

INGENUITY[®]

S Y S T E M S



IPA[®] Search & Explore Case Study for CNS

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CNS Search and Explore Examples

- Tell me about my gene of interest – *DRD2*
 - What Antibodies are available?
 - What canonical signalling pathways does it appear in?
 - What are the *transcriptional regulators* of this gene?
 - What other *GPCRs* are regulated by these Transcription Factors?
- What *ion channels and GPCRs* are involved in *cognition*?
 - How do they interconnect?
 - What other biological processes or functions are these genes involved in?
 - What are the molecular connections that link these genes to *growth factors* involved in *schizophrenia*?
 - What drugs target these genes?
- Tell me about *olanzapine*?
 - What clinical trials are running for olanzapine?
 - How does olanzapine treatment affect the gene expression of these cognition ion channels and GPCRs?
- What are the upstream regulators of the gene expression changes induced by olanzapine treatment?

Tell Me About My Gene of Interest

Genes and Chemicals | Functions and Diseases | Pathways and Tox Lists

dopamine [Advanced Search](#)

dopamine	chemical - endogenous mammalian
DOPAMINE D1 RECEPTOR	G-protein coupled receptor
Dopamine d2 receptor	G-protein coupled receptor
Dopamine d3 receptor	G-protein coupled receptor
DOPAMINE D4 RECEPTOR	G-protein coupled receptor
dopamine HCl	chemical - endogenous mammalian
dopamine lutine	chemical - endogenous mammalian
dopamine quinone	chemical toxicant
Dopamine receptor 4	G-protein coupled receptor
dopaminechrome	chemical toxicant

Auto-complete lists matching genes and chemical names
Use of auto-complete is optional, you can simply type and click Search

Search

[ADD TO MY PATHWAY](#) [ADD TO MY LIST](#) [CREATE DATASET](#) [CUSTOMIZE TABLE](#)

The search for Dopamine d2 receptor matched 1 items.

<input type="checkbox"/>	<input type="checkbox"/>	Symbol	Matched Term	Synonym(s)	Entrez Gene Name	Location	Type(s)	View/Open	Biomarker	Drug(s)	Target(s)	Species
<input type="checkbox"/>	1	DRD2	D2 DOPAMINE RECEPTOR, Dopamine d2 receptor	D2, D2 DOPAMINE RECEPTOR , D2 dopaminergic receptors, D2-like receptors, D2a dopamine receptors, D2DR, D2R, D2S, Dopamine d2 receptor , Dopamine D2L receptor, Dr2	dopamine receptor D2	Plasma Membrane	G-protein coupled receptor	Reagents and Interactions	Response	paliperidone, risperidone, buspirone, bifeprunox, iloperidone, blonanserin, asenapine, pardoprunox, ocaperidone, abaperidone		Human, Mouse, Rat

Examine Gene View Page (points to DRD2)

View All interactions and view Reagents page (points to Reagents and Interactions)

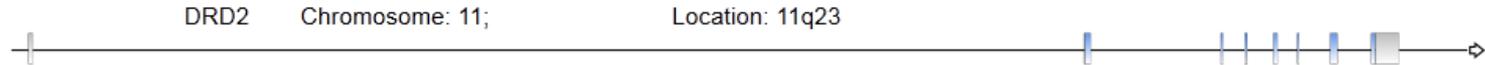
Examine Biomarker Usage (points to Response)

Examine Drug Chem View Page (points to Drug(s))

Gene View Page Details

Human Isoforms From RefSeq

[More Info](#)



Domains	Length (# of AA's)	# of findings
NM_000795.3 : NP_000786.1	443	203
NM_016574.3 : NP_057658.2	414	143

Literature Findings specific to different isoforms

Drug Information

Targeting Drug	Drug Brand Name(s)	Action
abaperidone		antagonist
amantadine	Endantadine; Gen-Amantadine; Mantadine; Pk-Merz; Symadine; Symmetrel	agonist
amitriptyline/perphenazine	Duo-Vil 2-10; Duo-Vil 2-25; Duo-Vil 4-10; Etrafon 2-10; Etrafon 2-25; Etrafon Forte	antagonist
apomorphine	Apokyn; Ixense; Uprima	agonist

Curated list of Drugs

Recently Added Literature Findings

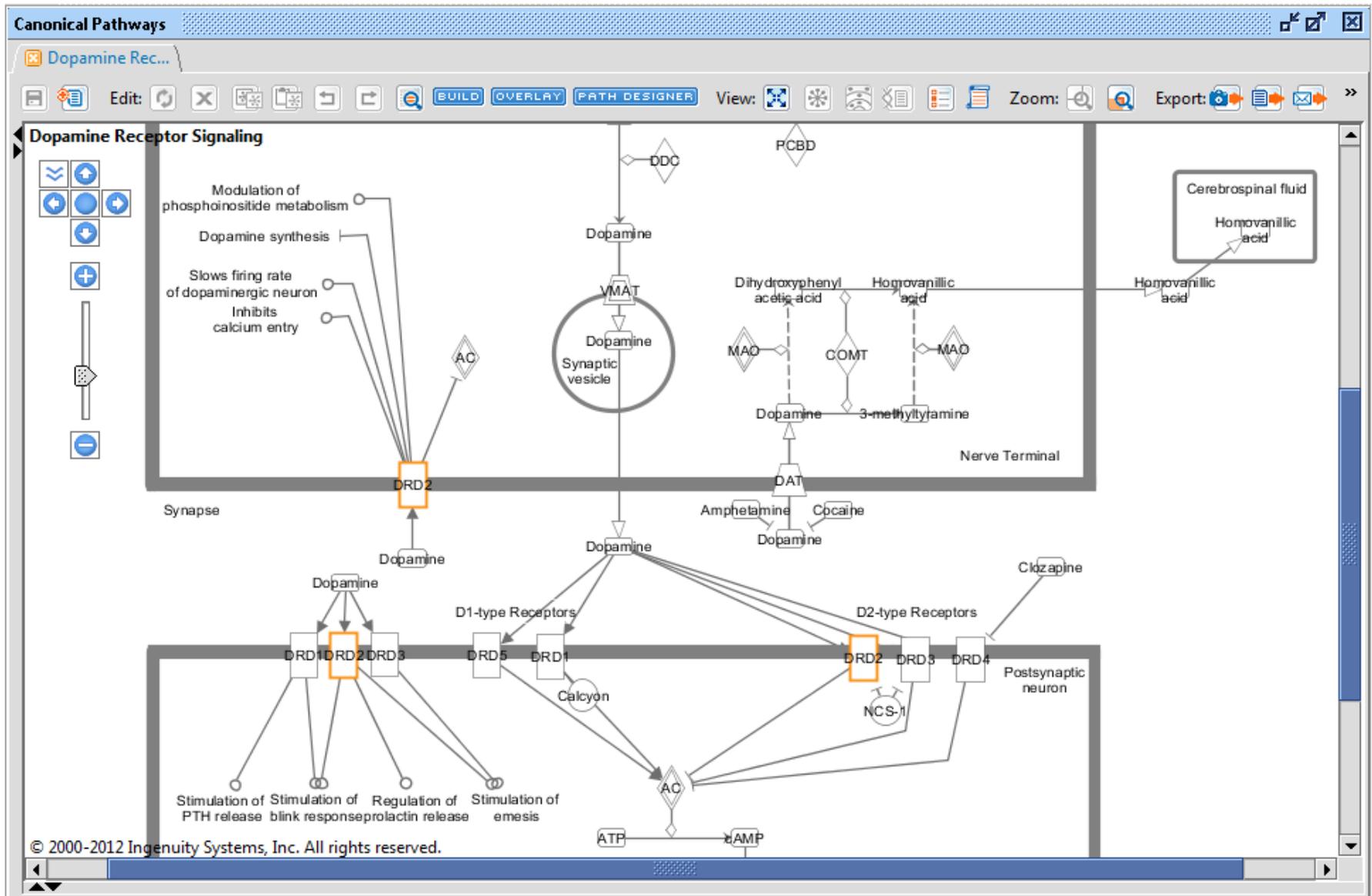
29 Recently Added Findings (show Findings)

3728 Categorized Literature Findings (hide details)

- Biomarker Information
- Functional Roles
- Mutant Information
- Modifications and Regulation
- Disease
- Expression and Localization
- Physical Interactions
- Additional Findings

Categorized Literature Findings

Dopamine Receptor Signalling Pathway



Transcriptional Regulators of DRD2

Search

ADD TO MY PATHWAY ADD TO MY LIST CREATE DATASET CUSTOMIZE TABLE

The search for Dopamine D2 receptor matched 1 items.

