

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

SEARCH
Advanced Search

dopamine
DOPAMINE D1 RECEPTOR
Dopamine d2 receptor
Dopamine d3 receptor
DOPAMINE D4 RECEPTOR
dopamine HCl
dopamine lutine
dopamine quinone
Dopamine receptor 4
dopaminechrome

chemical - endogenous mammalian
G-protein coupled receptor
G-protein coupled receptor
G-protein coupled receptor
G-protein coupled receptor
G-protein coupled receptor
chemical - endogenous mammalian
chemical - endogenous mammalian
chemical toxicant
G-protein coupled receptor
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.

	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 RE D2 dopaminergic D2-like receptors, D2a dopamine rec D2DR, D2R, D2S, Dopamine d2 rece Dopamine D2L rec Dr2	dopamine receptor D2	Plasma M G-protein	Reagents Interactions	Response t	paliperidone risperidone, buspirone, bifeprunox, iloperidone, blonanserin, asenapine, pardoprinox ocaperidone abaperidone		Human, Mouse, Rat

Examine Gene View Page

View All interactions and view Reagents page

Examine Biomarker Usage

Examine Drug Chem View Page

What Canonical Pathways Does it Appear In?

Gene View: DRD2 (Mammalian) > Interaction Network > View Reagents (191)

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

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

Summary Human Mouse Rat

Member Of: DOPAMINE D2 LIKE RECEPTOR, Gi-coupled receptor, Gpcr

Entrez Gene Name: dopamine receptor D2

Synonym(s): D2, D2a dopamine receptor, D2 DOPAMINE RECEPTOR, D2 dopaminergic receptor, D2DR, D2-like receptors, D2R, D2S, Dopamine D2L receptor, Dopamine d2 receptor, Dr2

NCBI CDD Domains (Superfamilies / Multi-Domains): --

Protein Functions / Functional Domains: cytoplasmic domain, cytoplasmic loop, dopamine D2 receptor-like receptor, dopamine receptor, drug binding, extracellular loop, G-protein coupled receptor, intracellular domain, intracellular loop, ionotropic glutamate receptor binding, protein binding, receptor binding, tail domain, third intracellular loop, transmembrane domain

Subcellular Location: acrosome, axons, axon terminals, cell periphery, cell surface, cellular membrane, Cytoplasm, cytoplasmic vesicles, dendrites, dendritic spines, endocytotic vesicle, flagella, intracellular membranes, intracellular space, lateral plasma membrane, membrane fraction, mitochondrial fraction, nerve ending, neurites, outer membranes, perikaryon, Plasma Membrane, postsynaptic density, presynaptic regions, soluble fraction, spine apparatus, synaptic vesicle membrane, synaptosomes

Canonical Pathway: cAMP-mediated signaling; Dopamine-DARPP32 Feedback in cAMP Signaling; Dopamine Receptor Signaling; Gap Junction Signaling; G-Protein Coupled Receptor Signaling

Targeted By miRNA Functional Cluster: miR-1207-5p (and other miRNAs w/seed GGCAGGG), miR-1252 (miRNAs w/seed GAAGGA), miR-1254 (and other miRNAs w/seed GCCUGGA), miR-150-5p (and other miRNAs w/seed CUCCCAA), miR-200a-3p (and other miRNAs w/seed AACACUG), miR-326 (and other miRNAs w/seed CUCUGGG), miR-34c-5p (and other miRNAs w/seed GGCAGUG), miR-4300 (and other miRNAs w/seed GGGAGCU), miR-484 (and other miRNAs w/seed CAGGCUC), miR-490-5p (and other miRNAs w/seed CAUGGAU), miR-561-3p (miRNAs w/seed AAGUUUU), miR-615-5p (and other miRNAs w/seed GAGGAGC), miR-619 (and other miRNAs w/seed GAGGAGC), miR-939 (miRNAs w/seed GGGGAGC), miR-9-5p (and other miRNAs w/seed CUUUGGU)

Click to View
Any Pathway

Top findings from Ingenuity Knowledge Base (show all 3728 categorized literature findings)

regulates: Adcy, Erk1/2, G ALPHA I/O, PRL, G protein alpha I, FOS, dopamine, cyclic AMP, Akt, Mapk, KCNJ6, MAPK3, Ca2+, GH1, TAC1

regulated by: HTT, dopamine, haloperidol, quinpirole, olanzapine, apomorphine, risperidone, aripiprazole, sulpiride, clozapine, bromocriptine, quetiapine, pergolide, ziprasidone, ropinirole

binds: dopamine, raclopride, haloperidol, guanosine 5'-O-(3-thiotriphosphate), spiperone, aripiprazole, olanzapine, apomorphine, quinpirole, pergolide, risperidone, clozapine, bromocriptine, lisuride, 7-hydroxy-2-N,N-dipropylaminotetralin

