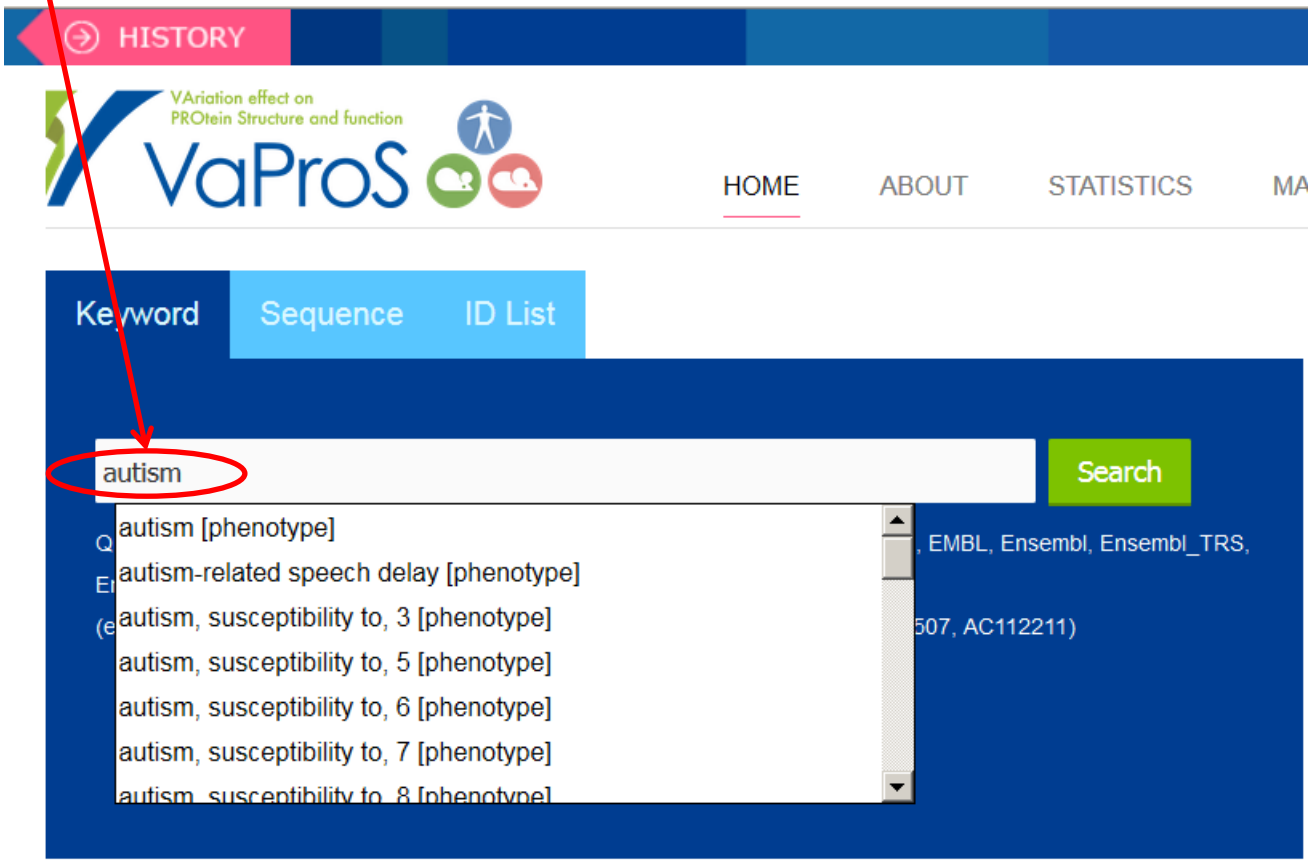
VaProSチュートリアル

＜VaProSを検索エンジンのように使用する＞

「自閉症の治療にペプチドホルモンであるオキシトシンが効果がある」(9/3)
「九大、自閉症引き起こす神経発達障害「レット症候群」の発症メカニズムの一端を解明」(9/22)
というニュースを見て自閉症と遺伝子の関係やリガンドとの結合に関して情報が得られないか。

まずkeywordで検索開始。



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Query: "autism"

	Hits
Gene/Protein	0
Ligand	0
Phenotype	24

Phenotype results にはoxytocinという語は見られない。
レット症候群の原因遺伝子(MECP2)についてmolecular interactions の数が61だが、EIF4Eでは154もある。とりあえずEIF4Eをクリック。

Gene/Protein results - hits: 0

Ligand results - hits: 0

Phenotype results - hits: 24

Details (Go)

