

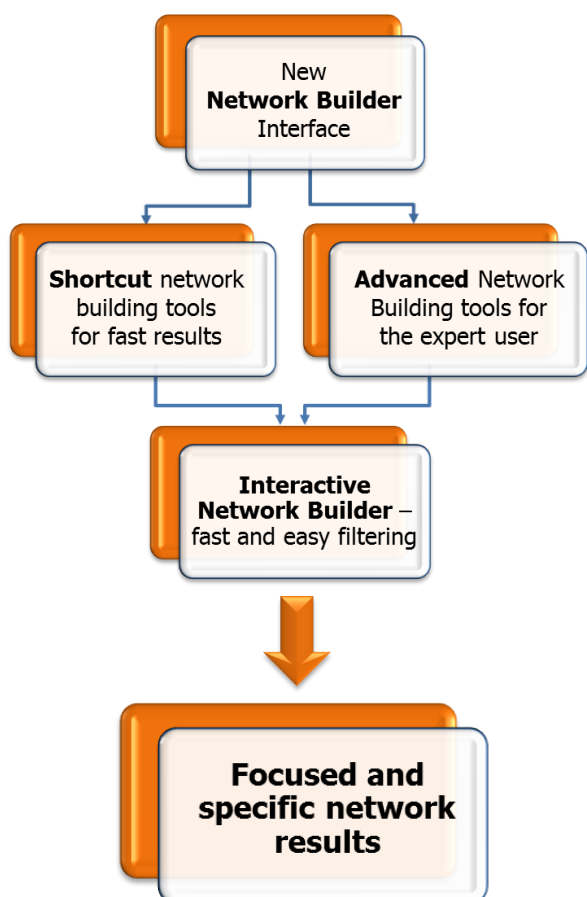
## Pathway Building in Pathway Studio® Web 11.4

### Introduction to Network Builder Basic (Shortcut Version) and the Interactive Network Builder

This document provides instructions for using the Network Builder Basic and the Interactive Network Builder.

Pathway Studio Network Builder makes pathway building fast, easy and intuitive. The interface provides a simple path to build and filter pathways, and short cuts that are designed to satisfy the novice user while still maintaining advanced filter options for the expert user as illustrated below. In addition, the Interactive Network Builder, adds powerful easy-to-use filtering tools to further refine networks, and set confidence levels is included in the Network Builder as an option.

Details on advance filtering in the Network Builder is provided in another support document.



Start your network building activities from the new **Network Builder** interface.

**Shortcut** menu options allow for quick visualization of network results from preset menus.

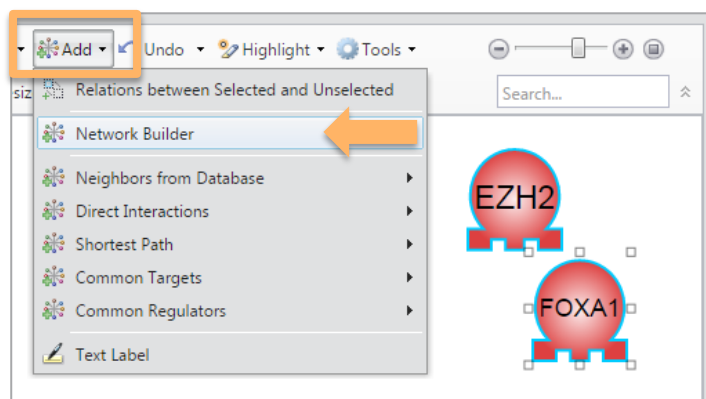
**Advanced** network building tools allow the expert user to apply specific entity and relation filters for more focused and specific results.

The **Interactive Network Builder** is simple-to-use interface for filtering larger networks to produce smaller, more manageable and focused results.

