Ingenuity Pathways Analysis (IPA)

Using the Ingenuity Knowledgebase understand genes and disease

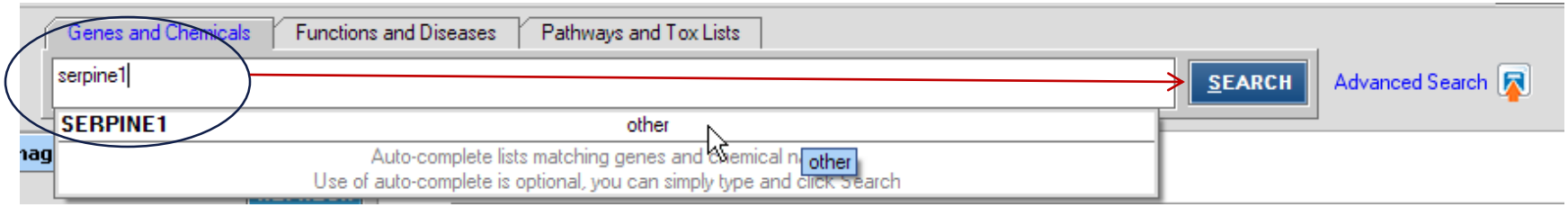
Some Questions IPA Can Answer

- What does my gene/protein/compound of interest do?
- What other compounds bind my target of interest?
- If I inhibit or activate a target protein, what cellular processes are likely to be affected that are beneficial or lead to adverse side effects?
- What are the upstream activators or downstream targets of my protein of interest?
- What can my microarray data tell me about changes in cellular functions, pathways, and toxicology?
- What genes are implicated in my disease of interest?
- What proteins might act as good biomarkers for drug efficacy?

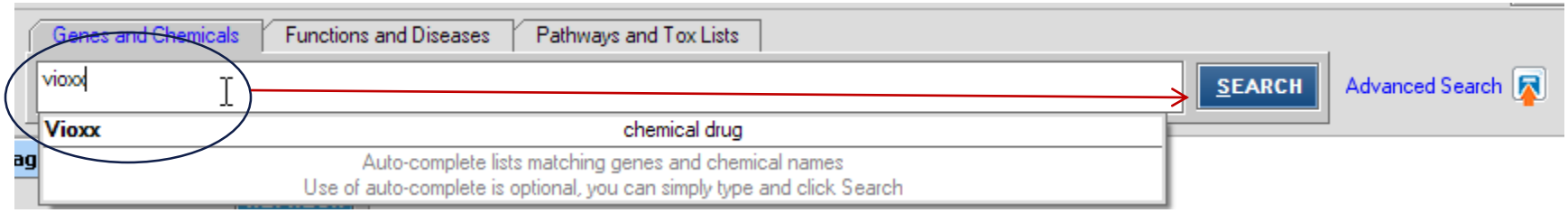
Basic gene and chemical search

Finding curated information about a gene/gene-product or drug, reagent or biochemical

Enter a gene or protein name in the search box



Enter a drug or chemical name in the search box



Search Basics, Continued

More than one search term can be entered at once

- Comma delimited
- Copy a column of IDs from MS Excel and past directly into the search box

Search terms can be any IPA supported identifier.

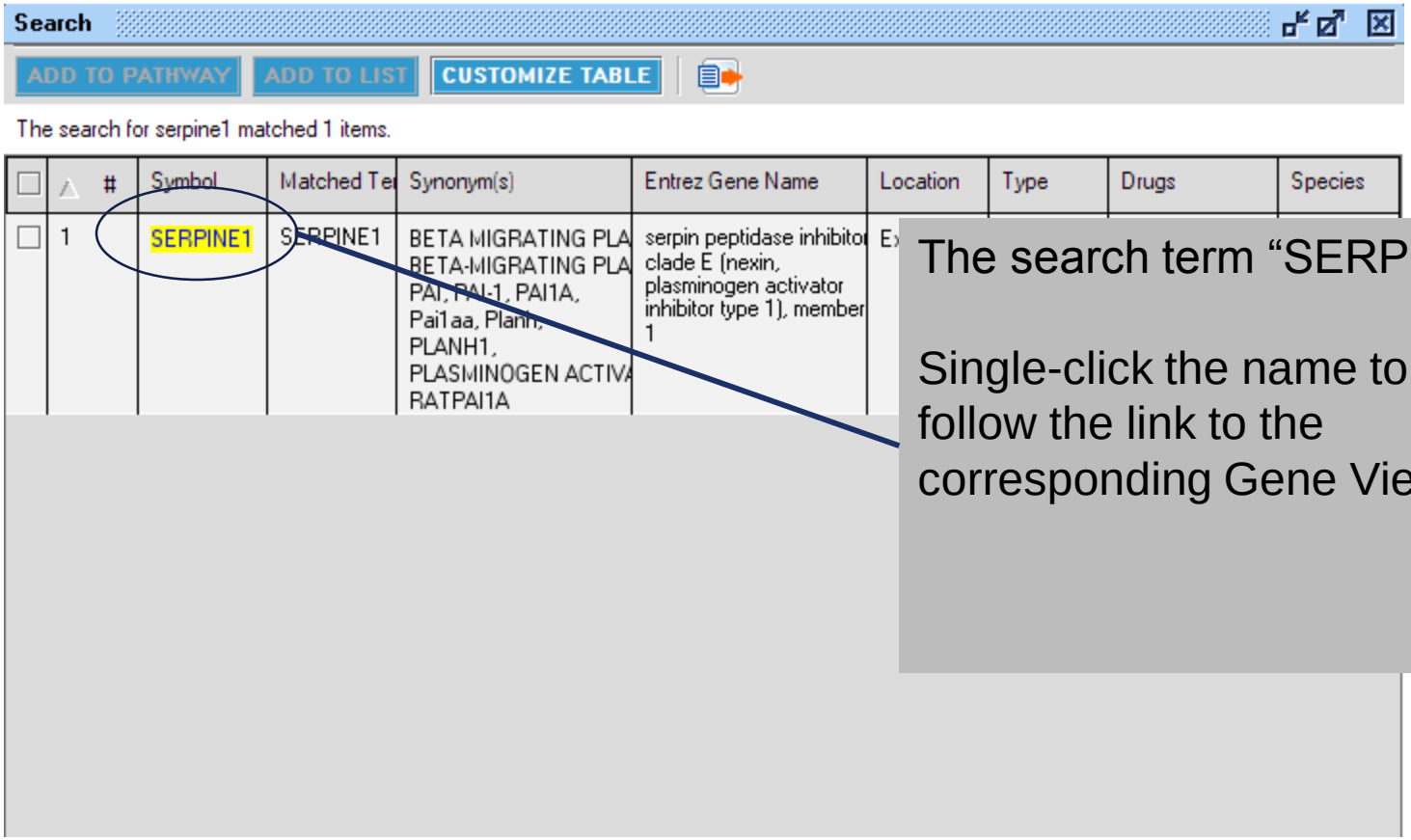
- Genbank, SwissProt, Affy probe ID, RefSeq, etc.
- See Help Manuel, “Data Upload Definitions” for complete list

Wildcard symbol should be used with searching with a partial gene name

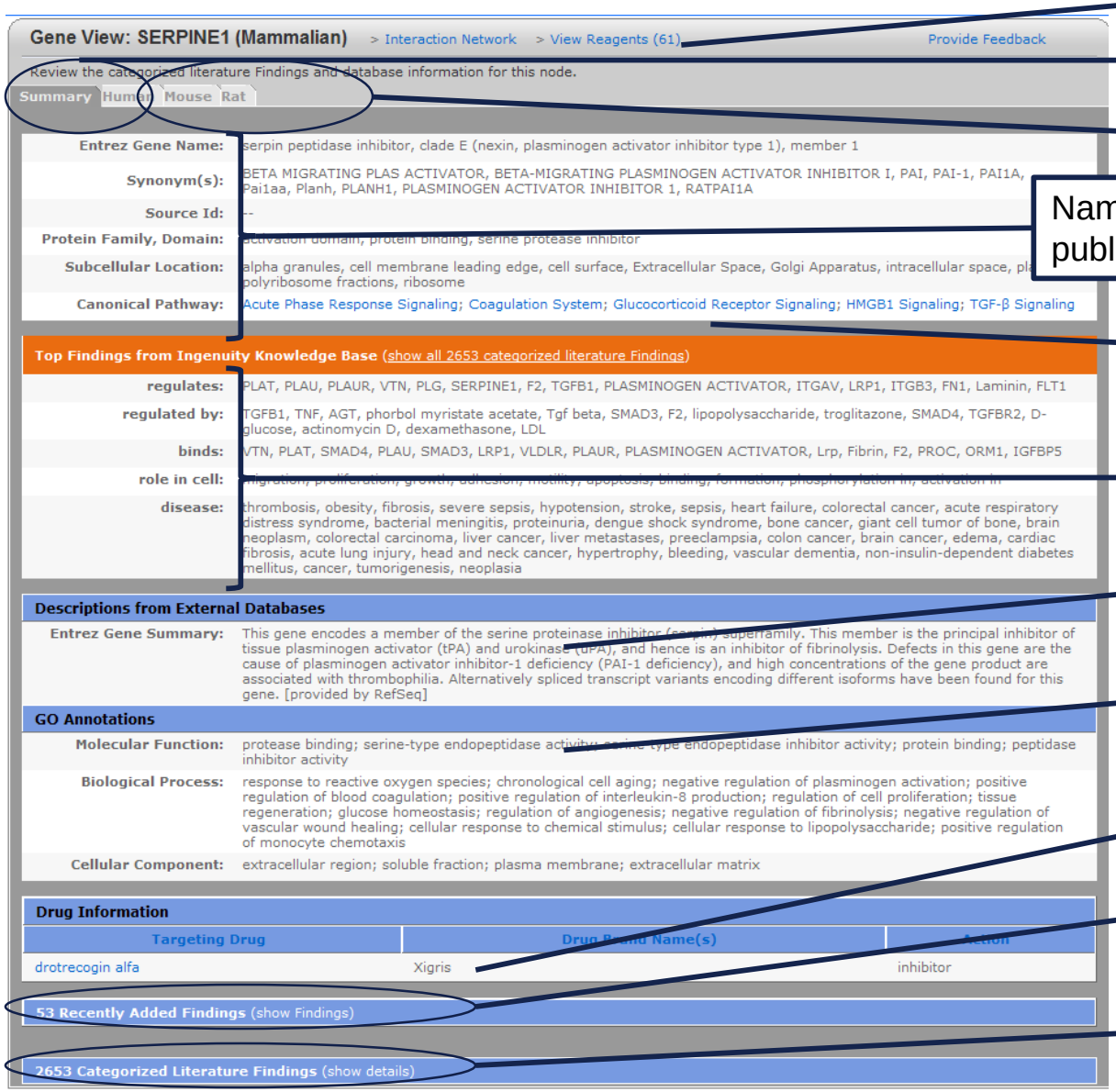
- When searching or expecting protein isoforms or related IDs, append a wildcard “*”
- Example: “SERPINE*” will find all gene and protein names that begin with SERPINE

List Result

Search results return as a list of entities that have a name or synonym that closely matches the search term



Gene View Page



Reagent View

Summary tab, partial view

Species specific information

Name and physical characteristics from public domain

Links to IPA Canonical Pathways

Summary of Ingenuity curated findings

Description

Gene Ontology information from public domain

Drug Information

Recently Added Findings

Link to full content

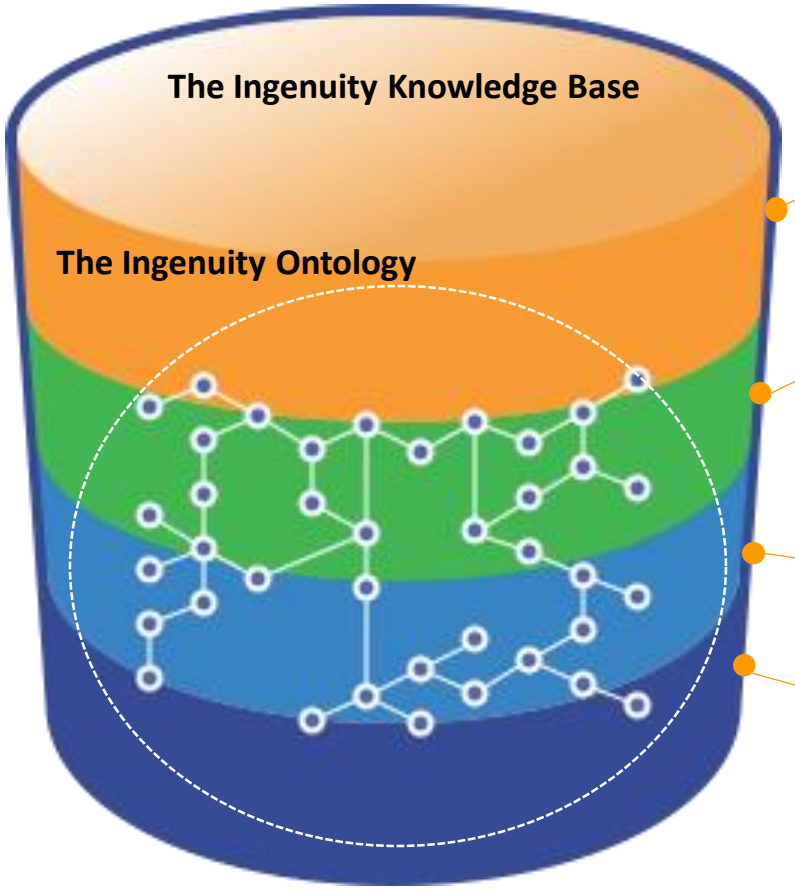
Curated Literature Findings

Header Links for navigation to point of interest.

Reference can be viewed by clicking the plus-sign, or “Expand All”.

Pubmed ID links to abstract.

The Ingenuity® Knowledge Base



Ingenuity Findings

Ingenuity® Expert Findings – Manually curated Findings that are reviewed, from the full-text, rich with contextual details, and are derived from top journals.

Ingenuity® ExpertAssist Findings – Automated text Findings that are reviewed, from abstracts, timely, and cover a broad range of publications.

Ingenuity Modeled Knowledge

Ingenuity® Expert Knowledge – Content we model such as pathways, toxicity lists, etc.

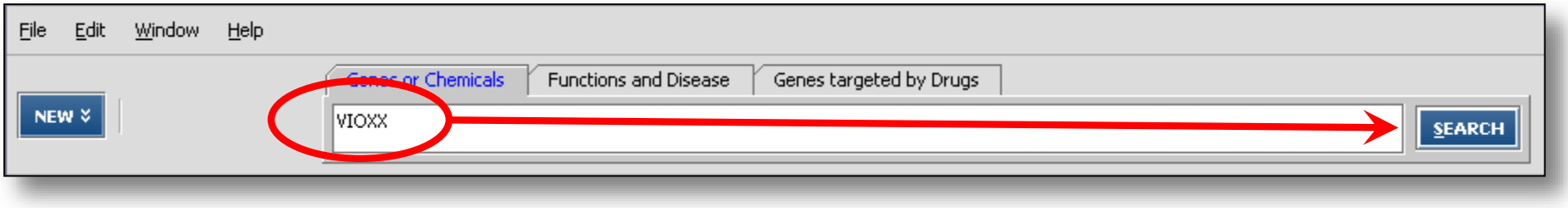
Ingenuity® Supported Third Party Information – Content areas include Protein-Protein, miRNA, biomarker, clinical trial information, and others

Ingenuity® Supported Third Party Information

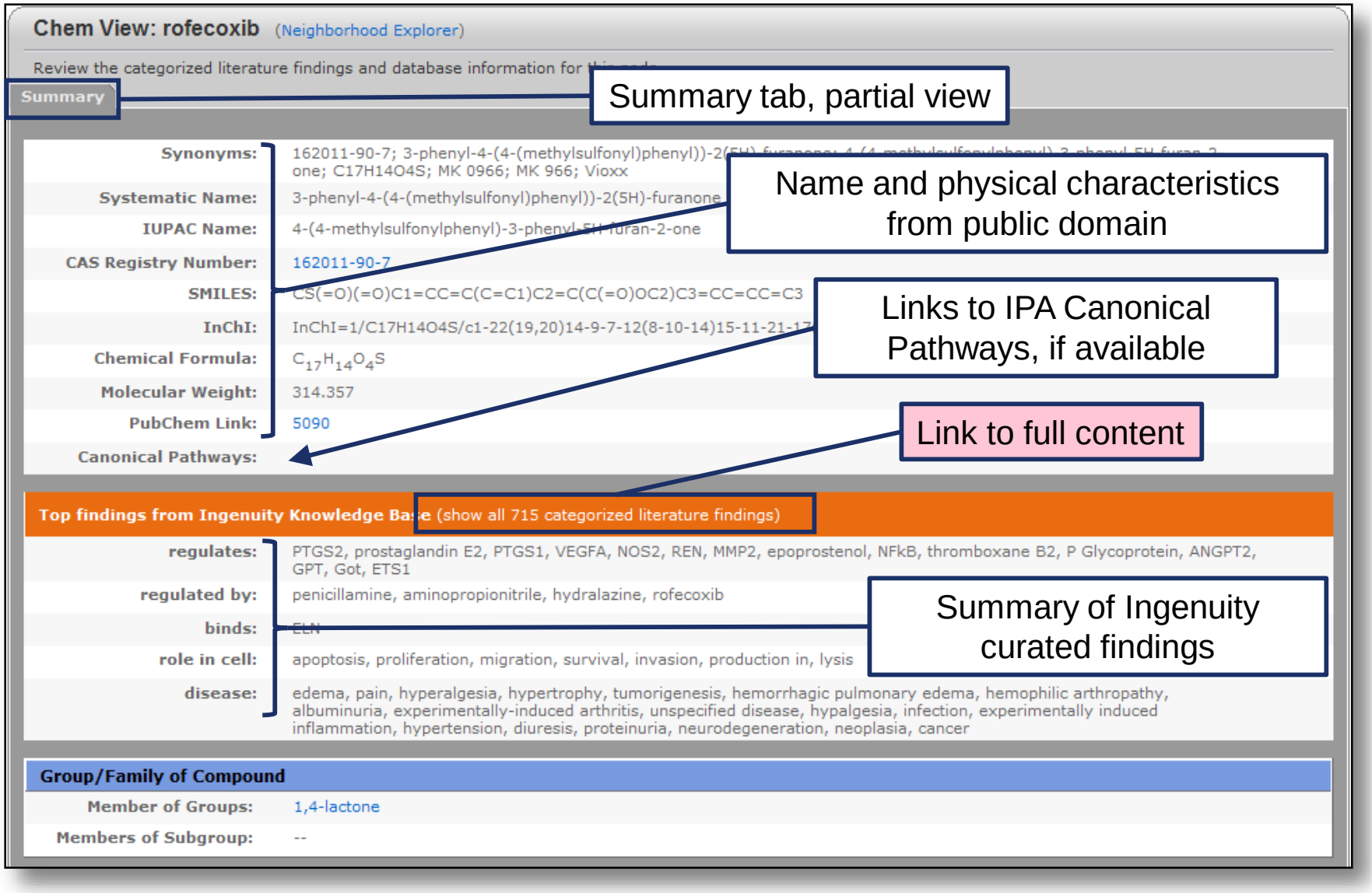
- Synonyms, Protein Family, Domains
  GO, Entrez Gene, Pfam
- Tissue and Biofluid Expression & Location
  GNF, Plasma Proteome
- Molecular Interactions
  BIND, DIP, MIPS, IntAct, Biogrid, MINT, Cognia, etc.
- miRNA/mRNA target databases
  TarBase, Argonaut 2
- Gene to Disease Associations
  OMIM, GWAS databases
- Exploratory Clinical Biomarkers
- Clinical Trial information
  clinical trials.gov

Search Basics

- Enter a drug or chemical name in the search box



Chem View Page



Chem View Continued

If the chemical is a drug, there will be additional information such as manufacturer, clinical trail status, target(s), and action

Drug Information

Brand Name(s):	Vioxx
Manufacturer(s):	MERCK
Therapeutic Categories:	non-narcotic analgesic; NSAID

Indication	FDA Approval Status	Trial Status	Clinical Trial Sponsor(s)	NCT#	Last Updated
malignant tumor of stomach	Phase III	Active, not recruiting	Chinese University of Hong Kong	NCT00164892	2005-11-16
osteoarthritis	Phase III	Completed	Novartis	NCT00637949	2008-03-17
brain tumor	Phase I	Terminated	M.D. Anderson Cancer Center	NCT00038389	2005-06-23
rheumatoid arthritis	Withdrawn	--			
osteoarthritis	Phase III	Completed	Novartis	NCT00637949	2008-03-17
colorectal cancer	Phase III	Active, not recruiting	Cancer Research Campaign Clinical Trials Centre	NCT00031863	2007-12-15
dysmenorrhea	Withdrawn	--			
prostatic carcinoma	Phase III	Completed	Merck	NCT00060476	2008-07-31
glioma	Phase I	Terminated	M.D. Anderson Cancer Center	NCT00038389	2005-06-23
prostate cancer	Phase III	Completed	Merck	NCT00060476	2008-07-31
malignant tumor of stomach	Phase III	Active, not recruiting	Chinese University of Hong Kong	NCT00164892	2005-11-16
pain	Phase II	Completed	National Institute of Dental and Craniofacial Research (NIDCR)	NCT00026819	2006-07-10

Target	Action
PTGS2	inhibitor

715 Categorized Literature Findings (show details)

Summary

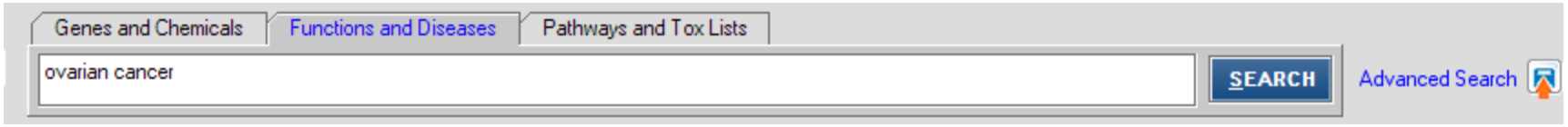
- IPA Search retrieves a wealth of experimental evidence for genes and proteins on the Gene View page, and Drug and Chemicals on the Chem View page.
- Gene and Chem pages display information that is explicitly known about a gene or molecule; there is no inferred or hypothetical information (this is done through custom pathway building).
- Gene and Chem View information is based primarily on literature findings taken from the full-text of journal articles but may come from other defined sources with references.

