Common Epigenetic Mechanism of SZ and ASD

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Overview

-This project will discover the common pathway (mechanism) of SZ and ASD

Methodology

- Gene list from DisGeNET

-The common genes related to ASD and SZ

-Used DAVID for analysis / Diagram

-4 Pathways selected

Neuroactive ligand-receptor interaction

GABAergic synapse

Glutamatergic synapse

Cell adhesion molecules

Gene list

Gene	Uniprot	Gene Full Name	Protein Class	pLI	DSI v	DPI v
KDM4C	Q9H3R0	lysine demethylase 4C		6.50E-07	0.601	0.615
PCDH15	Q96QU1	protocadherin related 15		8.00E-25	0.601	0.577
OPN1MW2	P04001 P0DN77 P0DN78	opsin 1, medium wave sensitive 2		0.24	0.601	0.769
OPN1MW3	P04001 P0DN77 P0DN78	opsin 1, medium wave sensitive 3			0.601	0.769
DRD5	P21918	dopamine receptor D5	G-protein coupled receptor	1.30E-16	0.603	0.423
NOS1AP	O75052	nitric oxide synthase 1 adaptor protein	Signaling	0.61	0.608	0.423
GPHN	Q9NQX3	gephyrin		1	0.608	0.538
ACTC1	P68032	actin alpha cardiac muscle 1	Cellular structure	0.74	0.61	0.538
FAN1	Q9Y2M0	FANCD2 and FANCI associated nuclease 1		1.70E-25	0.61	0.577
CAMK2A	Q9UQM7	calcium/calmodulin dependent protein kinase II alpha	Kinase	1	0.612	0.538
PRODH	O43272	proline dehydrogenase 1	Enzyme	5.40E-12	0.612	0.692
RHD	Q02161	Rh blood group D antigen		2.90E-05	0.612	0.654
BRINP1	O60477	BMP/retinoic acid inducible neural specific 1		0.99	0.615	0.615
JARID2	Q92833	jumonji and AT-rich interaction domain containing 2	Transcription factor	1	0.615	0.577
OXT	P01178	oxytocin/neurophysin I prepropeptide	Signaling	0.71	0.615	0.423
SLC38A1	Q9H2H9	solute carrier family 38 member 1	Transporter	0.93	0.615	0.769
EBPL	Q9BY08	EBP like	Enzyme	7.80E-05	0.615	0.577
CHRNB2	P17787	cholinergic receptor nicotinic beta 2 subunit	Ion channel	7.30E-04	0.617	0.308
NDUFV1	P49821	NADH:ubiquinone oxidoreductase core subunit V1		6.40E-11	0.617	0.538

Gene list

(cont.)

PLA2G12A	Q9BZM1	phospholipase A2 group XIIA		3.80E-04	0.805	0.192
LRRN3	Q9H3W5	leucine rich repeat neuronal 3	Receptor	3.20E-02	0.821	0.115
LRP2BP	Q9P2M1	LRP2 binding protein		2.40E-06	0.821	0.269
CNTNAP5	Q8WYK1	contactin associated protein family member 5		0.99	0.821	0.154
KCTD13	Q8WZ19	potassium channel tetramerization domain containing 13		9.20E-04	0.821	0.154
ARHGAP32	A7KAX9	Rho GTPase activating protein 32		1	0.839	0.115
ERMN	Q8TAM6	ermin		1.20E-05	0.861	0.115
CNTNAP3	Q9BZ76	contactin associated protein family member 3		1.70E-11	0.861	0.192
ATP13A4	Q4VNC1	ATPase 13A4		3.30E-26	0.861	0.077
KATNAL2	Q8IYT4	katanin catalytic subunit A1 like 2	Cellular structure	1.20E-06	0.89	0.03

-149 Genes total (Filtered by DSIv>0.6)

-DSIv: Disease Specificity Index for the gene —>genetic and genomic analysis to measure the specificity of a gene's association with a particular disease