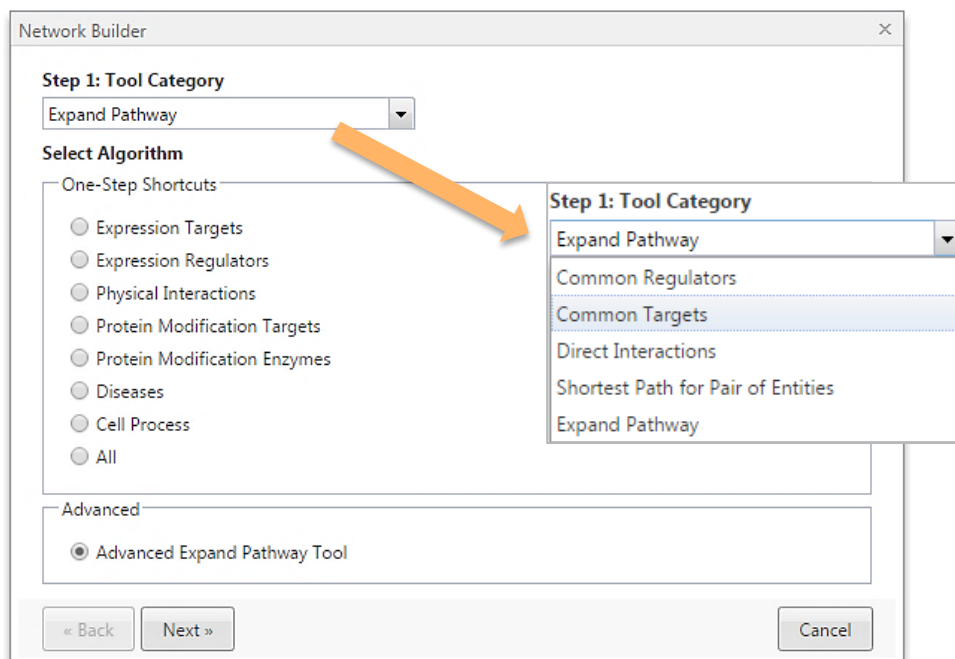
## Network Builder Basic (Shortcut) Version

The Network Builder Basic menus can be accessed from the **Network Builder** dialog found in the horizontal menu bar in the "Create Pathway" tool set.

Search for a gene or disease, then select "Create Pathway" from the menu bar located on the left side of the Pathway Studio page. From the result table that displays from the search, click on an entry or with a pathway view open, select the desired entity/entities to start. Go to the "Add" menu and select "Network Builder."



In the "Network Builder" dialog, first select the type of network you want to build from the Tool Category drop-down menu in Step 1. These are selected based on the research question that is being investigated as each will provide a different set of results.

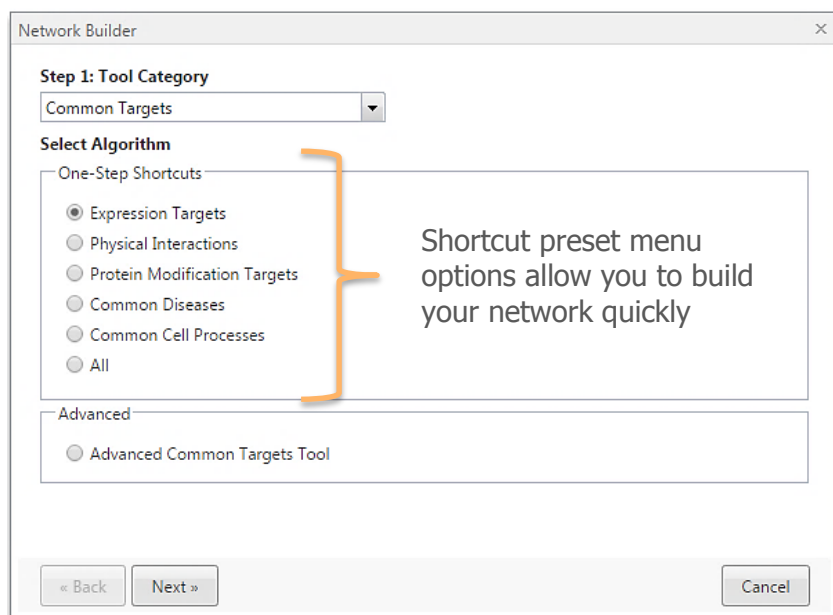


In Step 1, the tool definitions are as follows:

- **Direct Interactions:** find relationships between two or more selected entities
- **Shortest Path for a Pair of Entities:** find relationships between two selected entities, adding entities as needed to form the relationships
- **Expand Pathway:** find entities in the database directly connected to the entity /entities selected

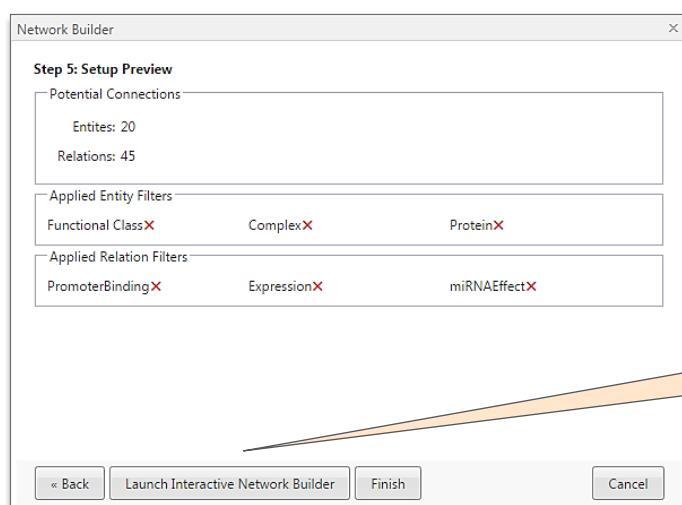
- **Common Targets:** find one or more downstream targets that are regulated by at least two or more of the selected entities
- **Common Regulators:** find one or more upstream regulators that regulate two or more of the selected entities

Once the desired build pathway algorithm is selected in Step 1, the One-Step Shortcuts menu directly below lists options that are available for that algorithm. Chose the desired shortcut and then select "Next." By selecting any one of the One-Step Shortcuts, you will bypass Steps 2-4 and go directly to Step 5 on the Advance Network Builder wizard. The example below illustrates a researcher interested in finding Common Targets to the entity they selected, and these targets are proteins, complexes, and functional classes related to expression, promoter binding, and miRNA effects. (see Appendix 1)



**Appendix One** lists definitions of of each shortcut option, including entity and relation selection, directionality and minimum limits where applicable.

Next, Step 5 Setup Preview dialog appears (you have bypassed Steps 2, 3 &4). This displays the applied entity and relation filters, each followed by a red "x." If you want to further refine your network at this point by removing an entity or relation category, select the "x" to remove that category. [Note: once removed, the only way to add the entity or relation type back is to start your network building workflow from the beginning.]



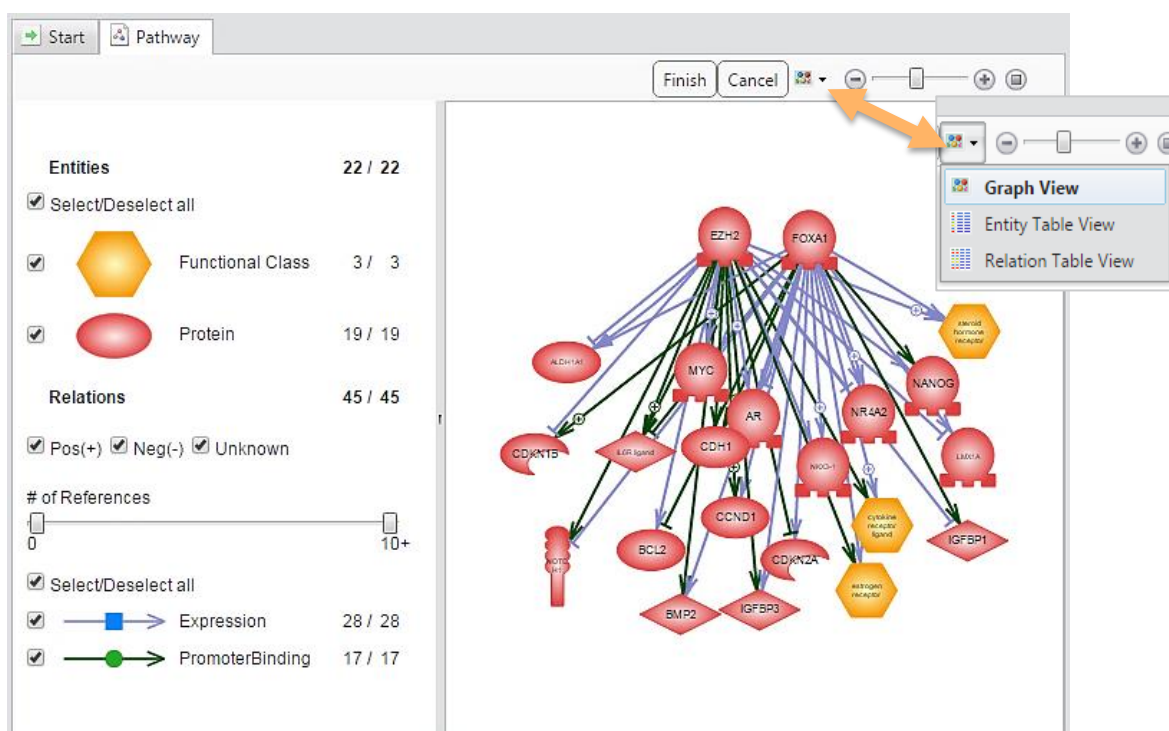
Interactive Network Builder is discussed below.