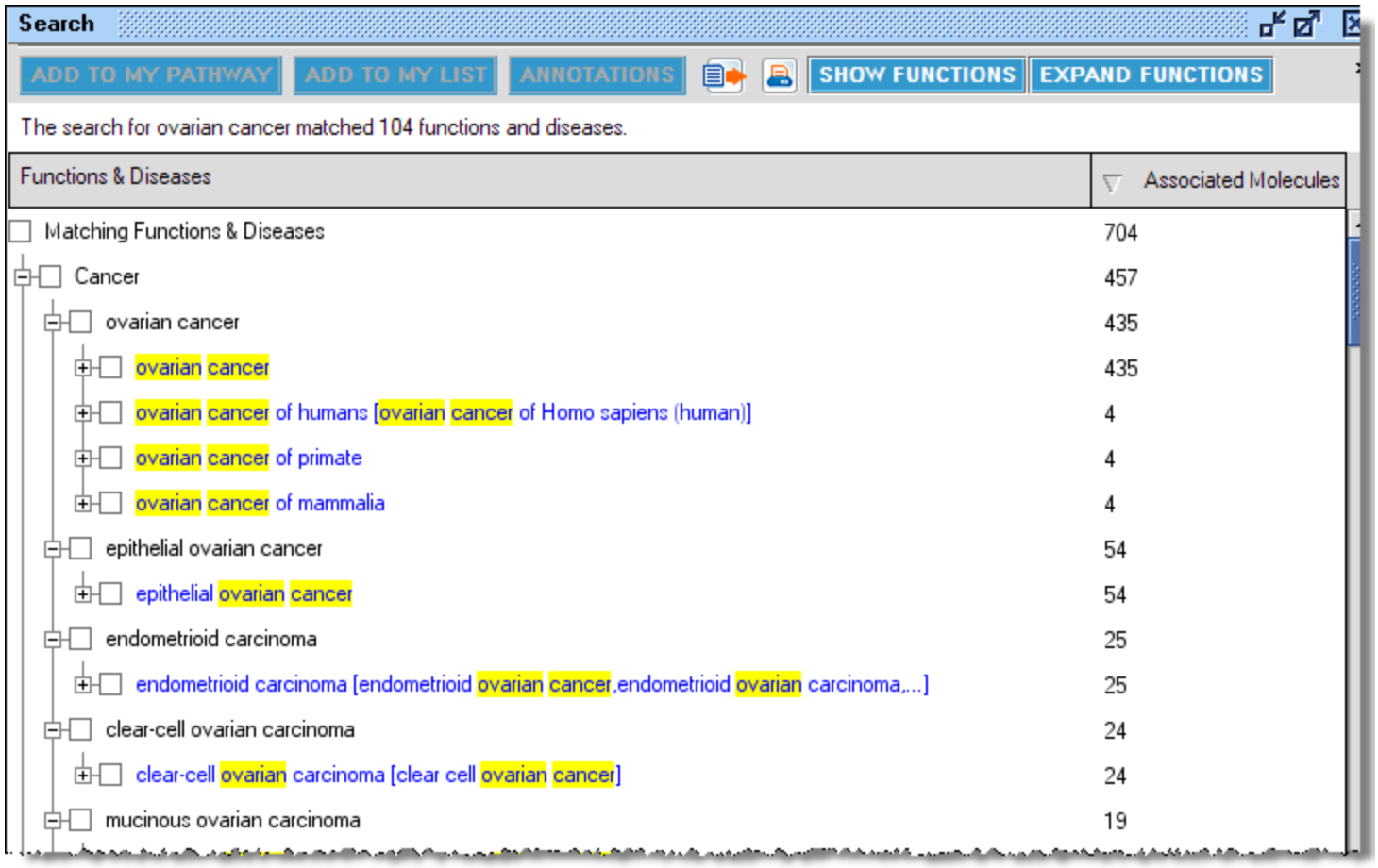
Function & Disease to Gene search

Finding gene and chemical entities associated with biological functions, processes, and diseases

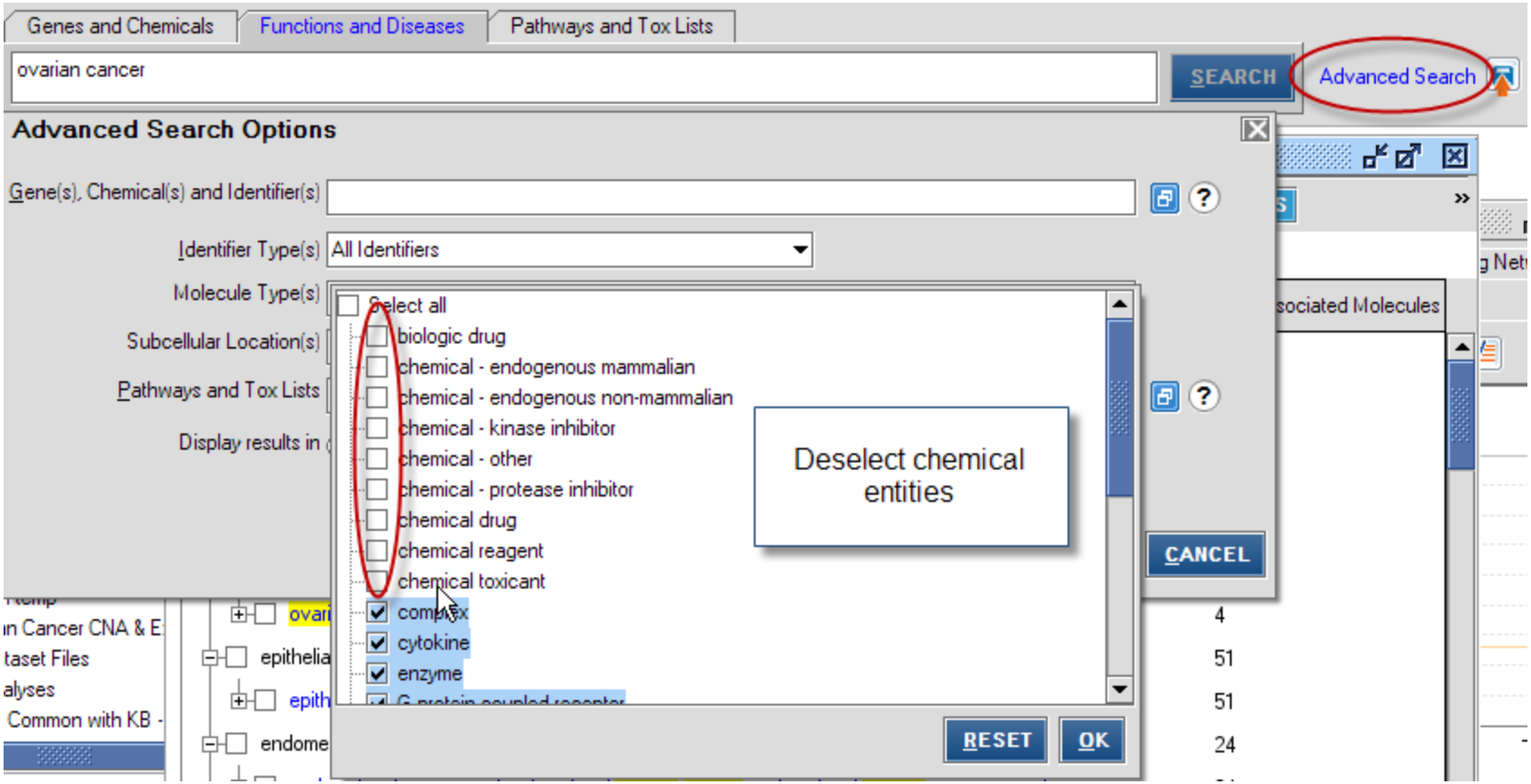
Function/Disease Search and Results

One can also find molecules (gene/chemicals) associated with a biological process or disease. Results are listed in a tree or list format.



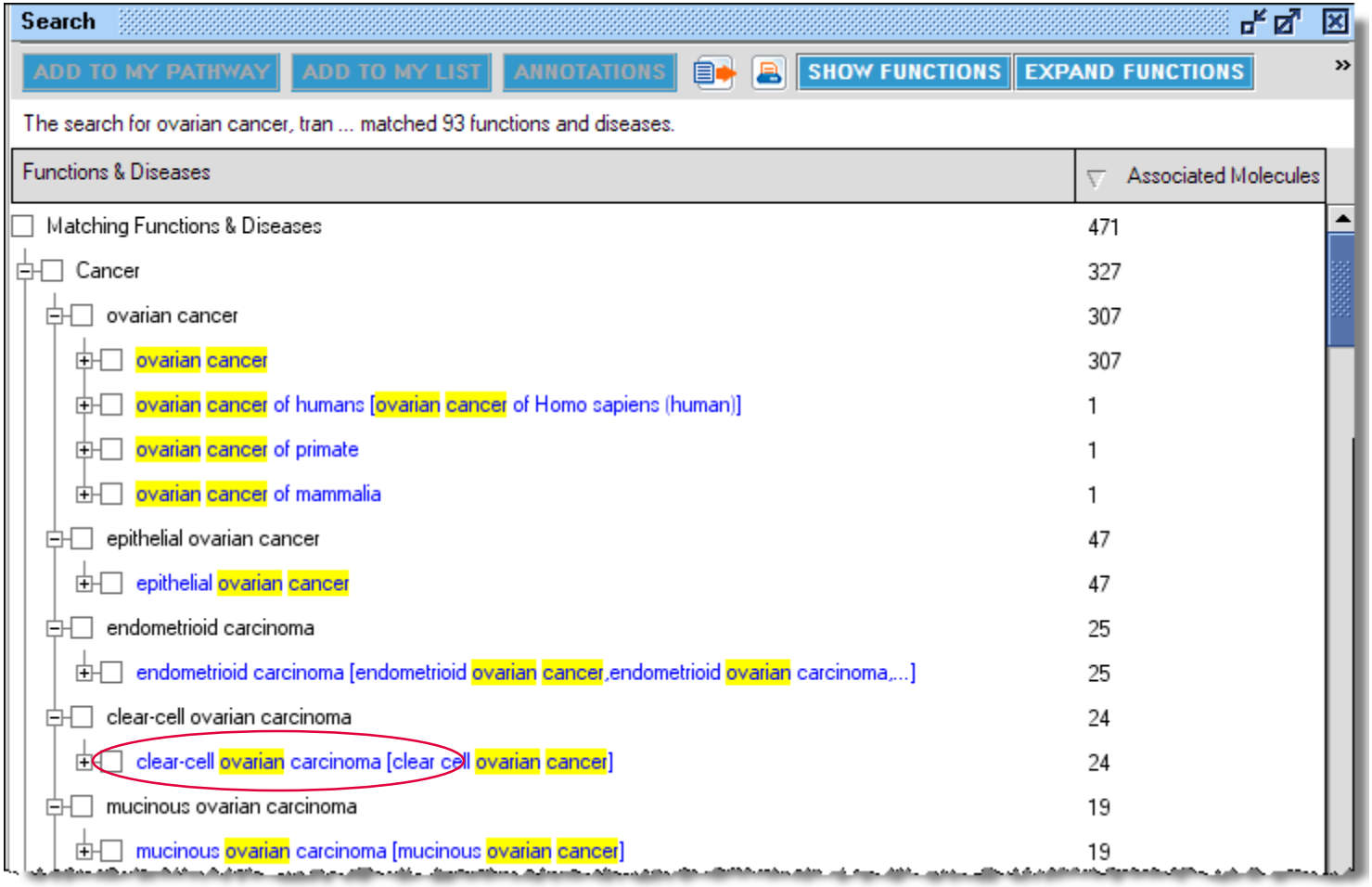


Limit Search to Exclude Chemical Entities using Advanced Search

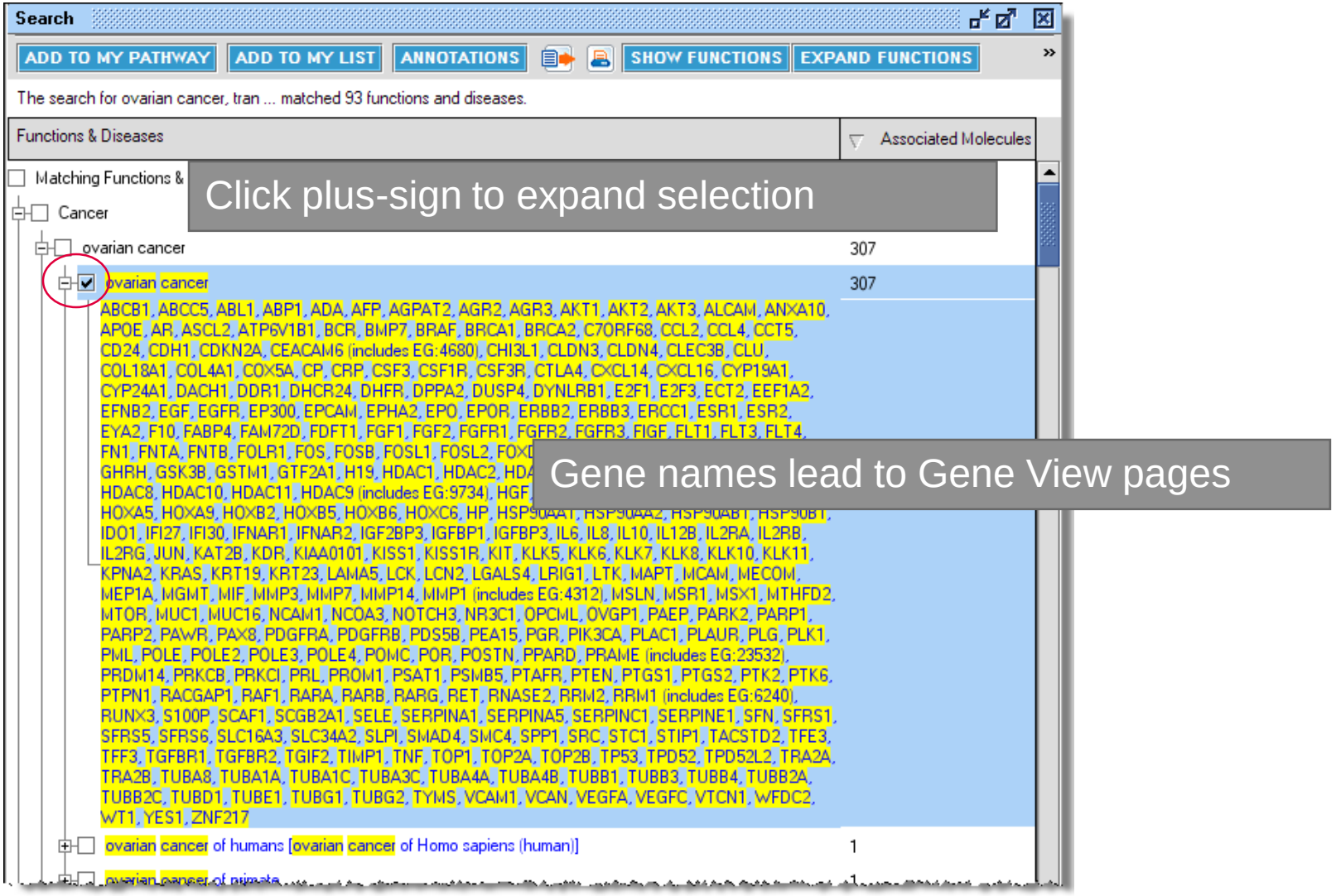


Effect on Function and Findings

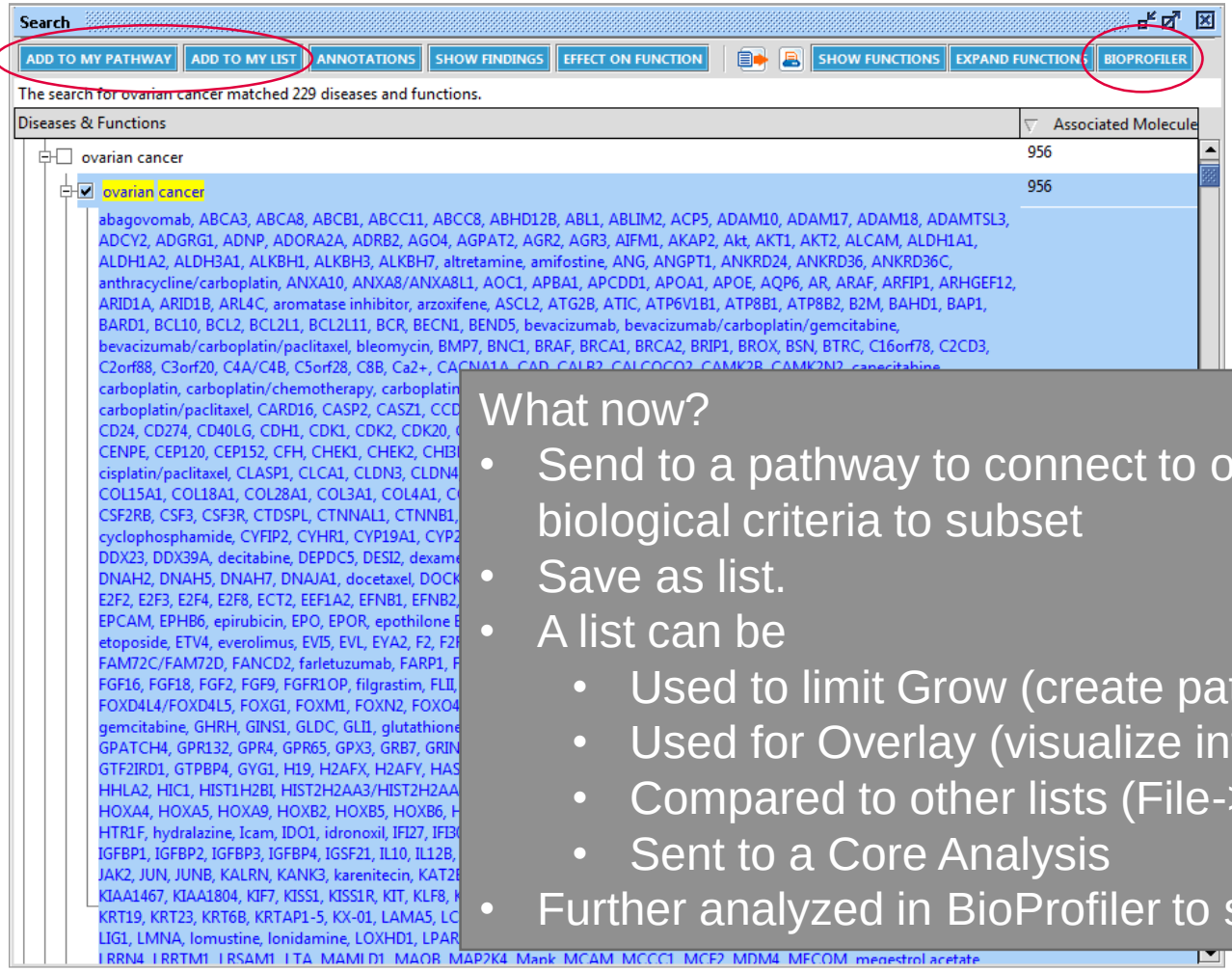
Clicking the function text to see the effect-on-function and then clicking to view findings works well there are a small number of results.



Gene/Chemical Names Link to View Pages



Function and Disease Results



What now?

- Send to a pathway to connect to other genes or overlay biological criteria to subset
- Save as list.
- A list can be
  - Used to limit Grow (create pathway to these genes)
  - Used for Overlay (visualize intersections)
  - Compared to other lists (File->New->Compare)
  - Sent to a Core Analysis
- Further analyzed in BioProfiler to subset

Advanced Analytics

Causal Networks

BioProfiler

Advanced Analytics requires an additional subscription fee

Questions BioProfiler Can Answer

- Which genes when [increased] in activity [increase] [COPD]?
- Which genes when [decreased] in activity [increase] [liver cholestasis]? What types of [genetic] evidence support this?
- Which genes are potential [diagnosis OR prognosis] biomarkers of [breast cancer] and are [upregulated] in breast cancer?
- Which genes are known to both [affect OR increase] [colorectal cancer AND obesity]?

Questions BioProfiler Can Answer

Targets of toxicity:

- Which genes when [decreased] in activity [increase] [liver cholestasis]? What types of [genetic] evidence support this?

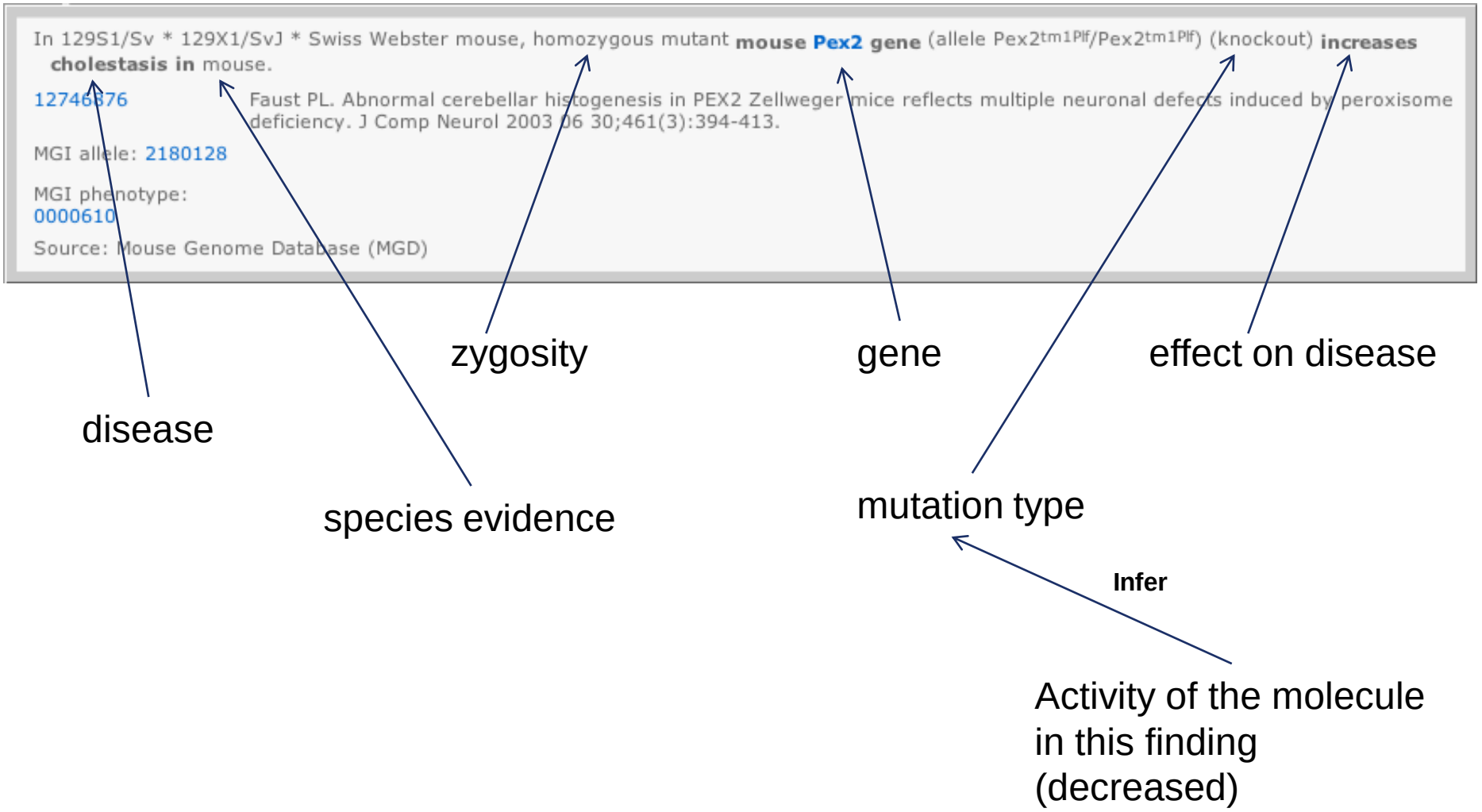
Target discovery:

- What [heterozygous knockouts] in [mouse] can [decrease] [asthma]?
- Which drugs or which targets have been in late stage clinical trials or approved to decrease [diabetes]?