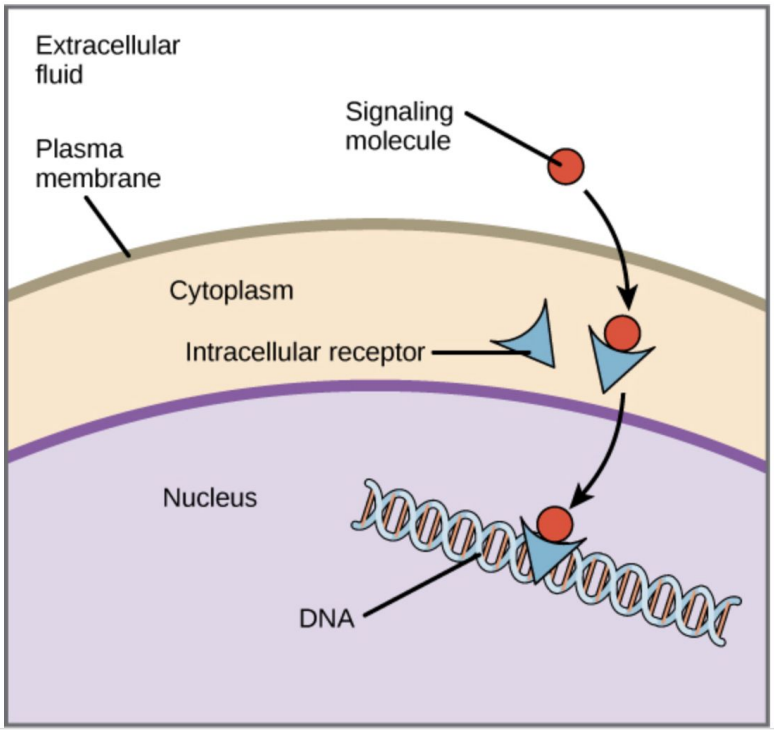
*Higher DSIv: the gene is specifically associated with a particular disease (or a narrow range of diseases)

*Lower DSIv: the gene may be more broadly involved in multiple diseases or biological processes

Neuroactive ligand-receptor interaction

-Neuroactive ligands influence neuronal function by binding to intracellular receptors, which has the capability of binding transcription factors and regulating gene expressions.J

-Neuroactive ligand-receptor interaction is important in important Biological processes like metabolism, neurotransmission and cellular signal transduction pathways.



Pathway

-ADR (aka ADRA1A):

Gene that encodes for the alpha-1A adrenergic receptor

-DRD:

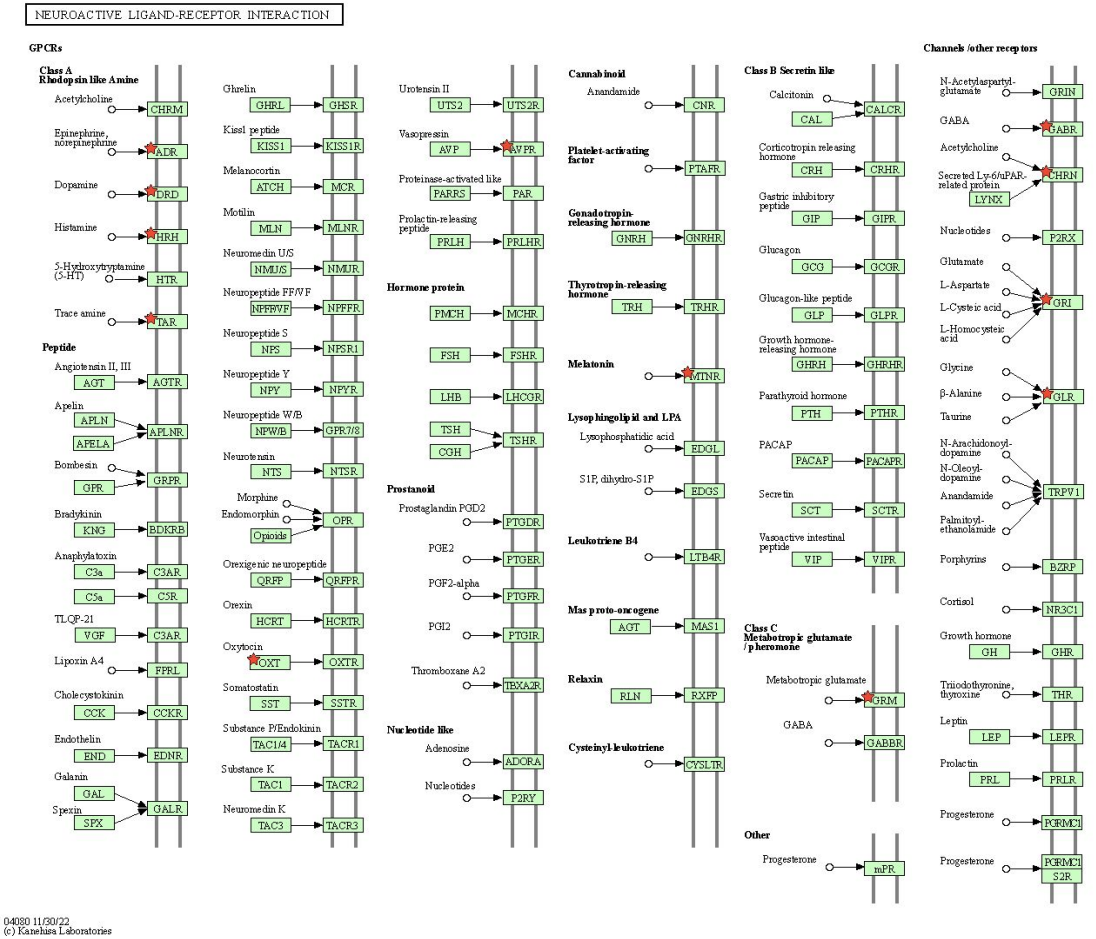
Gene that encode for dopamine receptors

-HRH

Genes that encode for histamine receptors

-TAR

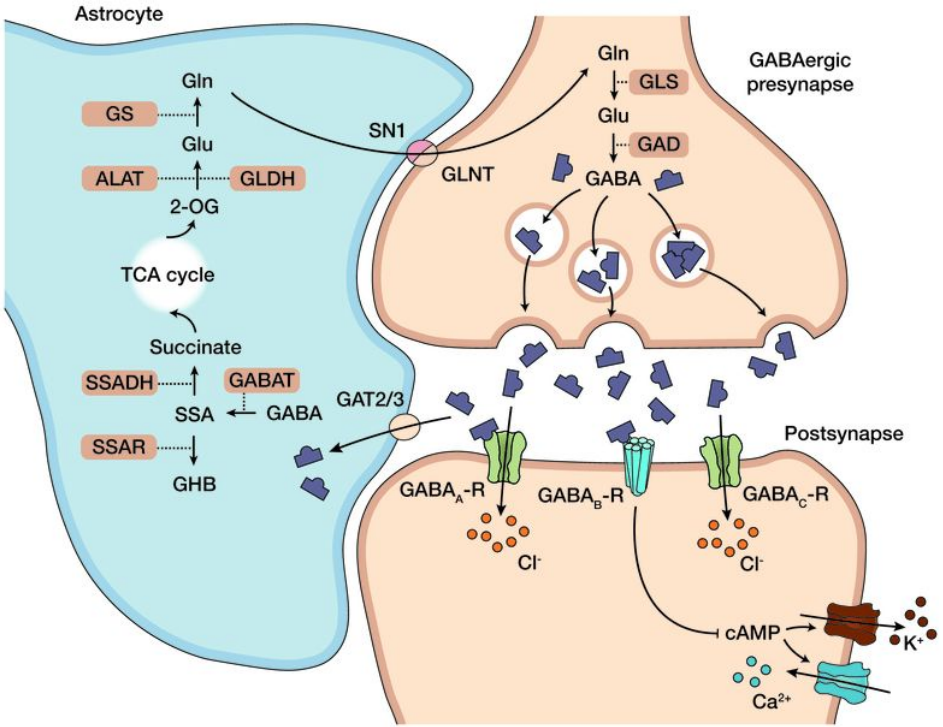
Gene that encodes the Trace amine-associated receptor 1 (TAAR1)



GABAergic synapse

-GABA: gamma-aminobutyric acid

-Provides the majority of synaptic inhibition that balances glutamatergic excitatory drive and thereby controls neuronal output.