<input checked="" type="checkbox"/>	Symbol	Matched Term	Synonym(s)	Entrez Gene Name
<input checked="" type="checkbox"/>	1 DRD2	DOPAMINE RECEPTOR, D2	D2, D2 DOPAMINE RECEPTOR, D2 dopaminergic receptor,	dopamine receptor D2

1. Select

2. Click and Add to New Pathway

My Pathways

New My Pathw...

Build Overlay Path Designer View: Zoom: Export:

Tool: <Select a tool>

Select a build tool from the options above.

4. Use the Build tools

5. Use Grow to grow out from selected nodes

3. Select

DRD2

Build Tools

- 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: 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

Use the Filter Options to Refine the Grow

Tool: Grow

Grow from selected molecules to molecules and relationships based on specified criteria. Click Apply to view new network.

Filter Summary
Consider all molecules and/or relationships

General Settings

Interactions
 Direct Indirect

Grow out...
 All molecules
 Get max of molecules at a time

...that are
Upstream or Downstream

...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
Relationship Types All
Publication Date Range All
Molecule Types All
Diseases All

RESET **APPLY**

General Settings

Interactions
 Direct Indirect

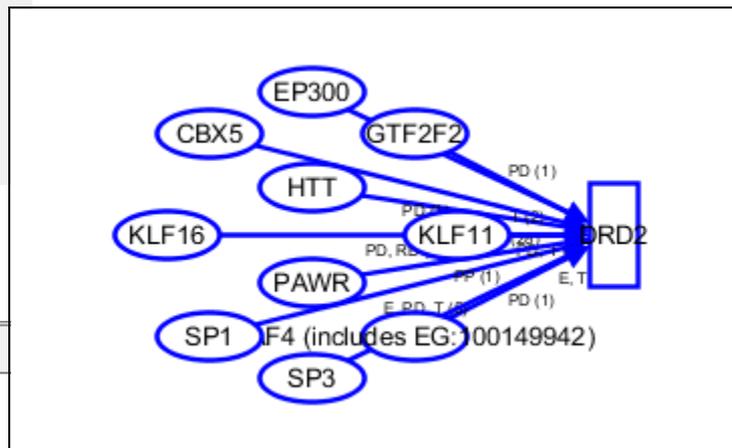
Grow out...
 All molecules
 Get max of molecules at a time

...that are
Upstream 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

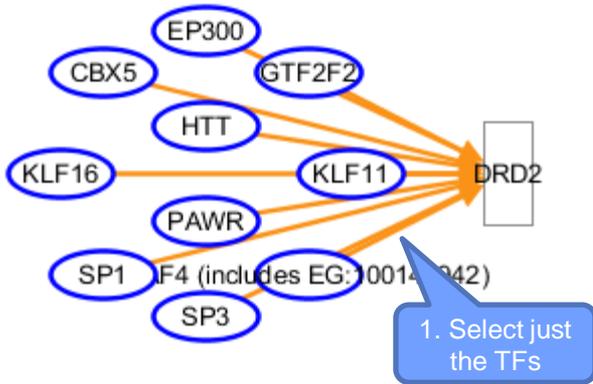
Molecule Types transcription regulator

- ligand-dependent nuclear receptor
- mature microRNA
- microRNA
- peptidase
- phosphatase
- transcription regulator
- translation regulator
- transmembrane receptor



Other refinements may be required or desired

Other GPCRs Regulated by these TFs



General Settings

Interactions
 Direct Indirect

Grow out...
 All molecules
 Get max of molecules at a time

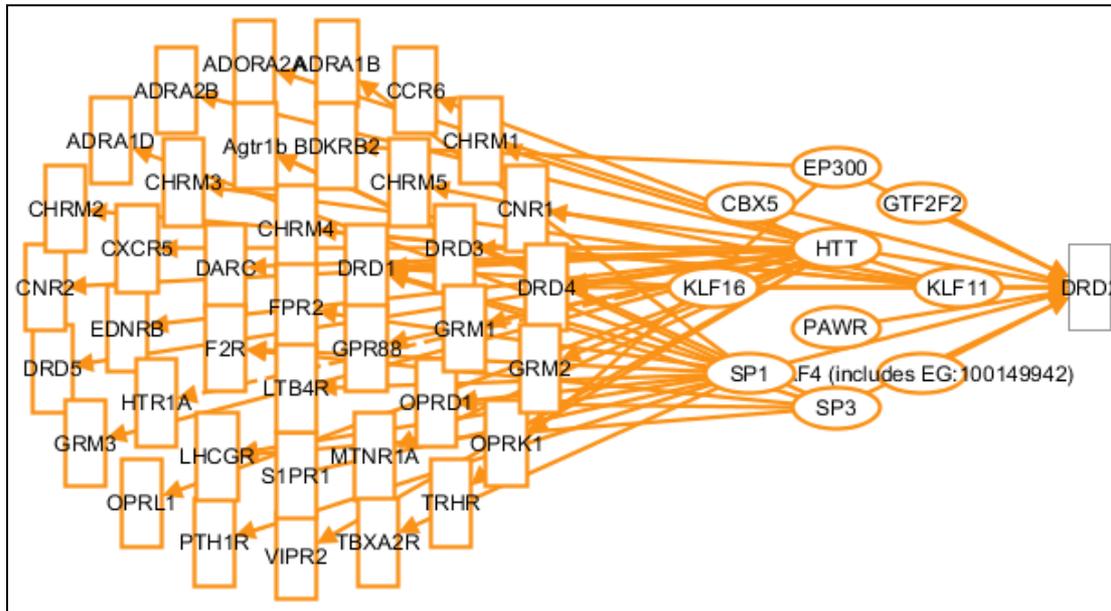
...that are
 Downstream of selected molecules ▼

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

Molecule Types G-protein coupled receptor

- enzyme
- G-protein coupled receptor
- group
- growth factor
- ion channel
- kinase
- ligand-dependent nuclear receptor
- mature microRNA

2. Grow Downstream to GPCRs

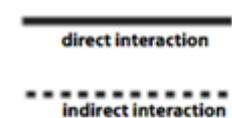
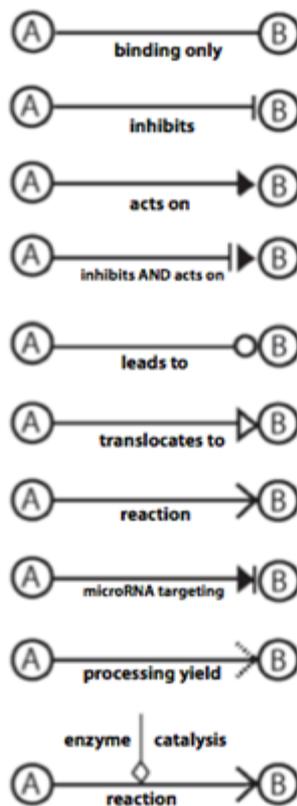


Network Legend

Network Shapes

-  Cytokine
-  Growth Factor
-  Chemical /Drug/ Toxicant
-  Enzyme
-  G-protein Coupled Receptor
-  Ion Channel
-  Kinase
-  Ligand-dependent Nuclear Receptor
-  Peptidase
-  Phosphatase
-  Transcription Regulator
-  Translation Regulator
-  Transmembrane Receptor
-  Transporter
-  Complex / Group
-  microRNA
-  Mature microRNA
-  Other

Relationships



Note: "Acts on" and "Inhibits" edges may also include a binding event.