Biomarker research:

- Which genes are potential [diagnosis OR prognosis] biomarkers of [breast cancer] and are [upregulated] in breast cancer?

BioProfiler enables precise filtering on the “components” of Ingenuity Findings



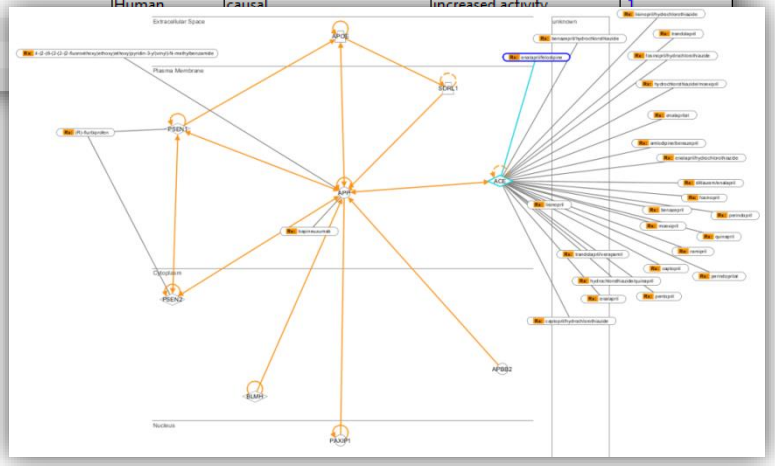
BioProfiler: quickly profile a disease, phenotype, or function

Identify genes known to be causally relevant as potential targets or identify targets of toxicity, associated known drugs, biomarkers and pathways

BioProfiler

ADD TO MY PATHWAY | ADD TO MY LIST

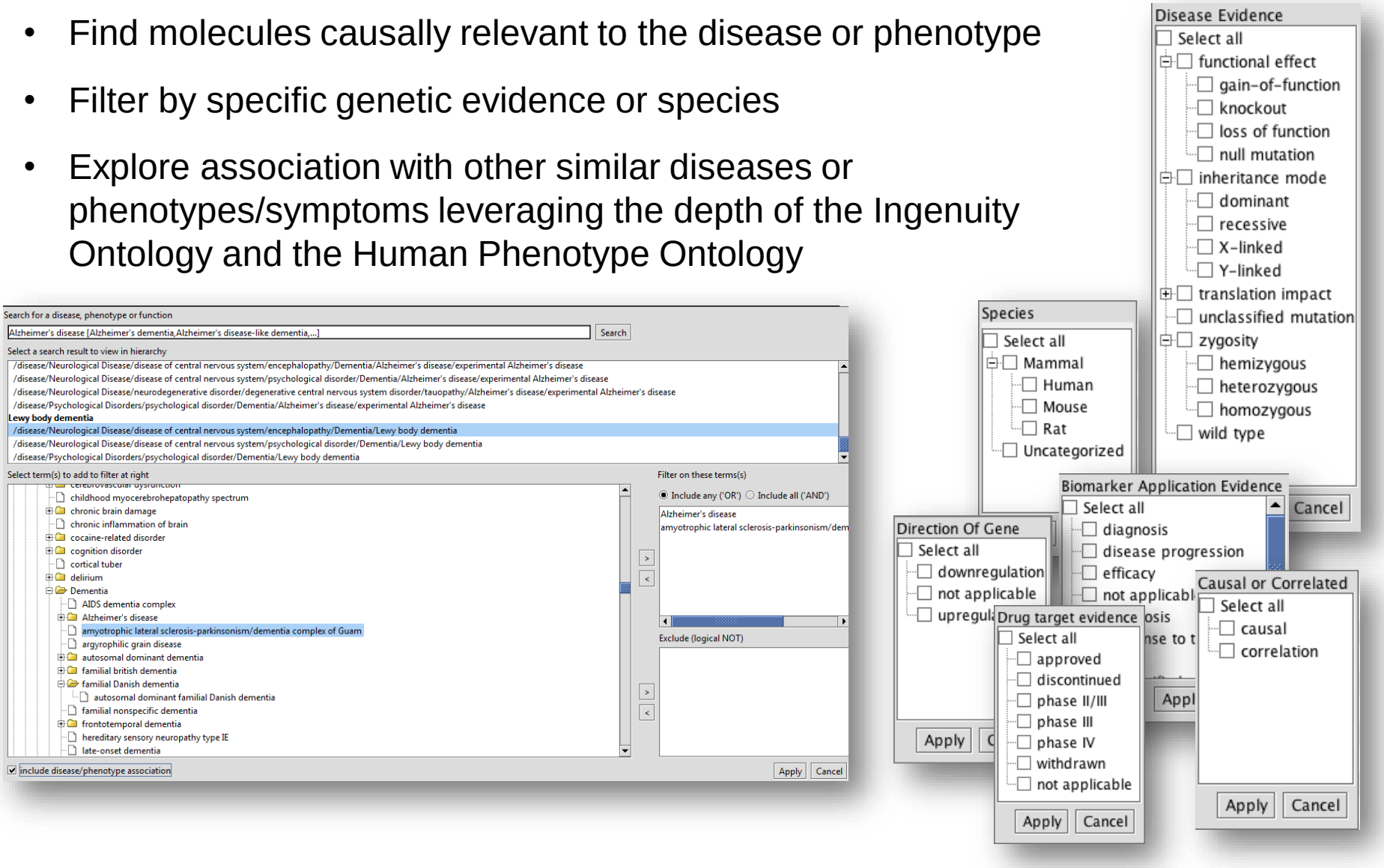
Molecule			Disease & Evidence						Add column(s)
Symbol	Molecule Type	Disease ...	Disease	Mut...	Effect on Disease/Function	Spe...	Causal or Correlated	Molecule Activity	Findings
ACE	peptidase	219	Alzheimer's disease	wild type	increases	Human	causal	increased activity	1
APBB2	other	55	Alzheimer's disease; late-onset Al ...	wild type	increases	Human	causal	increased activity	1
APOE	transporter	920	Alzheimer's disease	wild type	increases	Human	causal	increased activity	1
APP	other	1134	Alzheimer's disease	wild type	increases	Human	causal	increased activity	2
BLMH	peptidase	54	Alzheimer's disease	wild type	increases	Human	causal	increased activity	1
PAXIP1	other	63	Alzheimer's disease	wild type	increases	Human	causal	increased activity	1
PSEN1	peptidase	585	Alzheimer's disease	wild type	increases				
PSEN2	peptidase	277	Alzheimer's disease	wild type	increases				
SORL1	transporter	49	Alzheimer's disease	wild type	increases				



- Filter down to genes known to be causally associated with Alzheimer's
- Which genes when decreased in activity increase liver cholestasis?
- What types of genetic evidence support this?

BioProfiler: Find, Filter and Explore

- Find molecules causally relevant to the disease or phenotype
- Filter by specific genetic evidence or species
- Explore association with other similar diseases or phenotypes/symptoms leveraging the depth of the Ingenuity Ontology and the Human Phenotype Ontology



Find genes or chemicals that might be therapeutic for lung fibrosis (BioProfiler)

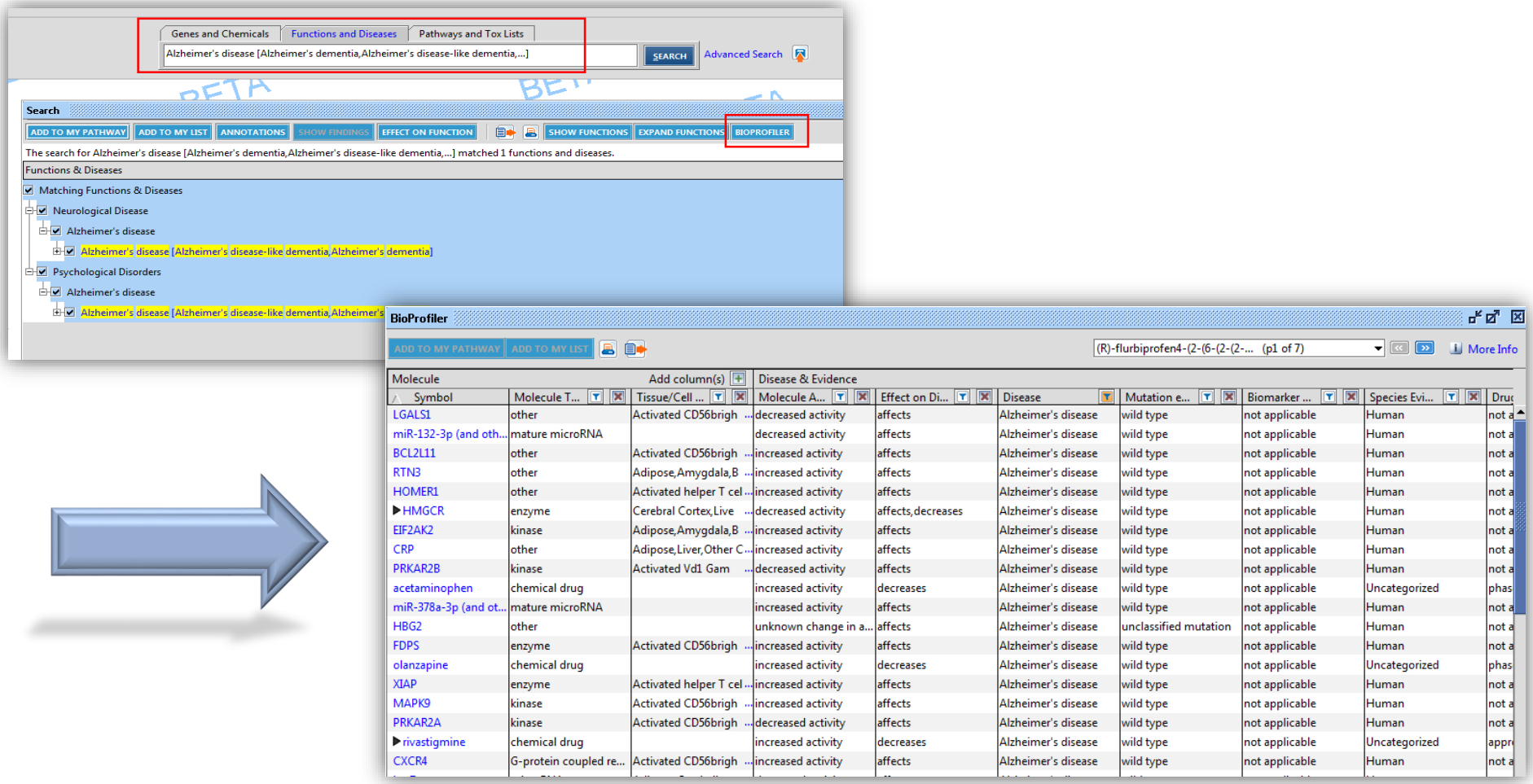
Molecule	Add column(s)	Disease, Phenotype & Evidence						Add column(s)
Symbol	Molec...	Molecule Acti...	Effect...	Disease	Mutation e...	Speci...	Caus...	Findings
ALOX5	enzyme	decreased activity	decreases	fibrosis of lung	homozygous,knockout	Mouse	causal	1
BAX	transporter	decreased activity	decreases	fibrosis of lung	homozygous,knockout	Mouse	causal	3
BID	other	decreased activity	decreases	fibrosis of lung	homozygous,knockout	Mouse	causal	4
CCL17	cytokine	decreased activity	decreases	fibrosis of lung	wild type	Mouse	causal	1
CCR2	G-protein cou...	decreased activity	decreases	fibrosis of lung	homozygous,knockout	Mouse	causal	3
CDH11	other	decreased activity	decreases	fibrosis of lung	homozygous,knockout	Mouse	causal	1
CXCL12	cytokine	decreased activity	decreases	fibrosis of lung	wild type	Mouse	causal	1
EGR1	transcription r...	decreased activity	decreases	fibrosis of lung	homozygous,knockout	Mouse	causal	2
ELANE	peptidase	decreased activity	decreases	fibrosis of lung	homozygous,knockout	Mouse	causal	1
FAS	transmembran...	decreased activity	decreases	fibrosis of lung	homozygous,loss of...	Mouse	causal	1
▶FASLG	cytokine	decreased activity	decreases	fibrosis of lung	homozygous,loss of...	Mouse	causal	2
▶ICAM1	transmembran...	decreased activity	decreases	fibrosis of lung	homozygous,knock...	Uncategorized...	causal	5
IKBKB	kinase	decreased activity	decreases	fibrosis of lung; ...	homozygous,knockout	Mouse	causal	1
IL11RA	transmembran...	decreased activity	decreases	fibrosis of lung	homozygous,knockout	Mouse	causal	1
▶IL12B	cytokine	decreased activity	decreases	fibrosis of lung	homozygous,knock...	Mouse	causal	4
IL13	cytokine	decreased activity	decreases	fibrosis of lung	homozygous,knockout	Mouse	causal	4
IL17A	cytokine	decreased activity	decreases	fibrosis of lung	wild type	Mouse	causal	9
IL1R1	transmembran...	decreased activity	decreases	fibrosis of lung	homozygous,knockout	Mouse	causal	1
IL4	cytokine	decreased activity	decreases	fibrosis of lung	homozygous,knockout	Mouse	causal	3
IL5	cytokine	decreased activity	decreases	fibrosis of bronchia; f ...	homozygous,knockout	Mouse	causal	1
ITGA5	transmembran...	decreased activity	decreases	fibrosis of lung	wild type	Mouse	causal	2

Drug targets: genes or proteins that when decreased in activity, decrease lung fibrosis

BioProfile Example

Alzheimer’s Disease
Identify and understand key molecules involved with the disease for potential target discovery

BioProfiler: Very simply search….and filter



Show me only those molecules that when increased are known to increase Alzheimer's disease.

Quickly identify 9 molecules causally relevant to Alzheimer's from 682 search results

BioProfiler

ADD TO MY PATHWAY | ADD TO MY LIST

ACEAPBB2APOEAPPBLMHPAXIP1PSEN1... (p1 of 1)

Molecule			Disease & Evidence							
Symbol	Molecule Type	Tissue/Cell ...	Molecule Activity	Effect on Disease...	Disease	Mutation e...	Species Evi...	Causal or C...	Findings
APP	other	Activated CD56brigh ...	increased activity	increases	Alzheimer's disease	wild type	Human	causal	2
PSEN1	peptidase	Adipose,Amygdala,B ...	increased activity	increases	Alzheimer's disease	wild type	Human	causal	1
ACE	peptidase	Dorsal Root Ganglio ...	increased activity	increases	Alzheimer's disease	wild type	Human	causal	1
PSEN2	peptidase	B lymphocytes not o ...	increased activity	increases	Alzheimer's disease	wild type	Human	causal	1
APBB2	other	Activated CD56dim ...	increased activity	increases	Alzheimer's disease; I ...	wild type	Human	causal	1
APOE	transporter	Activated Vd1 Gam ...	increased activity	increases	Alzheimer's disease	wild type	Human	causal	1
BLMH	peptidase	Activated Vd1 Gam ...	increased activity	increases	Alzheimer's disease	wild type	Human	causal	1
PAXIP1	other	Activated CD56brigh ...	increased activity	increases	Alzheimer's disease	wild type	Human	causal	1
SORL1	transporter	Activated CD56brigh ...	increased activity	increases	Alzheimer's disease	wild type	Human	causal	1

Filterable finding level attributes

Molecule Activity

- Whether the finding indicates increased or decreased activity
- Calculated using various factors
  - Observed upregulation or downregulation
  - Functional effect of mutations
  - Etc.

Effect on Disease/Function

- Whether the disease or function was increased or suppressed

Species evidence and Tissue/Cell line

- Select specific species e.g. mouse, and/or specific tissues e.g. lung

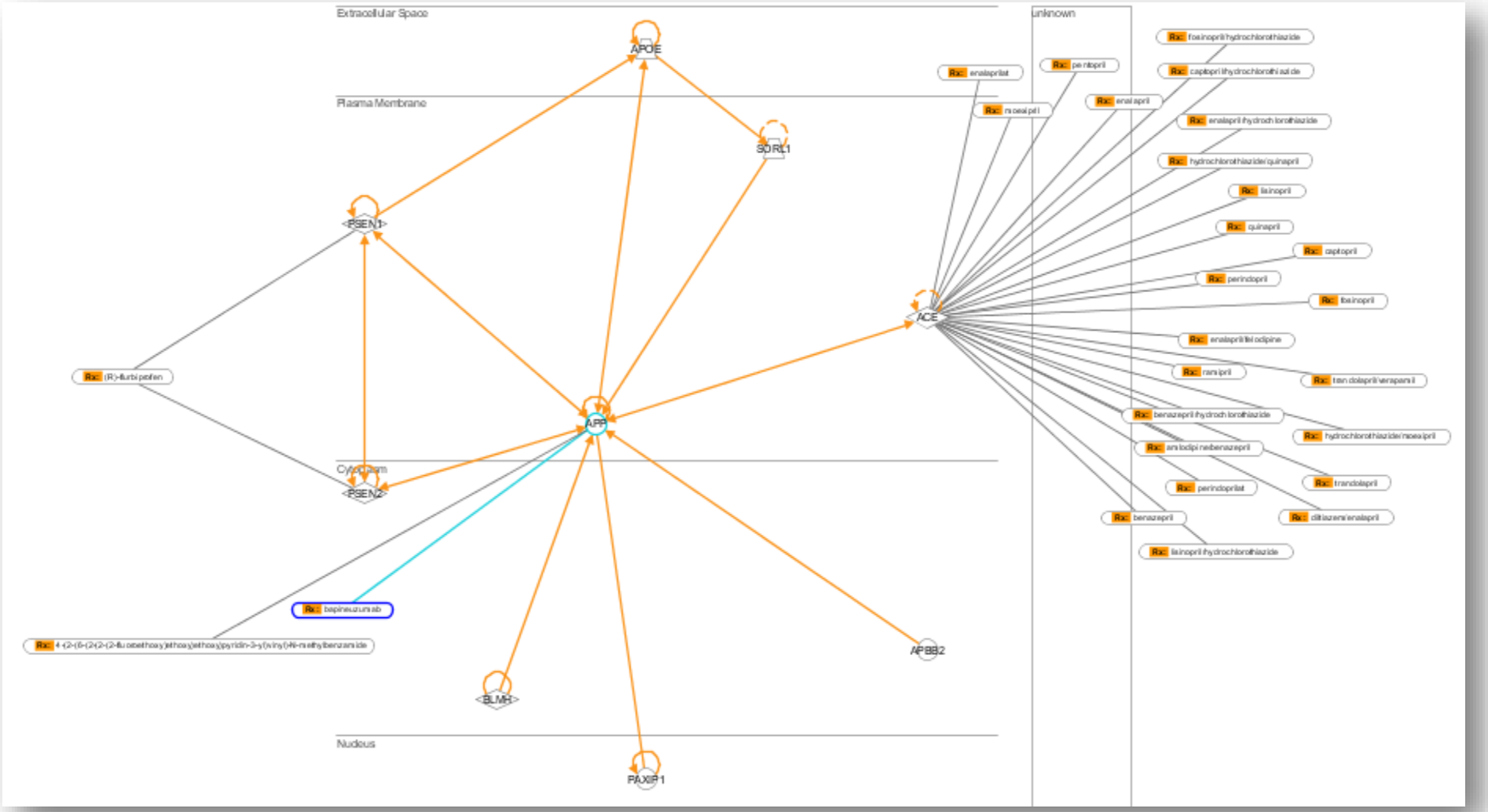
Mutation evidence

- Limit to certain mutation types e.g. homozygous, knockout

Causal v/s correlation

Find known drugs associated with key causally relevant molecules

Select molecules, place on a pathway and overlay drugs



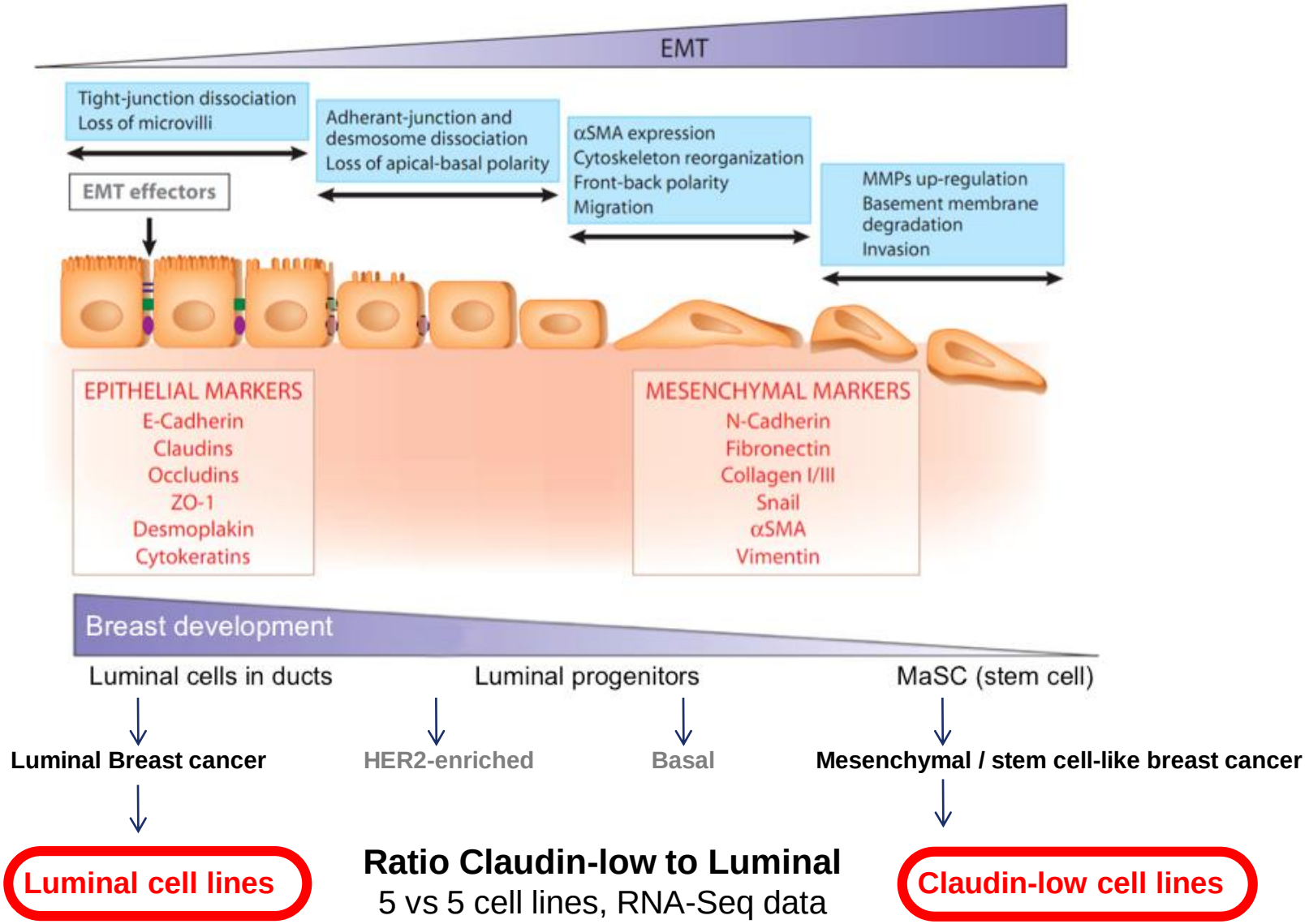
Analysis of the clinical aspect of EMT in Breast Cancer

Exploring the EMT molecules involved in breast cancer.

