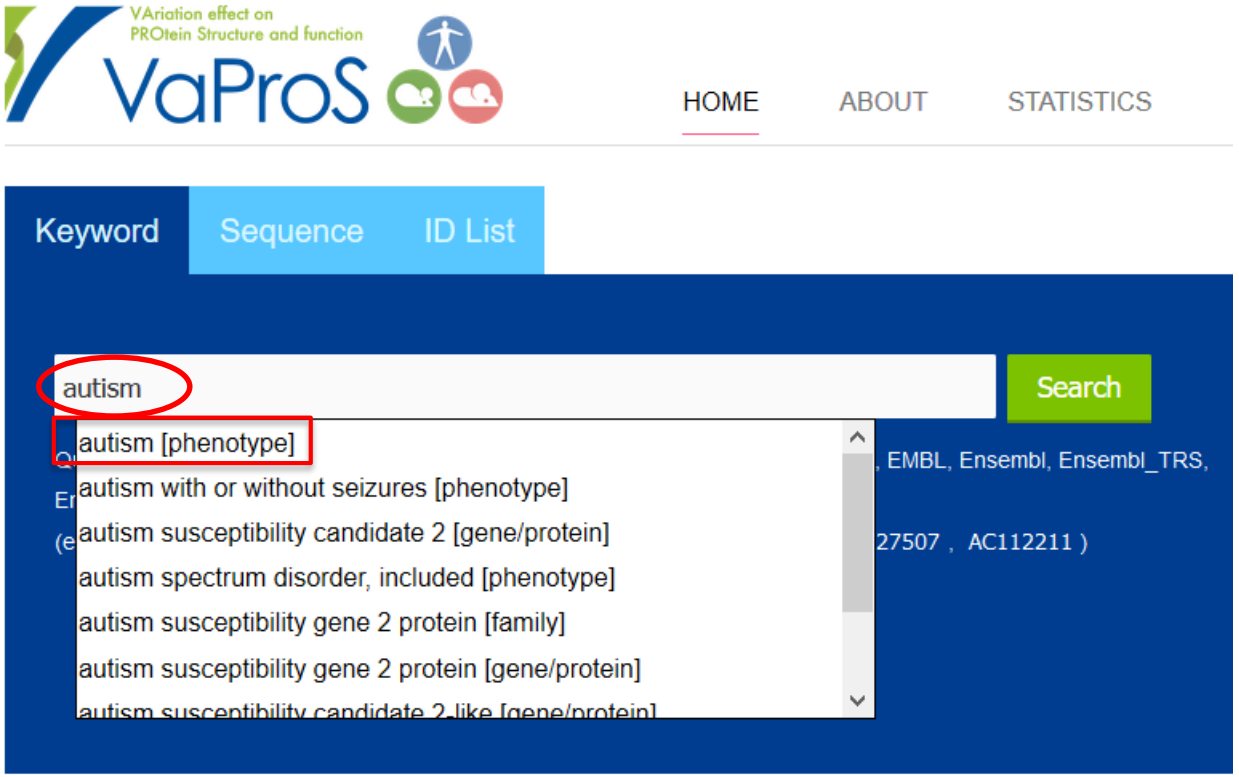
Vapros tutorial

In this tutorial, we demonstrate how to explore the molecular basis of autism and Rett syndrome and their relation with oxytocin using Vapros starting with the keyword “autism.”

Enter “autism” in the search window and select(click) one from the picklist displayed.



Query: "autism"

	Hits
Gene/Protein	0
Ligand	0
Phenotype	24

In the search results, we find 24 entries in phenotype category.

Gene/Protein results - hits: 0

Ligand results - hits: 0

Phenotype results - hits: 24

Details (Go)

In the list, we find the relation with Rett syndrome and MECP2 gene, and the gene has 89 molecular interactions. In addition, EIF4E is related with autism with 205 molecular interactions. The details of EIF4E can be found by ticking the far left check-box and click Details (Go) button.

Filtered by:

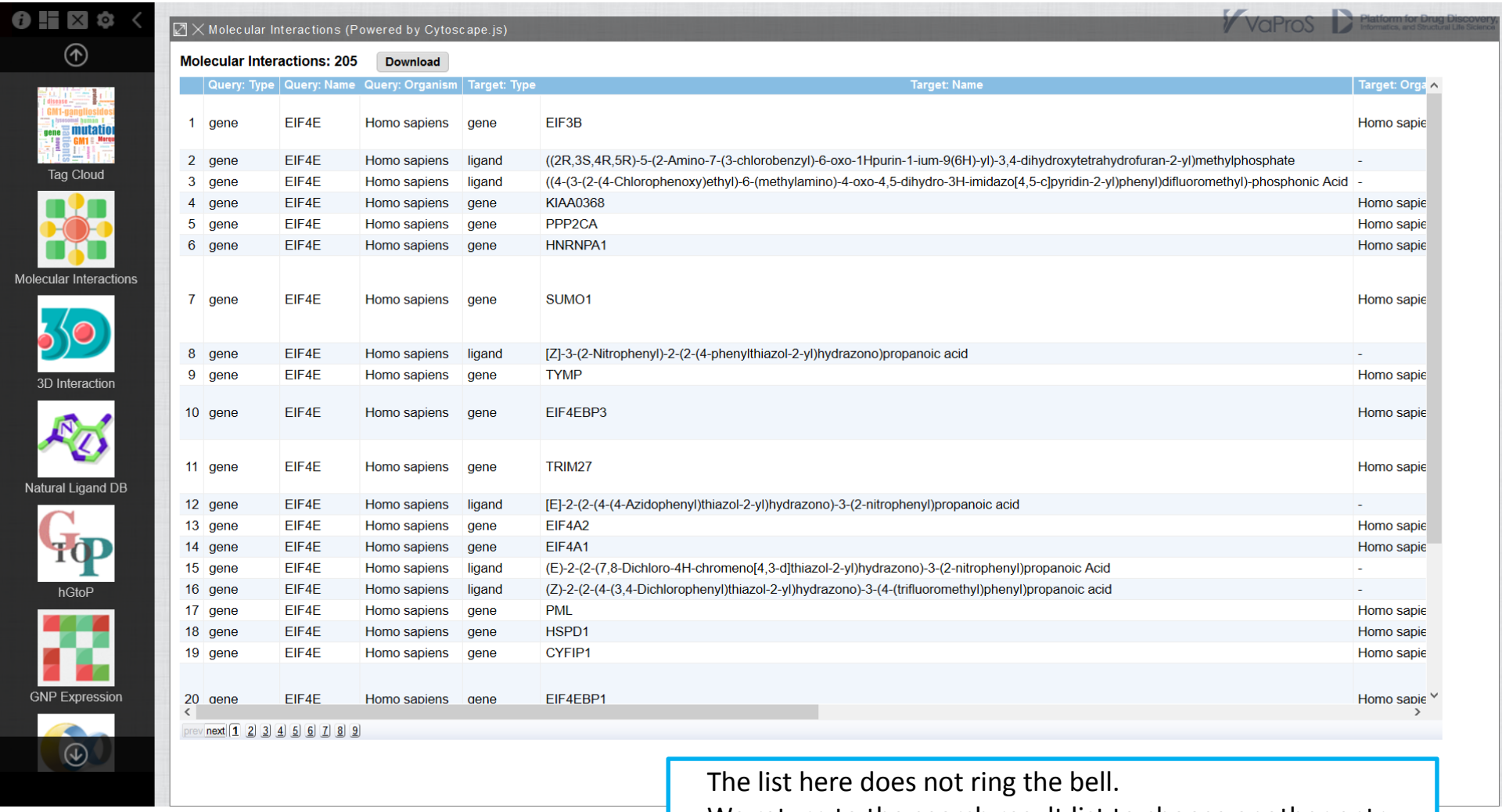
Molecule Type : molecule type Organism : organism TrEMBL : TrEMBL

