Glutamate decarboxylase

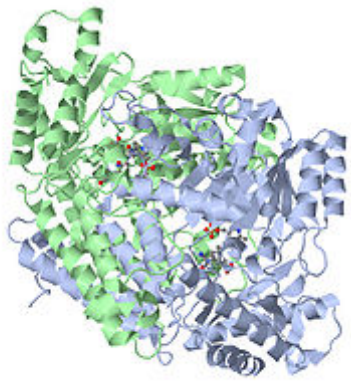
Glutamate decarboxylase or **glutamic acid decarboxylase** (**GAD**) is an enzyme that catalyzes the decarboxylation of glutamate to gamma-aminobutyric acid (GABA) and carbon dioxide (CO_2). GAD uses pyridoxal-phosphate (PLP) as a cofactor. The reaction proceeds as follows:

glutamate decarboxylase	
Identifiers	
EC no.	4.1.1.15 (https://www.enzyme-database.org/query.php?ec=4.1.1.15)
CAS no.	9024-58-2m
Databases	
IntEnz	IntEnz view (https://www.ebi.ac.uk/intenz/query?cmd=SearchEC&ec=4.1.1.15)
BRENDA	BRENDA entry (http://www.brenda-enzymes.org/enzyme.php?ecno=4.1.1.15)
ExPASy	NiceZyme view (https://enzyme.expasy.org/EC/4.1.1.15)
KEGG	KEGG entry (https://www.genome.jp/dbget-bin/www_bget?enzyme+4.1.1.15)
MetaCyc	metabolic pathway (https://biocyc.org/META/substring-search?type=NIL&object=4.1.1.15)
PRIAM	profile (http://priam.prabi.fr/cgi-bin/PRIAM_profiles_CurrentRelease.pl?EC=4.1.1.15)
PDB structures	RCSB PDB (https://www.rcsb.org/search?q=rcsb_polymer_entity.rcsb_ec_lineage.id:4.1.1.15) PDBe (https://www.ebi.ac.uk/pdbe/entry/search/index?ec_number:4.1.1.15) PDBsum (https://www.ebi.ac.uk/thornton-srv/

	databases/cgi-bin/enzymes/GetPage.pl?ec_number=4.1.1.15)
Gene Ontology	AmiGO (http://amigo.geneontology.org/amigo/term/GO:0004351) / QuickGO (https://www.ebi.ac.uk/QuickGO/term/GO:0004351)

Search	
PMC	articles (https://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&term=4.1.1.15%5BEC/RN%20Number%5D%20AND%20pubmed%20pmc%20local%5Bsb%5D)
PubMed	articles (https://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=pubmed&term=4.1.1.15%5BEC/RN%20Number%5D)
NCBI	proteins (https://www.ncbi.nlm.nih.gov/protein?term=4.1.1.15%5BEC/RN%20Number%5D)

Glutamic acid decarboxylase 1



GAD67 derived from PDB: 2okj (https://www.rcsb.org/structure/2okj)

Identifiers	
Symbol	GAD1
Alt. symbols	glutamate decarboxylase 1 (brain, 67kD); GAD67
NCBI gene	2571 (https://www.ncbi.nlm.nih.gov/gene?cmd=retri

	eve&dopt=default&list_uids=2571&rn=1)
HGNC	4092 (https://www.genenames.org/data/gene-symbol-report/#!/hgnc_id/HGNC:4092)
OMIM	605363 (https://omim.org/605363)
RefSeq	NM_000817 (https://www.ncbi.nlm.nih.gov/protein/NM_000817)
UniProt	Q99259 (https://www.uniprot.org/uniprot/Q99259)
Other data	
EC number	4.1.1.15 (https://www.genome.jp/dbget-bin/www_bget?enzyme+4.1.1.15)
Locus	Chr. 2 *q31 (https://omim.org/search/?index=geneMap&search=2q31)*
Search for	
Structures	Swiss-model (https://swissmodel.expasy.org/repository/uniprot/Q99259)
Domains	InterPro (https://www.ebi.ac.uk/interpro/protein/Q99259)

glutamic acid decarboxylase 2

Identifiers	
Symbol	GAD2
Alt. symbols	GAD65
NCBI gene	2572 (https://www.ncbi.nlm.nih.gov/gene?cmd=retrieve&dopt=default&list_uids=2572&rn=1)
HGNC	11284 (https://www.genenames.org/data/gene-symbol-report/#!/hgnc_id/HGNC:11284)
OMIM	4093 (https://omim.org/4093)