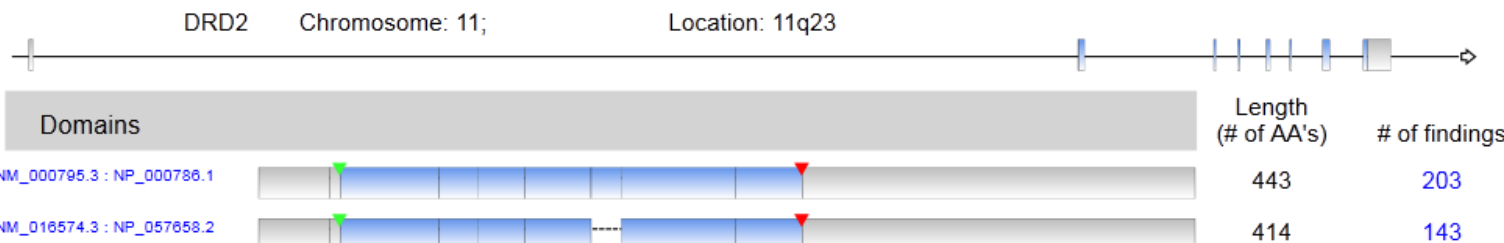
role in cell: proliferation, migration, number, synaptic transmission, response, activation in, transmission, function, excitotoxicity, mitosis

disease: Huntington's disease, schizophrenia, Parkinson's disease, bipolar disorder, agitation, bipolar I disorder, psychosis, depressive disorder, hyperprolactinemia, mania, neoplasia, hyperplasia, bradykinesia, weight gain, schizoaffective disorder, catalepsy, major depression, alcoholism, generalized anxiety disorder, restless legs syndrome, dementia, cognitive impairment, growth failure, bipolar depression, paranoid schizophrenia, hebephrenic schizophrenia, delirium, post-traumatic stress disorder, akinesia, mood disorder, non-insulin-dependent diabetes mellitus, Tourette syndrome, migraines, psychomotor agitation, hypotension, vomiting, nausea, gait disturbance, drug abuse, end stage renal disease, spontaneous ovarian hyperstimulation syndrome, ataxia, seizures, adenomyosis, tumorigenesis, hyperpigmentation, aphagia, polyuria, adrenal cortical hyperplasia, diabetes mellitus, restlessness, insulin resistance, bleeding, dyslipidemia, eating disorder, anorexia nervosa, hyperlipidemia, attention deficit hyperactivity disorder, hypothermia, panic disorder, psychological disorder, tic disorder, metabolic syndrome X, vascular dementia, tardive dyskinesia, bipolar II disorder, autism, insomnia, amyotrophic lateral sclerosis, cardiovascular disorder, hot flashes, obsessive-compulsive disorder, chronic hepatitis C, Alzheimer's disease-associated psychosis, anxiety disorder, fibromyalgia, schizophreniform psychosis, hyperaldosteronism, stroke, substance-related disorder, hypertension, arthritis, parkinsonism, cocaine-related disorder, pervasive developmental disorder, Asperger syndrome, hypoplasia, Alzheimer's disease, social anxiety disorder, Rett syndrome, rheumatoid arthritis, osteoarthritis, shock response, acromegaly, obesity, F, anxiety, heart failure, Lewy body dementia, extrapyramidal side-effects, motor dysfunction, myoclonic dystonia, gastroesophageal reflux, galactosemia, hypoplasia

Scroll down
for more
information

Gene View Page Details

Human Isoforms From RefSeq

[More Info](#)


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

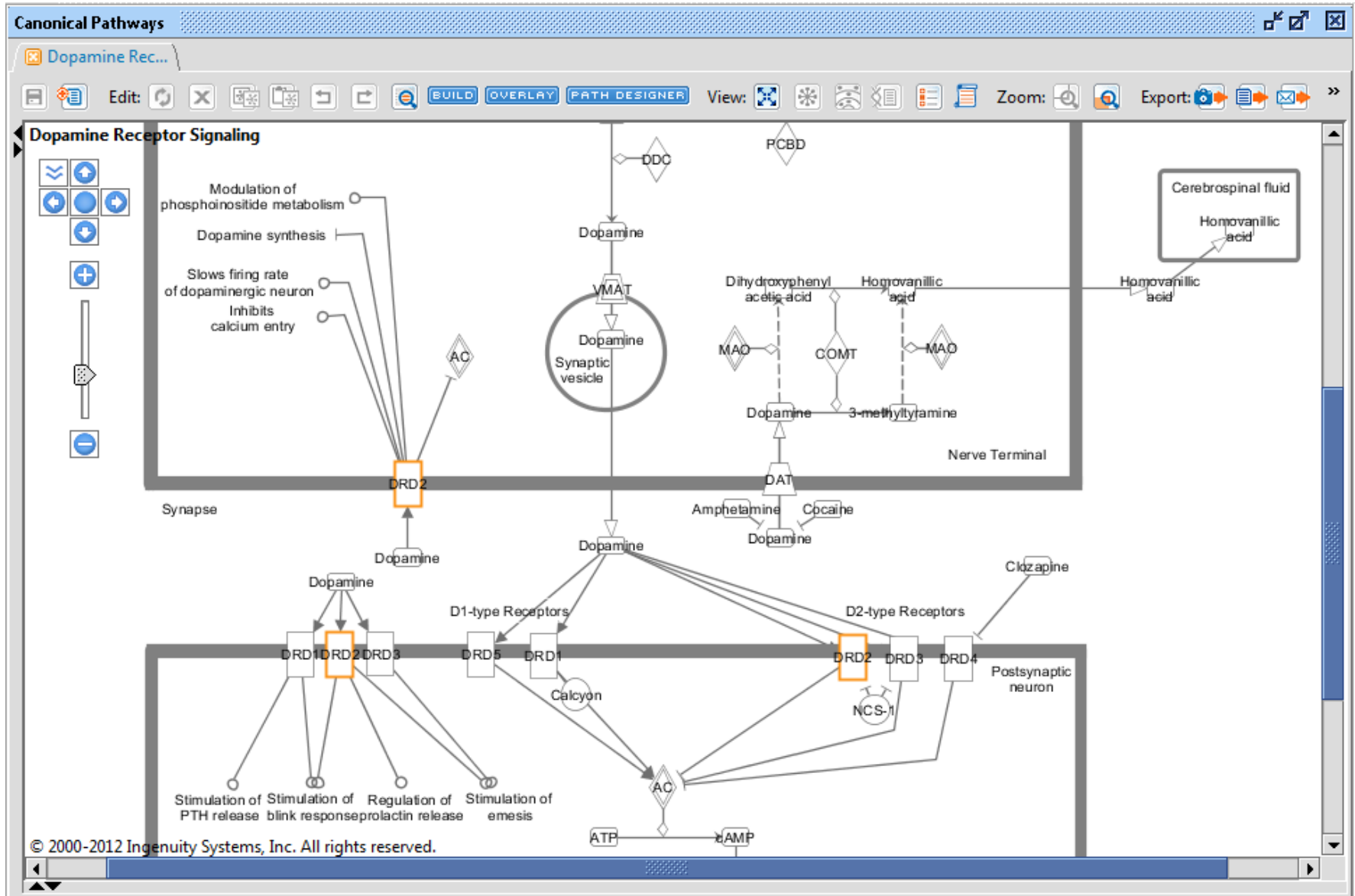
29 Recently Added Findings (show Findings)