Any Keyword :

			Type	Name	Organism	DB	Molecule Type	Molecule Symbol	EntrezGene ID	UniProtKB	TrEMBL	Molecular Interactions	PPI	3D Interaction	NLDB	hGtoP	GNP Expression	CC
1	☐	[synonym] AUTISM, SUSCEPTI...	phenotype	AUTISM, SUSCEPTIBILITY TO, X-L...	Homo sapiens	OMIM: 300847	gene/protein	RPL10	6134	P27635	none	634	634	1	0	1	1	1
2	☐	[synonym] AUTISM, SUSCEPTI...	phenotype	AUTISM, SUSCEPTIBILITY TO, 19	Homo sapiens	OMIM: 615091	gene/protein	EIF4E	1977	P06730	none	205	99	1	0	1	1	1
3	☐	[synonym] AUTISM, SUSCEPTI...	phenotype	AUTISM, SUSCEPTIBILITY TO, X-L...	Homo sapiens	OMIM: 300496	gene/protein	MECP2	4204	P51608	none	89	89	1	0	1	1	1
4	☐	[synonym] AUTISM, DEMENTIA...	phenotype	RETT SYNDROME	Homo sapiens	OMIM: 312750	gene/protein	MECP2	4204	P51608	none	89	89	1	0	1	1	1
5	☐	[synonym] AUTISM, SUSCEPTI...	phenotype	AUTISM, SUSCEPTIBILITY TO, 18	Homo sapiens	OMIM: 615032	gene/protein	CHD8	57680	Q9HCK8	none	80	80	1	1	1	1	1
6	☐	[synonym] AUTISM SPECTRUM ...	phenotype	AUTISM	Homo sapiens	OMIM: 209850	gene/protein	SNRPN	6638	P63163	none	51	51	1	0	1	1	1
7	☐	[synonym] AUTISM, SUSCEPTI...	phenotype	AUTISM, SUSCEPTIBILITY TO, 17	Homo sapiens	OMIM: 613436	gene/protein	SHANK2	22941	Q9UPX8	none	28	28	1	0	1	1	1
8	☐	[synonym] AUTISM, SUSCEPTI...	phenotype	AUTISM, SUSCEPTIBILITY TO, 15	Homo sapiens	OMIM: 612100	gene/protein	CNTNAP2	26047	Q9UHC6	none	12	12	1	0	1	1	1

Molecule Type	Molecule Symbol	EntrezGene ID	UniProtKB
gene/protein	RPL10	6134	P27635
gene/protein	EIF4E	1977	P06730

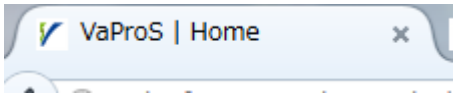
"Molecular interaction" viewer follows the **Details (Go)** button click and the interaction is displayed graphically. If the number of interactions is large, the data will be displayed in a table format.



	Query: Type	Query: Name	Query: Organism	Target: Type	Target: Name	Target: Orga
1	gene	EIF4E	Homo sapiens	gene	EIF3B	Homo sapie
2	gene	EIF4E	Homo sapiens	ligand	((2R,3S,4R,5R)-5-(2-Amino-7-(3-chlorobenzyl)-6-oxo-1Hpurin-1-ium-9(6H)-yl)-3,4-dihydroxytetrahydrofuran-2-yl)methylphosphate	-
3	gene	EIF4E	Homo sapiens	ligand	((4-(3-(2-(4-Chlorophenoxy)ethyl)-6-(methylamino)-4-oxo-4,5-dihydro-3H-imidazo[4,5-c]pyridin-2-yl)phenyl)difluoromethyl)-phosphonic Acid	-
4	gene	EIF4E	Homo sapiens	gene	KIAA0368	Homo sapie
5	gene	EIF4E	Homo sapiens	gene	PPP2CA	Homo sapie
6	gene	EIF4E	Homo sapiens	gene	HNRNPA1	Homo sapie
7	gene	EIF4E	Homo sapiens	gene	SUMO1	Homo sapie
8	gene	EIF4E	Homo sapiens	ligand	[Z]-3-(2-Nitrophenyl)-2-(2-(4-phenylthiazol-2-yl)hydrazono)propanoic acid	-
9	gene	EIF4E	Homo sapiens	gene	TYMP	Homo sapie
10	gene	EIF4E	Homo sapiens	gene	EIF4EBP3	Homo sapie
11	gene	EIF4E	Homo sapiens	gene	TRIM27	Homo sapie
12	gene	EIF4E	Homo sapiens	ligand	[E]-2-(2-(4-(4-Azidophenyl)thiazol-2-yl)hydrazono)-3-(2-nitrophenyl)propanoic acid	-
13	gene	EIF4E	Homo sapiens	gene	EIF4A2	Homo sapie
14	gene	EIF4E	Homo sapiens	gene	EIF4A1	Homo sapie
15	gene	EIF4E	Homo sapiens	ligand	(E)-2-(2-(7,8-Dichloro-4H-chromeno[4,3-d]thiazol-2-yl)hydrazono)-3-(2-nitrophenyl)propanoic Acid	-
16	gene	EIF4E	Homo sapiens	ligand	(Z)-2-(2-(4-(3,4-Dichlorophenyl)thiazol-2-yl)hydrazono)-3-(4-(trifluoromethyl)phenyl)propanoic acid	-
17	gene	EIF4E	Homo sapiens	gene	PML	Homo sapie
18	gene	EIF4E	Homo sapiens	gene	HSPD1	Homo sapie
19	gene	EIF4E	Homo sapiens	gene	CYFIP1	Homo sapie
20	gene	EIF4E	Homo sapiens	gene	EIF4EBP1	Homo sapie

prev next 1 2 3 4 5 6 7 8 9

The list here does not ring the bell.
We return to the search result list to choose another entry.



Back to the search result list by clicking the tab of the browser

Query: "autism"

	Hits
Gene/Protein	0
Ligand	0
Phenotype	24

Gene/Protein results - hits: 0

Ligand results - hits: 0

Phenotype results - hits: 24

By revisiting the search result,
we can move to OMIM description about autism and the relation with EIF4E.

