not installed the c-Mantic plugin then please follow the instructions provided here. Run Cytoscape and start the c-Mantic plugin



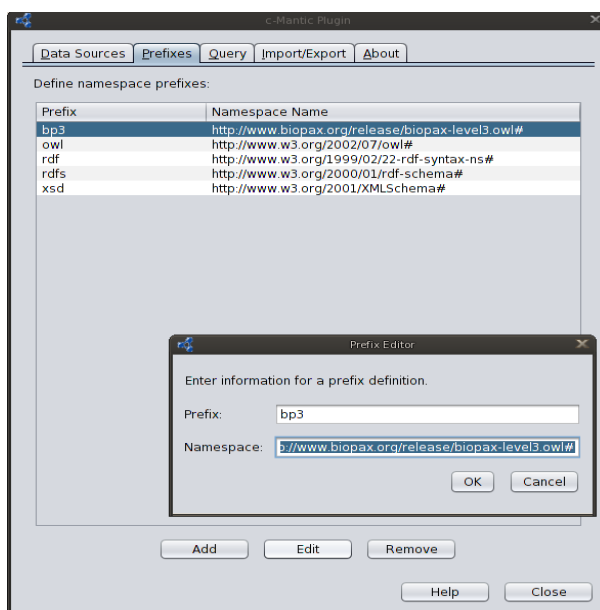
2. Select the "Data Source" tab in the main c-Mantic window and "Add" a KB for Reactome pathways – call it "reactome\_hs"



- Download the Reactome human pathways provided in BioPAX Level 3 format from here (reactome-homo-sapience.owl). Select the “Import/Export” tab in c-Mantic and select “reactome\_hs” as the “Local Data Source.” Click the “Import” button and select the Reactome file (reactome-homo-sapience.owl). This may take a few minutes depending on the speed of your computer – when it completes c-Mantic will let you know.