Relationship Labels

- A Activation
- B Binding
- C Causes/Leads to
- CC Chemical-Chemical interaction
- CP Chemical-Protein interaction
- E Expression (includes metabolism/ synthesis for chemicals)
- EC Enzyme Catalysis
- I Inhibition
- L Proteolysis (includes degradation for Chemicals)
- LO Localization
- M Biochemical Modification
- miT microRNA Targeting
- MB Group/complex Membership
- nTRR Non-Targeting RNA-RNA Interaction
- P Phosphorylation/Dephosphorylation
- PD Protein-DNA binding
- PP Protein-Protein binding
- PR Protein-RNA binding
- PY Processing Yields
- RB Regulation of Binding
- RE Reaction
- RR RNA-RNA Binding
- T Transcription
- TR Translocation

Ion Channels & GPCR Involved in Cognition

Genes and Chemicals | **Functions and Diseases** | Pathways and Tox Lists

cognition [Advanced Search](#)

1. Function & Disease Search

2. Refine with Advanced Search

Advanced Search Options

Gene(s), Chemical(s) and Identifier(s)

Identifier Type(s)

Molecule Type(s)

Subcellular Location(s)

Pathways and Tox Lists

Display results in Table Tree

3. Choose Molecule Types

The search for cognition, ion channel, G-protein coupled receptor, matched 3 functions and diseases.

Functions & Diseases	Associated Molecule
<input type="checkbox"/> Matching Functions & Diseases	76
<input type="checkbox"/> Behavior	63
<input type="checkbox"/> cognition	63
<input type="checkbox"/> cognition	63
ADORA1, ADORA2A, ADRA1B, ASIC1, CACNA1C, CACNA1E, CACNA1G, CACNB3, CHRNA4, CHRNA7, CHRN2, CNGA4, CRHR1, CX3CR1, DRD1, DRD2, DRD3, DRD4, DRD5, FZD9, GABBR1, GABBR2, GABRA1, GABRA5, GABRB3, GABRD, GALR2, GALR3, GLP1R, GRID2, GRIK1, GRIN1, GRIN2A, GRIN2B, GRM1, GRM4, GRM5, GRM7, GRPR, HCN1, HRH3, HTR1A, HTR1B, HTR2C, HTR4, HTR6, JPH3, KCNAB1, KCNAB2, KCNJ5, LYPD1, MCHR1, NPY2R, OPRM1, PSEN1, PTGER2, RYR3, SLC1A4, SLC24A2, TACR1, TACR3, VDAC1, VDAC3	

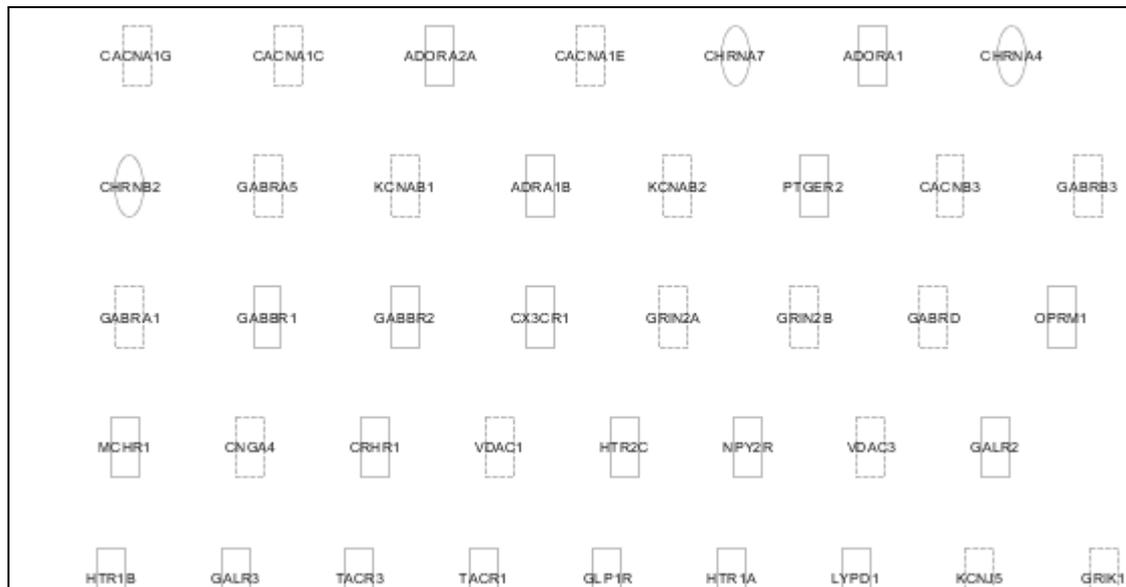
How Do They Interconnect?

The search for cognition channel, G-protein coupled receptor, matched 3 functions and diseases.

Functions & Disease	Associated Molecule
<input type="checkbox"/> Matching Function	76
<input type="checkbox"/> Behavior	63
<input checked="" type="checkbox"/> cognition	63
<input checked="" type="checkbox"/> cognition	63