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"/>	<input 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

New My Pathw...

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

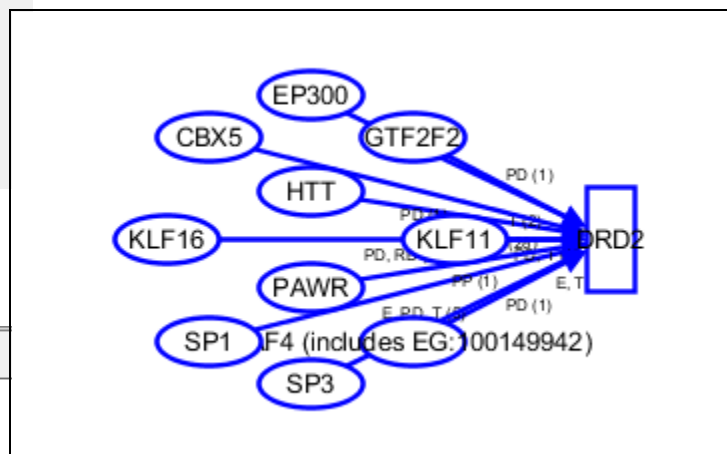
☐ peptidase

☐ phosphatase

☒ transcription regulator

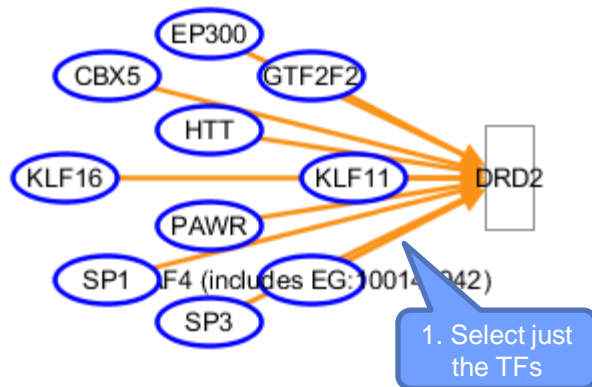
☐ translation regulator

☐ 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

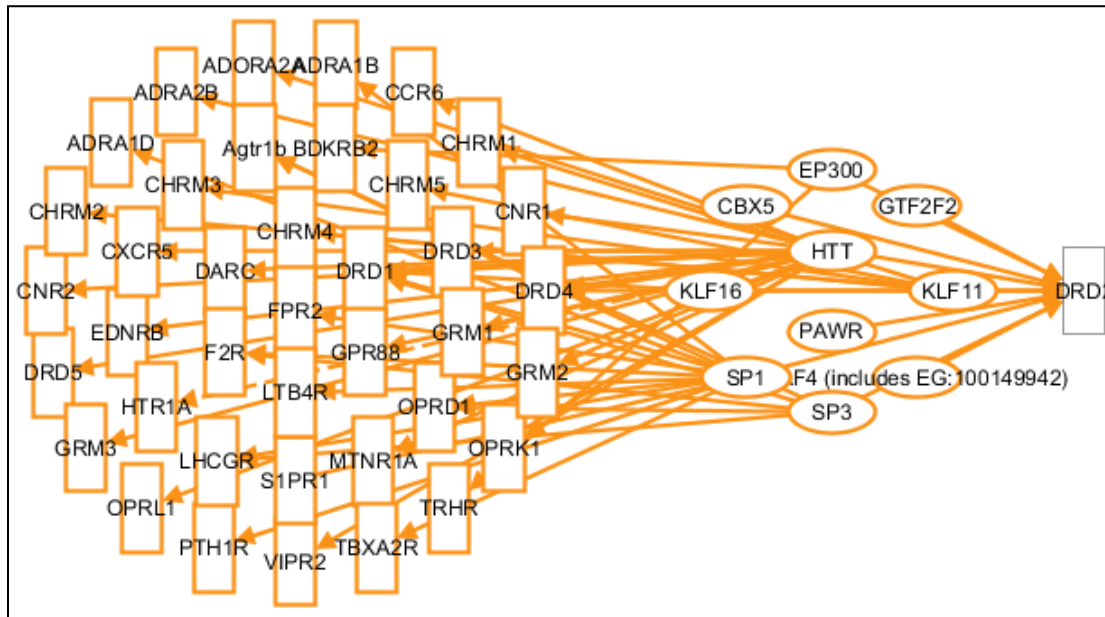
...that are
Downstream of selected molecules ▼