Filtered by:

Molecule Type : molecule type Organism : organism TrEMBL : TrEMBL

			Type	Name	Organism	DB	Molecule Type	Molecule Symbol	EntrezGene ID	UniProtKB	TrEMBL	Molecular Interaction
1	☐	[synonym] AUTISM, SUSCEPTI...	phenotype	AUTISM, SUSCEPTIBILITY TO, X-L...	Homo sapiens	OMIM: 300847	gene/protein	RPL	6134	P27635	none	
2	☐	[synonym] AUTISM, SUSCEPTI...	phenotype	AUTISM, SUSCEPTIBILITY TO, 19	Homo sapiens	OMIM: 615091	gene/protein	EIF4E	1977	P06730	none	154
3	☐	[synonym] AUTISM, SUSCEPTI...	phenotype	AUTISM, SUSCEPTIBILITY TO, 18	Homo sapiens	OMIM: 615032	gene/protein	CHD8	57680	Q9HCK8	none	62
4	☐	[synonym] AUTISM, SUSCEPTI...	phenotype	AUTISM, SUSCEPTIBILITY TO, X-L...	Homo sapiens	OMIM: 300496	gene/protein	MECP2	4204	P51608	none	61
5	☐	[synonym] AUTISM, DEMENTIA...	phenotype	RETT SYNDROME	Homo sapiens	OMIM: 312750	gene/protein	MECP2	4204	P51608	none	61
6	☐	[synonym] AUTISM SPECTRUM	phenotype	AUTISM	Homo sapiens	OMIM: 209850	gene/protein	SNRPN	6638	P63163	none	54

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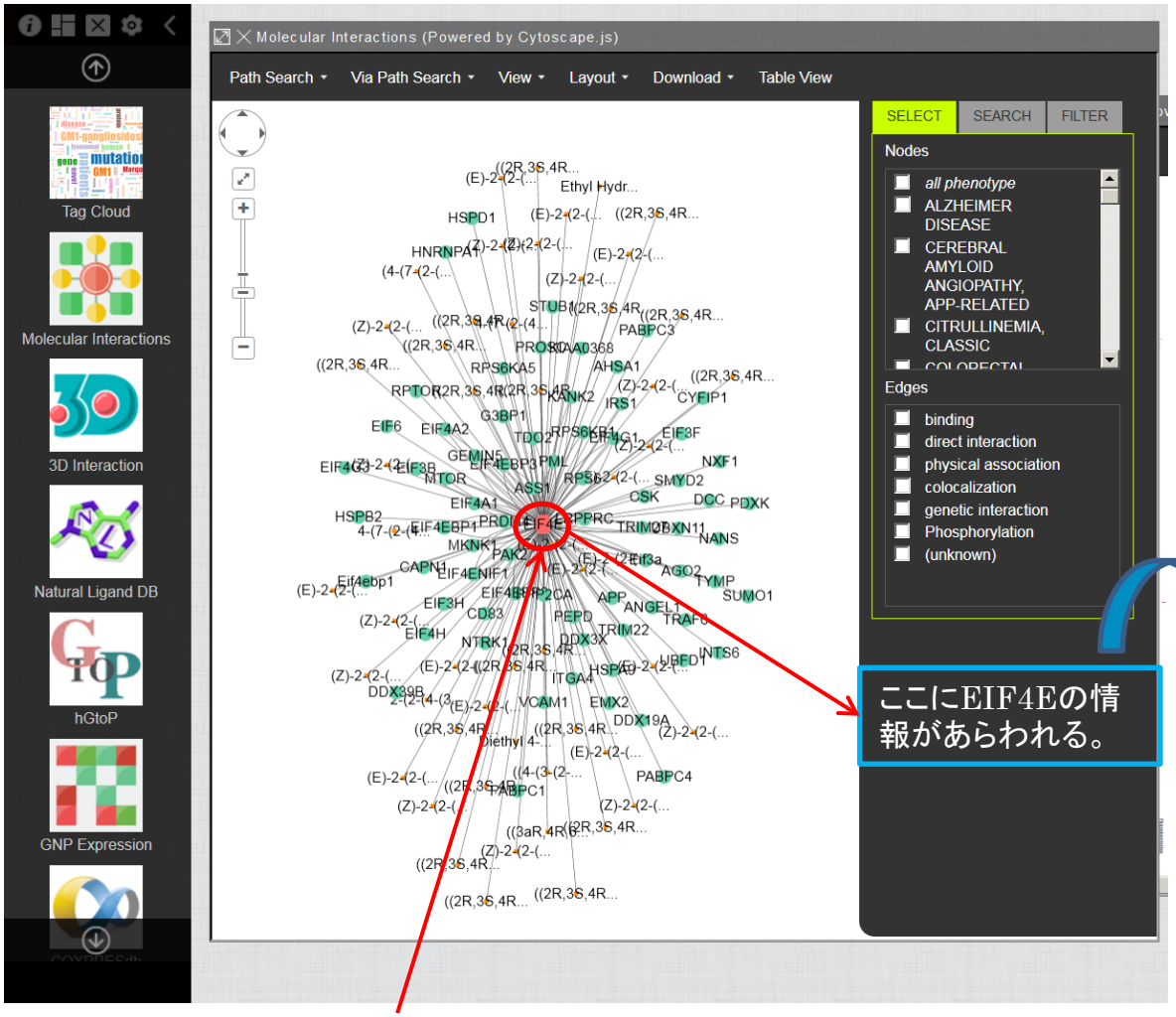