1. Highlight and Add to New My Pathway

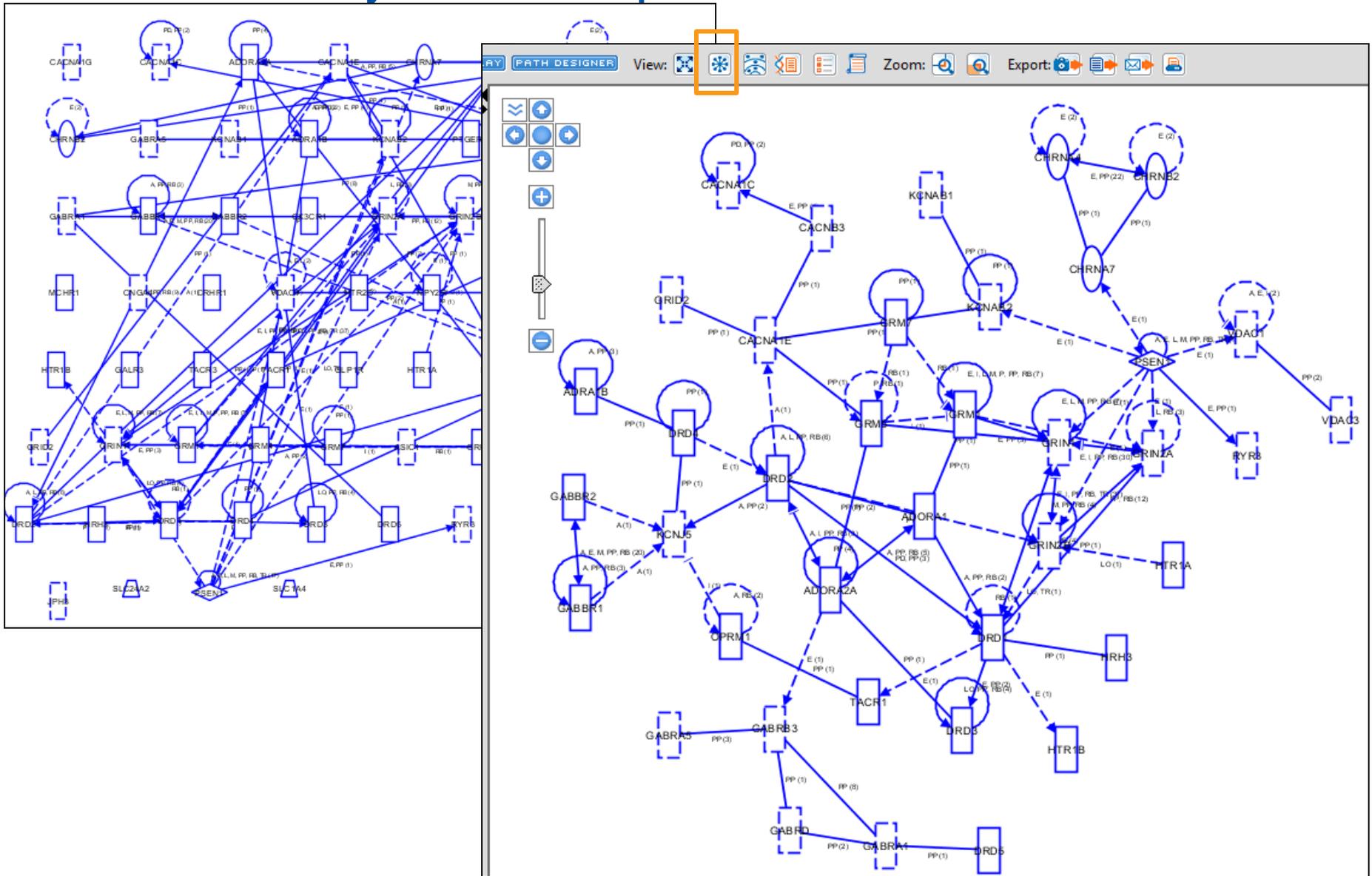
ADORA1, ADORA2A, ADRA1B, ASIC1, CACNA1C, CACNA1E, CACNA1G, CACNB3, CHRNA4, CHRNA7, CHRN2, CNGA4, CRHR1, CX3CR1, DRD1, DRD2, DRD3, DRD4, DRD5, FZD9, GABBR1, GABBR2, GABRA1, GABRA5, GABRB3, GABRD, GALR2, GALR3, GLP1R, GRID2, GRIK1, GRIN1, GRIN2A, GRIN2B, GRM1, GRM4, GRM5, GRM7, GRPR, HCN1, HRH3, HTR1A, HTR1B, HTR2C, HTR4, HTR6, JPH3, KCNAB1, KCNAB2, KCNJ5, LYPD1, MCHR1, NPY2R, OPRM1, PSEN1, PTGER2, RYR3, SLC14A, SLC24A2, TACR1, TACR3, VDAC1, VDAC3



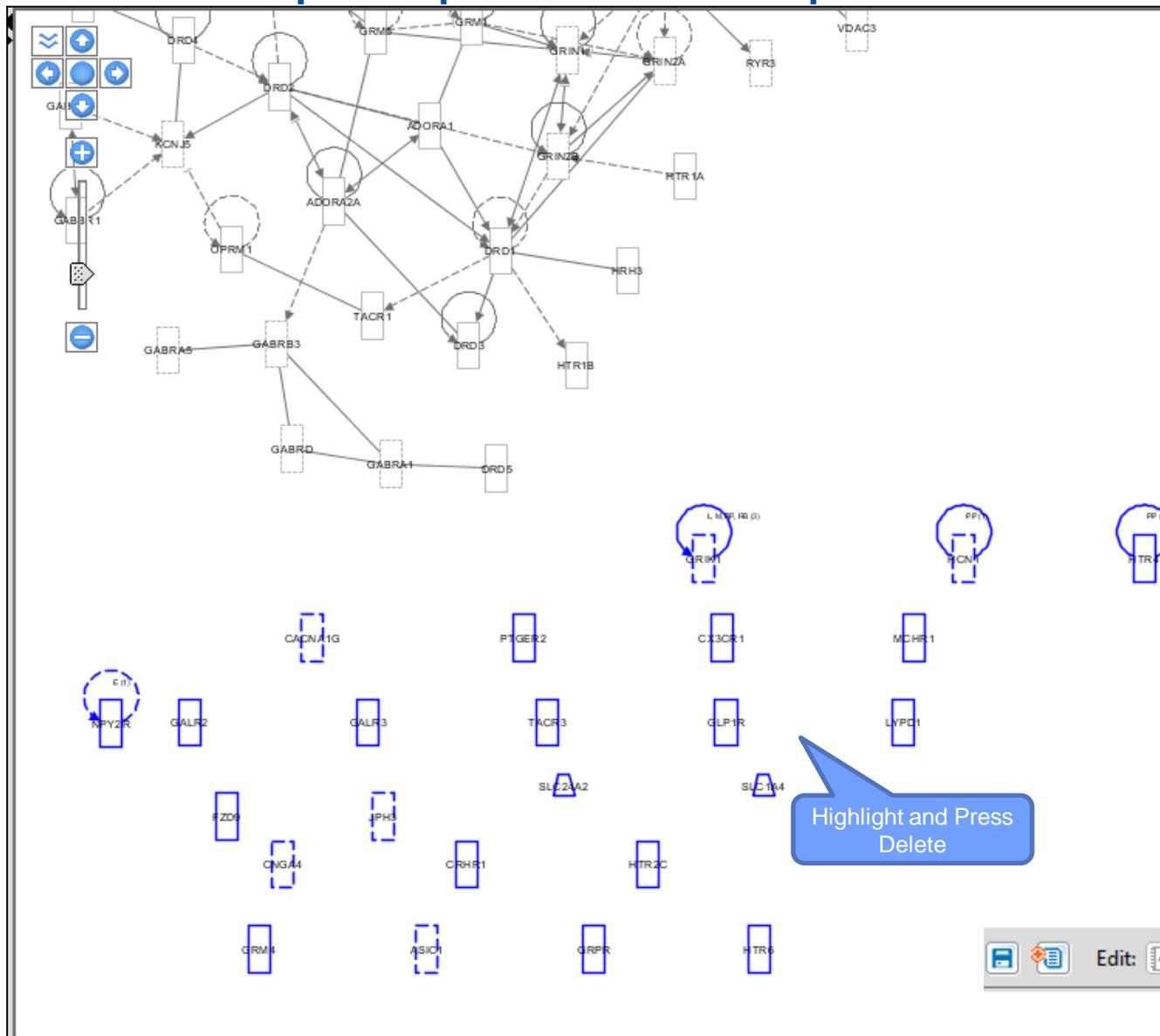
Use The Build Tool 'Connect' to Join Genes

The screenshot displays the Ingenuity Pathways Designer software interface. On the left, the 'Tool' dropdown is set to 'Connect'. Below it, a text box reads: 'Connect selected molecules based on specific criteria. Click Apply to view new connections.' A blue callout bubble points to the 'Connect' tool with the text: '1. Use Connect from the Build Tools'. Below this, the 'Filter Summary' section is visible, with the text: 'Consider all molecules and/or relationships'. The 'General Settings' section is expanded, showing 'Interactions' with 'Direct' and 'Indirect' checkboxes checked. Other sections include 'Data Sources All', 'Confidence Level All', 'Species All', 'Tissues & Cell Lines All', 'Mutation All', 'Relationship Types All', 'Publication Date Range All', 'Molecule Types All', 'Diseases All', and 'Biofluids All'. The main workspace contains a grid of gene symbols, each represented by a blue dashed box with the gene name inside. A blue callout bubble points to one of the symbols with the text: '2. Highlight'. At the bottom left, another blue callout bubble contains the text: '3. Refine, if necessary'. The top of the interface shows the 'My Pathways' title bar, navigation buttons, and a toolbar with options like 'BUILD', 'OVERLAY', 'PATH DESIGNER', 'View', 'Zoom', and 'Export'.