RefSeq	NM_001047 (https://www.ncbi.nlm.nih.gov/protein/NM_001047)
UniProt	Q05329 (https://www.uniprot.org/uniprot/Q05329)
Other data	
EC number	4.1.1.15 (https://www.genome.jp/dbget-bin/www_bget?enzyme+4.1.1.15)
Locus	Chr. 10 *p11.23 (https://omim.org/search/?index=geneMap&search=10p11.23)*
Search for	
Structures	Swiss-model (https://swissmodel.expasy.org/repository/uniprot/Q05329)
Domains	InterPro (https://www.ebi.ac.uk/interpro/protein/Q05329)

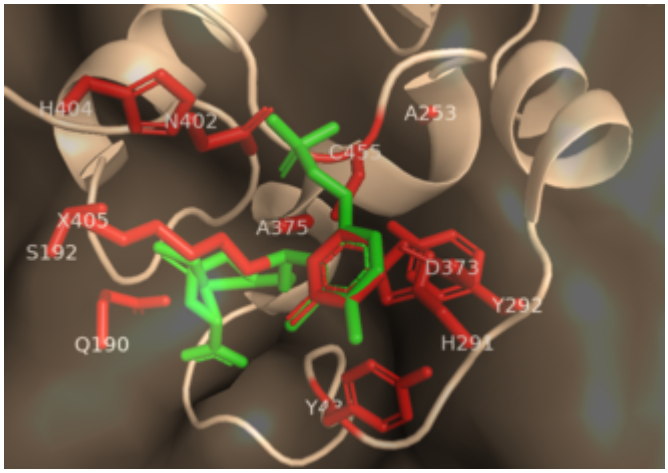
$$HOOC{-}CH_2{-}CH_2{-}CH(NH_2){-}COOH \rightarrow CO_2 + HOOC{-}CH_2{-}CH_2{-}CH_2NH_2$$

In mammals, GAD exists in two isoforms with molecular weights of 67 and 65 kDa (GAD_{67} and GAD_{65}), which are encoded by two different genes on different chromosomes (GAD1 and GAD2 genes, chromosomes 2 and 10 in humans, respectively).[1][2] GAD_{67} and GAD_{65} are expressed in the brain where GABA is used as a neurotransmitter, and they are also expressed in the insulin-producing β-cells of the pancreas, in varying ratios depending upon the species.[3] Together, these two enzymes maintain the major physiological supply of GABA in mammals,[2] though it may also be synthesized from putrescine in the enteric nervous system,[4] brain,[5][6] and elsewhere by the actions of diamine oxidase and aldehyde dehydrogenase 1a1.[4][6]

Several truncated transcripts and polypeptides of GAD_{67} are detectable in the developing brain,[7] however their function, if any, is unknown.

Structure and Mechanism

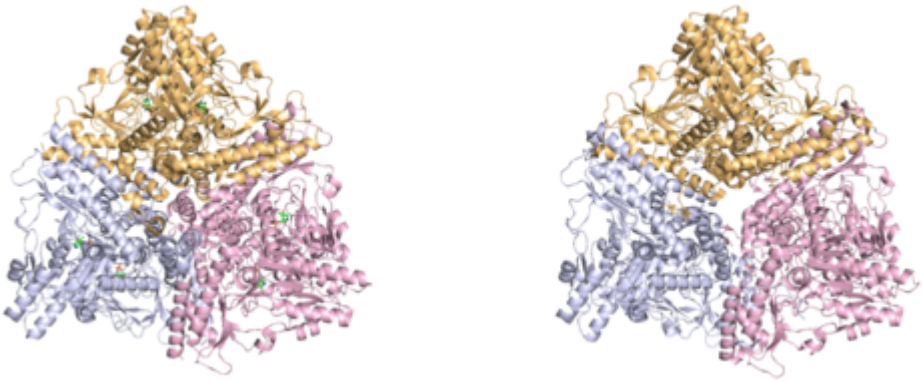
Both isoforms of GAD are homodimeric structures, consisting of 3 primary domains: the PLP, C-terminal and N-terminal domains. The PLP-binding domain of this enzyme adopts a type I PLP-dependent transferase-like fold.[8] The reaction proceeds via the canonical mechanism, involving Schiff base linkage between PLP and Lys405. PLP is held in place through base-stacking with an adjacent histidine residue, and GABA is positioned such that its carboxyl group forms a salt bridge with arginine and a hydrogen bond with glutamine.