Details (Go)

Filtered by:

Molecule Type : molecule type | Organism : organism | TrEMBL : TrEMBL

Any Keyword :

			Type	Name	Organism	DB	Molecule Type	Molecule Symbol	Entrez Gene ID	UniProtKB	TrEMBL	Molecular Interactions	PPI	3D Interaction	NLDB	hGtoPI	Expre
1	☐	[synonym] AUTISM, SUSCEPTI...	phenotype	AUTISM, SUSCEPTIBILITY TO, X-L...	Homo sapiens	OMIM: 300847	gene/protein	RPL10	6134	P27635	none	634	634	1	0	1	1
2	☐	[synonym] AUTISM, SUSCEPTI...	phenotype	AUTISM, SUSCEPTIBILITY TO, 19	Homo sapiens	OMIM: 615091	gene/protein	EIF4E	1977	P06730	none	205	99	1	0	1	1
3	☐	[synonym] AUTISM, SUSCEPTI...	phenotype	AUTISM, SUSCEPTIBILITY TO, X-L...	Homo sapiens	OMIM: 300496	gene/protein	MECP2	4204	P51608	none	89	89	1	0	1	1
4	☐	[synonym] AUTISM, DEMENTIA...	phenotype	RETT SYNDROME	Homo sapiens	OMIM: 312750	gene/protein	MECP2	4204	P51608	none	89	89	1	0	1	1
5	☐	[synonym] AUTISM, SUSCEPTI...	phenotype	AUTISM, SUSCEPTIBILITY TO, 18	Homo sapiens	OMIM: 615032	gene/protein	CHD8	57680	Q9HCK8	none	80	80	1	1	1	1
6	☐	[synonym] AUTISM SPECTRUM ...	phenotype	AUTISM	Homo sapiens	OMIM: 209850	gene/protein	SNRPN	6638	P63163	none	51	51	1	0	1	1
7	☐	[synonym] AUTISM, SUSCEPTI...	phenotype	AUTISM, SUSCEPTIBILITY TO, 17	Homo sapiens	OMIM: 613436	gene/protein	SHANK2	22941	Q9UPX8	none	28	28	1	0	1	1
8	☐	[synonym] AUTISM, SUSCEPTI...	phenotype	AUTISM, SUSCEPTIBILITY TO, 15	Homo sapiens	OMIM: 612100	gene/protein	CNTNAP2	26047	Q9UHC6	none	12	12	1	0	1	1

Organism	DB	Molecule Type	Molecule Symbol
Homo sapiens	OMIM: 300847	gene/protein	RPL10
Homo sapiens	OMIM: 615091	gene/protein	EIF4E

Jump to DB (OMIM)

TEXT

A number sign (#) is used with this entry because of evidence that variation in the EIF4E gene (133440) on chromosome 4q21-q25 influences susceptibility to autism.

For a phenotypic description and a discussion of genetic heterogeneity of autism, see 209850.

EIF4E gene locates on the 4th chromosome. A mutation on the gene may be a cause of the symptom.

Cytogenetics

Neves-Pereira et al. (2009) identified a boy with classic autism and a de novo balanced 46,XY,t(4;5)q23;q31.3) translocation. There was no family history of autism and the child had no dysmorphic features other than a double hair whorl on the crown. He demonstrated a typical and severe autistic phenotype. The breakpoint on chromosome 4 maps 56 kb downstream of EIF4E (133440), a region found to be associated with autism (Yonan et al., 2003; Schellenberg et al., 2006).

Molecular Genetics

To investigate a role for the EIF4E gene in autism susceptibility, Neves-Pereira et al. (2009) screened 120 multiplex families with 2 autistic sibs from the Autism Genetic Research Exchange (AGRE) collection for mutations in the coding regions and promoter of EIF4E. In 2 independent families direct sequencing revealed a heterozygous single-base insertion in the EIF4E promoter region (133440.0001) in the proband. In both of the families the variant was present in the second autistic sib and the father. The variant was not found in 1,020 anonymous control samples.

Model mouse has been established.

Animal Model

Gkogkas et al. (2013) demonstrated that knockout of the eukaryotic translation initiation factor 4E-binding protein 2 (EIF4EBP2; 602224), an EIF4E repressor downstream of MTOR, 601231) or Eif4e overexpression leads to increased translation of neuroligins, which are postsynaptic proteins that are causally linked to autism spectrum disorders (ASDs). Mice with knockout of Eif4ebp2 exhibit an increased ratio of excitatory to inhibitory synaptic inputs and autistic-like behaviors (i.e., social interaction deficits, altered communication, and repetitive/stereotyped behaviors). Pharmacologic inhibition of Eif4e activity or normalization of neuroligin-1 (600568), but not neuroligin-2 (606479), protein levels restored the normal excitation/inhibition ratio and rectified the social behavior deficits. Thus, Gkogkas et al. (2013) concluded that translational control by EIF4E regulates the synthesis of neuroligins, maintaining the excitation-to-inhibition balance, and its dysregulation engenders ASD-like phenotypes.

Santini et al. (2013) found that genetically increasing the levels of Eif4e in mice results in exaggerated cap-dependent translation and aberrant behaviors reminiscent of autism, including repetitive and perseverative behaviors and social interaction deficits. Moreover, these autistic-like behaviors are accompanied by synaptic pathophysiology in the medial prefrontal cortex, striatum, and hippocampus. The autistic-like behaviors displayed by the Eif4e transgenic mice are corrected by intracerebroventricular infusions of the cap-dependent translation inhibitor 4EGI-1. Santini et al. (2013) concluded that their findings demonstrated a causal relationship between exaggerated cap-dependent translation, synaptic dysfunction, and aberrant behaviors associated with autism.

Knock out of 4E-BP2, an EIF4E-binding protein, results in aberrant behavior of mice.