...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

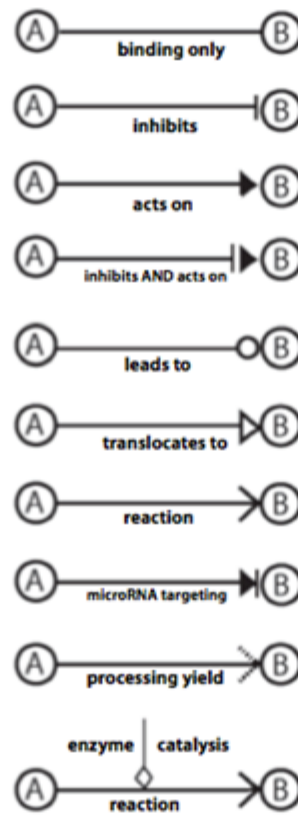


Network Legend

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



—————
direct interaction

indirect interaction


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 **SEARCH** Advanced Search 

1. Function & Disease Search

2. Refine with Advanced Search



Advanced Search Options

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


Identifier Type(s) All Identifiers

Molecule Type(s) ion channel, G-protein coupled receptor

Subcellular Location(s) Click here to select subcellular locations

Pathways and Tox Lists  

Display results in ☐ Table ☒ Tree

 **RESET** **SEARCH** **CANCEL**

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, IPH3, KCNAB1, KCNAB2, KCNJ5, LYPD1, MCHR1, NPY2R, OPRM1, PSEN1, PTGER2, RYR3, SLC1A4, SLC24A2, TACR1, TACR3, VDAC1, VDAC3	

How Do They Interconnect?

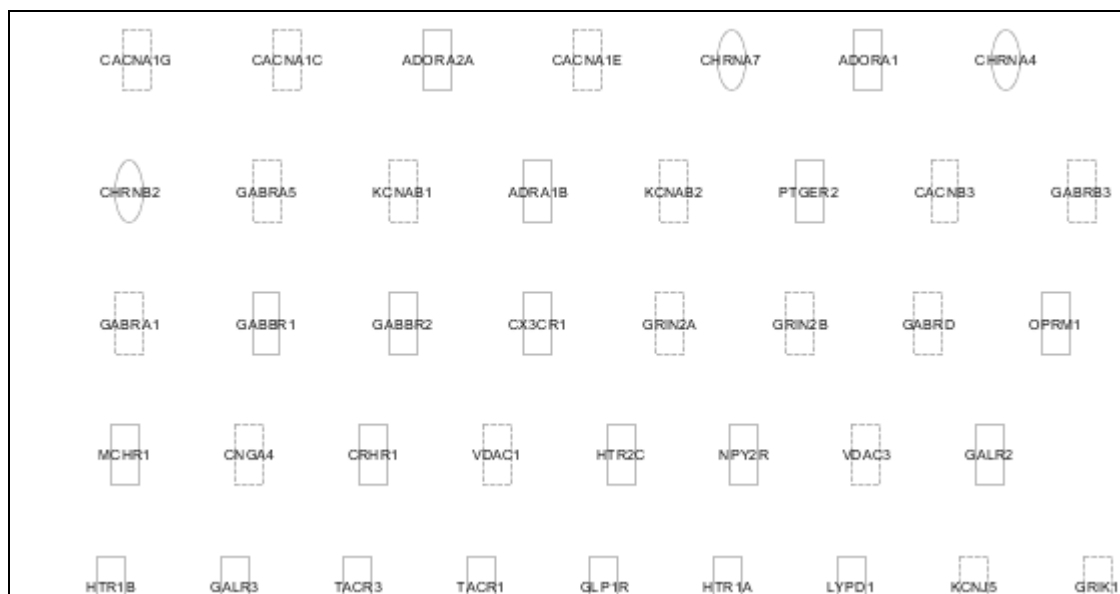
ADD TO MY PATHWAY ADD TO MY LIST ANNOTATIONS SHOW FINDINGS EFFECT ON FUNCTION SHOW FUNCTIONS EXPAND FUNCTIONS

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

Functions & Diseases	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, SLC1A4, SLC24A2, TACR1, TACR3, VDAC1, VDAC3



Use The Build Tool 'Connect' to Join Genes

My Pathways

New My Pathw... New My Pathw...