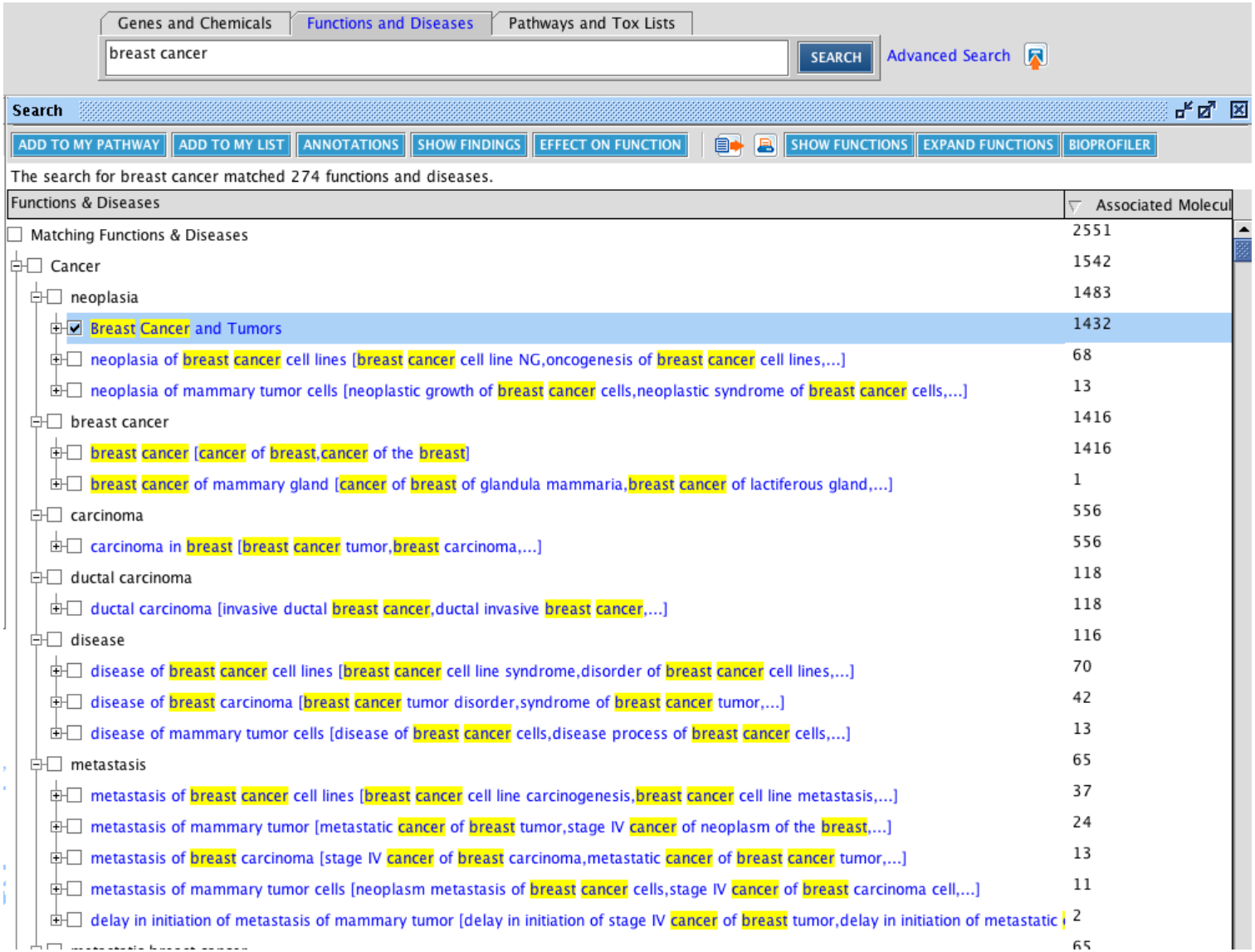
- Focusing on the Upstream Regulators predicted to be activated in the dataset to explore which ones if any would be of interest for therapeutic purposes.

Do any of these molecules of interest have biomarker application in breast cancer ?

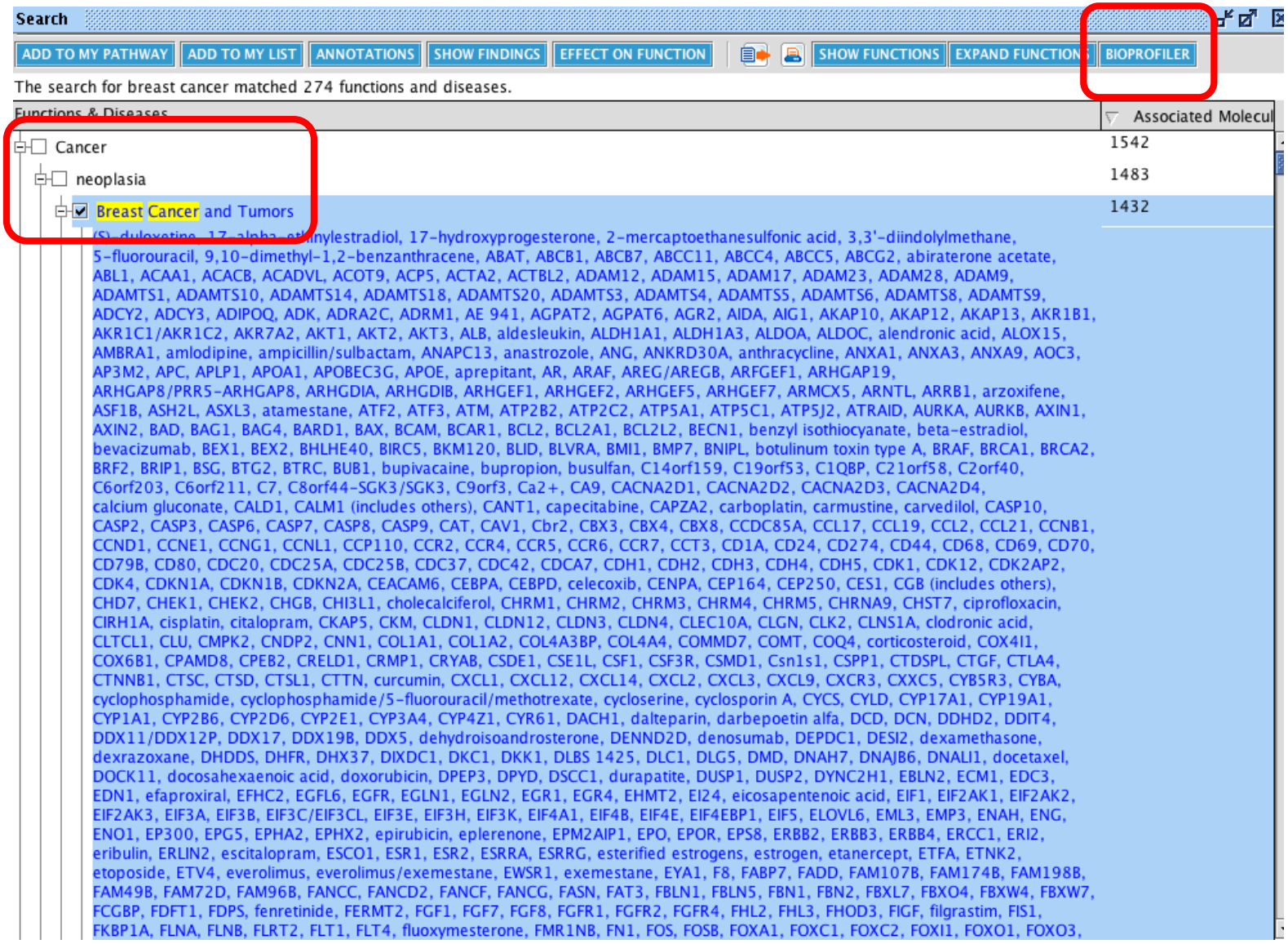
Epithelial to Mesenchymal Transition



All answers with BioProfiler!



1432 Molecules related with findings to Breast Cancer



1432 Molecules related with findings to Breast Cancer

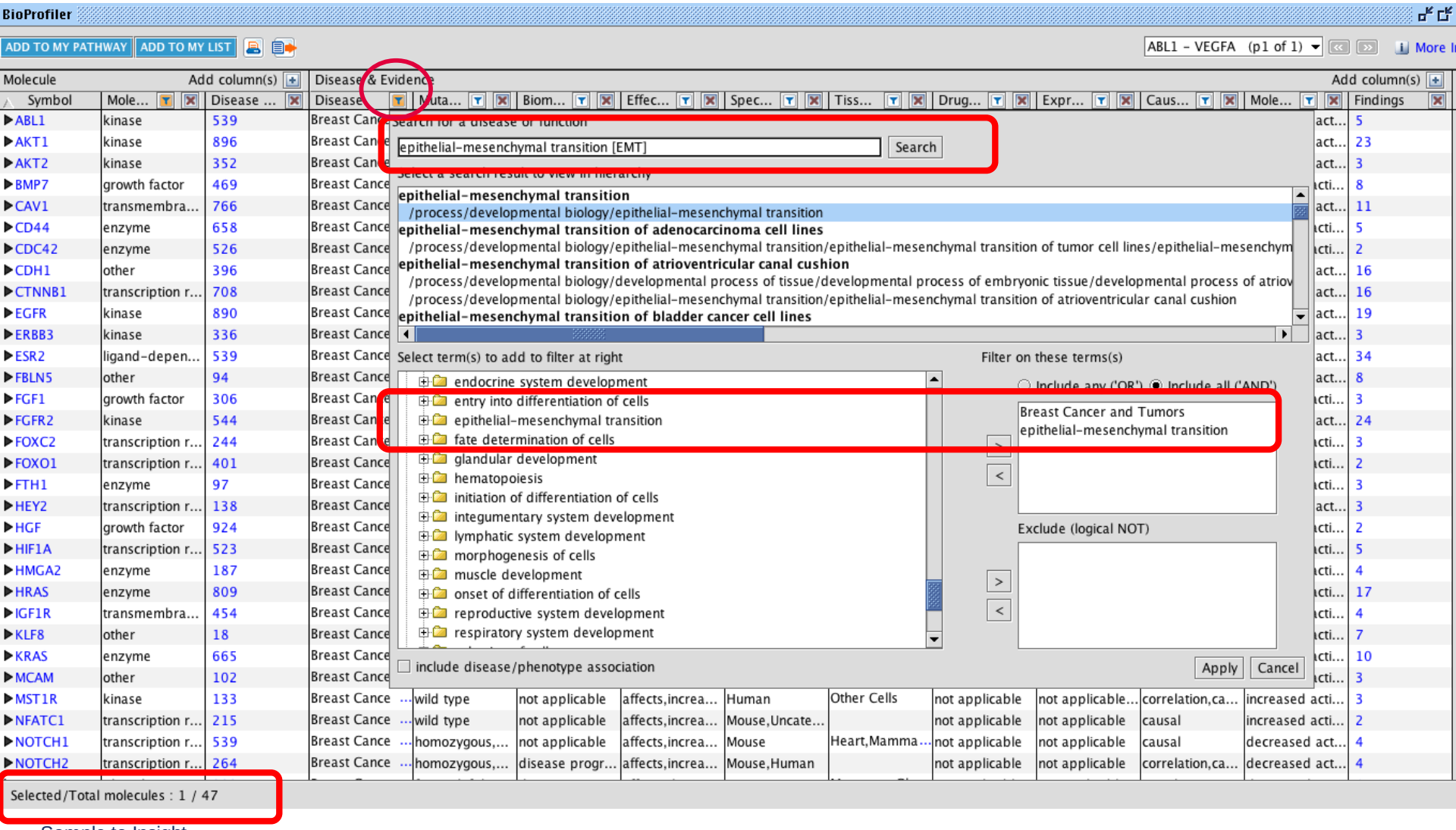
BioProfiler

ADD TO MY PATHWAY | ADD TO MY LIST | All Pages | More Info

Molecule			Disease & Evidence												Add column(s)
Symbol	Molecule Type	Diseas...	Disease	M...	Biom...	Eff...	Spe...	...	Drug...	Exp...	Caus...	Mole...	Findings
(S)-duloxetine	chemical drug	59	Breast Cance ...	wild type	not applicable	decreases	Uncategorized		phase III	not applicable	causal	increased acti...	3
▶17-alpha-ethinylestradiol	chemical drug	155	Breast Cance ...	wild type	not applicable	decreases	Uncategorized		approved,pha...	not applicable	causal	increased acti...	12
17-hydroxyprogesterone	chemical - endogenous...	15	Breast Cance ...	wild type	diagnosis	affects	Uncategorized		not applicable	not applicable	correlation	increased acti...	1
2-mercaptoethanesulfoni...	chemical drug	22	Breast Cance ...	wild type	not applicable	decreases	Uncategorized		phase III	not applicable	causal	increased acti...	1
▶3,3'-diindolylmethane	chemical drug	97	Breast Cance ...	wild type	not applicable	decreases	Uncategorized		not applicable...	not applicable	causal	increased acti...	3
▶5-fluorouracil	chemical drug	355	Breast Cance ...	wild type	not applicable	decreases	Uncategorized		approved,pha...	not applicable	causal	increased acti...	54
▶9,10-dimethyl-1,2-be...	chemical toxicant	258	Breast Cance ...	wild type	not applicable	increases	Rat,Mouse	Mammary ...	not applicable	not applicable	causal	increased acti...	7
ABAT	enzyme	44	Breast Cance ...	wild type	not applicable	affects	Human		not applicable	upregulation	correlation	increased acti...	1
▶ABCB1	transporter	212	Breast Cance ...	wild type	diagnosis,not ...	affects	Human		not applicable	not applicabl...	correlation	decreased act...	2
ABCB7	transporter	36	Breast Cance ...	wild type	unspecified a...	affects	Mouse		not applicable	upregulation	correlation	increased acti...	1
▶ABCC11	transporter	36	Breast Cance ...	homozygou...	not applicable	affects,decr...	Human		not applicable	not applicabl...	correlation,ca...	increased acti...	4
ABCC4	transporter	135	Breast Cance ...	unclassified...	not applicable	affects	Human		not applicable	not applicable	correlation	unknown chan...	1
ABCC5	transporter	60	Breast Cance ...	wild type	not applicable	affects	Human		not applicable	upregulation	correlation	increased acti...	1
ABCG2	transporter	162	Breast Cance ...	wild type	diagnosis	affects	Human		not applicable	not applicable	correlation	increased acti...	1
abiraterone acetate	chemical drug	17	Breast Cance ...	wild type	not applicable	decreases	Uncategorized		phase III	not applicable	causal	increased acti...	1
ABL1	kinase	540	Breast Cance ...	wild type	not applicable	affects	Human		not applicable	downregulation	correlation	decreased act...	2
ACAA1	enzyme	17	Breast Cance ...	wild type	unspecified a...	affects	Mouse		not applicable	upregulation	correlation	increased acti...	1
▶ACACB	enzyme	88	Breast Cance ...	wild type	not applicable	affects	Human		not applicable	upregulation	correlation	increased acti...	4
ACADVL	enzyme	53	Breast Cance ...	wild type	not applicable	affects	Mouse		not applicable	downregulation	correlation	decreased act...	1
ACOT9	enzyme	7	Breast Cance ...	wild type	not applicable	affects	Human	Other Or ...	not applicable	downregulation	correlation	decreased act...	2
▶ACP5	phosphatase	104	Breast Cance ...	wild type	unspecified a...	affects	Human		not applicable	upregulation	correlation	increased acti...	4
▶ACTA2	other	80	Breast Cance ...	wild type	not applicable	affects	Human	Other Ce ...	not applicable	upregulation	correlation	increased acti...	2
ACTBL2	other	7	Breast Cance ...	heterozygo...	not applicable	affects	Human	Other Or ...	not applicable	not applicable	correlation	unknown chan...	1
ADAM12	peptidase	140	Breast Cance ...	wild type	not applicable	affects	Human		not applicable	upregulation	correlation	increased acti...	1
ADAM15	peptidase	104	Breast Cance ...	wild type	not applicable	affects	Human		not applicable	upregulation	correlation	increased acti...	1
ADAM17	peptidase	227	Breast Cance ...	wild type	not applicable	affects	Human		not applicable	upregulation	correlation	increased acti...	1
ADAM23	peptidase	24	Breast Cance ...	wild type	not applicable	affects	Human		not applicable	not applicable	correlation	increased acti...	1
ADAM28	peptidase	32	Breast Cance ...	wild type	not applicable	affects	Human		not applicable	upregulation	correlation	increased acti...	2
ADAM9	peptidase	104	Breast Cance ...	wild type	not applicable	affects	Human		not applicable	upregulation	correlation	increased acti...	1
▶ADAMTS1	peptidase	156	Breast Cance ...	wild type	not applicable	affects	Human		not applicable	upregulation,...	correlation	decreased act...	2
ADAMTS10	peptidase	25	Breast Cance ...	wild type	not applicable	affects	Human		not applicable	downregulation	correlation	decreased act...	1

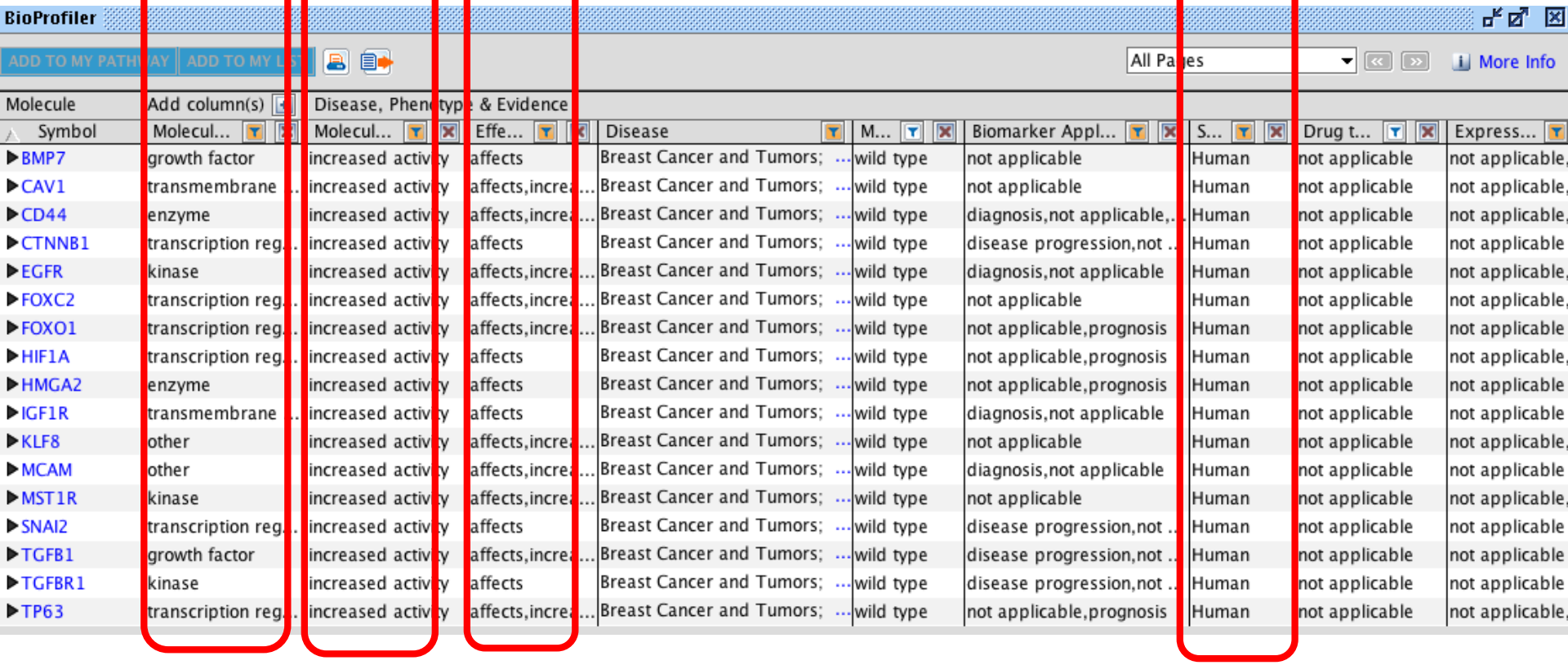
Selected/Total molecules : 0 / 1432

Narrowing down to Genes, RNAs and Proteins common to Breast Cancer and EMT: 47 molecules