Reference link to PubMed

Check 4E-BP2

Click 602224

REFERENCES

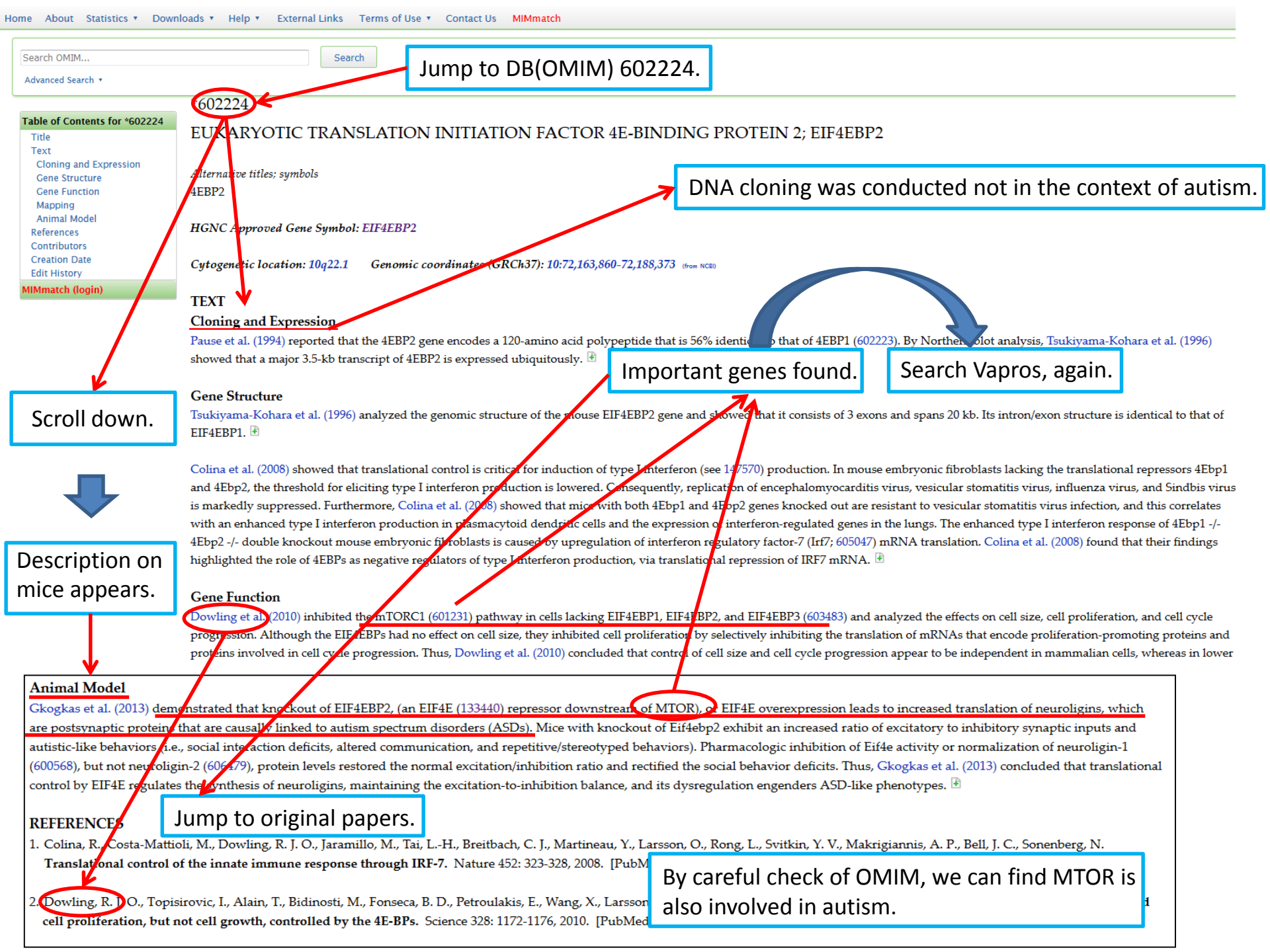
1. Gkogkas, C. G., Khoutorsky A., Ran, I., Rampakakis, E., Nevarko, T., Weatherill, D. B., Vasuta, C., Yee, S., Truitt, M., Dallaire, P., Major, F., Lasko, P., Ruggero, D., Nader, K., Lacaille, J.-C., Sonenberg, N. **Autism-related deficits via dysregulated eIF4E-dependent translational control.** Nature 493: 371-377, 2013. [PubMed: 23172145, related citations] [Full Text]

2. Neves-Pereira, M., Muller, B., Massie, D., Williams, J. H. G., O'Brien, P. C. M., Hughes, A., Shen, S.-B., St Clair, D., Miedzybrodzka, Z. **Deregulation of EIF4E: a novel mechanism for autism.** J. Med. Genet. 46: 759-765, 2009. Note: Erratum: J. Med. Genet. 48: 421 only, 2011. [PubMed: 19556253, related citations] [Full Text]

3. Santini, E., Huynh, T. N., MacAskill, A. F., Carter, A. G., Pierre, P., Ruggero, D., Kaphzan, H., Klann, E. **Exaggerated translation causes synaptic and behavioural aberrations associated with autism.** Nature 493: 411-415, 2013. [PubMed: 23263185, related citations] [Full Text]

4. Schellenberg, G. D., Dawson, G., Sung, Y. J., Estes, A., Munson, J., Rosenthal, E., Rothstein, J., Flodman, P., Smith, M., Coon, H., Leong, L., Yu, C.-E., Stodgell, C., Rodier, P. M., Spence, M. A., Minshew, N., McMahon, W. M., Wijsman, E. M. **Evidence for multiple loci from a genome scan of autism kindreds.** Molec. Psychiat. 11: 1049-1060, 2006. [PubMed: 16880825, related citations] [Full Text]

5. Yonan, A. L., Alarcon, M., Cheng, R., Magnusson, P. K. E., Spence, S. J., Palmer, A. A., Grunn, A., Juo, S.-H. H., Terwilliger, J. D., Liu, J., Cantor, R. M., Geschwind, D. H., Gilliam, T. C. **A genomewide screen of 345 families for autism-susceptibility loci.** Am. J. Hum. Genet. 73: 886-897, 2003. [PubMed: 13680528, related citations] [Full Text]