関連のある物質が多すぎるので、まず中央にあるEIF4Eをクリック。

ここにEIF4Eの情報があらわれる。

ここを眺めてもよくわからないのでもう一度リストに戻る。

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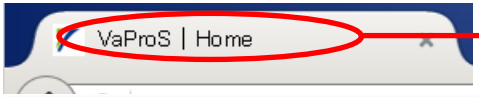

ホームに戻る。

Query: "autism"

	Hits
Gene/Protein	0
Ligand	0
Phenotype	24

Gene/Protein results - hits: 0

Ligand results - hits: 0

Phenotype results - hits: 24

Details (Go)

Filtered by:

Molecule Type : molecule type Organism : organism TrEMBL : TrEMBL

			Type	Name	Organism	DB	Molecule Type	Molecule Symbol	EntrezGene ID	UniProtKB	TrEMBL	Molecular Interactions	PPI	3D Interaction	NL
1	☐	[synonym] AUTISM, SUSCEPTI...	phenotype	AUTISM, SUSCEPTIBILITY TO, X-I...	Homo sapiens	OMIM: 300847	gene/protein	RPL10	6134	P27635	none	402	402	1	0
2	☐	[synonym] AUTISM, SUSCEPTI...	phenotype	AUTISM, SUSCEPTIBILITY T...	Homo sapiens	OMIM: 615091	gene/protein	EIF4E	1977	P06730	none	154	101	1	0
3	☐	[synonym] AUTISM, SUSCEPTI...	phenotype	AUTISM, SUSCEPTIBIL... TO, 18	Homo sapiens	OMIM: 615032	gene/protein	CHD8	57680	Q9HCK8	none	62	62	1	1
4	☐	[synonym] AUTISM, SUSCEPTI...	phenotype	AUTISM, SUSCEPTIB... TY TO, X-L...	Homo sapiens	OMIM: 300496	gene/protein	MECP2	4204	P51608	none	61	61	1	0
5	☐	[synonym] AUTISM, DEMENTIA...	phenotype	RETT SYNDROME	Homo sapiens	OMIM: 312750	gene/protein	MECP2	4204	P51608	none	61	61	1	0
6	☐	[synonym] AUTISM SPECTRUM ...	phenotype	AUTISM	Homo sapiens	OMIM: 209850	gene/protein	SNRPN	6638	P63163	none	54	54	0	0
7	☐	[synonym] AUTISM, SUSCEPTI...	phenotype	AUTISM, SUSCEPTIBI... Y TO, 17									26	1	0
8	☐	[synonym] AUTISM, SUSCEPTI...	phenotype	AUTISM, SUSCEPTIBILI... 15									2	1	0
9	☐	[synonym] AUTISM, SUSCEPTI...	phenotype	AUTISM, SUSCEPTIBILITY TO...									0	1	0
10	☐	[synonym] AUTISM, SUSCEPTI...	phenotype	EPSILON-TRIMETHYLLYSINE HYDRO...									2	1	1

EIF4Eと病気の関係を見るためにOMIMのDBをクリック。

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

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DB（OMIM）に跳ぶ。

Search OMIM... Search

Advanced Search | Search History

Table of Contents for #615091
- Title
- Phenotype-Gene Relationships
- Text
  - Cytogenetics
  - Molecular Genetics
  - Animal Model
- Phenotypic Series
- References
- Creation Date
- Edit History

MIMmatch (login)

ICD+

#615091

AUTISM, SUSCEPTIBILITY TO, 19; AUTS19

Phenotype-Gene Relationships

Location	Phenotype	Phenotype MIM number	Inheritance (in progress)	Phenotype mapping key	Gene/Locus	Gene/Locus MIM number
4q23	{Autism, susceptibility to, 19}	615091		3	EIF4E	133440

Phenotypic Series

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.