EMT-Breast Cancer molecules: Filter down further on molecules testable for therapeutic purposes: with interest in specific criteria and combining with previous Upstream Regulators Analysis: 17 molecules

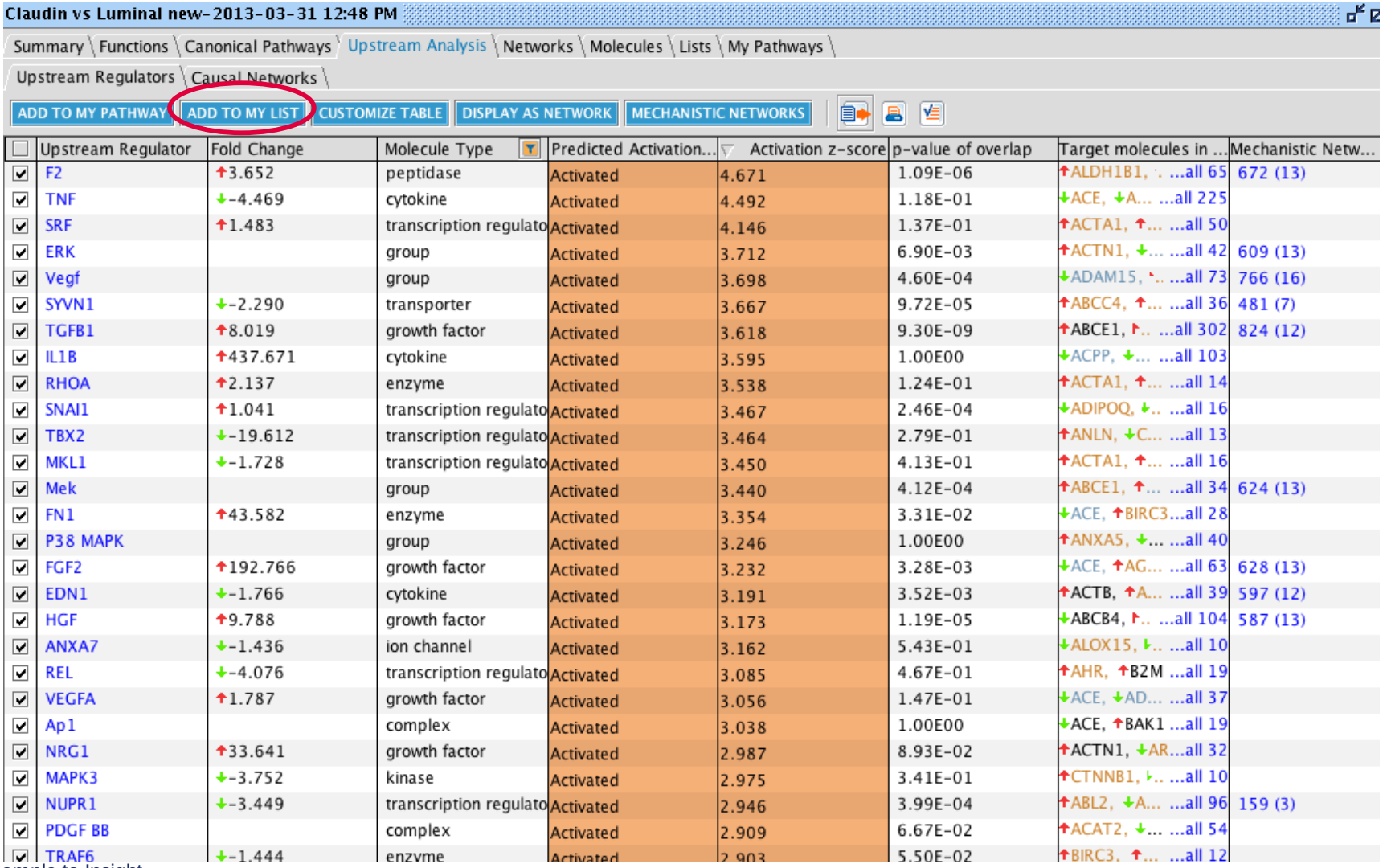
1 2 3 4



Symbol	Molecul...	Molecul...	Effe...	Disease	M...	Biomarker Appl...	S...	Drug t...	Express...
BMP7	growth factor	increased activity	affects	Breast Cancer and Tumors; ...	wild type	not applicable	Human	not applicable	not applicable,
CAV1	transmembrane ...	increased activity	affects,increa...	Breast Cancer and Tumors; ...	wild type	not applicable	Human	not applicable	not applicable,
CD44	enzyme	increased activity	affects,increa...	Breast Cancer and Tumors; ...	wild type	diagnosis,not applicable,...	Human	not applicable	not applicable,
CTNNB1	transcription reg...	increased activity	affects	Breast Cancer and Tumors; ...	wild type	disease progression,not ...	Human	not applicable	not applicable
EGFR	kinase	increased activity	affects,increa...	Breast Cancer and Tumors; ...	wild type	diagnosis,not applicable	Human	not applicable	not applicable,
FOXC2	transcription reg...	increased activity	affects,increa...	Breast Cancer and Tumors; ...	wild type	not applicable	Human	not applicable	not applicable,
FOXO1	transcription reg...	increased activity	affects,increa...	Breast Cancer and Tumors; ...	wild type	not applicable,prognosis	Human	not applicable	not applicable
HIF1A	transcription reg...	increased activity	affects	Breast Cancer and Tumors; ...	wild type	not applicable,prognosis	Human	not applicable	not applicable,
HMGA2	enzyme	increased activity	affects	Breast Cancer and Tumors; ...	wild type	not applicable,prognosis	Human	not applicable	not applicable
IGF1R	transmembrane ...	increased activity	affects	Breast Cancer and Tumors; ...	wild type	diagnosis,not applicable	Human	not applicable	not applicable
KLF8	other	increased activity	affects,increa...	Breast Cancer and Tumors; ...	wild type	not applicable	Human	not applicable	not applicable,
MCAM	other	increased activity	affects,increa...	Breast Cancer and Tumors; ...	wild type	diagnosis,not applicable	Human	not applicable	not applicable
MST1R	kinase	increased activity	affects,increa...	Breast Cancer and Tumors; ...	wild type	not applicable	Human	not applicable	not applicable,
SNAI2	transcription reg...	increased activity	affects	Breast Cancer and Tumors; ...	wild type	disease progression,not ...	Human	not applicable	not applicable
TGFB1	growth factor	increased activity	affects,increa...	Breast Cancer and Tumors; ...	wild type	disease progression,not ...	Human	not applicable	not applicable
TGFBR1	kinase	increased activity	affects	Breast Cancer and Tumors; ...	wild type	disease progression,not ...	Human	not applicable	not applicable
TP63	transcription reg...	increased activity	affects,increa...	Breast Cancer and Tumors; ...	wild type	not applicable,prognosis	Human	not applicable	not applicable,

Upstream Regulator Analysis indicated the predicted activated regulators in the dataset: 114 UR (Z-score > 2)

Click ADD TO MY LIST



Claudin vs Luminal new-2013-03-31 12:48 PM

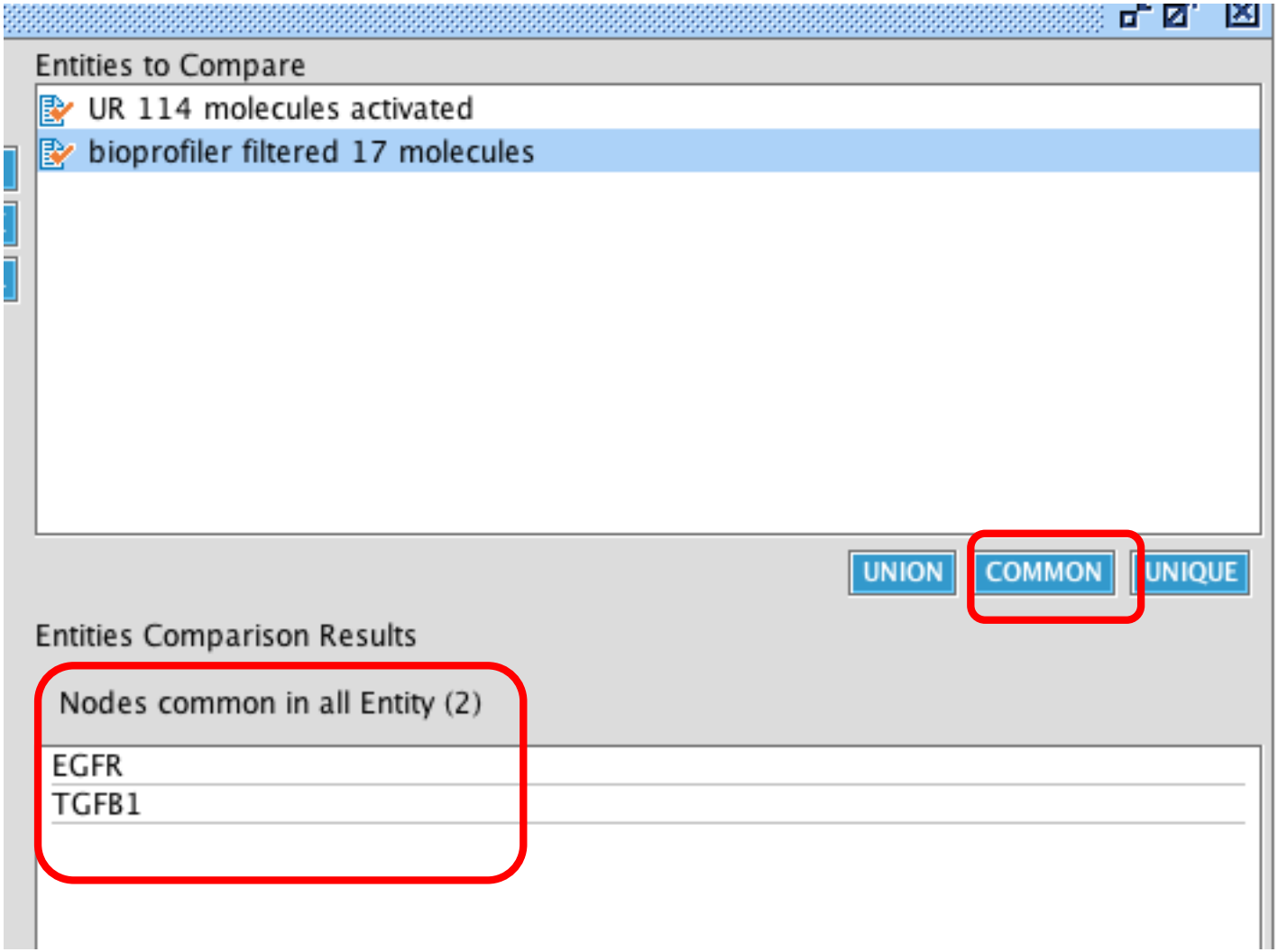
Summary | Functions | Canonical Pathways | Upstream Analysis | Networks | Molecules | Lists | My Pathways

Upstream Regulators | Causal Networks

ADD TO MY PATHWAY | ADD TO MY LIST | CUSTOMIZE TABLE | DISPLAY AS NETWORK | MECHANISTIC NETWORKS

Upstream Regulator	Fold Change	Molecule Type	Predicted Activation...	Activation z-score	p-value of overlap	Target molecules in ...	Mechanistic Netw...
F2	↑3.652	peptidase	Activated	4.671	1.09E-06	↑ALDH1B1, ...all 65	672 (13)
TNF	↓-4.469	cytokine	Activated	4.492	1.18E-01	↓ACE, ↓A... ...all 225	
SRF	↑1.483	transcription regulato	Activated	4.146	1.37E-01	↑ACTA1, ↑... ...all 50	
ERK		group	Activated	3.712	6.90E-03	↑ACTN1, ↓... ...all 42	609 (13)
Vegf		group	Activated	3.698	4.60E-04	↓ADAM15, ↑... ...all 73	766 (16)
SYVN1	↓-2.290	transporter	Activated	3.667	9.72E-05	↑ABCC4, ↑... ...all 36	481 (7)
TGFB1	↑8.019	growth factor	Activated	3.618	9.30E-09	↑ABCE1, ↑... ...all 302	824 (12)
IL1B	↑437.671	cytokine	Activated	3.595	1.00E00	↓ACPP, ↓... ...all 103	
RHOA	↑2.137	enzyme	Activated	3.538	1.24E-01	↑ACTA1, ↑... ...all 14	
SNAI1	↑1.041	transcription regulato	Activated	3.467	2.46E-04	↓ADIPOQ, ↓... ...all 16	
TBX2	↓-19.612	transcription regulato	Activated	3.464	2.79E-01	↑ANLN, ↓C... ...all 13	
MKL1	↓-1.728	transcription regulato	Activated	3.450	4.13E-01	↑ACTA1, ↑... ...all 16	
Mek		group	Activated	3.440	4.12E-04	↑ABCE1, ↑... ...all 34	624 (13)
FN1	↑43.582	enzyme	Activated	3.354	3.31E-02	↓ACE, ↑BIRC3...all 28	
P38 MAPK		group	Activated	3.246	1.00E00	↑ANXA5, ↓... ...all 40	
FGF2	↑192.766	growth factor	Activated	3.232	3.28E-03	↓ACE, ↑AG... ...all 63	628 (13)
EDN1	↓-1.766	cytokine	Activated	3.191	3.52E-03	↑ACTB, ↑A... ...all 39	597 (12)
HGF	↑9.788	growth factor	Activated	3.173	1.19E-05	↓ABCB4, ↑... ...all 104	587 (13)
ANXA7	↓-1.436	ion channel	Activated	3.162	5.43E-01	↓ALOX15, ↑... ...all 10	
REL	↓-4.076	transcription regulato	Activated	3.085	4.67E-01	↑AHR, ↑B2M ...all 19	
VEGFA	↑1.787	growth factor	Activated	3.056	1.47E-01	↓ACE, ↓AD... ...all 37	
Ap1		complex	Activated	3.038	1.00E00	↓ACE, ↑BAK1 ...all 19	
NRG1	↑33.641	growth factor	Activated	2.987	8.93E-02	↑ACTN1, ↓AR...all 32	
MAPK3	↓-3.752	kinase	Activated	2.975	3.41E-01	↑CTNNB1, ↑... ...all 10	
NUPR1	↓-3.449	transcription regulato	Activated	2.946	3.99E-04	↑ABL2, ↓A... ...all 96	159 (3)
PDGF BB		complex	Activated	2.909	6.67E-02	↑ACAT2, ↓... ...all 54	
TRAF6	↓-1.444	enzyme	Activated	2.903	5.50E-02	↑BIRC3, ↑... ...all 12	

Comparison of the 2 lists using File>New>Compare



Analysis of the clinical aspects of Breast Cancer (EMT focused)

Exploring the EMT molecules involved in breast cancer.

- Focusing on the Upstream Regulators predicted to be activated in the dataset to explore which ones if any would be of interest for therapeutic purposes. 2: EGFR, TGFB1

Do any of these molecules of interest have biomarker application in breast cancer ?

- EGFR: diagnosis
- TGFB1: disease progression

Is there biomarker application of EGFR or TGFB1?

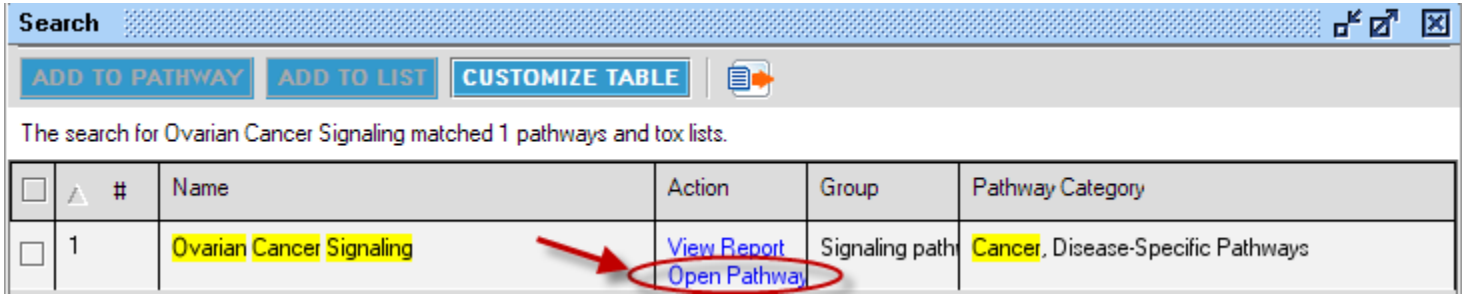
BioProfiler

ADD TO MY PATHWAY | ADD TO MY LIST | All Pages | More Inf

Molecule	Add column(s)	Disease, Phenotype & Evidence							
Symbol	Molecul...	Molecul...	Effe...	Disease	M...	Biomarker Appl...	S...	Drug t...	Express...
CD44	enzyme	increased activity	affects,increa...	Breast Cancer and Tumors; ...	wild type	diagnosis,disease progr...	Human	not applicable	not applicat
CTNNB1	transcription reg...	increased activity	affects	Breast Cancer and Tumors; ...	wild type	disease progression,not ...	Human	not applicable	not applicat
EGFR	kinase	increased activity	affects,increa...	Breast Cancer and Tumors; ...	wild type	diagnosis,not applicable,...	Human	not applicable	not applica
HIF1A	transcription reg...	increased activity	affects	Breast Cancer and Tumors; ...	wild type	not applicable,prognosis	Human	not applicable	not applicat
IGF1R	transmembrane ...	increased activity	affects	Breast Cancer and Tumors; ...	wild type	diagnosis,not applicable,...	Human	not applicable	not applicat
TGFBR1	kinase	increased activity	affects	Breast Cancer and Tumors; ...	wild type	disease progression,not ...	Human	not applicable	not applicat
TP63	transcription reg...	increased activity	affects,increa...	Breast Cancer and Tumors; ...	wild type	diagnosis,not applicable,...	Human	not applicable	not applicat

Ingenuity pathway search

Ingenuity Pathway Search



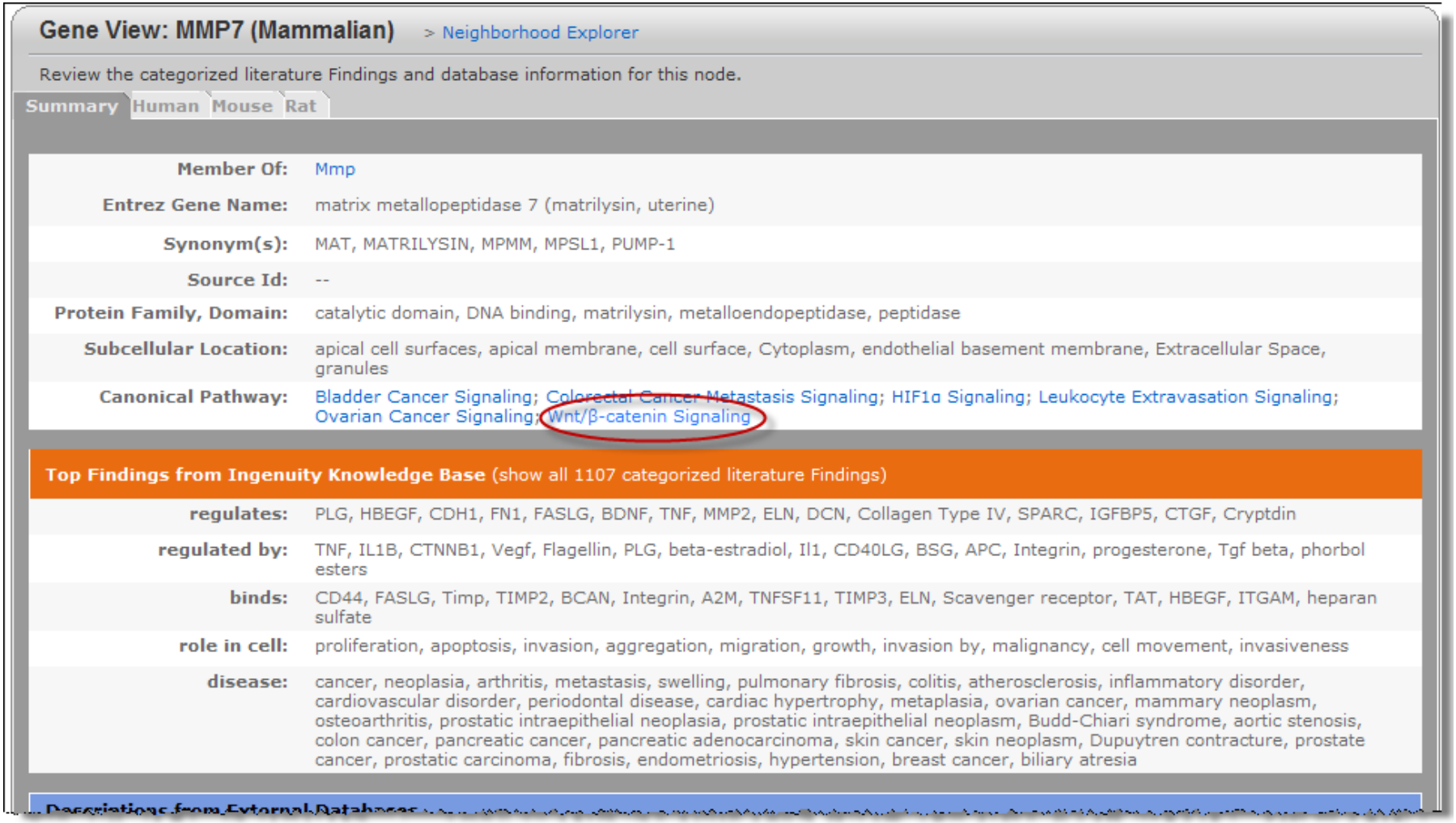
Most common workflow will be to open pathway after search

Understanding Canonical Pathways

IPA Canonical Pathways

- Canonical pathways are constructed, curated, IPA pathway diagrams for well established signaling and metabolic pathways
  - Vary in size
  - May contain one or more pathway branches or paths
    - Shows the canonical pathway in a large context
- Canonical Pathways can be modified and saved
  - Genes and molecules can be added or removed
  - Can be converted to Path Designer
- Canonical pathways show you both key biological and molecular roles of proteins and chemicals of interest.

From the Gene View Page



Gene View: MMP7 (Mammalian) > Neighborhood Explorer

Review the categorized literature Findings and database information for this node.