Pathway

-System A

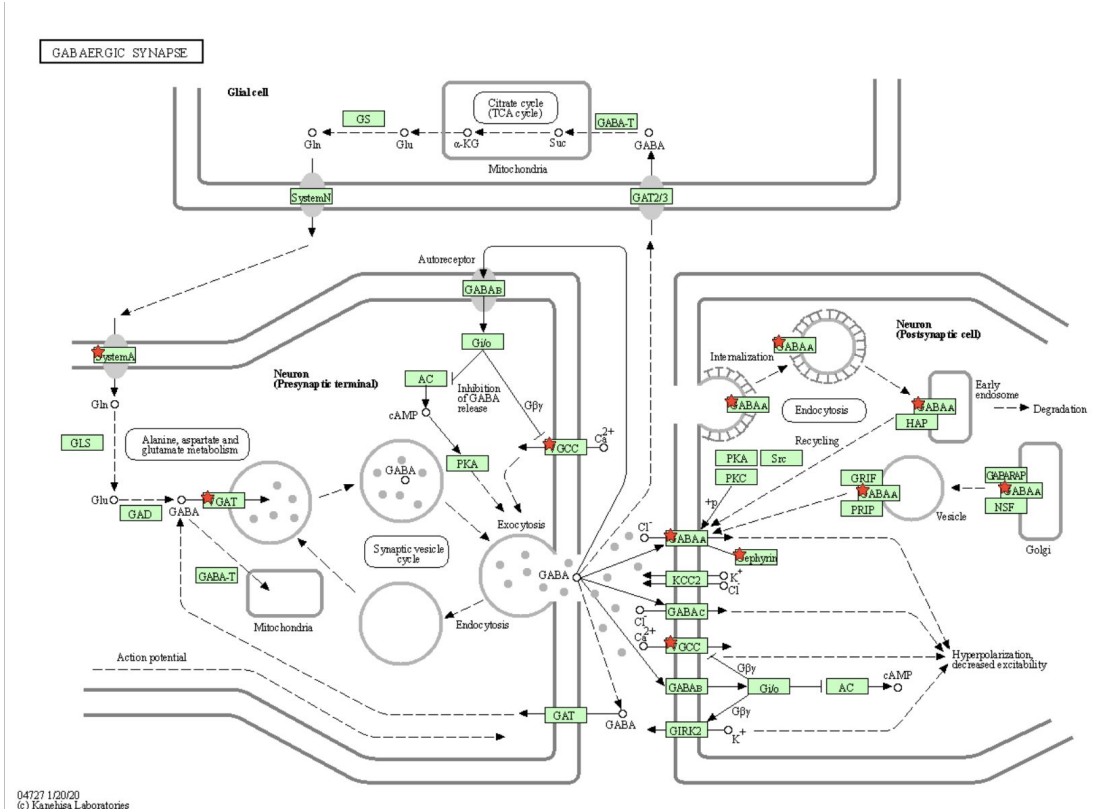
Reuptakes the neurotransmitter GABA from the synaptic cleft back into the presynaptic neuron