Build Overlay Path Designer View: Zoom: Export:

Tool: Connect

Connect selected molecules based on specific criteria. Click Apply to view new connections.

Filter Summary

Consider all molecules and/or relationships

General Settings

Interactions

☒ Direct ☒ Indirect

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

Biofluids All

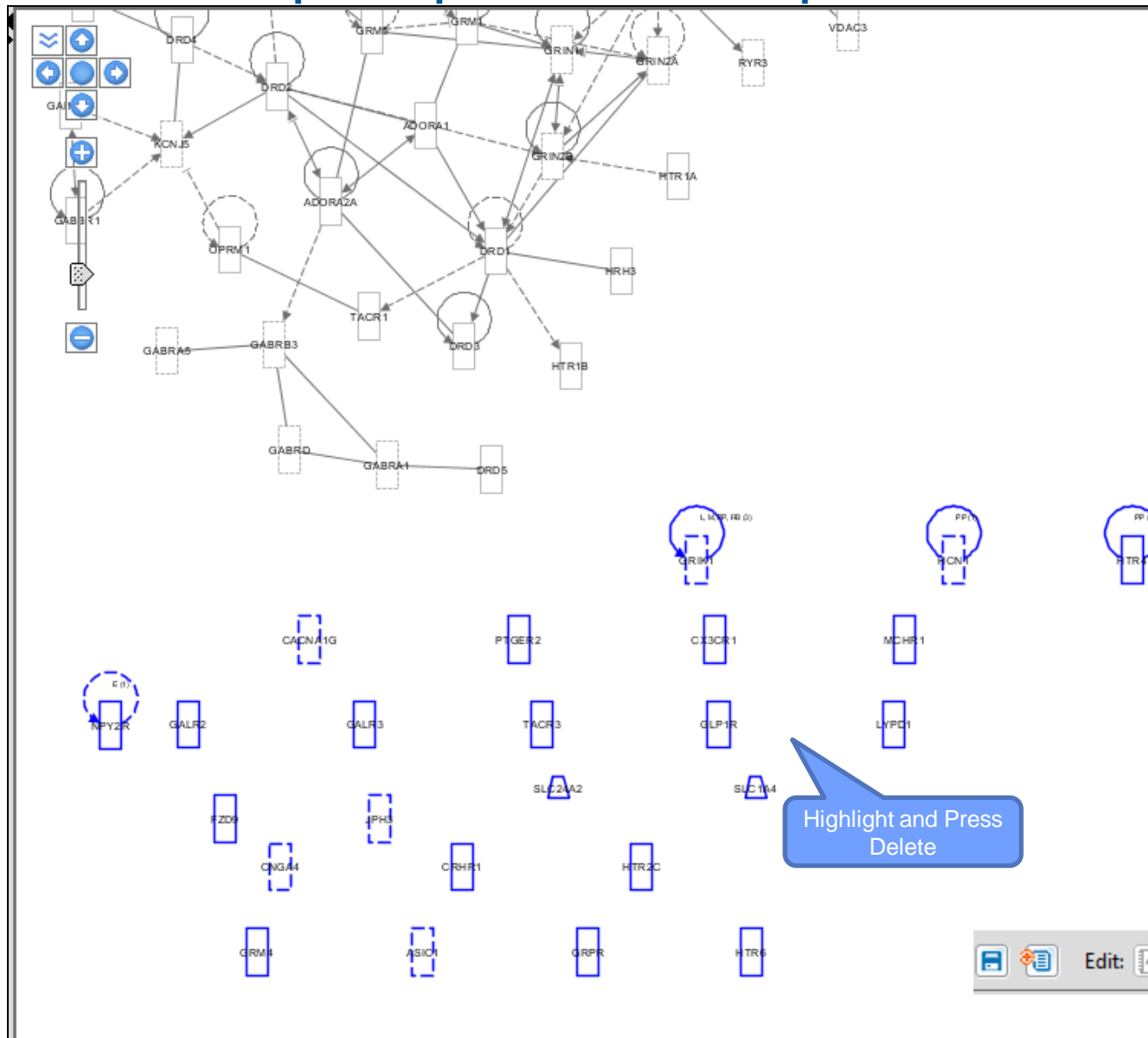
1. Use Connect from the Build Tools

2. Highlight

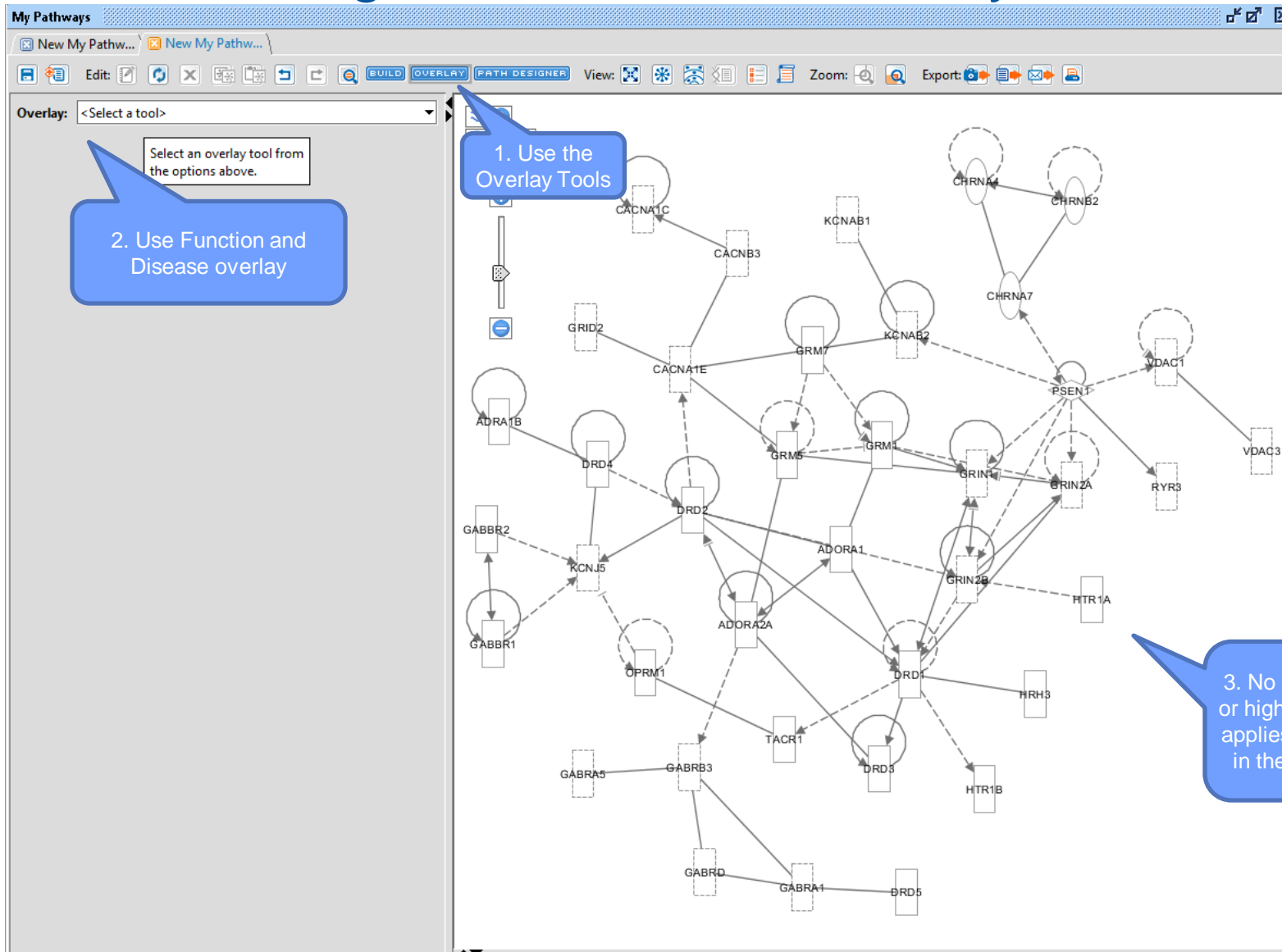
3. Refine, if necessary

[illegible]

Clean-up 'Orphans' if Required



What Biological Processes are they Involved In?



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 current	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 Function	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

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?

The screenshot shows the 'Functions and Diseases' tab in the Ingenuity Systems search interface. The search term 'schizophrenia' is entered in the main search bar. Below this, the 'Advanced Search Options' panel is visible. Callouts highlight three key steps: 1. 'Function & Disease Search' pointing to the search bar, 2. 'Refine with Advanced Search' pointing to the 'Advanced Search' link, and 3. 'Choose Molecule Types' pointing to the 'Molecule Type(s)' dropdown menu which is set to 'growth factor'. Other options include 'Identifier Type(s)' set to 'All Identifiers', 'Subcellular Location(s)' with a link to select locations, and 'Pathways and Tox Lists'. At the bottom, there are buttons for 'RESET', 'SEARCH', and 'CANCEL', along with radio buttons for 'Table' and 'Tree' display formats.

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

Functions & Diseases	Associated Molecule
<input type="checkbox"/> Matching Functions & Diseases	11
<input checked="" type="checkbox"/> Neurological Disease	11
<input checked="" type="checkbox"/> schizophrenia	11
<input checked="" type="checkbox"/> schizophrenia	11
<input type="checkbox"/> BDNF, CNTF, EGF (includes EG:13645), FGF1, GDNF, IL2, NELL1, NRG1 (includes EG:112400), NRG3, NTF3, VGF	.