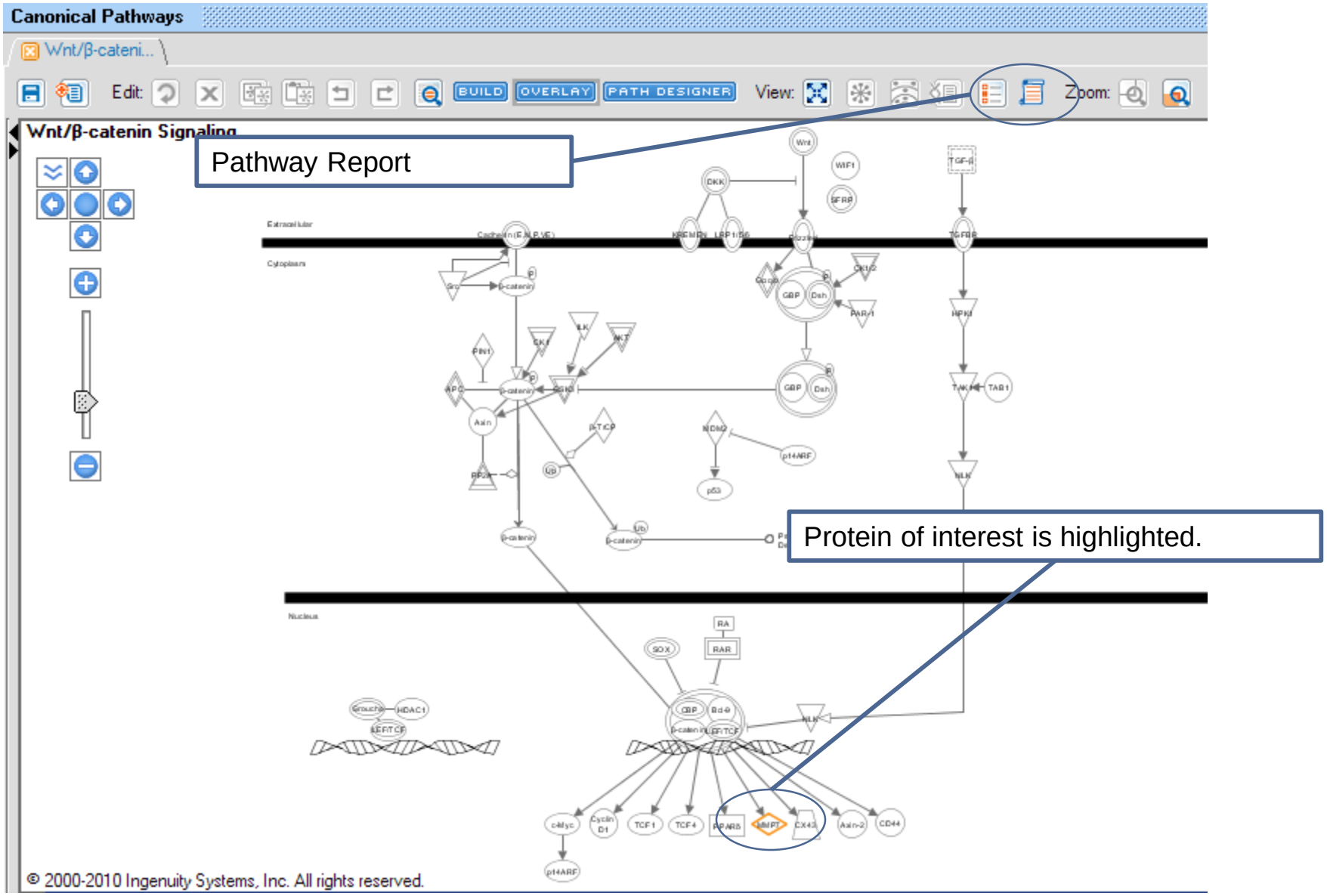
Summary | Human | Mouse | Rat

Member Of:	Mmp
Entrez Gene Name:	matrix metallopeptidase 7 (matrilysin, uterine)
Synonym(s):	MAT, MATRILYSIN, MPMM, MPSL1, PUMP-1
Source Id:	--
Protein Family, Domain:	catalytic domain, DNA binding, matrilysin, metalloendopeptidase, peptidase
Subcellular Location:	apical cell surfaces, apical membrane, cell surface, Cytoplasm, endothelial basement membrane, Extracellular Space, granules
Canonical Pathway:	Bladder Cancer Signaling; Colorectal Cancer Metastasis Signaling; HIF1α Signaling; Leukocyte Extravasation Signaling; Ovarian Cancer Signaling; Wnt/β-catenin Signaling

Top Findings from Ingenuity Knowledge Base (show all 1107 categorized literature Findings)

regulates:	PLG, HBEGF, CDH1, FN1, FASLG, BDNF, TNF, MMP2, ELN, DCN, Collagen Type IV, SPARC, IGFBP5, CTGF, Cryptdin
regulated by:	TNF, IL1B, CTNNB1, Vegf, Flagellin, PLG, beta-estradiol, Il1, CD40LG, BSG, APC, Integrin, progesterone, Tgf beta, phorbol esters
binds:	CD44, FASLG, Timp, TIMP2, BCAN, Integrin, A2M, TNFSF11, TIMP3, ELN, Scavenger receptor, TAT, HBEGF, ITGAM, heparan sulfate
role in cell:	proliferation, apoptosis, invasion, aggregation, migration, growth, invasion by, malignancy, cell movement, invasiveness
disease:	cancer, neoplasia, arthritis, metastasis, swelling, pulmonary fibrosis, colitis, atherosclerosis, inflammatory disorder, cardiovascular disorder, periodontal disease, cardiac hypertrophy, metaplasia, ovarian cancer, mammary neoplasm, osteoarthritis, prostatic intraepithelial neoplasia, prostatic intraepithelial neoplasm, Budd-Chiari syndrome, aortic stenosis, colon cancer, pancreatic cancer, pancreatic adenocarcinoma, skin cancer, skin neoplasm, Dupuytren contracture, prostate cancer, prostatic carcinoma, fibrosis, endometriosis, hypertension, breast cancer, biliary atresia

Descriptions from External Databases


Canonical Pathways
Wnt/β-cateni...
Edit:
BUILD
OVERLAY
PATH DESIGNER
View:
Zoom:
Wnt/β-catenin Signaling
Pathway Report
Protein of interest is highlighted.
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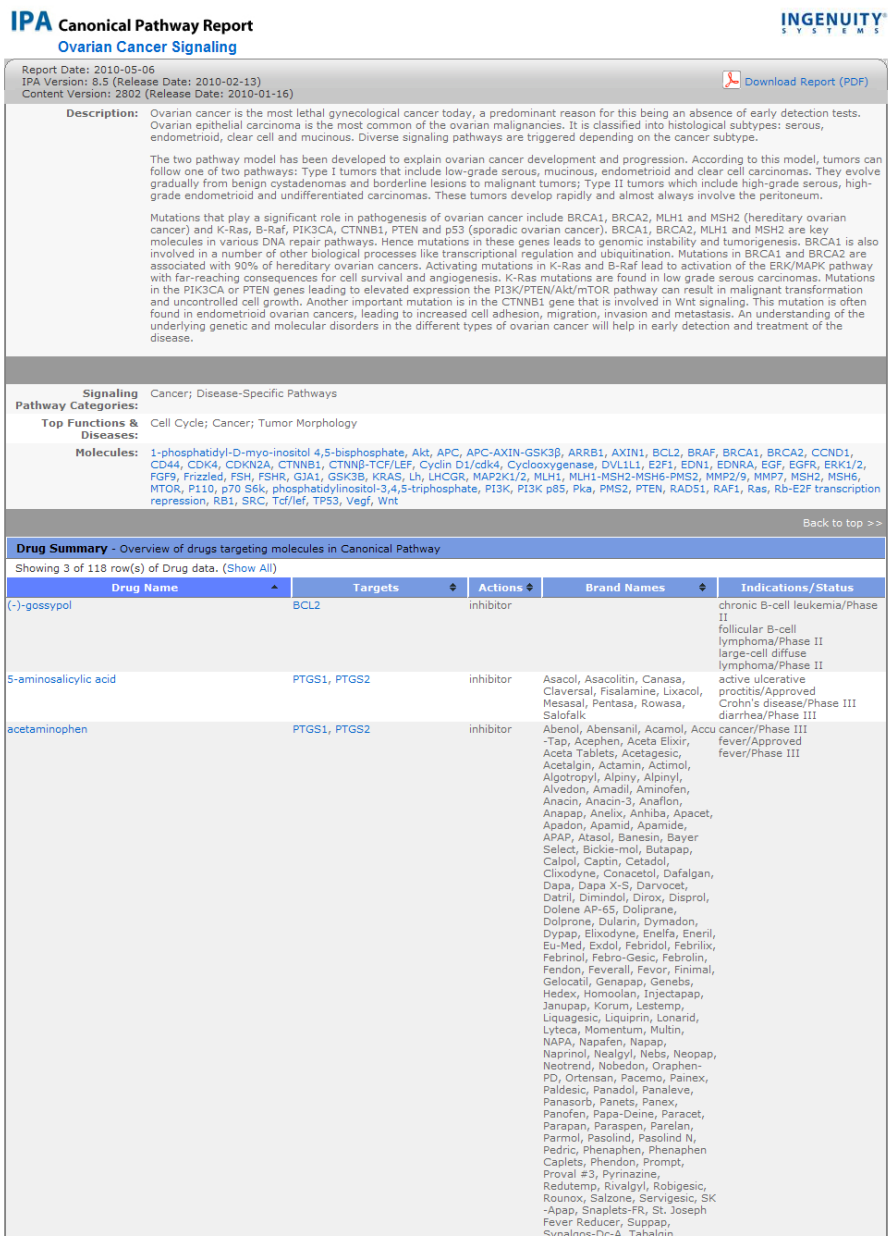
Pathway Reports

HTML and PDF formats

Reports contain

- Description
- Top functions
- Molecule list
- Drug Summary
- Target Information
- Link to references



IPA Canonical Pathway Report

Ovarian Cancer Signaling

INGENUITY SYSTEMS

Report Date: 2010-05-06
IPA Version: 8.5 (Release Date: 2010-02-13)
Content Version: 2802 (Release Date: 2010-01-16)

Download Report (PDF)

Description: Ovarian cancer is the most lethal gynecological cancer today, a predominant reason for this being an absence of early detection tests. Ovarian epithelial carcinoma is the most common of the ovarian malignancies. It is classified into histological subtypes: serous, endometrioid, clear cell and mucinous. Diverse signaling pathways are triggered depending on the cancer subtype.

The two pathway model has been developed to explain ovarian cancer development and progression. According to this model, tumors can follow one of two pathways: Type I tumors that include low-grade serous, mucinous, endometrioid and clear cell carcinomas. They evolve gradually from benign cystadenomas and borderline lesions to malignant tumors; Type II tumors which include high-grade serous, high-grade endometrioid and undifferentiated carcinomas. These tumors develop rapidly and almost always involve the peritoneum.

Mutations that play a significant role in pathogenesis of ovarian cancer include BRCA1, BRCA2, MLH1 and MSH2 (hereditary ovarian cancer) and K-Ras, B-Raf, PIK3CA, CTNNB1, PTEN and p53 (sporadic ovarian cancer). BRCA1, BRCA2, MLH1 and MSH2 are key molecules in various DNA repair pathways. Hence mutations in these genes leads to genomic instability and tumorigenesis. BRCA1 is also involved in a number of other biological processes like transcriptional regulation and ubiquitination. Mutations in BRCA1 and BRCA2 are associated with 90% of hereditary ovarian cancers. Activating mutations in K-Ras and B-Raf lead to activation of the ERK/MAPK pathway with far-reaching consequences for cell survival and angiogenesis. K-Ras mutations are found in low grade serous carcinomas. Mutations in the PIK3CA or PTEN genes leading to elevated expression the PI3K/PTEN/Akt/mTOR pathway can result in malignant transformation and uncontrolled cell growth. Another important mutation is in the CTNNB1 gene that is involved in Wnt signaling. This mutation is often found in endometrioid ovarian cancers, leading to increased cell adhesion, migration, invasion and metastasis. An understanding of the underlying genetic and molecular disorders in the different types of ovarian cancer will help in early detection and treatment of the disease.

Signaling Pathway Categories: Cancer; Disease-Specific Pathways

Top Functions & Diseases: Cell Cycle; Cancer; Tumor Morphology

Molecules: 1-phosphatidyl-D-myo-inositol 4,5-bisphosphate, Akt, APC, APC-AXIN-GSK3β, ARRB1, AXIN1, BCL2, BRAF, BRCA1, BRCA2, CCND1, CD44, CDK4, CDKN2A, CTNNB1, CTNNβ-TCF/LEF, Cyclin D1/cdk4, Cyclooxygenase, DVL1L1, E2F1, EDN1, EDNRA, EGF, EGFR, ERK1/2, FGF9, Frizzled, FSH, FSHR, GJA1, GSK3B, KRAS, Lh, LHCGR, MAP2K1/2, MLH1, MLH1-MSH2-MSH6-PMS2, MMP2/9, MMP7, MSH2, MSH6, MTOR, P110, p70 S6k, phosphatidylinositol-3,4,5-triphosphate, PI3K, PI3K p85, Pka, PMS2, PTEN, RAD51, RAF1, Ras, Rb-E2F transcription repression, RB1, SRC, Tcf/lef, TP53, Vegf, Wnt

Back to top >>

Drug Summary - Overview of drugs targeting molecules in Canonical Pathway

Showing 3 of 118 row(s) of Drug data. (Show All)

Drug Name	Targets	Actions	Brand Names	Indications/Status
(-)-gossypol	BCL2	inhibitor		chronic B-cell leukemia/Phase II follicular B-cell lymphoma/Phase II large-cell diffuse lymphoma/Phase II
5-aminosalicylic acid	PTGS1, PTGS2	inhibitor	Asacol, Asacolitin, Canasa, Claversal, Fisalamine, Lixacol, Mesasal, Pentasa, Rowasa, Salofalk	active ulcerative proctitis/Approved Crohn's disease/Phase III diarrhea/Phase III
acetaminophen	PTGS1, PTGS2	inhibitor	Abenol, Abensanil, Acamol, Accu-Tap, Acephen, Aceta Elixir, Aceta Tablets, Acetagesic, Acetalgin, Actamin, Actimol, Algotropyl, Alpiny, Alpinyl, Alvedon, Amadil, Aminofen, Anacin, Anacin-3, Anaflon, Anapap, Anelix, Anhiba, Apacet, Apadon, Apamid, Apamide, APAP, Atasol, Banesin, Bayer Select, Bickie-mol, Butapap, Calpol, Captin, Cetadol, Clixodyne, Conacetol, Dafalgan, Dapa, Dapa X-S, Darvocet, Datril, Dimindol, Dirox, Disprol, Dolene AP-65, Doliprane, Dolprone, Dularin, Dymadon, Dypap, Elixodyne, Enelfa, Eneril, Eu-Med, Exdol, Febridol, Febrilix, Febrinol, Febro-Gesic, Febrolin, Fendon, Feverall, Fevor, Finimal, Gelocatil, Genapap, Genebs, Hedex, Homoolan, Injectapap, Janupap, Korum, Lestemp, Liquagesic, Liquiprin, Lonarid, Lyteca, Momentum, Multin, NAPA, Napafen, Napap, Naprinol, Nealgyl, Nebs, Neopap, Neotrend, Nobedon, Oraphen-PD, Ortensan, Pacemo, Painex, Paldesic, Panadol, Panaleve, Panasorb, Panets, Panex, Panofen, Papa-Deine, Paracet, Parapan, Paraspen, Parelan, Parmol, Pasolind, Pasolind N, Pedric, Phenaphen, Phenaphen Caplets, Phendon, Prompt, Proval #3, Pyrinazine, Redutemp, Rivalgyl, Robigesic, Rounox, Salzone, Servigesic, SK-Apap, Snaplets-FR, St. Joseph Fever Reducer, Suppap,	cancer/Phase III fever/Approved fever/Phase III

Pathway Navigation

Scroll-wheel on mouse controls zoom, or use toolbar zoom buttons.

Left-click selects (turns blue)

Left-click-drag on nodes moves the node

Right-click hold-and-drag moves your view

Right-click brings up menu for controlling

- tool tip (mouse-over node pop-up)
- copy/past
- Highlight
- selection

Navigation Control

Node shapes indicate a protein's primary function, see Help>Legend

Relationship lines indicate the type of relationship and the mouse-over letter the type of relationship, see Help>Legend

Pathway Navigation, continued

Double-clicking a node brings up the node summary

- You can navigate to the Gene/Chem View page by clicking the protein name at the top of the summary window pane.

Double-clicking a relationship line brings up the relationship summary

- You can to the literature evidence findings by clicking the "View relationships between:…" link at the top of the summary window pane.

Groups

- Groups are represented by a double outline applicable to any molecule shape. These represent cases where findings use a general gene name to describe a gene class or group of isoforms
- Complexes of different proteins are also given a double outline
  - View members by left-click selecting, then right-click>Show Membership

Building Custom pathways

Some Questions That Can Be Answered by Creating Custom Pathways

- What other compounds bind my target of interest?
- If I inhibit (LOF) or activate (GOF) a protein (gene), what cellular processes are likely to be affected and how will they change?
  - What are the upstream activators or downstream targets of my protein of interest?
  - Might there be adverse effects of a drug
  - Explain how a loss-of-function mutation results in a disease phenotype
- What proteins might act as good biomarkers for molecular drug effect?

How to Implement the Build Tools

1. Select nodes that you want to operate on
2. Click the BUILD button to open the build toolbox
   - Not necessary if the build window pane is already open
3. Choose a build tool in the pull-down
4. Set tool parameters and filters
   - Highly recommended to use filters
5. APPLY

Build Tools

- **Grow**: Adds new molecules and their relationships given the criteria that the user specifies
  - **Disease & Functions:** Adds nodes representing diseases or biological function/processes based on gene enrichment of pathway genes
- **Path Explorer**: Calculates the “Shortest Path” between 2 molecules or 2 sets of molecules
- **Connect**: Connects molecules given the criteria that the user specifies
- **Trim**: Removes molecules/relationships that meet the criteria that the user specifies
- **Keep**: Keeps molecules/relationships that meet the criteria that the user specifies
- **Add Molecule/Relationship**: Add a custom molecules or relationship to the current pathway that does not exist in Ingenuity’s Knowledge Base as well as ones that already exist

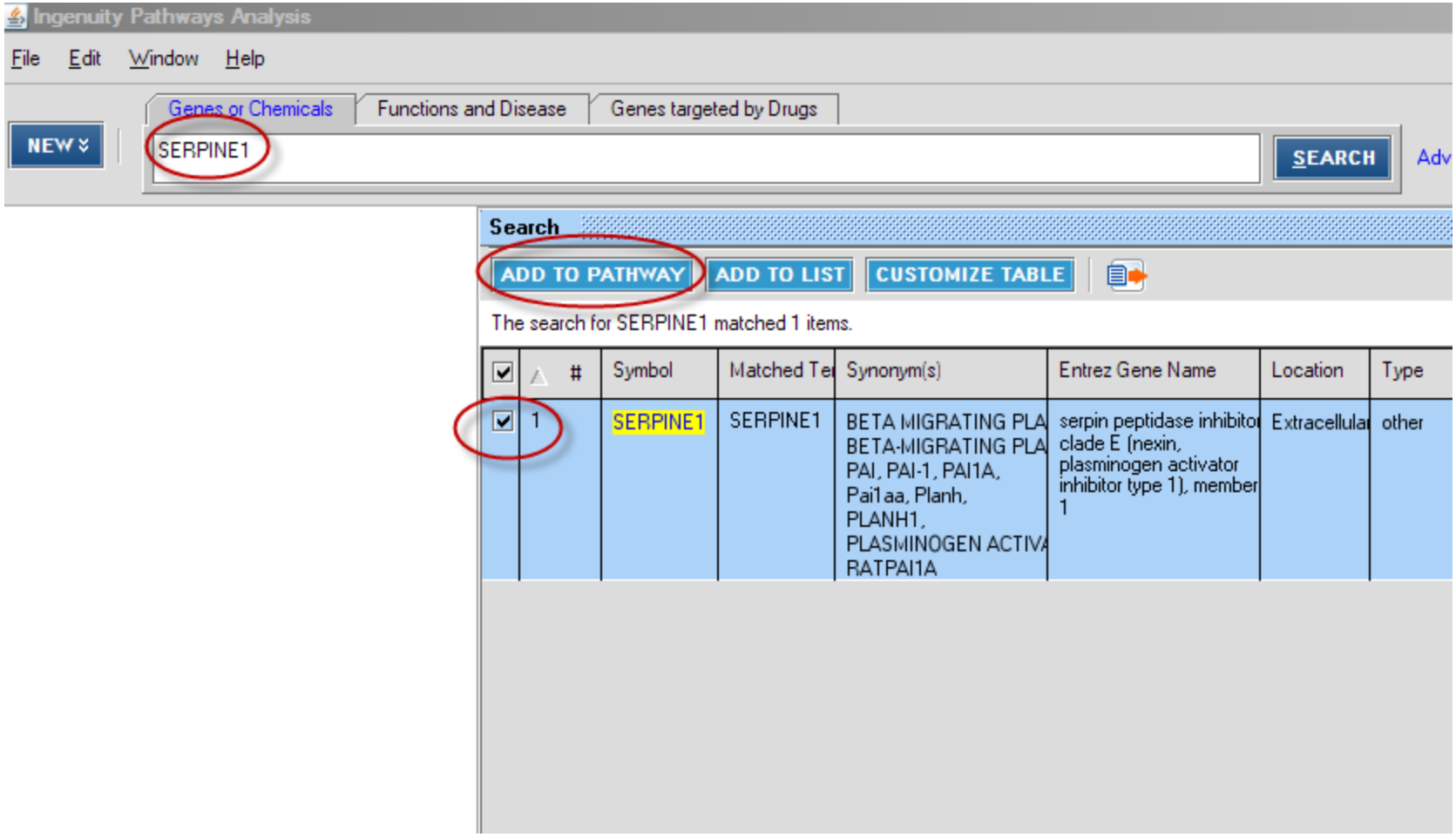
How Grow Works

- Adds new molecules and their relationships given the criteria that the user specifies
- Recommend growing to “All molecules” and using relationship, molecule type, or other filters to limit grow
- If specifying “Add max of ‘x’ molecules”:
  - Priority is given to those molecules that have a high degree of connectivity
    - Prefers to add molecules that interact with the many molecules on the pathway instead of molecules not on the pathway
  - De-emphasis on “hub” molecules that interact promiscuously with many molecules that are not on the pathway