Use Auto-Layout to Re-position



Clean-up 'Orphans' if Required



What Biological Processes are they Involved In?

The screenshot shows the 'My Pathways' software interface. At the top, there are tabs for 'BUILD', 'OVERLAY', and 'PATH DESIGNER'. The 'OVERLAY' tab is active. Below the tabs is a toolbar with various icons for editing and viewing. On the left side, there is a panel labeled 'Overlay:' with a dropdown menu set to '<Select a tool>'. Below this panel, there are three callout boxes:

- Callout 1: A blue speech bubble pointing to the 'Overlay:' dropdown menu, containing the text "1. Use the Overlay Tools".
- Callout 2: A blue speech bubble pointing to the 'Overlay:' dropdown menu, containing the text "2. Use Function and Disease overlay".
- Callout 3: A blue speech bubble pointing to the network diagram, containing the text "3. No Need to select or highlight – Overlay applies to everything in the My Pathway".

The network diagram itself consists of numerous nodes (represented by rectangles and circles) and edges (represented by solid and dashed lines). The nodes are labeled with gene symbols such as CACNA1C, CACNB3, KCNA1E, GRM7, GRM5, GRM1, GRIN1, GRIN2A, GRIN2B, DRD1, DRD2, DRD3, DRD4, DRD5, ADORA1, ADORA2A, GABBR1, GABBR2, GABBR3, GABRA5, GABRA1, GABRD, OPRM1, TACR1, HTR1A, HTR1B, HTR3, RYR3, VDAC1, VDAC3, CHRNA4, CHRNB2, CHRNB7, KCNAB1, KCNAB2, and PSEN1. The diagram illustrates a complex network of interactions between these genes.

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

Browse and Select from Function Tree

Overlay: Function & Disease

FUNCTIONS SHOW FUNCTIONS

Functions and Diseases	p-value Δ	# Molecules
<input type="checkbox"/> Relevant Biological Functions		39
<input type="checkbox"/> Behavior	6.6E-68 - 2.99E-5	39
<input type="checkbox"/> Cell-To-Cell Signaling and Interaction	1.11E-42 - 2.99E-5	36
<input type="checkbox"/> neurotransmission	1.11E-42 - 1.11E-...	30
<input type="checkbox"/> synaptic transmission	5.59E-41 - 1.79E-6	28
<input type="checkbox"/> long-term potentiation	6.37E-25 - 2.99E-5	19
<input type="checkbox"/> action potential	1.3E-19 - 6.7E-15	13
<input checked="" type="checkbox"/> plasticity	4.3E-17 - 4.3E-17	11
<input type="checkbox"/> release	3.46E-14 - 6.26E-...	18
<input type="checkbox"/> synaptic depression	2.57E-14 - 3.57E-...	10
<input type="checkbox"/> secretion	8.97E-...	10
<input type="checkbox"/> long term	4.74E-6	9
<input type="checkbox"/> excitatory postsynaptic potential	1.74E-11 - 4.55E-8	8
<input type="checkbox"/> metabolism	1.75E-9 - 1.75E-9	5
<input type="checkbox"/> quantity	7.67E-9 - 7.67E-9	9
<input type="checkbox"/> concentration	5.35E-8 - 5.35E-8	7
<input type="checkbox"/> binding	1.74E-7 - 1.74E-7	3
<input type="checkbox"/> GABA-mediated receptor currents	5.93E-7 - 5.93E-7	3
<input type="checkbox"/> NMDA-mediated synaptic current	2.24E-6 - 2.24E-6	3
<input type="checkbox"/> nicotine-mediated receptor curren	3E-6 - 3E-6	2
<input type="checkbox"/> excitation	1.55E-5 - 1.55E-5	4
<input type="checkbox"/> activation	1.79E-5 - 1.79E-5	2
<input type="checkbox"/> Nervous System Development and Fu	1.11E-42 - 4.06E-5	38
<input type="checkbox"/> Neurological Disease	6.82E-37 - 3.94E-5	36
<input type="checkbox"/> Psychological Disorders	6.82E-37 - 2.99E-5	32
<input type="checkbox"/> Hereditary Disorder	1.58E-30 - 1.79E-5	32
<input type="checkbox"/> Skeletal and Muscular Disorders	2.89E-23 - 7.51E-6	25
<input type="checkbox"/> Nutritional Disease	1.93E-22 - 2.01E-7	18
<input type="checkbox"/> Organismal Injury and Abnormalities	4.9E-22 - 2.14E-1	26
<input type="checkbox"/> Molecular Transport	1.69E-20 - 5.37E-5	36
<input type="checkbox"/> Cardiovascular Disease	3.55E-19 - 2.47E-1	25
<input type="checkbox"/> Cell Morphology	4.3E-17 - 4.06E-5	20

1. Select to Label Relevant Nodes

2. Double-Click to view literature Findings for this association

Ex: plasticity of synapse

Findings View

Findings: plasticity of synapse

Review the information that supports the gene-to-function relationship. Click the plus icon to view the reference information.

PlainText ▾

[EXPORT REFERENCES](#)

Findings 1 to 20 of 20

Mouse **Psen1** is involved in plasticity of synapse.

[15066262](#)

Saura CA, Choi SY, Beglopoulos V, Malkani S, Zhang D, Shankaranarayana Rao BS, Chattarji S, Kelleher RJ, Kandel ER, Duff K, Kirkwood A, Shen J. Loss of presenilin function causes impairments of memory and synaptic plasticity followed by age-dependent neurodegeneration. *Neuron* 2004 04 8;42(1):23-36.

[0048167](#)

Source: Gene Ontology (GO)

Mouse **Grin2b** is involved in plasticity of synapse.

[16710293](#)

Nakazawa T, Komai S, Watabe AM, Kiyama Y, Fukaya M, Arima-Yoshida F, Horai R, Sudo K, Ebine K, Delawary M, Goto J, Umemori H, Tezuka T, Iwakura Y, Watanabe M, Yamamoto T, Manabe T. NR2B tyrosine phosphorylation modulates fear learning as well as amygdaloid synaptic plasticity. *EMBO J* 2006 06 21;25(12):2867-77.

[0048167](#)

Source: Gene Ontology (GO)

Rat **Drd1a** is involved in plasticity of synapse.

[16855100](#)

Lemon N, Manahan-Vaughan D. Dopamine D1/D5 receptors gate the acquisition of novel information through hippocampal long-term potentiation and long-term depression. *J Neurosci* 2006 07 19;26(29):7723-9.

[0048169](#)

Source: Gene Ontology (GO)

How do Growth Factors Involved in Schizophrenia Link to these Genes?

Genes and Chemicals | **Functions and Diseases** | Pathways and Tox Lists

schizophrenia SEARCH [Advanced Search](#)

Advanced Search Options

Gene(s), Chemical(s) and Identifier(s) ?