GAD67 active site containing PLP-glutamate complex (shown in green), with Schiff base linkage at Lys405. Side chain residues shown in red.

Dimerization is essential to maintaining function as the active site is found at this interface, and mutations interfering with optimal association between the 2 chains has been linked to pathology, such as schizophrenia.[9][10] Interference of dimerization by GAD inhibitors such as 2-keto-4-pentenoic acid (KPA) and ethyl ketopentenoate (EKP) were also shown to lead to dramatic reductions in GABA production and incidence of seizures.[11][8]

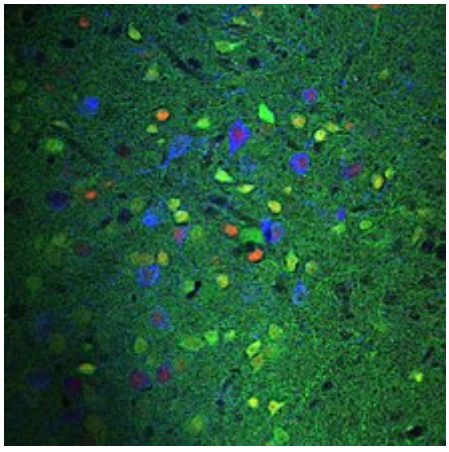
Catalytic activity is mediated by a short flexible loop at the dimer interface (residues 432–442 in GAD67, and 423–433 in GAD65). In GAD67 this loop remains tethered, covering the active site and providing a catalytic environment to sustain GABA production; its mobility in GAD65 promotes a side reaction that results in release of PLP, leading to autoinactivation.[12] The conformation of this loop is intimately linked to the C-terminal domain, which also affects the rate of autoinactivation.[13] Moreover, GABA-bound GAD65 is intrinsically more flexible and exists as an ensemble of states, thus providing more opportunities for autoantigenicity as seen in Type 1 diabetes.[14][15] GAD derived from *Escherichia coli* shows additional structural intricacies, including a pH-dependent conformational change. This behavior is defined by the presence of a triple helical bundle formed by the N-termini of the hexameric protein in acidic environments.[16]


Hexameric E. coli GAD conformational transition: low-pH (left), neutral pH (right).

Regulation of GAD65 and GAD67

Despite an extensive sequence similarity between the two genes, GAD65 and GAD67 fulfill very different roles within the human body. Additionally, research suggests that GAD65 and GAD67 are regulated by distinctly different cellular mechanisms.

GAD_{65} and GAD_{67} synthesize GABA at different locations in the cell, at different developmental times, and for functionally different purposes.[17][18] GAD_{67} is spread evenly throughout the cell while GAD_{65} is localized to nerve terminals.[17][19][20] GAD_{67} synthesizes GABA for neuron activity unrelated to neurotransmission, such as synaptogenesis and protection from neural injury.[17][18] This function requires widespread, ubiquitous presence of GABA. GAD_{65}, however, synthesizes GABA for neurotransmission,[17] and therefore is only necessary at nerve terminals and synapses. In order to aid in neurotransmission, GAD_{65} forms a complex with heat shock cognate 70 (HSC_{70}), cysteine string protein (CSP) and vesicular GABA transporter VGAT, which, as a complex, helps package GABA into vesicles for release during neurotransmission.[21] GAD_{67} is transcribed during early development, while GAD_{65} is not transcribed until later in life.[17] This developmental difference in GAD_{67} and GAD_{65} reflects the functional properties of each isoform; GAD_{67} is needed throughout development for normal cellular functioning, while GAD_{65} is not needed until slightly later in development when synaptic inhibition is more prevalent.[17]



Gad65 in red, Gad67 in green, and tyrosine hydroxylase (blue) in the ventral tegmental area of the mouse brain