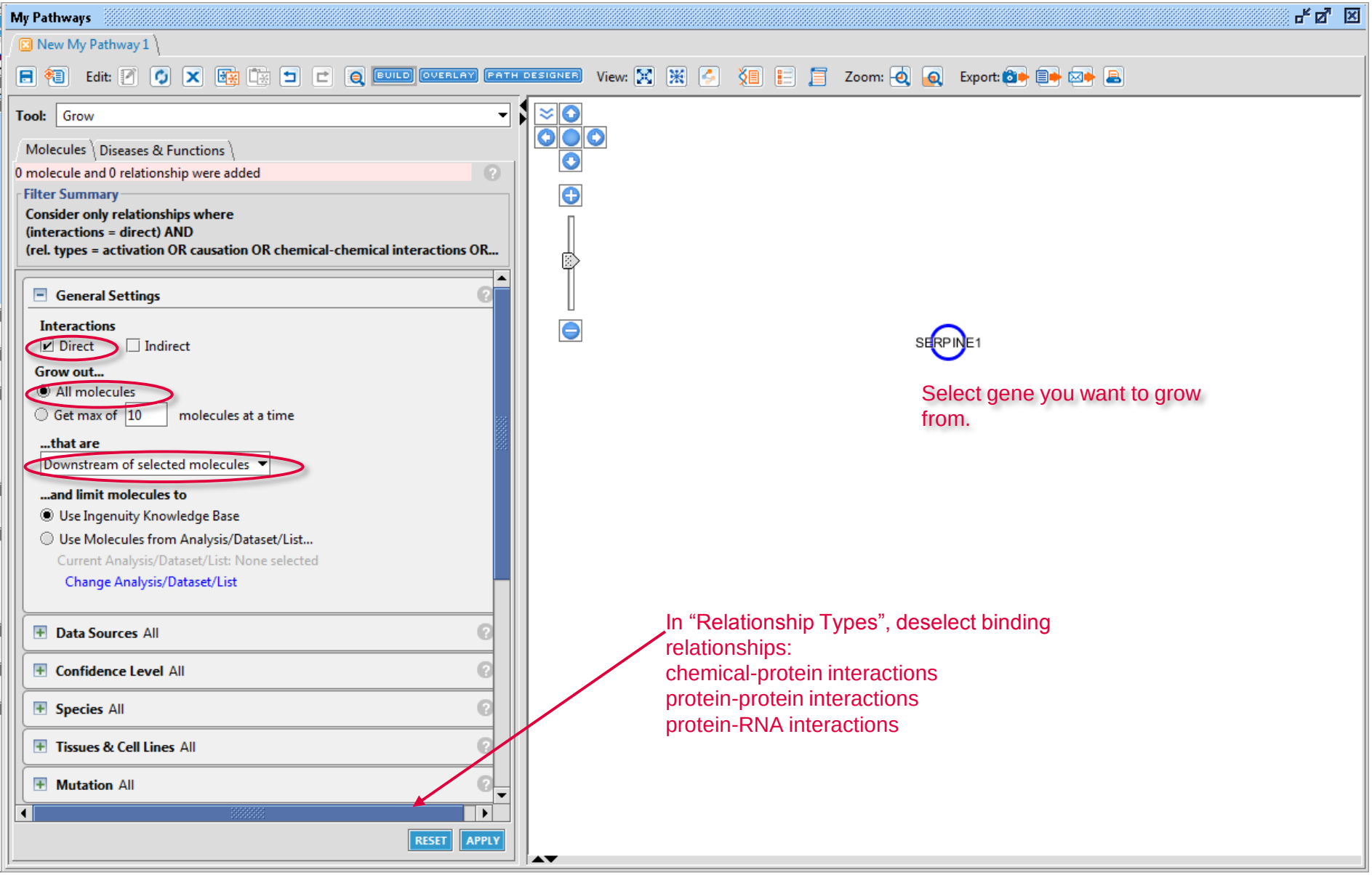
Tips on Using the Grow Tool

- Genes (proteins, chemicals) will not be added if already present somewhere on the pathway.
  - Know if the molecule you are growing from already connects to others in the pathway using Connect or Path Explore
- Newly grown out nodes do not automatically CONNECT to other nodes in a pathway.
  - Use Connect or Path Explorer after Grow to see these relationships.
- Protein-Protein (PP) relationships and other binding relationships will be added when growing either upstream, downstream, or both directions.
  - Recommend as a separate Grow step.
- If Grow is used directionally, only the specific directional interactions (edges) will be displayed.
  - Select new nodes following Grow and use the connect tool to add all interactions from the Knowledge Base.

Search and Add to Pathway



Grow Downstream



My Pathways

New My Pathway 1

Edit: BUILD OVERLAY PATH DESIGNER View: Zoom: Export:

Tool: Grow

Molecules | Diseases & Functions

8 molecules and 8 relationships were added

Filter Summary

Consider only relationships where
(interactions = direct) AND
(rel. types = activation OR causation OR chemical-chemical interactions OR...

General Settings

Interactions
☑ Direct ☐ Indirect

Grow out...
◉ All molecules
○ Get max of 10 molecules at a time

...that are
Downstream of selected molecules

...and limit molecules to
◉ Use Ingenuity Knowledge Base
○ Use Molecules from Analysis/Dataset/List...
Current Analysis/Dataset/List: None selected
Change Analysis/Dataset/List

Data Sources All

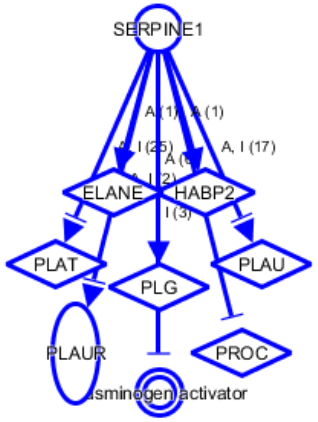
Confidence Level All

Species All

Tissues & Cell Lines All

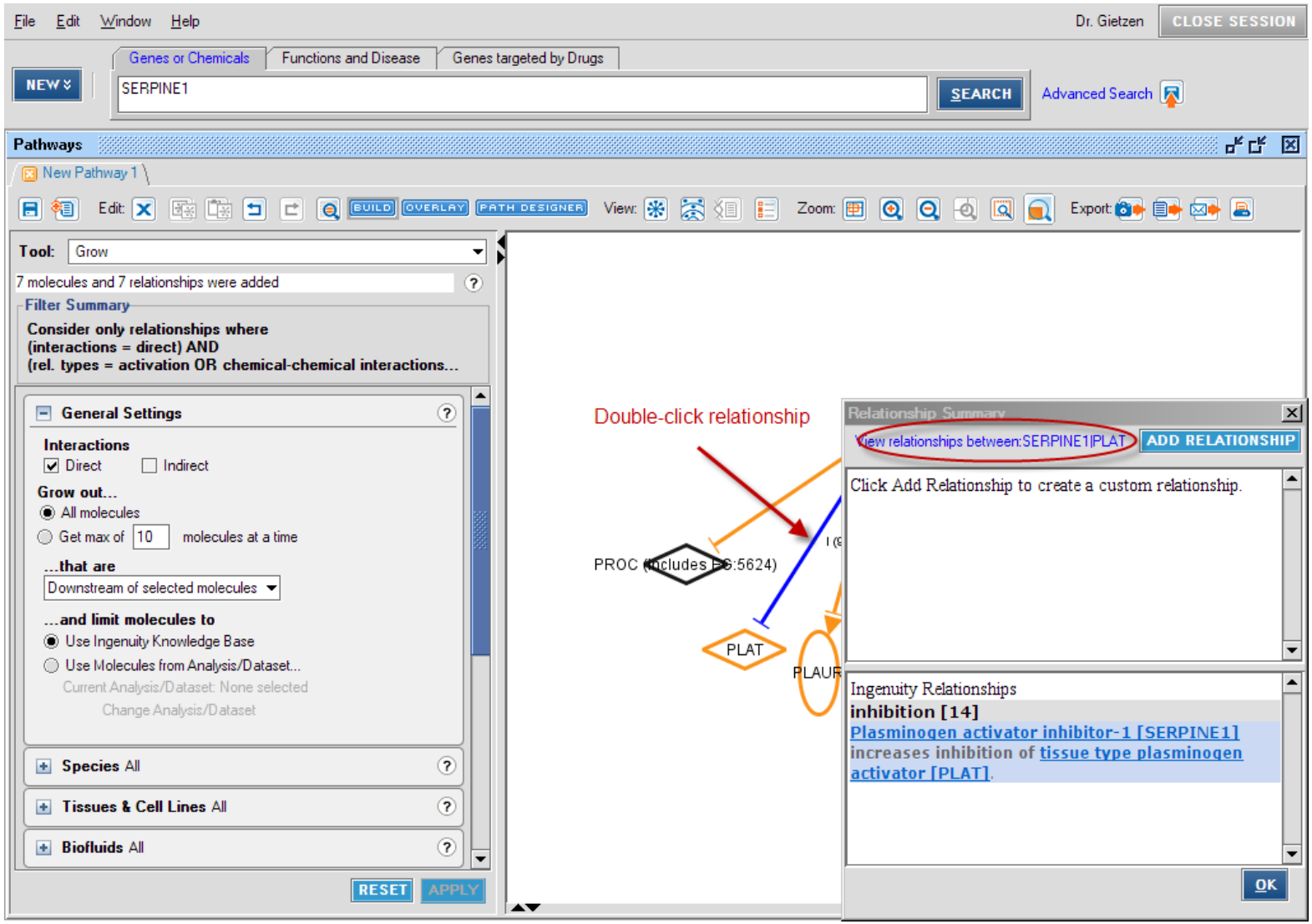
Mutation All

RESET APPLY

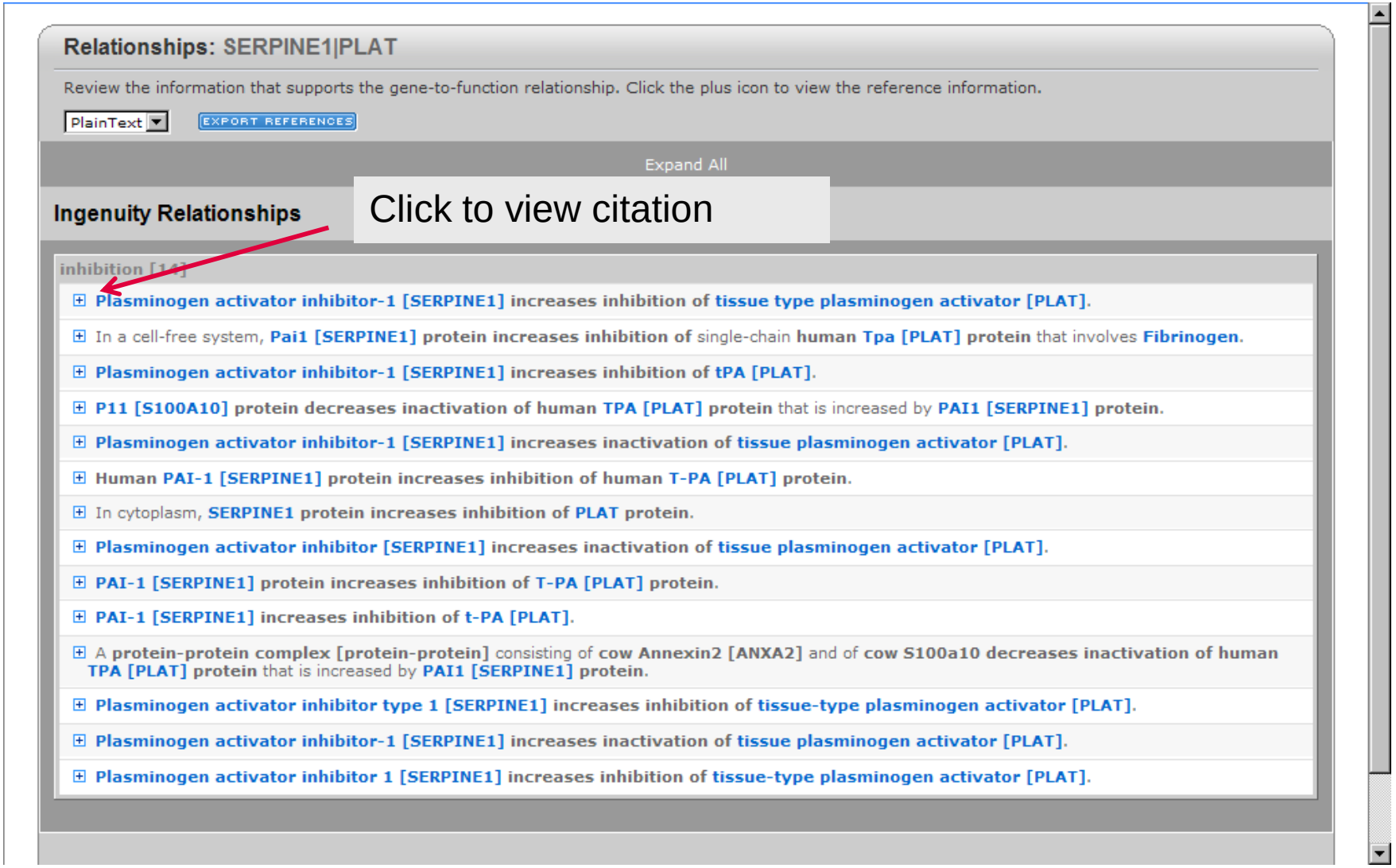


- Click in white-space to deselect
- Right-click to “Reset Highlight”

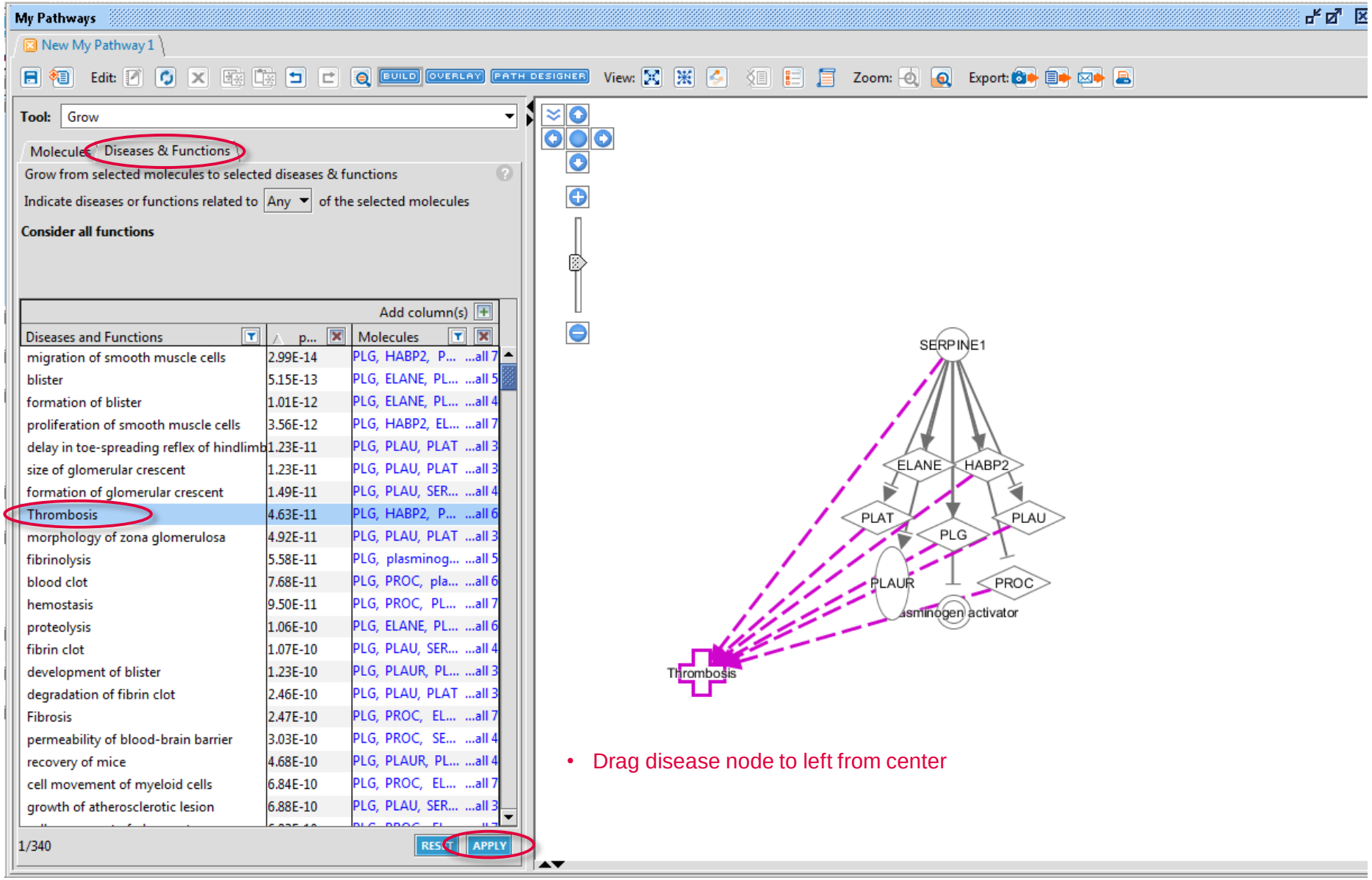
Investigate Relationships



View Literature Findings

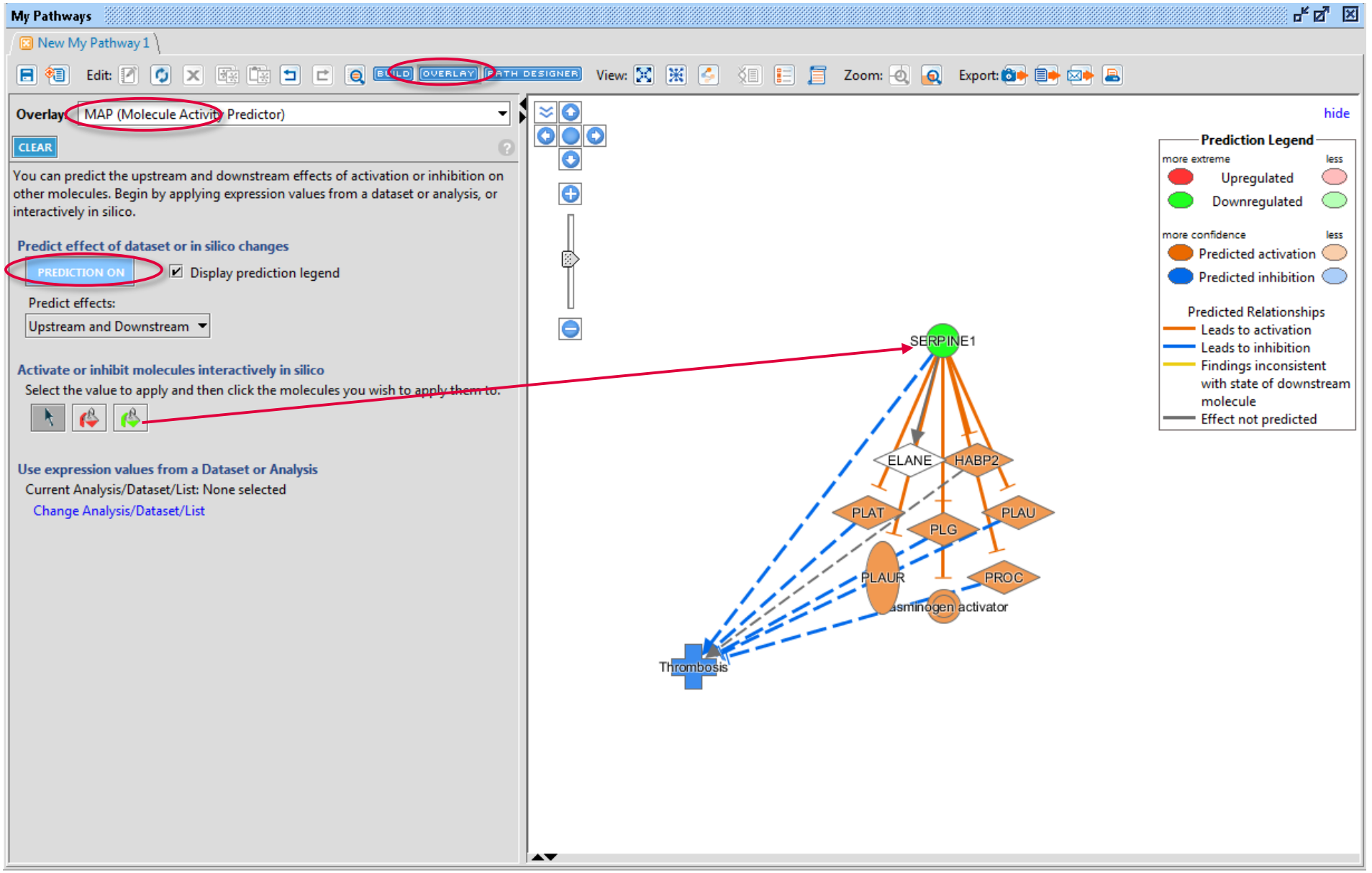


GROW to Disease & Functions



- Drag disease node to left from center

Model Gene Effect on Disease Using MAP



Overlay Tools

- Analysis/ Dataset: Expression/data values that have been uploaded into IPA
- Drug: Known drugs that target the molecules on pathway
- Function & Disease: Functions and Diseases that overlap
- My List/My pathway: User created lists/pathways saved within IPA that overlap
- Canonical Pathway: Canonical Pathways that overlap
- Biomarkers: Displays the molecules that are known biomarkers for specific Applications and Diseases
- Ingenuity Tox List: Ingenuity created toxicity related lists that overlap
- Highlight: Outline molecules that match specified criteria

Find Existing Drug Targets

Use the drug overlay tool to identify drugs that target proteins on the pathway.