Identifier Type(s) All Identifiers ?

Molecule Type(s) growth factor

Subcellular Location(s) [Click here to select subcellular locations](#)

Pathways and Tox Lists ?

Display results in Table Tree

? RESET SEARCH CANCEL

1. Function & Disease Search

2. Refine with Advanced Search

3. Choose Molecule Types

The search for schizophrenia, growth factor, matched 3 functions and diseases.

Functions & Diseases	Associated Molecule
<input type="checkbox"/> Matching Functions & Diseases	11
<input type="checkbox"/> Neurological Disease	11
<input type="checkbox"/> schizophrenia	11
<input type="checkbox"/> schizophrenia	11
<ul style="list-style-type: none"> BDNF, CNTF, EGF (includes EG:13645), FGF1, GDNF, IL2, NELL1, NRG1 (includes EG:112400), NRG3, NTF3, VGF 	.

Add Molecules to Existing My Pathway

The screenshot displays a software interface for managing biological pathways. At the top, a search bar contains the text "schizophrenia growth factor". Below the search bar are several action buttons: "ADD TO MY PATHWAY", "ADD TO MY LIST", "ANNOTATIONS", "SHOW FINDINGS", "EFFECT ON FUNCTION", "SHOW FUNCTIONS", and "EXPAND FUNCTIONS".

The search results section shows "The search for schizophrenia growth factor, matched 3 functions and diseases." Under "Functions & Diseases", a tree view shows "Neurological Disease" expanded to "schizophrenia", which is further expanded to "schizophrenia". A list of genes is displayed below, including "BDNF, CNTF, EGF (includes EG:13645), FGF1, GDNF, IL2, NELL1, NRG1 (includes EG:112400), NRG3, NTF3, VGF".

The pathway diagram below shows a network of genes. Existing genes in the pathway are shown in solid boxes, while newly added genes are shown in dashed boxes. A legend on the right lists the genes: BDNF, CNTF (includes EG:13645), FGF1, GDNF, IL2, NRG1 (includes EG:112400), NRG3, NTF3, and VGF. The newly added genes (BDNF, CNTF, FGF1, NRG1, NRG3, NTF3, VGF) are highlighted with blue dashed boxes.

Annotations include:

- "1. Select the set of genes" pointing to the search results list.
- "2. Add to the already open My Pathway" pointing to the "ADD TO MY PATHWAY" button.
- "Existing genes in My Pathway" pointing to the solid boxes in the pathway diagram.
- "Newly added Schizophrenia-related Growth Factors automatically selected" pointing to the dashed boxes in the pathway diagram.

Link the Sets of Molecules with Path Explorer

Tool: Path Explorer

Add molecules to set A and B and explore shortest path(s) based on user-defined criteria. Click Apply to view list of shortest path(s).

Filter Summary

Consider only relationships where interactions = direct

General Settings

Interactions

Direct Indirect

Set A

BDNF
CNTF
EGF (includes EG:13645)

Direction: From Set A to Set B

Set B

ADORA1
ADORA2A
ADRA1B

Data Sources All

1. Use the Path Explorer tool from the Build Tools
2. Add the set of Growth Factors to Set A
3. Highlight the other genes and Add to Set B
4. Refine options throughout the left-hand panel

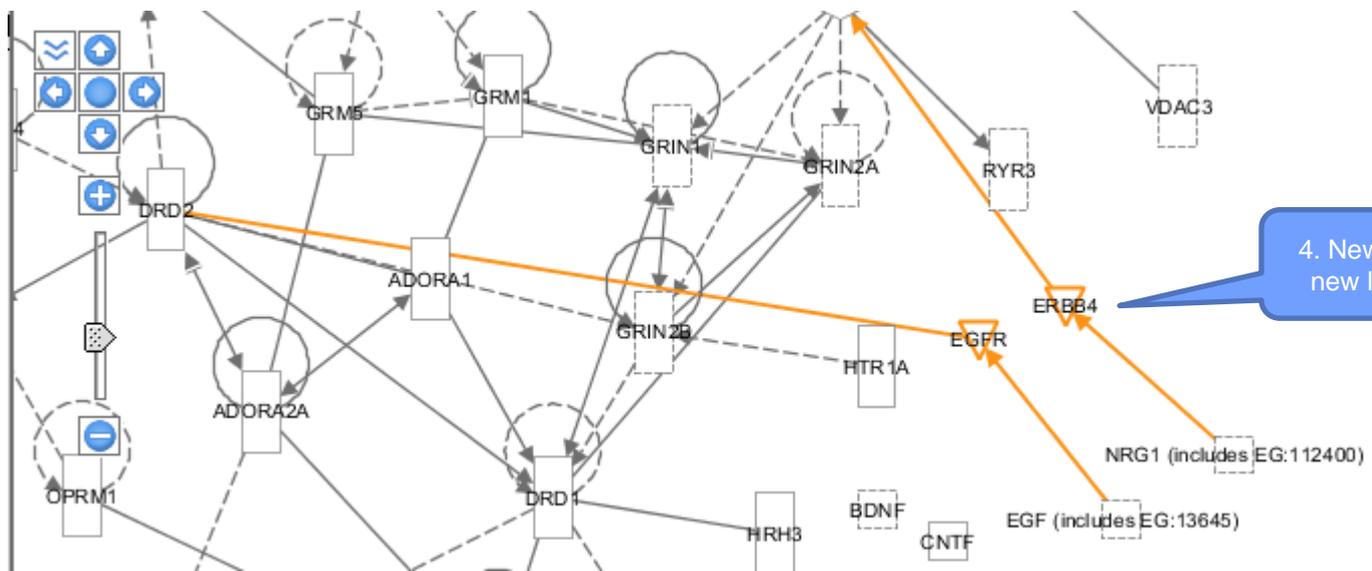
Add Required Paths to Pathway

Paths	Set A Molecules	Molecules 1	Set B Molecules
<input checked="" type="checkbox"/>	1 EGF (includes EG:13645)	EGFR	DRD2
<input type="checkbox"/>	2 BDNF	NTRK2	GRIN2A
<input type="checkbox"/>	3 BDNF	NTRK2	GRIN1
<input type="checkbox"/>	4 BDNF	HTT	DRD2
<input checked="" type="checkbox"/>	5 NRG1 (includes EG:112400)	ERBB4	PSEN1
<input type="checkbox"/>	6 NRG1 (includes EG:112400)	DLG4	GRIN2B

1. Click Apply to see Path Explorer Results

3. Select any or all paths to the pathway

2. The Shortest Path may require one or more additional layers of molecules between Set A and Set B



4. New nodes and new links added

What Drugs Target these Genes?