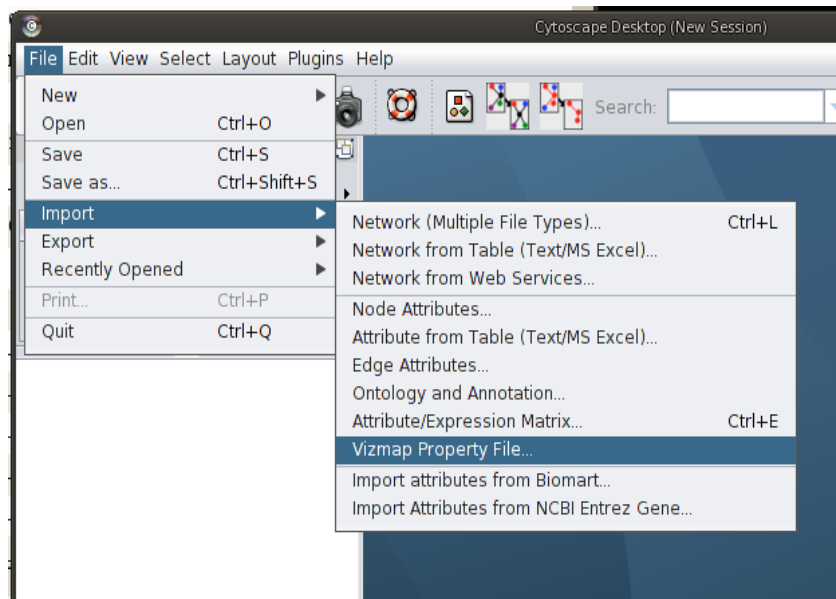


4. Select the “Prefixes” tab and add “bp3” as an abbreviation for:  
<http://www.biopax.org/release/biopax-level3.owl#>



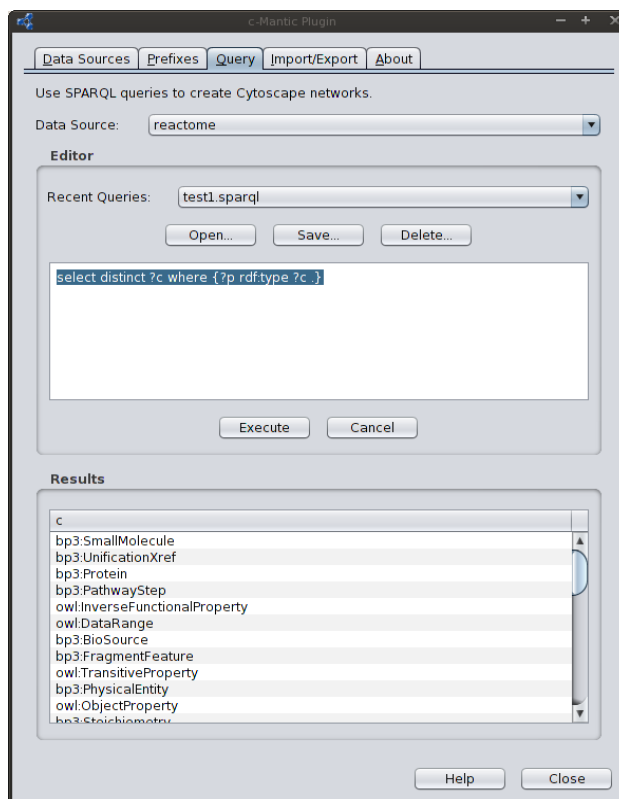
## Querying and Visualizing Reactome Pathways

1. Before visualizing Cytoscape networks, download this vizmap properties file – which has been customized for viewing BioPAX Level 3 information using c-Mantic. Load this file from the Cytoscape menu: “File -> Import -> Vizmap Property File”. A visual legend for this property file is included at the end of this document.



- Now you can query the Reactome KB in the “Query” tab. Choose “reactome\_hs” as the “Data Source” and enter the following SPARQL in the input area:

```
select distinct ?c where {?p rdf:type ?c .}
```



- Select the “Query” tab in c-Mantic, choose data source “reactome\_hs”. Enter the following SPARQL in the query input area to visualize components of the cell cycle pathway. (For a newer version of Reactome, you will need the URI for the cell cycle pathway.)

```

construct {
  ?pax rdf:type ?pt; bp3:name ?pn .
  ?pax bp3:pathwayComponent ?pc1; bp3:pathwayComponent ?pc2 .
  ?pc1 rdf:type ?pc1t; bp3:name ?pc1n .
  ?pc2 rdf:type ?pc2t; bp3:name ?pc2n .
  ?pax bp3:pathwayOrder ?ps1; bp3:pathwayOrder ?ps2 .
  ?ps1 rdf:type ?ps1t . ?ps2 rdf:type ?ps2t .
  ?ps1 bp3:stepProcess ?pc1; bp3:nextStep ?ps2 .
  ?ps2 bp3:stepProcess ?pc2 .
} where {
  ?pax rdf:type ?pt; bp3:name ?pn .
  ?pax bp3:pathwayComponent ?pc1; bp3:pathwayComponent ?pc2 .
  ?pc1 rdf:type ?pc1t; bp3:name ?pc1n .
  ?pc2 rdf:type ?pc2t; bp3:name ?pc2n .
  ?pax bp3:pathwayOrder ?ps1; bp3:pathwayOrder ?ps2 .
  ?ps1 rdf:type ?ps1t . ?ps2 rdf:type ?ps2t .
  ?ps1 bp3:stepProcess ?pc1; bp3:nextStep ?ps2 .
  ?ps2 bp3:stepProcess ?pc2 .
}
filter(?pax = <http://www.reactome.org/biopax#Cell_Cycle_Mitotic>
)

```

When c-Mantic completes this query it will show the number of results and will ask if you want to visualize these as a Cytoscape network. If you select “yes” then these results will appear as a new Cytoscape network. (This is helpful when a query produces millions of results.) You can customize this network using our settings by choosing the “BP3” visual style.