-VGAT

Responsible for loading GABA into synaptic vesicles in GABAergic neurons

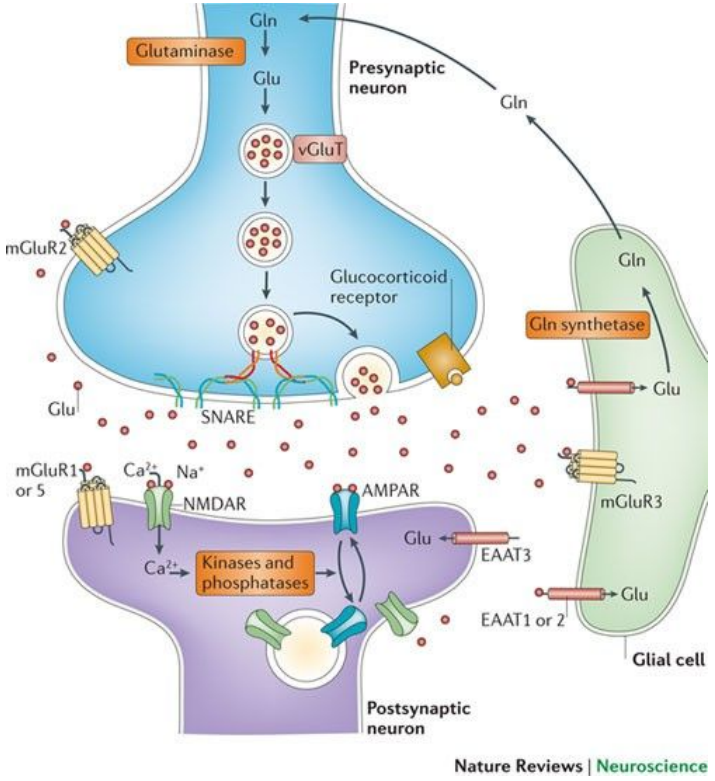
-VGCC

Voltage-Gated Calcium Channels



Glutamatergic synapse

-Excitatory relay stations between presynaptic nerve terminals and postsynaptic dendritic spines (axo-dendritic synapses) or adjacent nerve endings (axo-axonal synapses)