Overlay: Drug

DRUG SUMMARY

Select drug labels from table to be displayed on pathway

<input type="checkbox"/>	Drug Name	# Molecul...	Target(s)
<input checked="" type="checkbox"/>	olanzapine	10	ADRA1B, DRD1, DRD2, D...
<input type="checkbox"/>	fluoxetine/olanzapine	9	ADRA1B, DRD1, DRD2, D...
<input type="checkbox"/>	iloperidone	7	ADRA1B, DRD1, DRD2, D...
<input type="checkbox"/>	asenapine	7	ADRA1B, DRD1, DRD2, D...
<input type="checkbox"/>	felbamate	7	GABRA1, GABRA5, GABR...
<input type="checkbox"/>	ziprasidone	7	ADRA1B, DRD1, DRD2, D...
<input type="checkbox"/>	isoflurane	7	CHRNA4, CHRNA7, CHR...
<input type="checkbox"/>	enflurane	7	CHRNA4, CHRNA7, CHR...
<input type="checkbox"/>	amobarbital	6	CHRNA4, CHRNA7, CHR...
<input type="checkbox"/>	dopamine	6	ADRA1B, DRD1, DRD2, D...
<input type="checkbox"/>	apomorphine	6	DRD1, DRD2, DRD3, DRD4...
<input type="checkbox"/>	promazine	5	DRD1, DRD2, DRD3, DRD4...
<input type="checkbox"/>	acetaminophen/butalbit...	5	ADORA2A, GABRA1, GAB...
<input type="checkbox"/>	fluphenazine	5	DRD1, DRD2, DRD3, DRD4...
<input type="checkbox"/>	haloperidol decanoate	5	DRD1, DRD2, DRD3, DRD4...
<input type="checkbox"/>	clozapine	5	DRD1, DRD2, DRD3, DRD4...
<input type="checkbox"/>	amitriptyline/perphenazine	5	DRD1, DRD2, DRD3, DRD4...
<input type="checkbox"/>	prochlorperazine	5	DRD1, DRD2, DRD3, DRD4...
<input type="checkbox"/>	thioridazine	5	DRD1, DRD2, DRD3, DRD4...
<input type="checkbox"/>	fluphenazine enanthate	5	DRD1, DRD2, DRD3, DRD4...
<input type="checkbox"/>	aripiprazole	5	ADRA1B, DRD2, DRD3, D...
<input type="checkbox"/>	pergolide	5	DRD1, DRD2, DRD3, DRD4...
<input type="checkbox"/>	trimethobenzamide	5	DRD1, DRD2, DRD3, DRD4...
<input type="checkbox"/>	dihydroergocryptine	5	DRD1, DRD2, DRD3, DRD4...
<input type="checkbox"/>	thiothixene	5	DRD1, DRD2, DRD3, DRD4...
<input type="checkbox"/>	lisuride	5	DRD1, DRD2, DRD3, DRD4...
<input type="checkbox"/>	pramipexol	5	DRD1, DRD2, DRD3, DRD4...

1. Use the Drug Overlay Tool

2. Double-Click to view Chem View page for Drug

Chem View Page for Drug

Chem View: olanzapine > [Interaction Network](#) > [View Reagents \(0\)](#)

[Provide Feedback](#) | [Live Support](#)

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

Summary

Synonyms: 132539-06-1; 2-methyl-4-(4-methyl-1-piperazinyl)-10H-thieno(2,3-b)(1,5)benzodiazepine; 2-methyl-4-(4-methylpiperazin-1-yl)-5H-thieno[3,2-c][1,5]benzodiazepine; C17H20N4S; LY 170053; Olansek; Zydys; Zyprexa; Zyprexa Intramuscular; Zyprexa Zydys

Systematic Name: 2-methyl-4-(4-methyl-1-piperazinyl)-10H-thieno(2,3-b)(1,5)benzodiazepine

IUPAC Name: 2-methyl-4-(4-methylpiperazin-1-yl)-5H-thieno[3,2-c][1,5]benzodiazepine

CAS Registry Number: 132539-06-1

SMILES: CC1=CC2=C(NC3=CC=CC=C3N=C2S1)N4CCN(CC4)C

InChI: InChI=1S/C17H20N4S/c1-12-11-13-16(21-9-7-20(2)8-10-21)18-14-5-3-4-6-15(14)19-17(13)22-12/h3-6,11,18H,7-10H2,1-2H3

Chemical Formula: C₁₇H₂₀N₄S

Molecular Weight: 312.43250

PubChem Link: [4585](#)

HMDB Link: [HMDB05012](#)

Canonical Pathways: --

Top findings from Ingenuity Knowledge Base (show all 2657 categorized literature findings)

regulates: DRD2, HTR2A, DRD1, HRH1, DRD3, DRD4, ADRA1A, ADRA1B, HTR2C, CHRM1, ADRA1D, ADRA1E, ADRA1F, ADRA1G, ADRA1H, ADRA1I, ADRA1J, ADRA1K, ADRA1L, ADRA1M, ADRA1N, ADRA1O, ADRA1P, ADRA1Q, ADRA1R, ADRA1S, ADRA1T, ADRA1U, ADRA1V, ADRA1W, ADRA1X, ADRA1Y, ADRA1Z, ADRA1AA, ADRA1AB, ADRA1AC, ADRA1AD, ADRA1AE, ADRA1AF, ADRA1AG, ADRA1AH, ADRA1AI, ADRA1AJ, ADRA1AK, ADRA1AL, ADRA1AM, ADRA1AN, ADRA1AO, ADRA1AP, ADRA1AQ, ADRA1AR, ADRA1AS, ADRA1AT, ADRA1AU, ADRA1AV, ADRA1AW, ADRA1AX, ADRA1AY, ADRA1AZ, ADRA1BA, ADRA1BB, ADRA1BC, ADRA1BD, ADRA1BE, ADRA1BF, ADRA1BG, ADRA1BH, ADRA1BI, ADRA1BJ, ADRA1BK, ADRA1BL, ADRA1BM, ADRA1BN, ADRA1BO, ADRA1BP, ADRA1BQ, ADRA1BR, ADRA1BS, ADRA1BT, ADRA1BU, ADRA1BV, ADRA1BW, ADRA1BX, ADRA1BY, ADRA1BZ, ADRA1CA, ADRA1CB, ADRA1CC, ADRA1CD, ADRA1CE, ADRA1CF, ADRA1CG, ADRA1CH, ADRA1CI, ADRA1CJ, ADRA1CK, ADRA1CL, ADRA1CM, ADRA1CN, ADRA1CO, ADRA1CP, ADRA1CQ, ADRA1CR, ADRA1CS, ADRA1CT, ADRA1CU, ADRA1CV, ADRA1CW, ADRA1CX, ADRA1CY, ADRA1CZ, ADRA1DA, ADRA1DB, ADRA1DC, ADRA1DD, 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regulated by: PEROXIDASE, MPO, fluoxetine

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List Clinical Trials for this Drug