The screenshot displays two windows. The left window is c-Mantic, showing the 'Query' tab with the SPARQL query entered in the editor. A dialog box is open over the results, asking 'The query returned 3360 statements. Do you want to create a network?' with 'No' and 'Yes' buttons. The right window is Cytoscape 2.8.2, showing a network visualization of the cell cycle pathway. The network consists of nodes representing phases (G2 Phase, M Phase, S Phase, G1 Phase) and transitions (G2/M Transition, M/G1 Transition, G1/S Transition). Edges represent step processes and pathway orders. The 'Visual Mapping Browser' on the left of the Cytoscape window shows the 'BP3' visual style selected for the network.

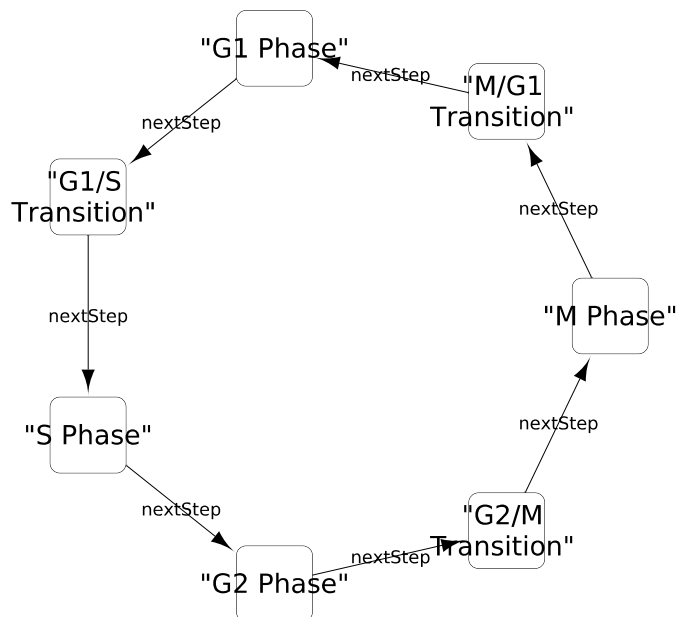
4. For a more intuitive view of cell cycle progression try the following query.

```

construct {
  ?pc1 rdf:type ?pc1t; bp3:name ?pc1n .
  ?pc2 rdf:type ?pc2t; bp3:name ?pc2n .
  ?pc1 bp3:nextStep ?pc2 .
} where {
  ?pax rdf:type ?pt; bp3:name ?pn .
  ?pax bp3:pathwayComponent ?pc1; bp3:pathwayComponent ?pc2 .
  ?pc1 rdf:type ?pc1t; bp3:name ?pc1n .
  ?pc2 rdf:type ?pc2t; bp3:name ?pc2n .
  ?pax bp3:pathwayOrder ?ps1; bp3:pathwayOrder ?ps2 .
  ?ps1 rdf:type ?ps1t . ?ps2 rdf:type ?ps2t .
  ?ps1 bp3:stepProcess ?pc1; bp3:nextStep ?ps2 .
  ?ps2 bp3:stepProcess ?pc2 .
filter(?pax = <http://www.reactome.org/biopax#Cell_Cycle__Mitotic>)
}

```

Here we have used SPARQL to construct a network in which pathway components are ordered using the "nextStep" relationship.