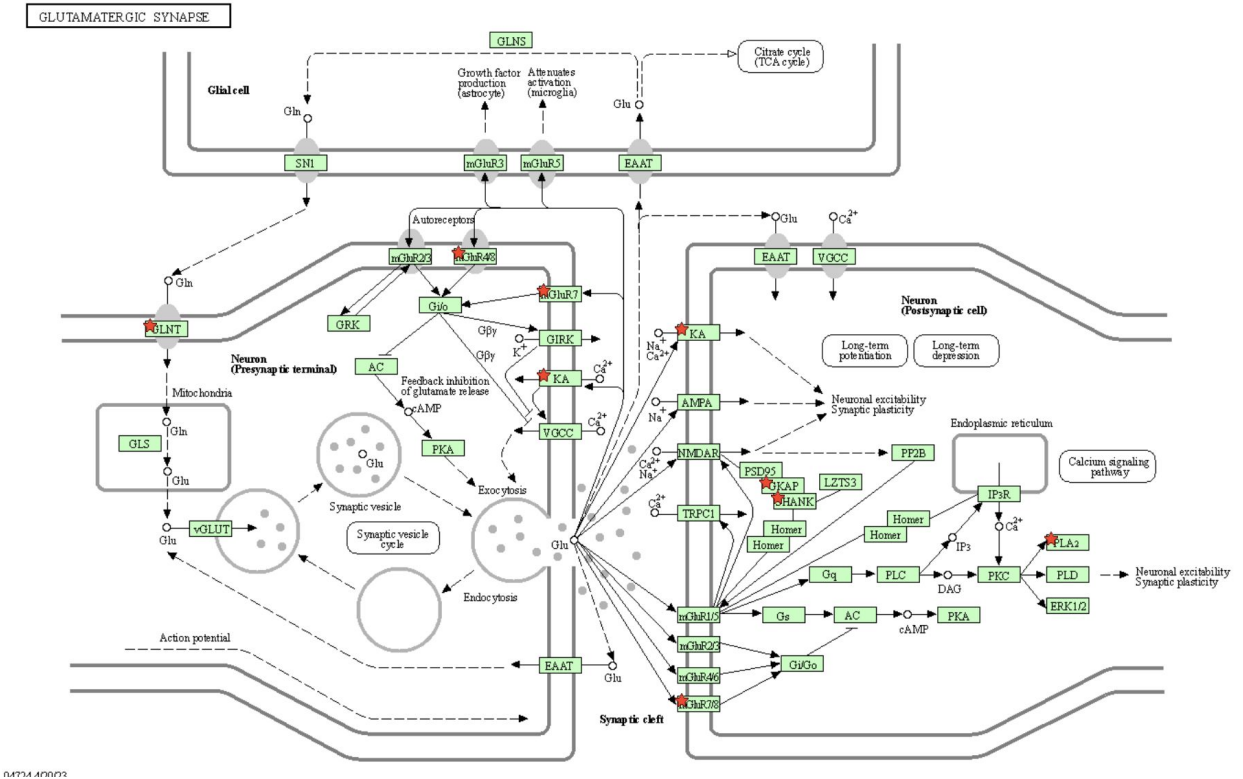
Pathway

-mGluR4/8, mGluR7

Members of the metabotropic glutamate receptor (mGluR) family
*They play important roles in glutamatergic synapses in the central nervous system

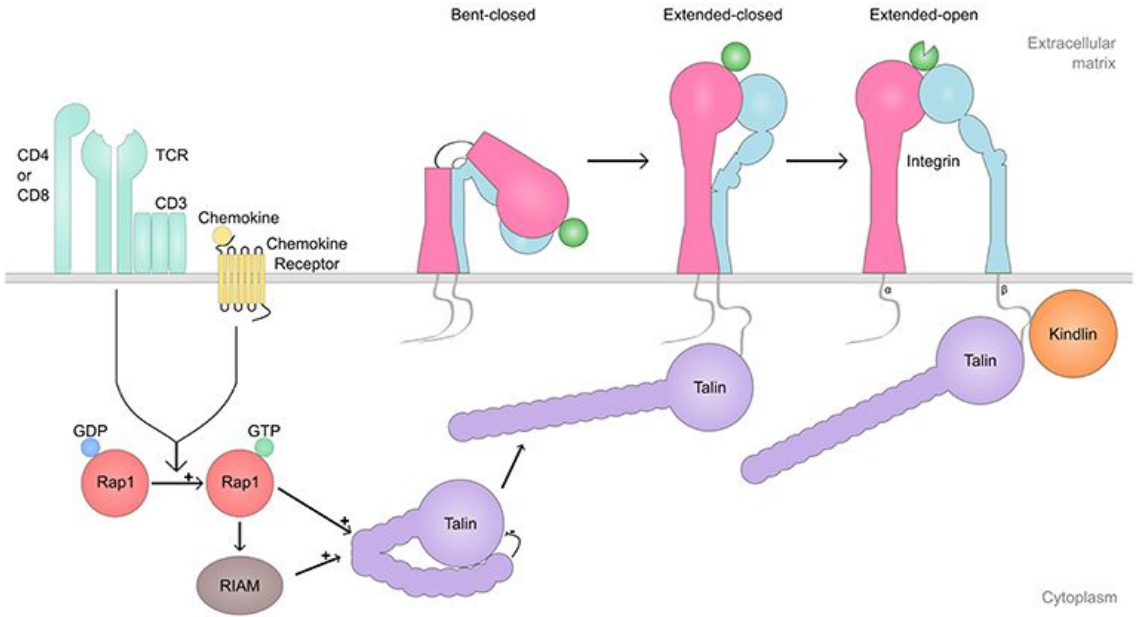
-KA

Kainate receptors. Type of ionotropic glutamate receptor and are named after the natural compound kainic acid, which selectively activates these receptors.



Cell adhesion molecules

-Cell adhesion molecules (CAMs) are (glyco)proteins expressed on the cell surface and play a critical role in a wide array of biologic processes that include hemostasis, the immune response, inflammation, embryogenesis, and development of neuronal tissue.



Pathway

-NEGR1

Promote neurite outgrowth and axonal guidance during neural development, contributing to the establishment of neuronal connections.

-NGL2

involved in mediating interactions between neurons and plays a critical role in synaptic connectivity and plasticity

-b-NRXN

Interacts with various postsynaptic proteins, such as neuroligins, leucine-rich repeat transmembrane proteins (LRRTMs), and cerebellin/GluD complexes. These interactions are crucial for establishing and maintaining synaptic connections between neurons.