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.

読んでみると、、、

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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遺伝子が4番目の染色体にあって、
この部分の遺伝子異常で病気になるらしい。

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

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すでにモデルマウスも作られているらしい。

Animal Model

Gkogkas et al. (2013) demonstrated that knockout of the eukaryotic translation initiation factor 4E-binding protein-2 (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.

EIF4Eに結合するタンパク質（4E-BP2 ）をノックアウトするとマウスの行動に異常が出てくる。

参考文献もPubMedから跳べる。

4E-BP2を見る。

602224をクリック。

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]

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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]

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VaProSのトップページのKeyword検索に戻り、mtorと入力し、mtor [gene/protein]を選択すると検索結果のオーバービューの画面が現れる。

Query: "mtor"

	Hits
Gene/Protein	12
Ligand	0
Phenotype	0

Gene/Protein results - hits: 12

Details (Go)

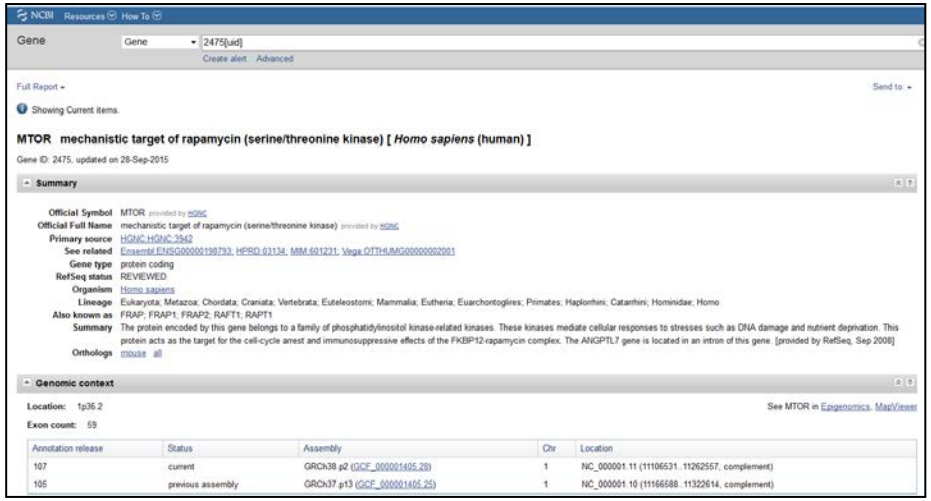
Filtered by:

Type : molecule type Organism : organism TrEMBL : TrEMBL

			Type	Name	Full Name	Organism	EntrezGene ID	UniProtKB	TrEMBL	Molecular Interactions	PPI	3D Interaction	NLDB	hGtoP	GNP Expression	COXPRESdb	Pathway DB	Phenotype	S-VAR
1		[synonym] mTOR	gene/protein	MTOR	Serine/threonine-protein kinas...	Homo sapiens	2475	P42345	none	4316	223	1	3	1	1	1	8	0	link
2		[synonym] Mtor	gene/protein	Mtor	Serine/threonine-protein kinas...	Mus musculus	56717	Q9JLN9	none	120	47	0	3	1	1	1	0	0	link
3		[synonym] MTOR associate...	gene/protein	MLST8	MTOR associated protein, LST8 ...	Homo sapiens	64223	Q9BVC4	none	59	59	1	0	1	1	1	0	0	link
4		[synonym] Mtor	gene/protein	Mtor	Serine/threonine-protein kinas...	Rattus norvegicus	56718	P42346	none	42	10	0	3	0	0	1	0	0	link
5		[synonym] MTOR associate...	gene/protein	Mlst8	MTOR associated protein, LST8 ...	Mus musculus	56716	Q9DCJ1	none	6	6	0	0	1	1	1	0	0	link
6		[synonym] mTORC2	gene/protein	Crtc2	CREB regulated transcription c...	Mus musculus	74343	Q3U182	none	5	5	0	0	1	1	1	0	0	link
7		[synonym] Mtor	protein	Mtor	Serine/threonine-protein kinas...	Rattus norvegicus		A0A0G2JX74	yes	0	0	0	0	0	0	0	0	0	link