Drug Information

Brand Name(s): Olansek; Zydys; Zyprexa; Zyprexa Intramuscular; Zyprexa Zydys

Manufacturer(s): BARR PHARMS; LILLY; MYLAN PHARMA; PHARMAFORCE; ROXANE; SANDOZ; TEVA PHARMS

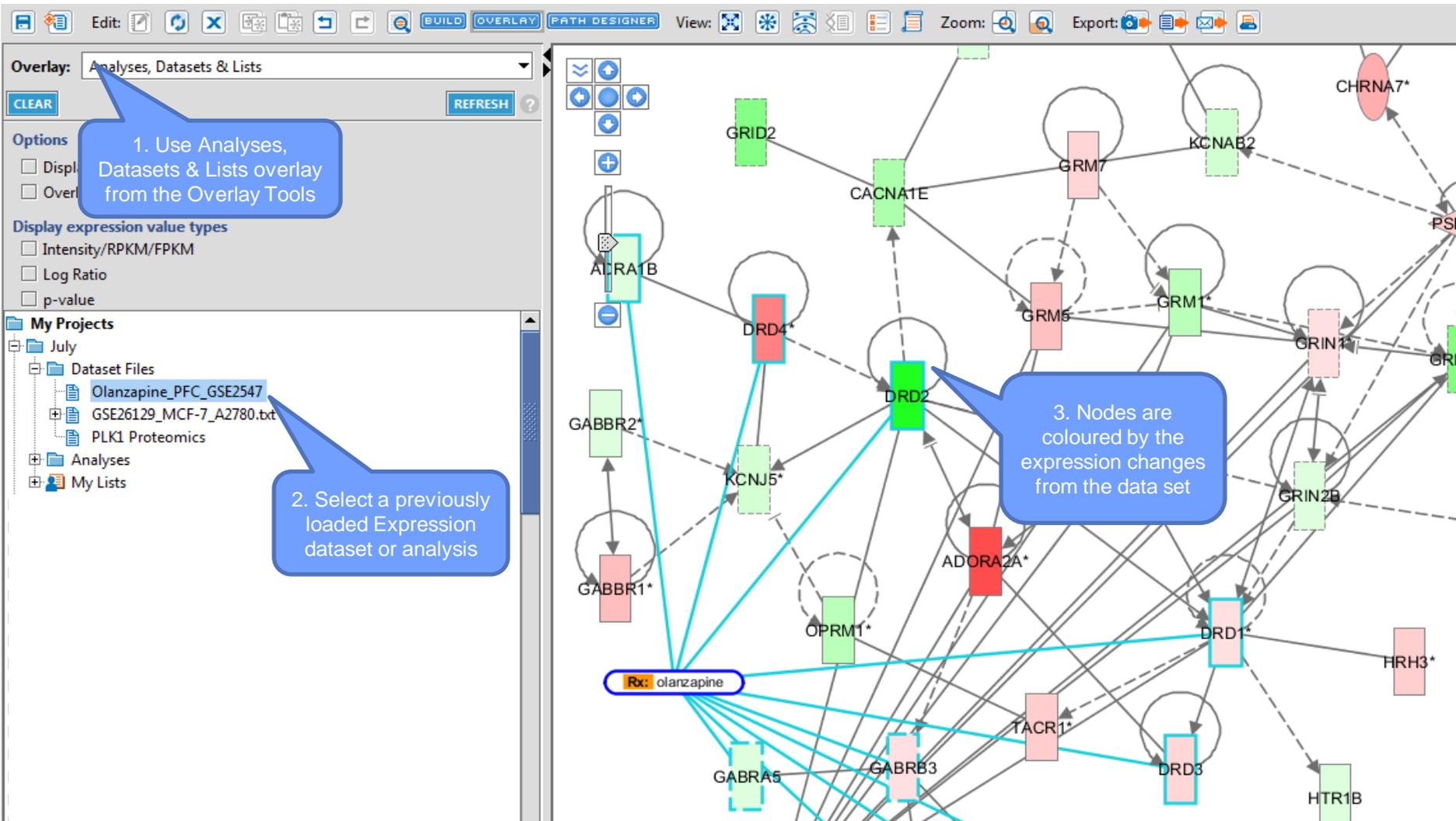
Therapeutic Categories: antipsychotic

Sort Columns

Indication	FDA Approval Status	Trial Status	Clinical Trial Sponsor(s)	NCT#	Last Updated
bipolar disorder	Phase IV	Completed	National Institute of Mental Health (NIMH)	NCT00048802	2008-08-20
hyperglycemia	Phase IV	Completed	Nathan Kline Institute for Psychiatric Research	NCT00287820	2011-07-22
hyperglycemia	Phase IV	Completed	Eli Lilly and Company	NCT00287820	2011-07-22
obsessive-compulsive disorder	Unspecified phase	Completed	National Institute of Mental Health (NIMH)	NCT00000373	2005-12-06
bipolar disorder	Phase III	Completed	Organon	NCT00159796	2008-08-11
bipolar disorder	Phase III	Completed	Pfizer	NCT00159796	2008-08-11
anorexia nervosa	Phase IV	Completed	North Shore Long Island Jewish Health System	NCT00592930	2008-01-11
anorexia nervosa	Phase IV	Completed	Eli Lilly and Company	NCT00592930	2008-01-11
schizophrenia	Unspecified phase	Recruiting	National Center for Research Resources (NCRR)	NCT00006195	2006-10-11
schizophrenia	Unspecified phase	Recruiting	Janssen, LP	NCT00006195	2006-10-11
schizophrenia	Unspecified phase	Recruiting	Washington University School of Medicine	NCT00006195	2006-10-11
diabetes mellitus	Phase IV	Recruiting	National Institute of Mental Health (NIMH)	NCT00895921	2009-06-25
psychosis	Phase IV	Completed	University of Bergen	NCT00932529	2010-05-24
alcoholism	Phase III	Completed	The Mind Research Network	NCT00746785	2012-03-12

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trial information

How Does Olanzapine Effect Gene Expression of these Genes?



Upstream Regulators of Olanzapine Pharmacology

DataSet Record GDS2608: Expression Profiles Data Analysis Tools Sample Subsets	
Title:	Antipsychotic agent olanzapine effect on the brain frontal cortex
Summary:	Analysis of brain frontal cortices of albino Sprague-Dawley males treated with olanzapine for 21 days. Olanzapine is a second generation antipsychotic agent. Results provide insight into the molecular basis of the clinical response to olanzapine.

Summary Functions Canonical Pathways Upstream Regulators Networks Network Explorer Overlapping Networks Molecules Lists My Pathways							
ADD TO MY PATHWAY		ADD TO MY LIST		CUSTOMIZE TABLE		DISPLAY AS NETWORK	
p-value of over... 8.14E-05 - 1.24E-02 (p1 of 3) << >> More Info							
<input type="checkbox"/>	Upstream Regulator	Log Ratio	Molecule Type	Predicted Activation Sta...	Activation z-score	p-value of overlap	Target molecules in dat...
<input type="checkbox"/>	olanzapine		chemical drug	Activated	3.357	8.14E-05	↑CAPN8, ↓CT... ...all 15
<input type="checkbox"/>	arachidonic acid		chemical - endogenous		0.888	2.21E-04	↓ACOX1, ↓CD83 ...all 12
<input type="checkbox"/>	LY294002		chemical - kinase inhibit	Inhibited	-2.860	4.92E-04	↑ABCB1, ↓BAD, ...all 37
<input type="checkbox"/>	AGT	↑0.209	growth factor	Activated	2.068	4.95E-04	↓ACE2 (include... ...all 35
<input type="checkbox"/>	APLP2	↓-0.119	other			6.35E-04	↑EGFR, ↓PRNP, ↑...all 3
<input type="checkbox"/>	Z-IETD-FMK		chemical - protease inhib			6.35E-04	↑EGFR, ↓GRIA3, ↑...all 3
<input type="checkbox"/>	SPDEF	↓-0.090	transcription regulator	Inhibited	-2.155	7.30E-04	↑COL16A1, ↑C... ...all 10
<input type="checkbox"/>	AKT1	↑0.908	kinase	Activated	2.146	9.15E-04	↑ABCB1, ↓BAD, ...all 20

Effects of antipsychotic drugs on cell growth, survival, metabolism and phosphoinositide 3-kinase/Akt and extracellular signal-regulated kinase pathways

by Lu, Xiao-Hong, Ph.D., Louisiana State University Health Sciences Center - Shreveport, 2004, 284 pages; AAT 3155914

Abstract (Summary)

A number of second generation antipsychotic drugs (SGAs) have been reported to stimulate neurogenesis, provide neuroprotection, and stem the progressive gray matter loss in schizophrenic brains. We hypothesized that some SGAs may produce positive in vitro effects on cell growth, proliferation, differentiation, and metabolism. Signal transduction pathways such as phosphoinositide 3-kinase, PI3K/Akt pathway and extracellular signal-regulated kinase (ERK) pathways were investigated in relation to the growth effects of antipsychotic drugs.

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