Add Molecules to Existing My Pathway

Search

ADD TO MY PATHWAY **ADD TO MY LIST** **ANNOTATIONS** **SHOW FINDINGS** **EFFECT ON FUNCTION** **SHOW FUNCTIONS** **EXPAND FUNCTIONS**

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

Functions & Diseases

☐ Matching Function

☐ Neurological Disease

☒ schizophrenia

☒ schizophrenia

BDNF, CNTF, EGF (includes EG:13645), FGF1, GDNF, IL2, NELL1, NRG1 (includes EG:112400), NRG3, NTF3, VGF

1. Select the set of genes

2. Add to the already open My Pathway

Existing genes in My Pathway

Newly added Schizophrenia-related Growth Factors automatically selected

Link the Sets of Molecules with Path Explorer

The screenshot shows the Path Explorer software interface. The top toolbar includes buttons for BUILD, OVERLAY, and PATH DESIGNER. The left panel contains a 'Filter Summary' section with the text 'Consider only relationships where interactions = direct'. Below this is the 'General Settings' section, which includes 'Interactions' (with 'Direct' checked and 'Indirect' unchecked), 'Set A' (containing BDNF, CNTF, and EGF (includes EG:13645)), 'Direction' (set to 'From Set A to Set B'), and 'Set B' (containing ADORA1, ADORA2A, and ADORA1B). The right panel displays a complex network diagram with nodes and edges. Four blue callout boxes provide instructions: 1. 'Use the Path Explorer tool from the Build Tools' (pointing to the BUILD button), 2. 'Add the set of Growth Factors to Set A' (pointing to the ADD button for Set A), 3. 'Highlight the other genes and Add to Set B' (pointing to the ADD button for Set B), and 4. 'Refine options throughout the left-hand panel' (pointing to the General Settings section).

Tool: Path Explorer

Add molecules to set A and B and explore shortest path(s) based on 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
ADORA1B

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

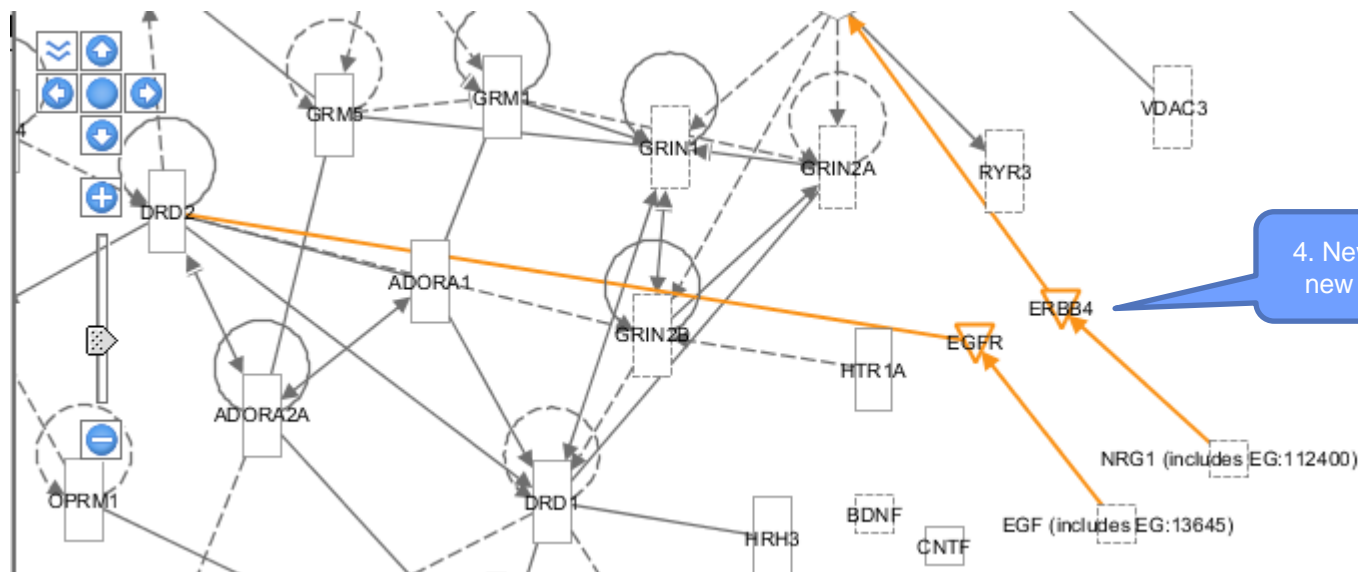
Add Required Paths to Pathway

		ADD TO MY PATHWAY	HIGHLIGHT	View	Shortest Paths (86)	Paths	1 - 50
<input type="checkbox"/>	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

1. Use the Drug Overlay Tool

<input type="checkbox"/>	Drug Name	# Molecule	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...