At this point you can select "Finish" to see the resultant network or continue to Interactive Network Builder to further refine the network.

### The Interactive Network Builder

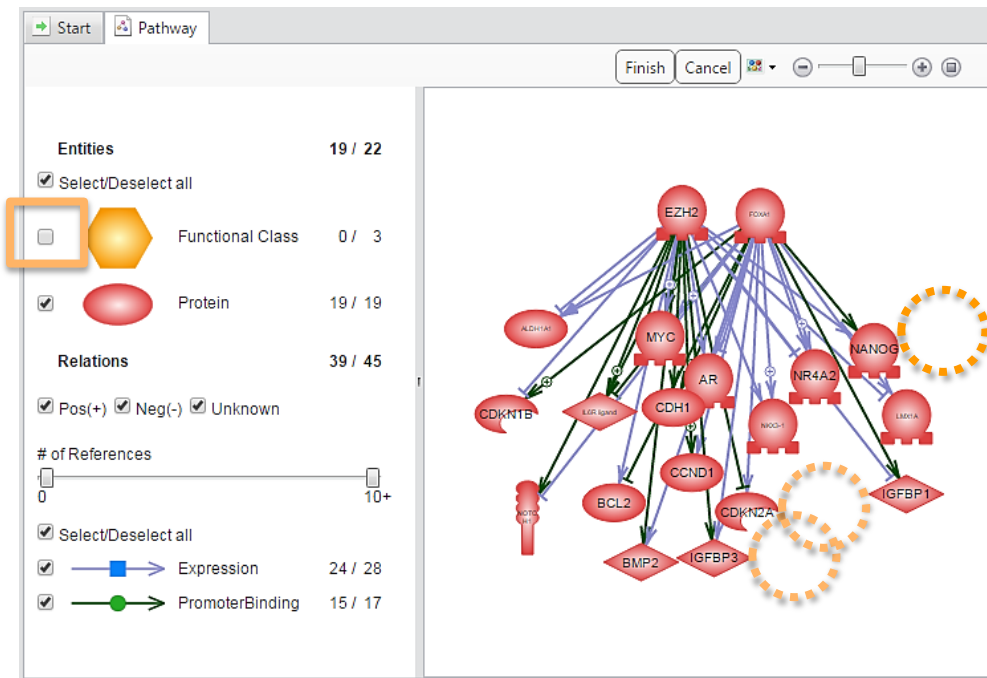
From the workflow above you can alternatively,select "Launch Interactive Network Builder." This will allow you to see statistics of your network for entities and relations. It will allow you to filter your network by entity type, relation type, relation effect (positive, negative, unknown) and by the reference count for the relations.

The **Interactive Network Builder** is a powerful easy-to-use dialog to facilitate reducing larger networks to smaller more precise results.