Home About Statistics Downloads Help External Links Terms of Use Contact Us MIMmatch
Search OMIM...
Search
Advanced Search
Jump to DB(OMIM) 602224.
602224
Table of Contents for *602224
Title
Text
Cloning and Expression
Gene Structure
Gene Function
Mapping
Animal Model
References
Contributors
Creation Date
Edit History
MIMmatch (login)
EUKARYOTIC TRANSLATION INITIATION FACTOR 4E-BINDING PROTEIN 2; EIF4EBP2
Alternative titles; symbols
4EBP2
HGNC Approved Gene Symbol: EIF4EBP2
Cytogenetic location: 10q22.1
Genomic coordinates (GRCh37): 10:72,163,860-72,188,373
DNA cloning was conducted not in the context of autism.
TEXT
Cloning and Expression
Pause et al. (1994) reported that the 4EBP2 gene encodes a 120-amino acid polypeptide that is 56% identi to that of 4EBP1 (602223). By Northe blot analysis, Tsukiyama-Kohara et al. (1996) showed that a major 3.5-kb transcript of 4EBP2 is expressed ubiquitously.
Important genes found.
Search Vapros, again.
Scroll down.
Gene Structure
Tsukiyama-Kohara et al. (1996) analyzed the genomic structure of the mouse EIF4EBP2 gene and showed that it consists of 3 exons and spans 20 kb. Its intron/exon structure is identical to that of EIF4EBP1.
Colina et al. (2008) showed that translational control is critical for induction of type I interferon (see 147570) production. In mouse embryonic fibroblasts lacking the translational repressors 4Ebp1 and 4Ebp2, the threshold for eliciting type I interferon production is lowered. Consequently, replication of encephalomyocarditis virus, vesicular stomatitis virus, influenza virus, and Sindbis virus is markedly suppressed. Furthermore, Colina et al. (2008) showed that mice with both 4Ebp1 and 4Ebp2 genes knocked out are resistant to vesicular stomatitis virus infection, and this correlates with an enhanced type I interferon production in plasmacytoid dendritic cells and the expression of interferon-regulated genes in the lungs. The enhanced type I interferon response of 4Ebp1 -/- 4Ebp2 -/- double knockout mouse embryonic fibroblasts is caused by upregulation of interferon regulatory factor-7 (Irf7; 605047) mRNA translation. Colina et al. (2008) found that their findings highlighted the role of 4EBPs as negative regulators of type I interferon production, via translational repression of IRF7 mRNA.
Description on mice appears.
Gene Function
Dowling et al. (2010) inhibited the mTORC1 (601231) pathway in cells lacking EIF4EBP1, EIF4EBP2, and EIF4EBP3 (603483) and analyzed the effects on cell size, cell proliferation, and cell cycle progression. Although the EIF4EBPs had no effect on cell size, they inhibited cell proliferation by selectively inhibiting the translation of mRNAs that encode proliferation-promoting proteins and proteins involved in cell cycle progression. Thus, Dowling et al. (2010) concluded that control of cell size and cell cycle progression appear to be independent in mammalian cells, whereas in lower
Animal Model
Gkogkas et al. (2013) demonstrated that knockout of EIF4EBP2, (an EIF4E (133440) repressor downstream of MTOR), or EIF4E overexpression leads to increased translation of neuroligins, which are postsynaptic proteins that are causally linked to autism spectrum disorders (ASDs). Mice with knockout of Eif4ebp2 exhibit an increased ratio of excitatory to inhibitory synaptic inputs and autistic-like behaviors (i.e., social interaction deficits, altered communication, and repetitive/stereotyped behaviors). Pharmacologic inhibition of Eif4e activity or normalization of neuroligin-1 (600568), but not neuroligin-2 (606479), protein levels restored the normal excitation/inhibition ratio and rectified the social behavior deficits. Thus, Gkogkas et al. (2013) concluded that translational control by EIF4E regulates the synthesis of neuroligins, maintaining the excitation-to-inhibition balance, and its dysregulation engenders ASD-like phenotypes.
Jump to original papers.
REFERENCES
1. Colina, R., Costa-Mattioli, M., Dowling, R. J. O., Jaramillo, M., Tai, L.-H., Breitbach, C. J., Martineau, Y., Larsson, O., Rong, L., Svitkin, Y. V., Makrigiannis, A. P., Bell, J. C., Sonenberg, N. Translational control of the innate immune response through IRF-7. Nature 452: 323-328, 2008. [PubM
2. Dowling, R. J. O., Topisirovic, I., Alain, T., Bidinosti, M., Fonseca, B. D., Petroulakis, E., Wang, X., Larsson cell proliferation, but not cell growth, controlled by the 4E-BPs. Science 328: 1172-1176, 2010. [PubMed
By careful check of OMIM, we can find MTOR is also involved in autism.

Query: "mtor"

	Hits
Gene/Protein	52
Ligand	0
Phenotype	0

According to the inspiration obtained by OMIM link, “mtor” is used as a new query. “mtor” is short, so simple keyword search will produce many false positive results, which can be prevented by limiting the search for gene and proteins with “[gene/protein]” tag. As a result, we can easily find 12 related entries. Similar filtering can be achieved by using pull-down menu for type above the search result table. We can also select the genes for human by using a pull-down menu for organisms.

Gene/Protein results - hits: 52

Details (Go)

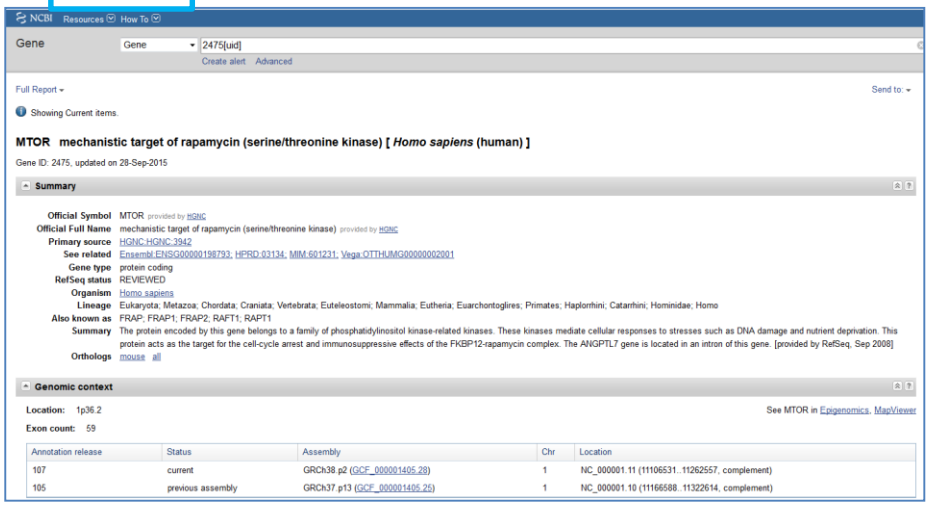
Filtered by:

Type : molecule type | Organism : organism | TrEMBL : TrEMBL

Any Keyword :

			Type	Name	Full Name	Organism	EntrezGene ID	UniProtKB	TrEMBL	Molecular Interactions	PPI	3D Interaction	NLDB	hGtoP	GNP Expression
1	☐	[synonym] mTOR	gene/protein	MTOR	Serine/threonine-protein kinas...	Homo sapiens	2475	P42345	none	4477	250	1	3	1	1
2	☐	[synonym] ...rotein of mTOR	gene/protein	RPTOR	Regulatory-associated protein ...	Homo sapiens	57521	Q8N122	none	131	131	1	0	1	1
3	☐	[synonym] mTOR	gene/protein	Mtor	Serine/threonine-protein kinas...	Mus musculus	56717	Q9JLN9	none	120	47	1	3	1	1
4	☐	[synonym] ... MAPK and MTOR activator...	gene/protein	LAMTOR5	Ragulator complex protein LAMTOR5	Homo sapiens	10542	O43504	none	113	113	1	0	1	1
5	☐	[synonym] ...panion of mTOR	gene/protein	RICTOR	Rapamycin-insensitive companio...	Homo sapiens	253260	Q6R327	none	107	106	1	0	1	1
6	☐	[synonym] ... MAPK and MTOR activator...	gene/protein	LAMTOR3	Ragulator complex protein LAMTOR3	Homo sapiens	8649	Q9UHA4	none	104	104	1	0	1	1

To NCBI



To UniProt

NCBI tells that MTOR is a Ser/Thr kinase and is bound by rapamycin.

NCBI Resources How To

Gene | Gene | 2475[uid]

Create alert Advanced

Full Report

Showing Current items.

MTOR mechanistic target of rapamycin (serine/threonine kinase) [*Homo sapiens* (human)]

Gene ID: 2475, updated on 28-Sep-2015

UniProt tells the sequence and binding partners of MTOR.