NCBIへ

UniProtへ



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NCBIからMTORがrapamycinのターゲットでセリン/スレオニン キナーゼであることがわかる。

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

NCBIだけでなくUniProtからもMTORの遺伝子配列や作用、複合体形成などたくさんの情報を得ることができる。

たとえばUniProtの最初の画面で下の方を見てみるとInteractionというところがあってそこにEIF-4EBP1の記述がある。

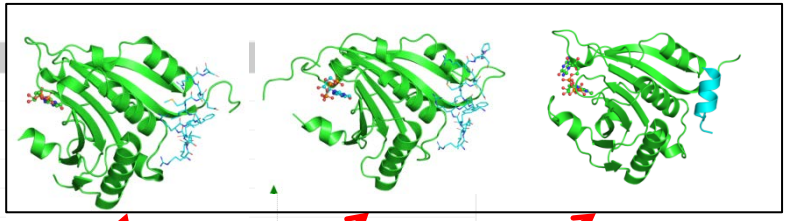
Interaction

Subunit structure

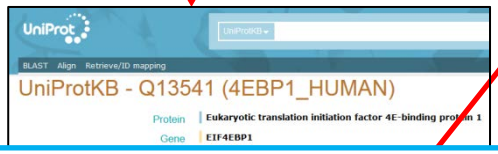
Part of the mammalian target of rapamycin complex 1 (mTORC1) which contains MTOR, MLST8, RPTOR, AKT1S1/PRAS40 and DEPTOR. The mTORC1 complex is a 1 Md obligate dimer of two stoichiometric heterotetramers with overall dimensions of 290 A x 210 A x 135 A. It has a rhomboid shape and a central cavity, the 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 PPAPDC3 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-5239949



ここをクリックするとUniProtに跳ぶ。



UniProtの画面の下の方を見てみるとStructureにぶつかる。

PDBIDをクリック。

Structure

Secondary structure

Legend: Helix Turn Beta strand

Show more details

3D structure databases

Select the link destinations: PDBe RCSB PDB PDBj

	Method	Resolution (Å)
1EJ4	X-ray	2.25
	X-ray	2.10
2JGB	X-ray	1.70
2JGC	X-ray	2.40
2V8W	X-ray	2.30
2V8X	X-ray	2.30
	X-ray	2.10
3HXG	X-ray	2.10
	X-ray	1.80
3M93	X-ray	2.90
3M94	X-ray	2.05
3U7X	X-ray	2.10
4UED	X-ray	1.75

複合体構造を見ることができる。

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OMIM 602224に戻る

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]

MTORの下流にEIF4Eに結合する4EBP2があり、MTORがrapamycin結合のターゲットということはタンパク質の発現の調節ができる可能性があるということか？

自閉症発症の原因は単純ではなさそうだが、ゲノム解析で4番目の染色体のEIF4E遺伝子の異常が原因の場合には治療ができるようになるのかもしれない。

次にMCP2がかかわる自閉症について調べてみよう。

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Query: "autism"

	Hits
Gene/Protein	0
Ligand	0
Phenotype	24

Gene/Protein results - hits: 0

Ligand results - hits: 0

Phenotype results - hits: 24

Details (Go)

Filtered by:

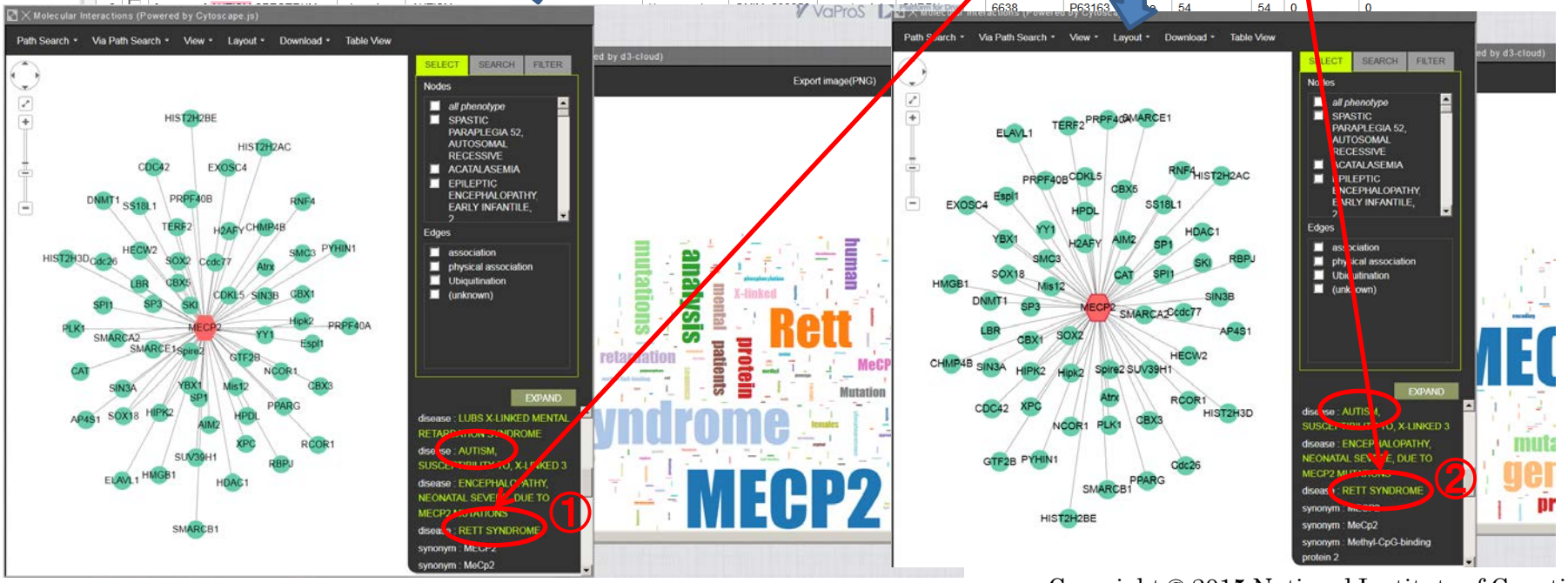
Molecule Type : molecule type Organism : organism TrEMBL : TrEMBL

			Type	Name	Organism		Molecule Type	Molecule Symbol	EntrezGene ID	UniProtKB	TrEMBL	Molecular Interactions	PPI	3D Interaction	NL
1	☐	[synonym] AUTISM, SUSCEPTI...	phenotype	AUTISM, SUSCEPTIBILITY TO, X-L...	Homo sapiens	OMIM: 300847		RPL10	6134	P27635	none	402	402	1	0
2	☐	[synonym] AUTISM, SUSCEPTI...	phenotype	AUTISM, SUSCEPTIBILITY TO	Homo sapiens	OMIM: 615091		EIF4B	1977	P06730	none	154	101	1	0
3	☐	[synonym] AUTISM, SUSCEPTI...	phenotype	AUTISM, SUSCEPTIBILITY 18	Homo sapiens	OMIM: 615032		HDA8	57	Q96KK8	none	62	62	1	1
4	☐	[synonym] AUTISM, SUSCEPTI...	phenotype	AUTISM, SUSCEPTIBILITY TO, X-L...	Homo sapiens	OMIM: 300496		MECP2	4204	P51608	none	61	61	1	0
5	☐	[synonym] AUTISM, DEMENTIA...	phenotype	RETT SYNDROME	Homo sapiens	OMIM: 312750		MECP2	4204	P51608	none	61	61	1	0

最初に戻ってMECP2を探すと2つ見つかったのでそれぞれをクリックしてみる。

図形の並び方は違うが基本的には同じ。

まずはレット症候群とは何かを調べるためにRETT SYNDROMEをクリック。



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表からは①と②ではID番号が異なる（①:#300496、②:#312750）が、どちらもcontributorsは同じ人であることがわかった。図の方のRETT SYNDROMEをクリックするとどちらも②が表示され、こちらの方が内容が充実しているが、DBの更新日は①の方が少し新しい。まず①の方をクリック。

#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	

Clinical Synops… | Phenotypic Series

Phenotypic Seriesとは？
気になるのでクリック。

MECP2はAUTSX3とも関係している遺伝子

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.

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.

自閉症の遺伝子が染色体のどこにあるか、遺伝子名など有益な情報の一覧をみつけた。
（ちなみにこの情報は②には載っていない。）

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次に②の方をクリック。

#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とはmethyl-CpG-binding protein-2 のこと。

それではmethyl-CpG-binding protein-2とはどのようなタンパク質なのだろう。

ここをクリック。

*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は神経系の発達に大変重要なタンパク質であり、しかも、X染色体にある遺伝子で、劣性致死遺伝子らしいといったいろいろな情報を得ることができる。

このように、VaProSを検索エンジンのように使用すると、通常の検索エンジンで調べるよりも、確実な情報をreference付きで、しかも、自分で確かめながら得ることができます。

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