Labels provide links to Chem Views

Highlight Mode at bottom of Overlay pane provides easy visualization of drug targets

Drug summary provides indications and clinical status of drugs that target the pathway

Pathways

New Pathway 1

Edit: BUILD OVERLAY PATH DESIGNER View: Zoom: Export:

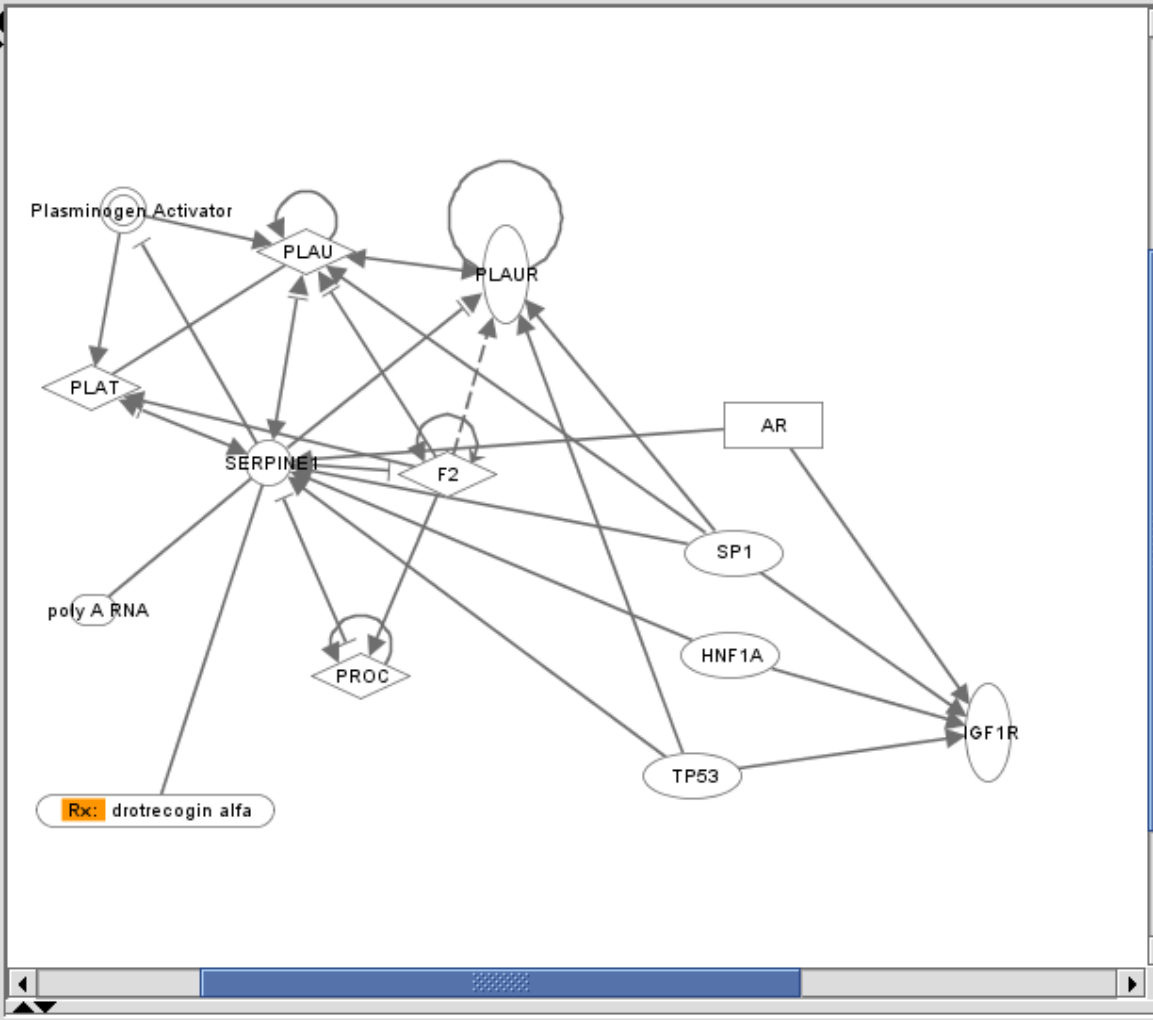
Overlay: Drug

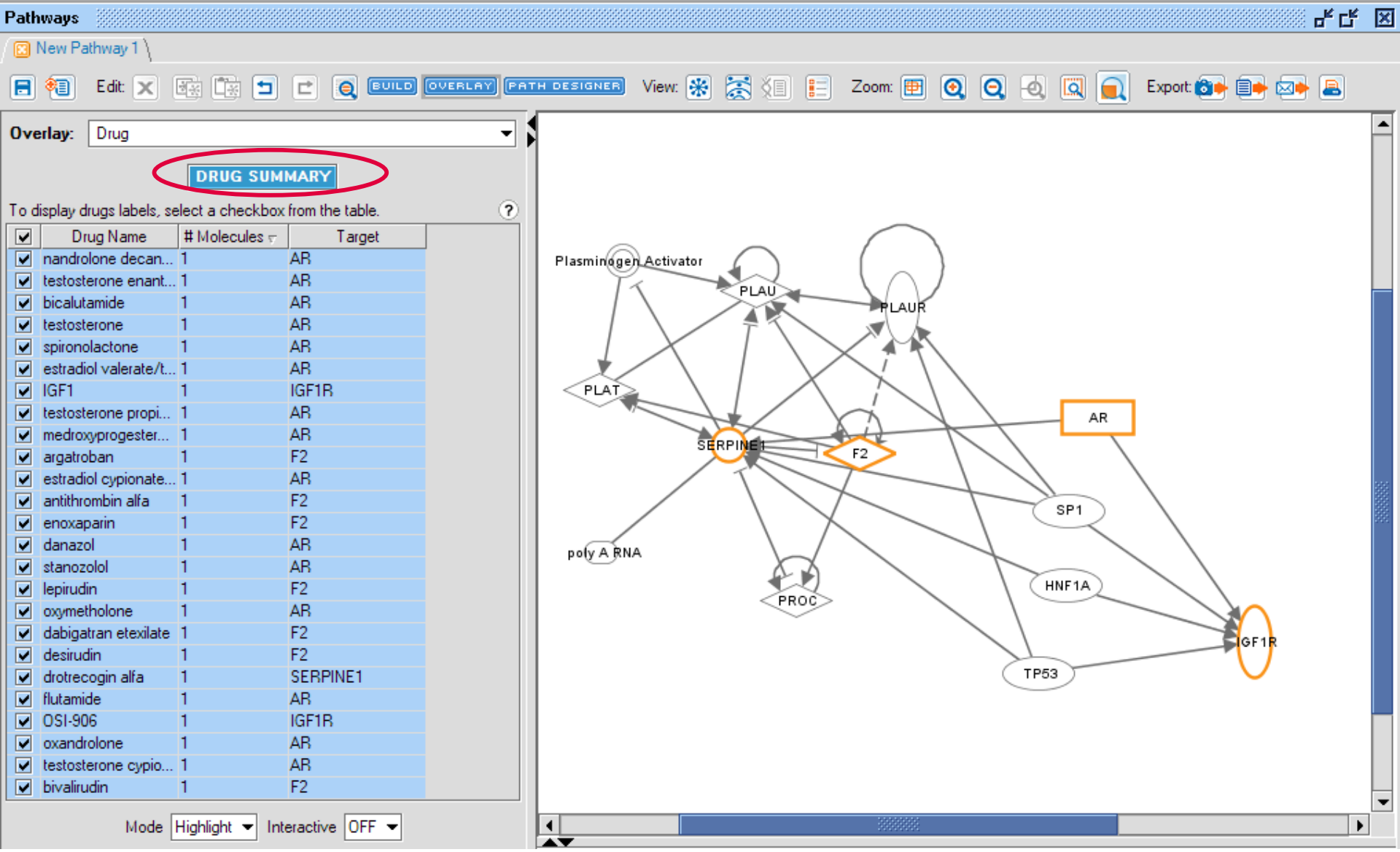
DRUG SUMMARY

To display drugs labels, select a checkbox from the table.

Drug Name	# Molecules	Target
nandrolone decan...	1	AR
testosterone enant...	1	AR
bicalutamide	1	AR
testosterone	1	AR
spironolactone	1	AR
estradiol valerate/t...	1	AR
IGF1	1	IGF1R
testosterone propi...	1	AR
medroxyprogester...	1	AR
argatroban	1	F2
estradiol cypionate...	1	AR
antithrombin alfa	1	F2
enoxaparin	1	F2
danazol	1	AR
stanozolol	1	AR
lepirudin	1	F2
oxymetholone	1	AR
dabigatran etexilate	1	F2
desirudin	1	F2
drotrecogin alfa	1	SERPINE1
flutamide	1	AR
OSI-906	1	IGF1R
oxandrolone	1	AR
testosterone cypio...	1	AR
bivalirudin	1	F2

Mode Label Interactive OFF




Pathways
New Pathway 1
Edit:
BUILD
OVERLAY
PATH DESIGNER
View:
Zoom:
Export:
Overlay: Drug
DRUG SUMMARY
To display drugs labels, select a checkbox from the table.
Drug Name
Molecules
Target
nandrolone decan... 1 AR
testosterone enant... 1 AR
bicalutamide 1 AR
testosterone 1 AR
spironolactone 1 AR
estradiol valerate/t... 1 AR
IGF1 1 IGF1R
testosterone propi... 1 AR
medroxyprogester... 1 AR
argatroban 1 F2
estradiol cypionate... 1 AR
antithrombin alfa 1 F2
enoxaparin 1 F2
danazol 1 AR
stanozolol 1 AR
lepirudin 1 F2
oxymetholone 1 AR
dabigatran etexilate 1 F2
desirudin 1 F2
drotrecogin alfa 1 SERPINE1
flutamide 1 AR
OSI-906 1 IGF1R
oxandrolone 1 AR
testosterone cypio... 1 AR
bivalirudin 1 F2
Mode Highlight
Interactive OFF
Plasminogen Activator
PLAU
PLAUR
PLAT
SERPINE1
F2
AR
SP1
poly A RNA
PROC
HNF1A
IGF1R
TP53

Drug Summary:New Pathway 1

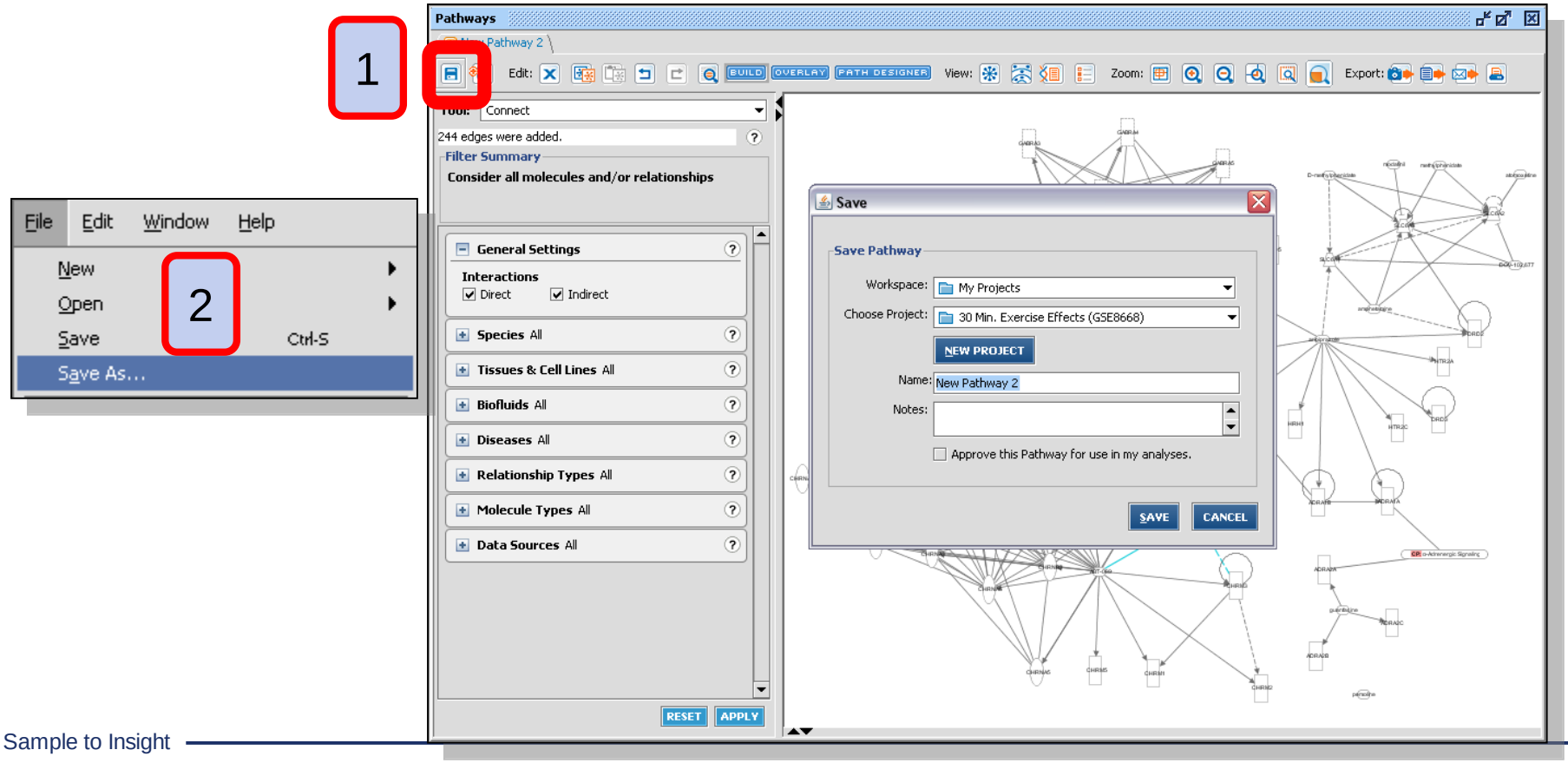
Review the details of drugs associated with a network.

Drug Name ▲	Targets	Actions	Brand Names	Indications/Status
antithrombin alfa	F2	inhibitor	ATryn	disseminated intravascular coagulation/Phase II thromboembolism/Approved
argatroban	F2	inhibitor	Acova	heparin-induced thrombocytopenia/Approved heparin-induced thrombocytopenia/Phase III heparin-induced thrombocytopenia/Phase III coronary artery disease/Phase II
bicalutamide	AR	antiandrogen	Casodex	prostate cancer/Phase III prostate cancer/Phase III prostate cancer/Phase III prostatic carcinoma/Phase III prostatic carcinoma/Phase III prostatic carcinoma/Phase III prostate cancer/Phase III prostatic carcinoma/Phase III prostate cancer/Phase III prostatic carcinoma/Approved prostatic carcinoma/Phase II breast cancer/Phase II breast cancer/Phase II prostate cancer/Phase II
bivalirudin	F2	inhibitor	Angiox, Angiomax	heparin-induced thrombocytopenia/Approved hematological disorder/Phase III cardiovascular disorder/Phase III thrombosis/Phase II angioplasty/Approved

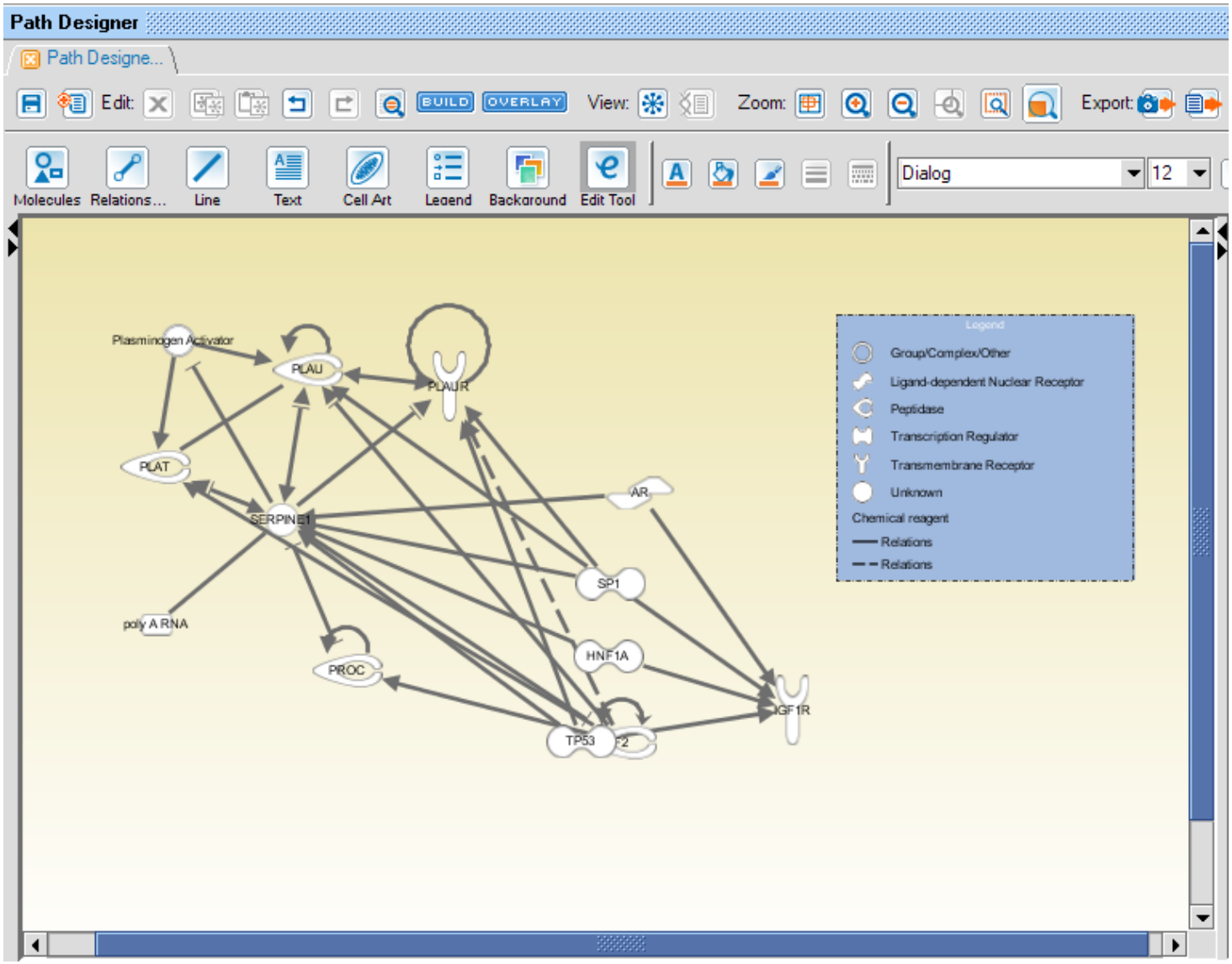
Saving a Pathway

Once a pathway is complete, make sure to save it

1. Using the save icon in the tool bar if you are saving a new one
2. Using File>Save or File>Save As… if you edit an existing one



Send to Path Designer for Image Editing



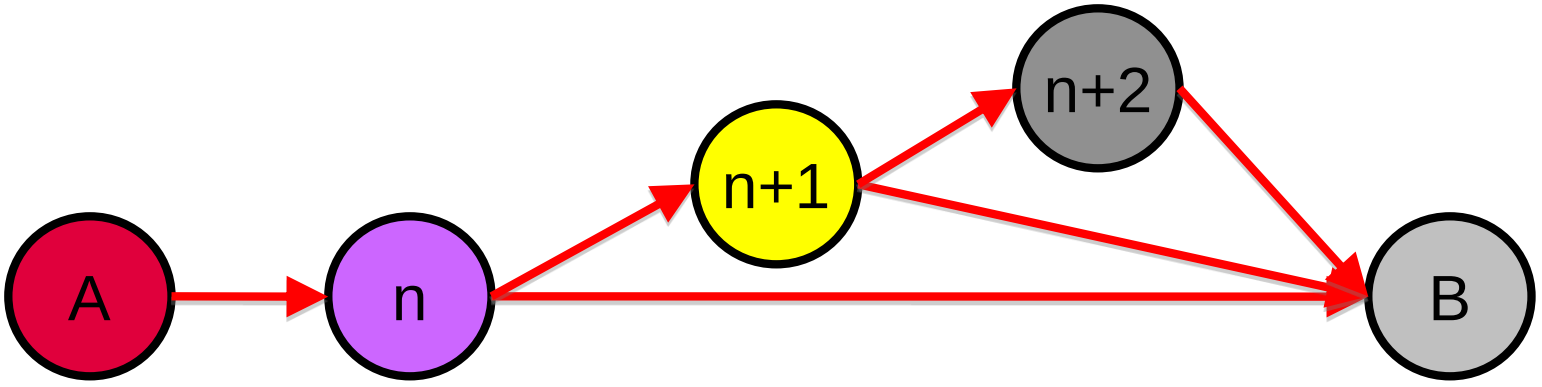
Search and Explore Review

How Path Explorer Works

Calculates the “Shortest Path” between 2 molecules or 2 sets of molecules

If 2 molecules/sets don’t have specific connections in IPA, Path Explorer will find how many and which molecules can be added to this pathway to create the shortest path

- Shortest Path (n)
- Shortest Path + 1 (n+1)
- Shortest Path + 2 (n+2)



General Pathway Navigation

Tool Bar in Pathway/Network view that contains a variety of functions

- **Save:** Save molecules in the pathway as a graphic or as a list
- **Edit:** Delete, Copy, Paste, Undo, Redo, and Find
- **Build:** Grow, Path Explorer, Connect, Trim, Keep, and Add Molecules/Relationships
- **Overlay:** Analyzed Dataset, Molecule Activity Predictor, Drugs, Function & Disease, My List, Canonical Pathway, My Pathway, Ingenuity Tox List, and Highlight
- **Path Designer:** Make a publish/presentation quality version
- **View:** Auto Layout, Sub Cellular Layout, View Annotations, and Preference Settings
- **Zoom:** Overview, Zoom In, Zoom Out, Zoom Selected, Fit to Window, and Magnifying Lens
- **Export:** Image, Data, e-Mail, and Print

Grow: Adds new molecules and their relationships given the criteria that the user specifies

Path Explorer: Calculates the “Shortest Path” between 2 molecules or 2 sets of molecules

Connect: Connects molecules given the criteria that the user specifies

Trim: Removes molecules/relationships that meet the criteria that the user specifies

Keep: Keeps molecules/relationships that meet the criteria that the user specifies

Add Molecule/Relationship: Allows adding a custom molecules or relationship to the current pathway that does not exist in Ingenuity’s KB as well as ones that already exist

Analysis/ Dataset: Expression/data values that have been uploaded into IPA

Molecule Activity Predictor (MAP): Uses expression or user-defined activation states to predict the activity of neighboring molecules

Drug: Known drugs that target the molecules on pathway

Function & Disease: Functions and Diseases that overlap

My List/My Pathway: User created lists/pathways saved within IPA that overlap

Canonical Pathway: Canonical Pathways that overlap

Biomarkers: Displays the molecules that are known biomarkers for specific Applications and Diseases

Ingenuity Tox List: Ingenuity created toxicity related lists that overlap

Highlight: Outline molecules that match specified criteria