UniProt describes an interaction between MTOR and EIF-4EBP1 at the Interaction section.

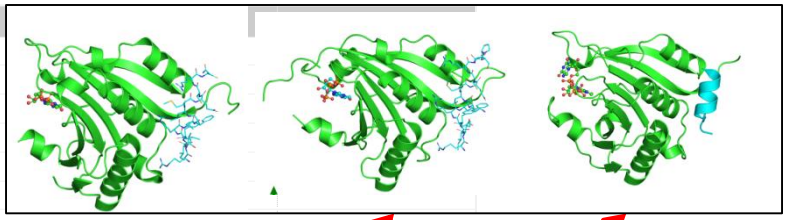
Interaction

Subunit structure

Part of the mammalian target of rapamycin complex 1 (mTORC1) which contains MTOR, MLST8, RPTOR, AKT1S1/PRAS40 and DEPTOR. The mTORC1 complex is a 1 Md obligate dimer of two stoichiometric heterotetramers with overall dimensions of 290 A x 210 A x 135 A. It has a rhomboid shape and a central cavity, the dimeric interfaces are formed by interlocking interactions between the two MTOR and the two RPTOR subunits. the MLST8 subunits forms distal foot-like protuberances, and contacts only one MTOR within the complex, while the small PRAS40 localizes to the midsection of the central core, in close proximity to RPTOR. Part of the mammalian target of rapamycin COmplex 2 (mTORC2) which contains MTOR, MLST8, PRR5, RICTOR, MAPKAP1 and DEPTOR. Interacts with RPAPDC3 and PML. Interacts with PRR5 and RICTOR; the interaction is direct within the mTORC2 complex. Interacts with UBQLN1. Interacts with TTI1 and TELO2. Interacts with CLIP1; phosphorylates and regulates CLIP1. Interacts with NBN. Interacts with HTR6 (PubMed:23027611). Interacts with BRAT1. 22 Publications

Binary interactions

With	Entry	#Exp.	IntAct
AKT1	P31749	2	EBI-359260,EBI-296087
DEPTOR	Q8TB45	5	EBI-359260,EBI-2359040
EIF4EBP1	Q13541	2	EBI-359260,EBI-74090
FKBP1	P62942	2	EBI-359260,EBI-1027571
MLST8	Q9BVC4	4	EBI-359260,EBI-1387471
PREX1	Q8TCU6	11	EBI-359260,EBI-1046542
RAB1A	P62820	4	EBI-359260,EBI-716845
RICTOR	Q6R327	27	EBI-359260,EBI-1387196
RPTOR	Q8N122	32	EBI-359260,EBI-1567928
SIRT1	Q96EB6	2	EBI-359260,EBI-1802965
TPCN2	Q8NHX9	2	EBI-359260,EBI-5239940



Jump to UniProt

Structure

Secondary structure

1

Legend: Helix Turn Beta strand

Show more details

3D structure databases

Select the link destinations: PDBe RCSB PDB PDBj

Entry	Method	Resolution (Å)
1EJ4	X-ray	2.25
1WKW	X-ray	2.10
2JGB	X-ray	1.70
2JGC	X-ray	2.40
2V8W	X-ray	2.30
2V8X	X-ray	2.30
2V8Y	X-ray	2.10
3HXG	X-ray	2.10
3HXI	X-ray	1.80

3D structure in complex can be found.

UniProt description has “Structure” at the bottom.

Click PDB ID

Return to the page for OMIM602224.

Animal Model

Gkogkas et al. (2013) demonstrated that knockout of EIF4EBP2, (an EIF4E (133440) repressor downstream of MTOR), or EIF4E overexpression leads to increased translation of neuroligins, which are postsynaptic proteins that are causally linked to autism spectrum disorders (ASDs). Mice with knockout of Eif4ebp2 exhibit an increased ratio of excitatory to inhibitory synaptic inputs and autistic-like behaviors (i.e., social interaction deficits, altered communication, and repetitive/stereotyped behaviors). Pharmacologic inhibition of Eif4e activity or normalization of neuroligin-1 (600568), but not neuroligin-2 (606479), protein levels restored the normal excitation/inhibition ratio and rectified the social behavior deficits. Thus, Gkogkas et al. (2013) concluded that translational control by EIF4E regulates the synthesis of neuroligins, maintaining the excitation-to-inhibition balance, and its dysregulation engenders ASD-like phenotypes.

REFERENCES

1. Colina, R., Costa-Mattioli, M., Dowling, R. J. O., Jaramillo, M., Tai, L.-H., Breitbach, C. J., Martineau, Y., Larsson, O., Rong, L., Svitkin, Y. V., Makrigiannis, A. P., Bell, J. C., Sonenberg, N. **Translational control of the innate immune response through IRF-7.** Nature 452: 323-328, 2008. [PubMed: 18272964, related citations] [Full Text]

2. Dowling, R. J. O., Topisirovic, I., Alain, T., Bidinosti, M., Fonseca, B. D., Petroulakis, E., Wang, X., Larsson, O., Selvaraj, A., Liu, Y., Kozma, S. C., Thomas, G., Sonenberg, N. **mTORC1-mediated cell proliferation, but not cell growth, controlled by the 4E-BPs.** Science 328: 1172-1176, 2010. [PubMed: 20508131, related citations] [Full Text]

4EBP2 which binds EIF4E is located downstream of MTOR. MTOR is targeted by rapamycin. Hence rapamycin has potential to regulate protein expression.

The cause of autism should be complex. Yet autism caused by the aberrant EIF4E on the 4th chromosome may have a way for cure.

Investigate autism caused by aberrant MCP2 next.

Query: "autism"

	Hits
Gene/Protein	0
Compound	0
Phenomenon	25

Gene/Protein result - hits: 0

Compound result - hits: 0

Phenomenon result - hits: 25

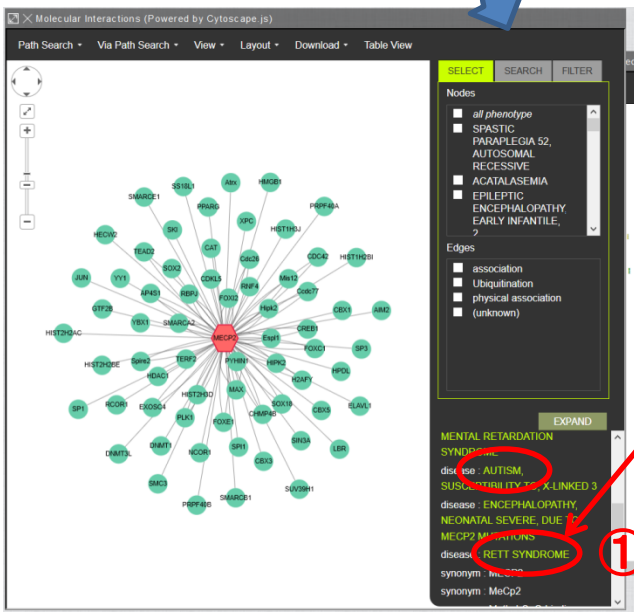
Details (Go)