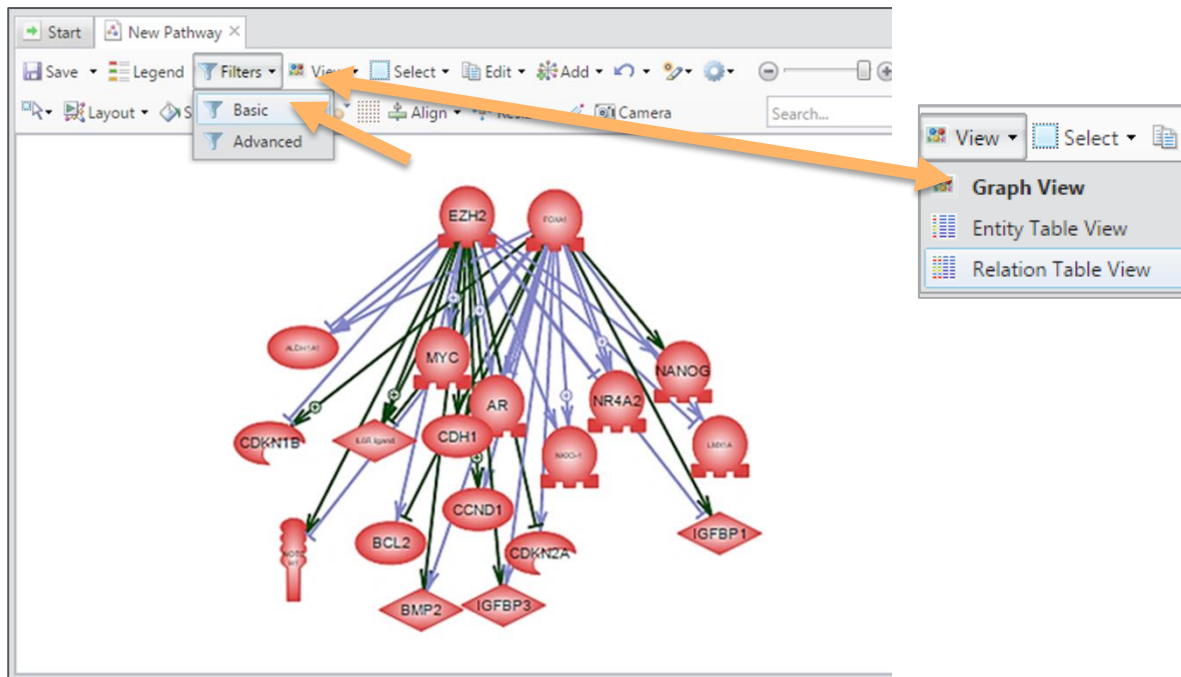


Note: If the network is larger than 200 entities, the graph view will not display on the right. Instead the Entity Table View will display. The checkbox filters on the left are still available.

In the example below, the Functional Class entity type was deselected (uncheck box). This removes the functional class entities from the resultant network as indicated with the dotted circles in the image below.