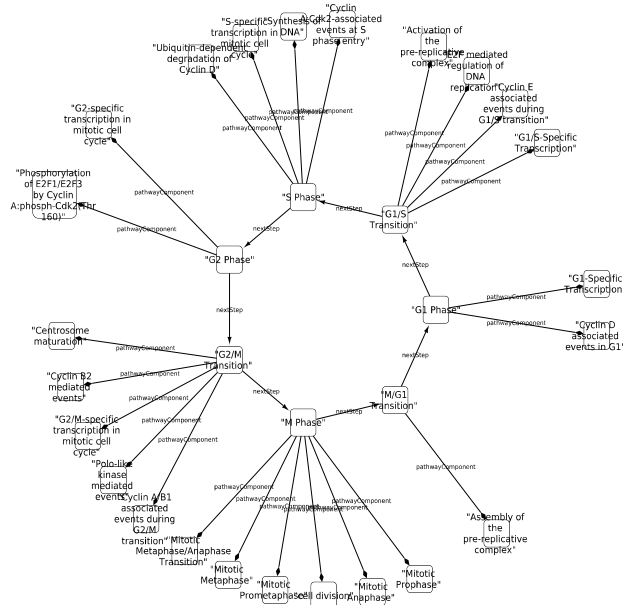


5. To visualize additional components of cell cycle stages try the following query:

```

construct {
  ?pc1 rdf:type ?pc1t; bp3:name ?pc1n .
  ?pc2 rdf:type ?pc2t; bp3:name ?pc2n .
  ?pc1 bp3:nextStep ?pc2 .
  ?pc1 bp3:pathwayComponent ?pc1c .
  ?pc1c rdf:type ?pc1ct; bp3:name ?pc1cn .
  ?pc2 bp3:pathwayComponent ?pc2c .
  ?pc2c rdf:type ?pc2ct; bp3:name ?pc2cn .
}
where {
  ?pax rdf:type ?pt; bp3:name ?pn .
  ?pax bp3:pathwayComponent ?pc1; bp3:pathwayComponent ?pc2 .
  ?pc1 rdf:type ?pc1t; bp3:name ?pc1n .
  ?pc2 rdf:type ?pc2t; bp3:name ?pc2n .
  ?pax bp3:pathwayOrder ?ps1; bp3:pathwayOrder ?ps2 .
  ?ps1 rdf:type ?ps1t . ?ps2 rdf:type ?ps2t .
  ?ps1 bp3:stepProcess ?pc1; bp3:nextStep ?ps2 .
  ?ps2 bp3:stepProcess ?pc2 .
  ?pc1 bp3:pathwayComponent ?pc1c .
  ?pc1c rdf:type ?pc1ct; bp3:name ?pc1cn .
  ?pc2 bp3:pathwayComponent ?pc2c .
  ?pc2c rdf:type ?pc2ct; bp3:name ?pc2cn .
  filter(?pax = <http://www.reactome.org/biopax#Cell_Cycle_Mitotic>)
}