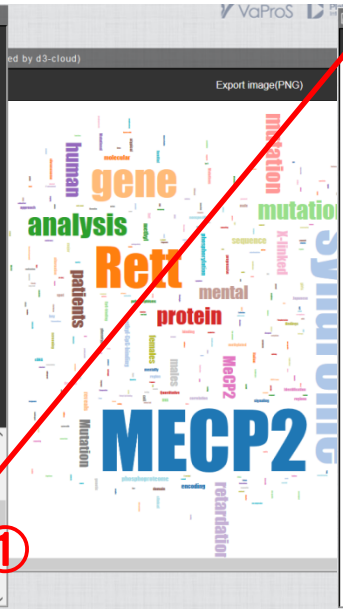
		TYPE	NAME	TAXONOMY	DB	MOLECULE TYPE	MOLECULE SYMBOL	MOLECULE TAXONOMY	ENTREZGENE ID	UNIPROTKB AC	HGTOP	3D INTERACTOME	NLDB	GNP EXPRESSION	COXPRESDB	MOLECULAR INTERACTIONS	PATHWAY	DISEASE	S-VAR
1		disease	AUTISM, SUSCEPTIBILITY TO, 19	Homo sapiens	OMIM: 615091	gene/protein	EIF4E	Homo sapiens	1977	P06730	0	0	0	1	1	127	0	1	open
2		disease	AUTISM	Homo sapiens	OMIM: 209850	gene/protein	SNRPN	Homo sapiens	6638	P63164	0	0	0	1	1	46	0	2	open
3		disease	AUTISM, SUSCEPTIBILITY TO, 18	Homo sapiens	OMIM: 615032	gene/protein	CHD8	Homo sapiens	57680	Q9HCK8	0	1		1	1	35	0	1	open
4		disease	AUTISM, SUSCEPTIBILITY TO, X-LINKED 5	Homo sapiens	OMIM: 300847	gene/protein	RPL10	Homo sapiens	6134	P27635	3	1	0	1	1	18	0	1	open
5		disease	AUTISM, SUSCEPTIBILITY TO, 17	Homo sapiens	OMIM: 613436	gene/protein	SHANK2	Homo sapiens	22941	Q9UPX8	0	1	0	1	1	11	0	1	open
6		disease	EPSILON-TRIMETHYLLYSINE HYDROXYLASE DEFICIENCY	Homo sapiens	OMIM: 300872	gene/protein	TMLHE	Homo sapiens	55217	Q9NVH6	0	1	1	1	1	10	0	1	open
7		disease	AUTISM, SUSCEPTIBILITY TO, 15	Homo sapiens	OMIM: 612100	ge	CNTNAP2	Homo sapiens	26047	B2RC34	0	1	0	1	1	9	0	2	open
8		disease	AUTISM, SUSCEPTIBILITY TO, X-LINKED 1	Homo s	OMIM: 300425	gene/prot	NLGN3		54413	Q9NZ94	0	0	0	1	1	8	0	2	open
9		disease	AUTISM, SUSCEPTIBILITY TO, X-LINKED 3	Hom	OMIM: 300496	gene/protein	MECP2	Homo sapiens	04	P51608	0	1	0	1	1	7	0	6	open
10		disease	RETT SYNDROME	Ho	OMIM: 312750	gene/protein	MECP2	Homo sapiens		P51608	0	1	0	1	1	7	0	6	open

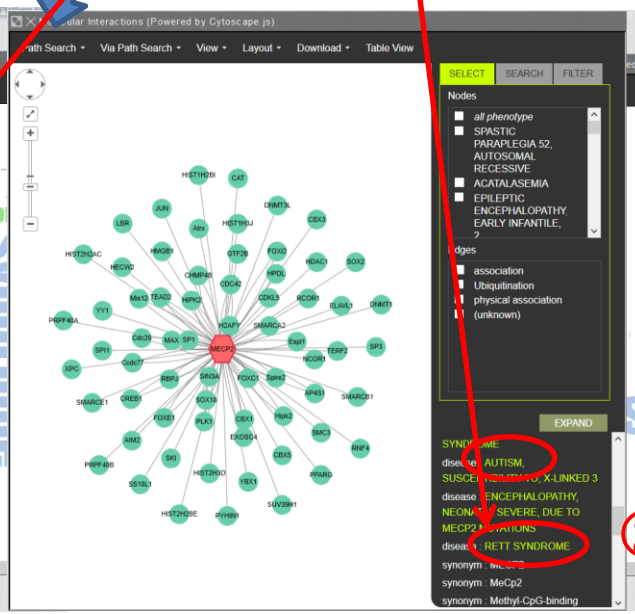
Return to the first search-result table and find two hits. Click each hit.

The Molecular Interactions shown in both links are topologically the same, although they look different.

By clicking “RETT SYNDROME”, the detail of the syndrome can be found in the link.







Two links (#300496 and #312750) were found. Both descriptions were contributed by the same person. Click #300496 which is the latest.

#300496

AUTISM, SUSCEPTIBILITY TO, X-LINKED 3; AUTSX3

Phenotype-Gene Relationships

Location	Phenotype	Phenotype MIM number	Inheritance (in progress)	Phenotype mapping key	Gene/Locus	Gene/Locus MIM number
Xq28	{Autism susceptibility, X-linked 3}	300496	XL, IC, Mu	3	MECP2	300005

Clinical Synops… | Phenotypic Series

Click!

MECP2 is related to AUTSX3.

TEXT

A number sign (#) is used with this entry because X-linked autism-3 (AUTSX3) is associated with mutation in the MECP2 gene (300005) on Xq28.

Description

Autism, the prototypic pervasive developmental disorder (PDD), is usually apparent by 3 years of age. It is characterized by a triad of limited or absent verbal communication, a lack of reciprocal social interaction or responsiveness, and restricted, stereotypic, and ritualized patterns of interests and behavior (Bailey et al., 1996; Risch et al., 1999). 'Autism spectrum disorder,' sometimes referred to as ASD, is a broader phenotype encompassing the less severe disorders Asperger syndrome (see ASPG1; 608638) and pervasive developmental disorder, not otherwise specified (PDD-NOS). 'Broad autism phenotype' includes individuals with some symptoms of autism, but who do not meet the full criteria for autism or other disorders. Mental retardation coexists in approximately two-thirds of individuals with ASD, except for Asperger syndrome, in which mental retardation is conspicuously absent (Jones et al., 2008). Genetic studies in autism often include family members with these less stringent diagnoses (Schellenberg et al., 2006).

For a discussion of genetic heterogeneity of autism, see 209850.

The list of genes for autism was found. This information was not described in #312750.