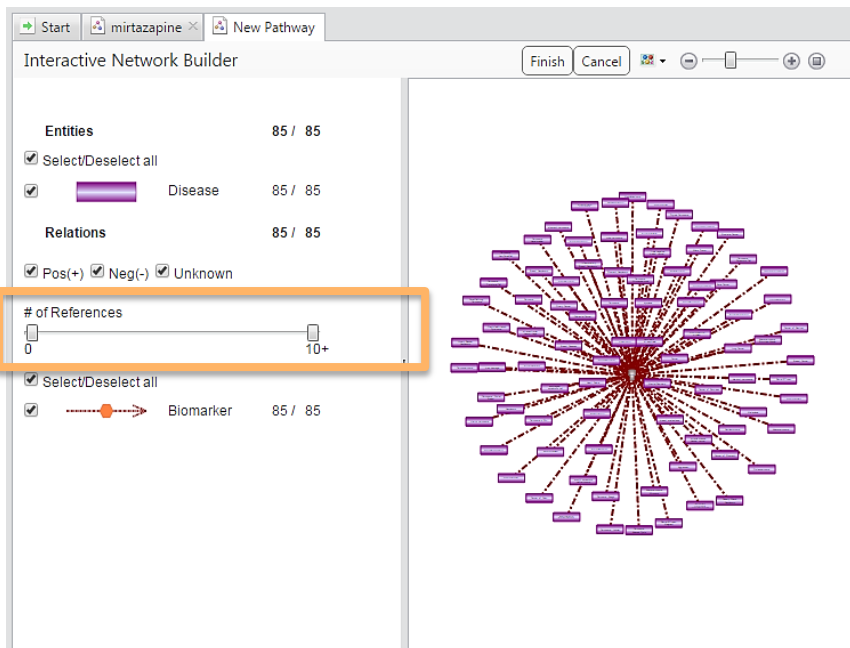


After using the Interactive Network Builder to apply the desired filters, select the “Finish” button to see the resultant network. If your network is still large and you would like to apply additional filters, you can access the Interactive Network Builder again by selecting Filters > Basic from the graph view.

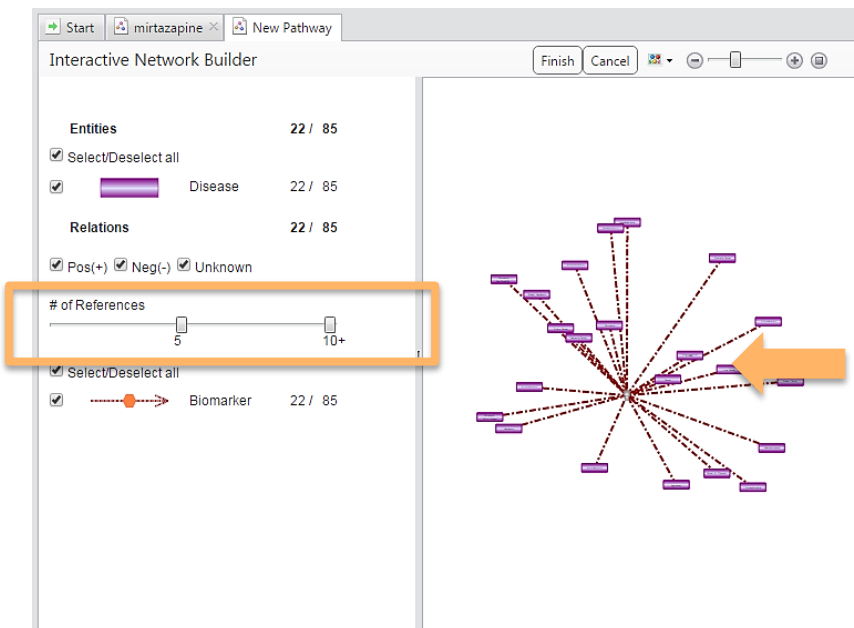


Network results can always be viewed in tabular form by selecting either “Entity Table View” or “Relation Table View” from the View menu.

In the Interactive Network Builder example shown in the following two figures a relation reference count filter of  $\geq 5$  references is applied to a network.