```

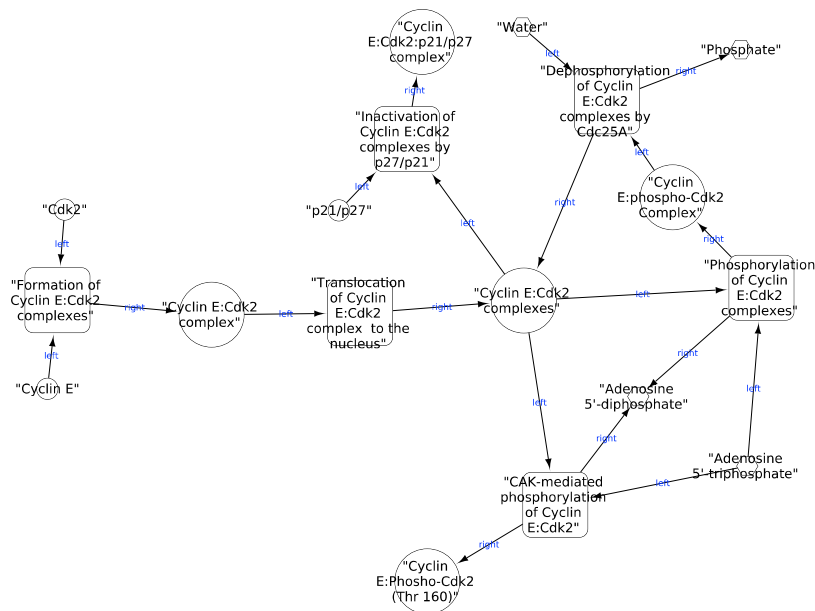


6. Finally, the Cyclin E associated biochemical interactions during G1/S transition are visualized using this query:

```

construct {
  ?pc1 bp3:left ?pc1l; bp3:right ?pc1r .
  ?pc1l rdf:type ?pc1lt; bp3:name ?pc1ln .
  ?pc1r rdf:type ?pc1rt; bp3:name ?pc1rn .
}
where {
  ?pax rdf:type ?pt; bp3:name ?pn .
  ?pax bp3:pathwayComponent ?pc1; bp3:pathwayComponent ?pc2 .
  ?pc1 rdf:type ?pc1t; bp3:name ?pc1n .
  ?pc1 bp3:left ?pc1l; bp3:right ?pc1r .
  ?pc1l rdf:type ?pc1lt; bp3:name ?pc1ln .
  ?pc1r rdf:type ?pc1rt; bp3:name ?pc1rn .
filter(?pax=<http://www.reactome.org/biopax#Cyclin\_E\_associated\_events\_during\_G1\_S\_transition\_>)
}

```



**Visual Legend for BP3**






**Edge Label is displayed as UnPrefixedName**

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**Node Label is displayed as <http://www.biopax.org/release/biopax-level3.owl#name>**

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**Node Shape Mapping**

Node Shape	<a href="http://www.w3.org/1999/02/22-rdf-syntax-ns#type">http://www.w3.org/1999/02/22-rdf-syntax-ns#type</a>
	<a href="http://www.biopax.org/release/biopax-level3.owl#BiochemicalReaction">http://www.biopax.org/release/biopax-level3.owl#BiochemicalReaction</a>
	<a href="http://www.biopax.org/release/biopax-level3.owl#Complex">http://www.biopax.org/release/biopax-level3.owl#Complex</a>
	<a href="http://www.biopax.org/release/biopax-level3.owl#Pathway">http://www.biopax.org/release/biopax-level3.owl#Pathway</a>
	<a href="http://www.biopax.org/release/biopax-level3.owl#PathwayStep">http://www.biopax.org/release/biopax-level3.owl#PathwayStep</a>
	<a href="http://www.biopax.org/release/biopax-level3.owl#PhysicalEntity">http://www.biopax.org/release/biopax-level3.owl#PhysicalEntity</a>
	<a href="http://www.biopax.org/release/biopax-level3.owl#Protein">http://www.biopax.org/release/biopax-level3.owl#Protein</a>
	<a href="http://www.biopax.org/release/biopax-level3.owl#SmallMolecule">http://www.biopax.org/release/biopax-level3.owl#SmallMolecule</a>

**Node Size Mapping**

Node Size	<a href="http://www.w3.org/1999/02/22-rdf-syntax-ns#type">http://www.w3.org/1999/02/22-rdf-syntax-ns#type</a>
<b>60.0</b>	<a href="http://www.biopax.org/release/biopax-level3.owl#BiochemicalReaction">http://www.biopax.org/release/biopax-level3.owl#BiochemicalReaction</a>
<b>30.0</b>	<a href="http://www.biopax.org/release/biopax-level3.owl#Complex">http://www.biopax.org/release/biopax-level3.owl#Complex</a>
<b>20.0</b>	<a href="http://www.biopax.org/release/biopax-level3.owl#PathwayStep">http://www.biopax.org/release/biopax-level3.owl#PathwayStep</a>
<b>10.0</b>	<a href="http://www.biopax.org/release/biopax-level3.owl#PhysicalEntity">http://www.biopax.org/release/biopax-level3.owl#PhysicalEntity</a>
<b>20.0</b>	<a href="http://www.biopax.org/release/biopax-level3.owl#Protein">http://www.biopax.org/release/biopax-level3.owl#Protein</a>
<b>20.0</b>	<a href="http://www.biopax.org/release/biopax-level3.owl#SmallMolecule">http://www.biopax.org/release/biopax-level3.owl#SmallMolecule</a>

**Edge Target Arrow Shape Mapping**

Edge Target Arrow Shape	UnPrefixedName
	nextStep
	pathwayComponent
	pathwayOrder
	stepProcess

Cytoscape Visual Legend for BioPAX Level 3