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, ADRA1DE, ADRA1DF, ADRA1DG, ADRA1DH, ADRA1DI, ADRA1DJ, ADRA1DK, ADRA1DL, ADRA1DM, ADRA1DN, ADRA1DO, ADRA1DP, ADRA1DQ, ADRA1DR, ADRA1DS, ADRA1DT, ADRA1DU, ADRA1DV, ADRA1DW, ADRA1DX, ADRA1DY, ADRA1DZ, ADRA1EA, ADRA1EB, ADRA1EC, ADRA1ED, ADRA1EE, ADRA1EF, ADRA1EG, ADRA1EH, ADRA1EI, ADRA1EJ, ADRA1EK, ADRA1EL, ADRA1EM, ADRA1EN, ADRA1EO, ADRA1EP, ADRA1EQ, ADRA1ER, ADRA1ES, ADRA1ET, ADRA1EU, ADRA1EV, ADRA1EW, ADRA1EX, ADRA1EY, ADRA1EZ, ADRA1FA, ADRA1FB, ADRA1FC, ADRA1FD, ADRA1FE, ADRA1FF, ADRA1FG, ADRA1FH, ADRA1FI, ADRA1FJ, ADRA1FK, ADRA1FL, ADRA1FM, ADRA1FN, ADRA1FO, ADRA1FP, ADRA1FQ, ADRA1FR, ADRA1FS, ADRA1FT, ADRA1FU, ADRA1FV, ADRA1FW, ADRA1FX, ADRA1FY, ADRA1FZ, ADRA1GA, ADRA1GB, ADRA1GC, ADRA1GD, ADRA1GE, ADRA1GF, ADRA1GG, ADRA1GH, ADRA1GI, ADRA1GJ, ADRA1GK, ADRA1GL, ADRA1GM, ADRA1GN, ADRA1GO, ADRA1GP, ADRA1GQ, ADRA1GR, ADRA1GS, ADRA1GT, ADRA1GU, ADRA1GV, ADRA1GW, ADRA1GX, ADRA1GY, ADRA1GZ, ADRA1HA, ADRA1HB, ADRA1HC, ADRA1HD, ADRA1HE, ADRA1HF, ADRA1HG, ADRA1HH, ADRA1HI, ADRA1HJ, ADRA1HK, 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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

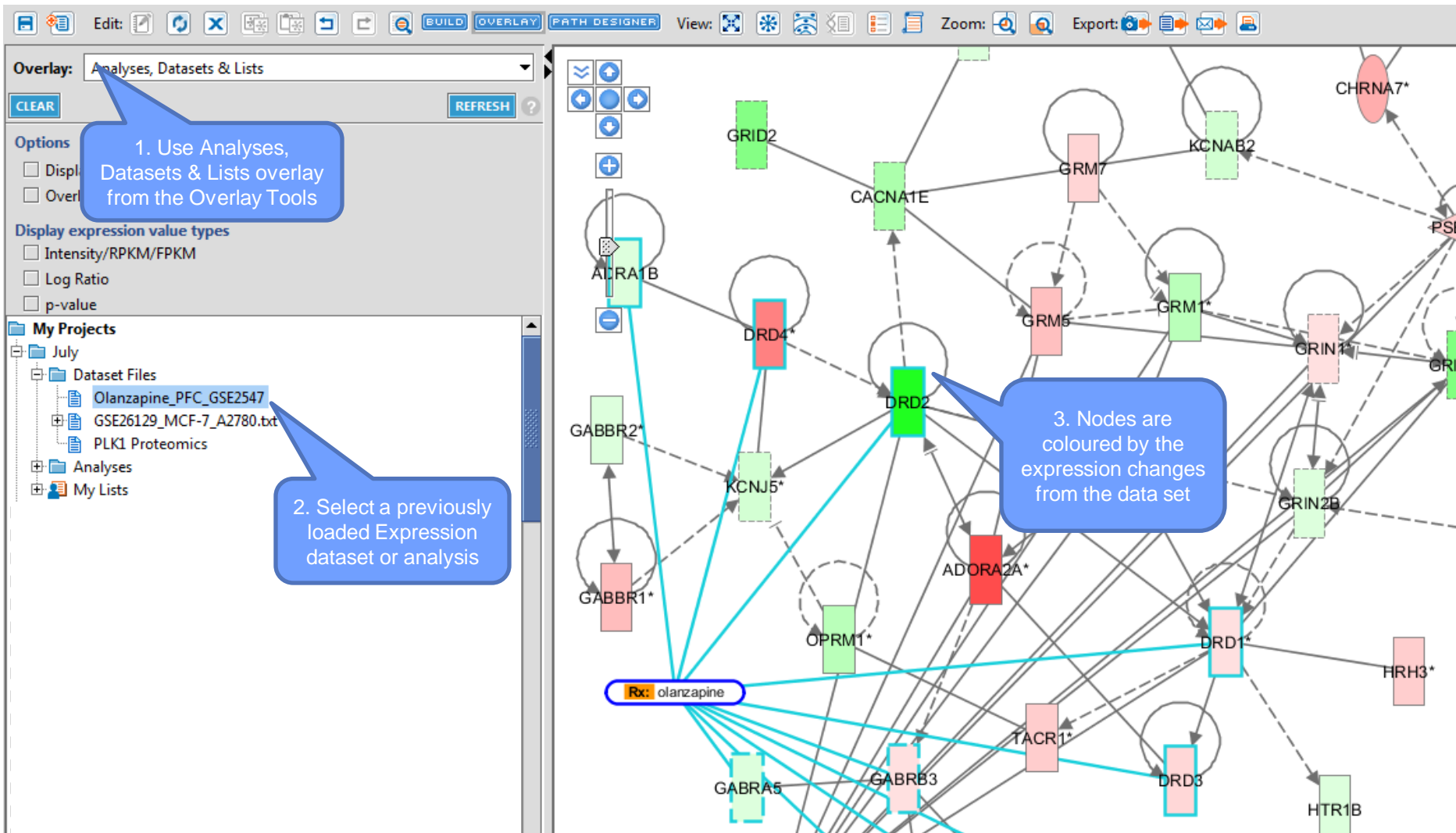
Therapeutic Categories: antipsychotic

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)	
<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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