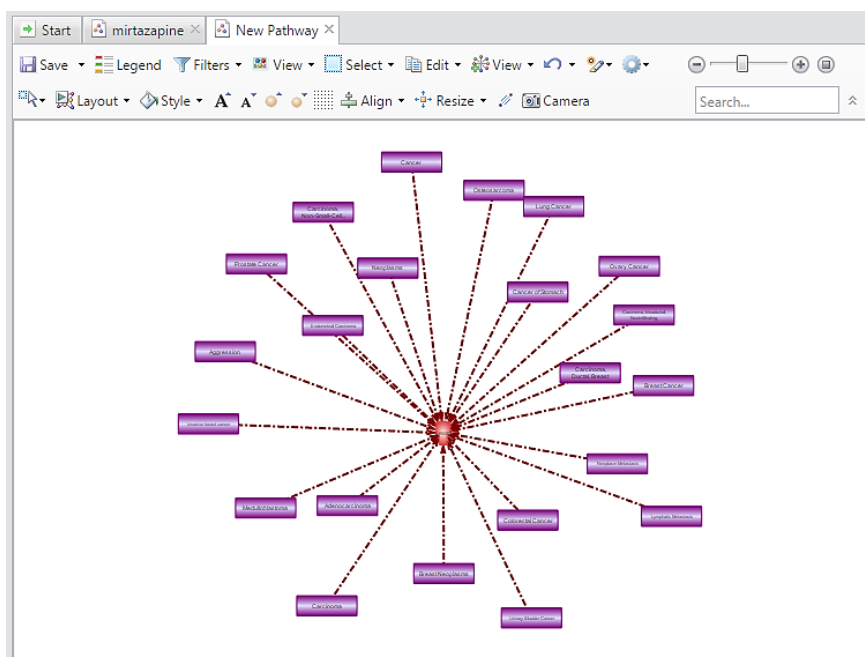


By moving the scroll bar for # of References to five, only relations with a reference of five or above remain.



The confidence level of the network is increased by including only relations with higher numbers of literature references.

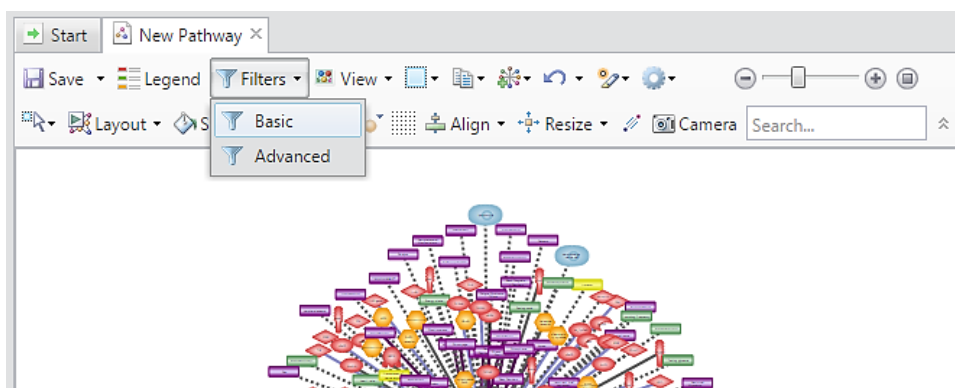
Select "Finish" to view the resultant network in the graph view.



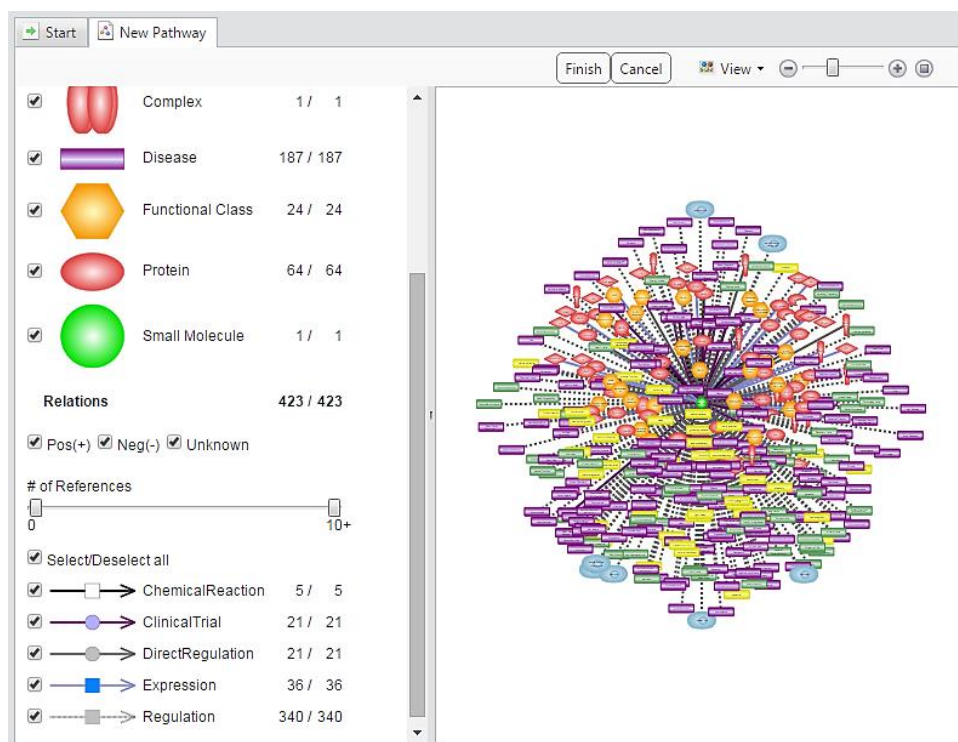
Once a network is completed, additional subtractive filters can be applied to reduce the network to more specific results. Alternatively, a subset of the network can be selected for further analysis.