Autism, susceptiblity to - PS209850 - 26 Entries

Location ▲	Phenotype	Phenotype mapping key	Phenotype MIM number	Gene/Locus	Gene/Locus MIM number
1q41-q42	{Autism susceptibility 11}	2	610836	AUTS11	610836
2q	{Autism susceptibility 5}	2	606053	AUTS5	606053
3q24	?{Autism susceptibility 16}	3	613410	SLC9A9, AUTS16	608396
3q25-q27	{Autism susceptibility 8}	2	607373	AUTS8	607373
4q23	{Autism, susceptibility to, 19}	3	615091	EIF4E, EIF4EL1, AUTS19	133440
7q22	{Autism susceptibility 1}	2	209850	AUTS1	209850
7q31	{Autism, susceptibility to, 9}	2	611015	AUTS9	611015
7q35-q36	{Autism susceptibility 15}	3	612100	CNTNAP2, CASPR2, NRXN4, CDFE, AUTS15, PTHSL1	604569
7q36	{Autism, susceptibility to, 10}	2	611016	AUTS10	611016
11q13.3-q13.4	{Autism susceptibility 17}	3	613436	SHANK2, CORTBP1, AUTS17	603290
12q14.2	{Autism susceptibility 13}	2	610908	AUTS13	610908
13q14.2-q14.1	{Autism susceptibility 3}	2	608049	AUTS3	608049
14q11.2	{Autism, susceptibility to, 18}	3	615032	CHD8, DUPLIN, KIAA1564, AUTS18	610528
15q11	{Autism susceptibility 4}	2	608636	AUTS4	608636
16p11.2	Chromosome 16p11.2 deletion syndrome, 593kb	4	611913	DEL16p11.2, C16DELp11.2, AUTS14A	611913
16p11.2	{Autism susceptibility 14A}	2	611913	DEL16p11.2, C16DELp11.2, AUTS14A	611913
17q11	{Autism susceptibility 6}	2	609378	AUTS6	609378
17q21	{Autism susceptibility 7}	2	610676	AUTS7	610676
21p13-q11	{Autism susceptibility 12}	2	610838	AUTS12	610838
Xp22.32-p22.31	Mental retardation, X-linked	3	300495	NLGN4, KIAA1260, AUTSX2, ASPGX2	300427
Xp22.32-p22.31	{Autism susceptibility, X-linked 2}	3	300495	NLGN4, KIAA1260, AUTSX2, ASPGX2	300427
Xp22.11	{Autism susceptibility, X-linked 4}	4	300830	DELXp22.11, CXDELp22.11, AUTSX4	300830
Xq13.1	{Autism susceptibility, X-linked 1}	3	300425	NLGN3, ASPGX1, AUTSX1	300336
Xq28	{Autism susceptibility, X-linked 3}	3	300496	MECP2, RTT, PPMX, MRX16, MRX79, AUTSX3, MRXSL, MRXS13, MRX79, MRX16	300005
Xq28	{Autism, susceptibility to, X-linked 5}	3	300847	RPL10, DXS648, QM, AUTSX5	312173
Xq28	Epsilon-trimethyllysine hydroxylase deficiency	3	300872	TMLHE, BBOX2, TMLH, TMLHED, AUTSX6	300777

Phenotype Mapping Key

1 - the disorder is placed on the map due to its association with a gene, but the underlying defect is not known.
2 - the disorder was placed on the map by statistical methods.
3 - the molecular basis of the disorder is known.
4 - a contiguous gene duplication or deletion syndrome in which multiple genes are involved.

Click #312750

#312750

RETT SYNDROME; RTT

Alternative titles; symbols

RTS

AUTISM, DEMENTIA, ATAXIA, AND LOSS OF PURPOSEFUL HAND USE

Other entities represented in this entry:

RETT SYNDROME, ZAPPELLA VARIANT, INCLUDED

RETT SYNDROME, PRESERVED SPEECH VARIANT, INCLUDED

RETT SYNDROME, ATYPICAL, INCLUDED

Phenotype-Gene Relationships

Location	Phenotype	Phenotype MIM number	Inheritance (in progress)	Phenotype mapping key	Gene/Locus	Gene/Locus MIM number
Xq28	Rett syndrome	312750	XLD	3	MECP2	300005
Xq28	Rett syndrome, preserved speech variant	312750	XLD	3	MECP2	300005
Xq28	Rett syndrome, atypical	312750	XLD	3	MECP2	300005

Clinical Synopsis

TEXT

A number sign (#) is used with this entry because Rett syndrome (RTT) is caused by mutation in the gene encoding methyl-CpG-binding protein-2 (MECP2; 300005).

See also the congenital variant of Rett syndrome (613454), which is caused by mutation in the FOXG1 gene (164874) on chromosome 14q13.

MECP2 is the same as methyl-CpG-binding protein-2.

What kind of protein is methyl-CpG-binding protein-2?

click

*300005

METHYL-CpG-BINDING PROTEIN 2; MECP2

HGNC Approved Gene Symbol: *MECP2*

Cytogenetic location: *Xq28* ***Genomic coordinates (GRCh37):*** *X:153,287,024-153,363,187* (from NCBI)

Gene-Phenotype Relationships

Location	Phenotype	Phenotype MIM number	Inheritance (in progress)	Phenotype mapping key
Xq28	Encephalopathy, neonatal severe	300673	XLR	3
	Mental retardation, X-linked syndromic, Lubs type	300260	XLR	3
	Mental retardation, X-linked, syndromic 13	300055	XLR	3
	Rett syndrome	312750	XLD	3
	Rett syndrome, atypical	312750	XLD	3
	Rett syndrome, preserved speech variant	312750	XLD	3
	{Autism susceptibility, X-linked 3}	300496	XL, IC, Mu	3

TEXT

Description

MECP2, which binds methylated CpGs, is a chromatin-associated protein that can both activate and repress transcription. It is required for maturation of neurons and is developmentally regulated (summary by Swanberg et al., 2009). Mutations in MECP2 can cause Rett syndrome, mental retardation, or encephalopathy, and have been implicated in autism susceptibility.

Cloning and Expression

Lewis et al. (1992) identified and cloned Mecp2 from a rat brain cDNA library. The deduced 492-amino acid protein has a molecular mass of 53 kD and is rich in basic amino acids and potential phosphorylation sites. Immunofluorescent staining showed that the distribution of Mecp2 along chromosomes parallels that of methyl-CpG. In the mouse, Mecp2 is concentrated in pericentromeric heterochromatin, which contains about 40% of all genomic 5-methylcytosine. Unlike methyl-CpG-binding protein-1 (MBD1; 156535), MECP2 is able to bind a single methyl-CpG pair. Nan et al. (1993) cloned the rat Mecp2 gene and defined the methyl-CpG-binding domain (MBD). The MBD is 85 amino acids long and binds exclusively to DNA that contains one or more symmetrically methylated CpGs.

MECP2 is one of the key proteins for neurogenesis. The gene is located on X chromosome, hence lethal recessive inherited gene.

Vapros realizes speedy and reliable search compared with other search engines. The evidence for any statement can be found on the linked DBs.