### Subtractive Filter - Basic

To apply a subtractive filter to a network, in the graph view select Filter > Basic.



This will open the Interactive Network Builder. From here you can select to remove any entity or relation type, remove relations based on effect (positive, negative, or unknown), or filter relations based on the number of literature references. Simply uncheck the box to remove a specific category, or move the scroll bar to set the threshold for references for all relation.



When done, select the "Finish" button to see the resultant network. Be sure to save your results in your Project Folder for future use.

Provide your feedback on this and other issue by contacting [pathway@elsevier.com](mailto:pathway@elsevier.com)



**Appendix One: Pathway building shortcut definitions.**

Category	Sub-Category	Relationship(s)	Entity(ies)	Direction	Minimum Limits
<b>Neighbors from DB</b>	Expression Targets	Expression, PromoterBinding, miRNAEffect	Proteins, Complexes, Functional Classes	Downstream	NA
	Expression Regulators	Expression, PromoterBinding, miRNAEffect	Proteins, Complexes, Functional Classes, small molecules	Upstream	NA
	Physical Interactions	DirectRegulation, Binding	Proteins, Complexes, Functional Classes, small molecules	All	NA
	Protein Modification Targets	ProtModification	Proteins, Complexes, Functional Classes	Downstream	NA
	Protein Modification Enzymes	ProtModification	Proteins, Complexes, Functional Classes	Upstream	NA
	Diseases	Biomarker, ClinicalTrial, GeneticChange, QuantitiveChange, Regulation, StateChange	Diseases	All	NA
	Cell Processes	ClinicalTrials, Regulation	Cell Processes	Downstream	NA
	All	All	All	All	NA
	<b>Direct Interactions</b>	Physical Interactions	DirectRegulation, Binding	Proteins, Complexes, Functional Classes	All
Expression Regulation		Expression, PromoterBinding, miRNAEffect	Proteins, Complexes, Functional Classes	All	NA
Protein Modification		ProtModification	Proteins, Complexes, Functional Classes	All	NA
All		All	All	All	NA
<b>Shortest Path</b>	Physical Interactions	DirectRegulation, Binding	Proteins, Complexes, Functional Classes	All	NA
	Expression Regulation	Expression, PromoterBinding, miRNAEffect	Proteins, Complexes, Functional Classes	All	NA
	Protein Modification	ProtModification	Proteins, Complexes, Functional Classes	All	NA
	All	DirectRegulation, Binding, Expression, PromoterBinding, miRNAEffect, ProtModification, Chemical Reaction, MolSythesis, MolTransport	Proteins, Complexes, Functional Classes, small molecule	All	NA
<b>Common Targets</b>	Expression Targets	Expression, PromoterBinding, miRNAEffect	Proteins, Complexes, Functional Classes	Downstream	2
	Physical Interactions	DirectRegulation, Binding	Proteins, Complexes, Functional Classes	Downstream	2
	Protein Modification Targets	ProtModification	Proteins, Complexes, Functional Classes	Downstream	2

	Common Diseases	Regulation, Clinical Trial	Diseases	Downstream	2
	Common Cell Processes	Regulation, Clinical Trial	Cell Processes	Downstream	2
	All	All	All	Downstream	2
<b>Common Regulators</b>	Expression Regulators	Expression, PromoterBinding, miRNAEffect	Proteins, Complexes, Functional Classes	Upstream	2
	Physical Interactions	DirectRegulation, Binding	Proteins, Complexes, Functional Classes	Upstream	2
	Protein Modification Enzymes	ProtModification	Proteins, Complexes, Functional Classes	Upstream	2
	Common Diseases	Biomarker, GeneticChange, QuantitiveChange, Regulation, StateChange	Diseases	Upstream	2
	All	All	All	Upstream	2