GAD_{67} and GAD_{65} are also regulated differently post-translationally. Both GAD_{65} and GAD_{67} are regulated via phosphorylation of a dynamic catalytic loop,[22][12] but the regulation of these isoforms differs; GAD_{65} is activated by phosphorylation while GAD_{67} is inhibited by phosphorylation. GAD67 is predominantly found activated (~92%), whereas GAD65 is predominantly found inactivated (~72%).[23] GAD_{67} is phosphorylated at threonine 91 by protein kinase A (PKA), while GAD_{65} is phosphorylated, and therefore regulated by, protein kinase C (PKC). Both GAD_{67} and GAD_{65} are also regulated post-translationally by pyridoxal 5'-phosphate (PLP); GAD is activated when bound to PLP and inactive when not bound to PLP.[23] Majority of GAD_{67} is bound to PLP at any given time, whereas GAD_{65} binds PLP when GABA is needed for neurotransmission.[23] This reflects the functional properties of the two isoforms; GAD_{67} must be active at all times for normal cellular functioning, and is therefore constantly activated by PLP, while GAD_{65} must only be activated when GABA neurotransmission occurs, and is therefore regulated according to the synaptic environment.

Studies with mice also show functional differences between Gad67 and Gad65. GAD67−/− mice are born with cleft palate and die within a day after birth while GAD65−/− mice survive with a slightly increased tendency in seizures. Additionally, GAD65+/- have symptoms defined similarly to attention deficit hyperactivity disorder (ADHD) in humans.[24]

Role in the nervous system

Both GAD67 and GAD65 are present in all types of synapses within the human nervous system. This includes dendrodendritic, axosomatic, and axodendritic synapses. Preliminary evidence suggests that GAD65 is dominant in the visual and neuroendocrine systems, which undergo more phasic changes. It is also believed that GAD67 is present at higher amounts in tonically active neurons.[25]

Role in pathology

Autism

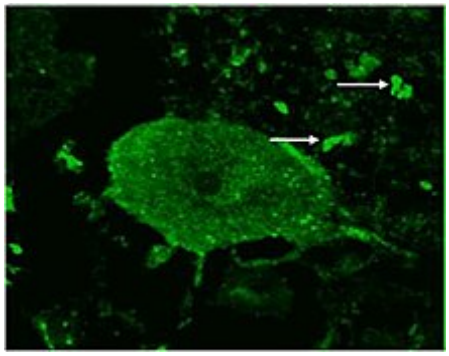
Both GAD65 and GAD67 experience significant downregulation in cases of autism. In a comparison of autistic versus control brains, GAD65 and GAD67 experienced a downregulation average of 50% in parietal and cerebellar cortices of autistic brains.[26] Cerebellar Purkinje cells also reported a 40% downregulation, suggesting that affected cerebellar nuclei may disrupt output to higher order motor and cognitive areas of the brain.[18]

Diabetes

Both GAD_{67} and GAD_{65} are targets of autoantibodies in people who later develop type 1 diabetes mellitus or latent autoimmune diabetes.[27][28] Injections with GAD_{65} in ways that induce immune tolerance have been shown to prevent type 1 diabetes in rodent models.[29][30][31] In clinical trials, injections with GAD_{65} have been shown to preserve some insulin production for 30 months in humans with type 1 diabetes.[32][33] A Cochrane systematic review also examined 1 study showing improvement of C-peptide levels in cases of Latent Autoimmune Diabetes in adults, 5 years following treatment with GAD_{65} .Still, it is important to highlight that the studies available to be included in this review presented considerable flaws in quality and design.[34]

Stiff person syndrome

High titers of autoantibodies to glutamic acid decarboxylase (GAD) are well documented in association with stiff person syndrome (SPS).[35] Glutamic acid decarboxylase is the rate-limiting enzyme in the synthesis of γ-aminobutyric acid (GABA), and impaired function of GABAergic neurons has been implicated in the pathogenesis of SPS. Autoantibodies to GAD might be the causative agent or a disease marker.[36]



Stiff man human cerebellum stained with a reference anti-GAD65 monoclonal antibody. Thin arrows show presynaptic terminals staining only with the anti-GAD65 monoclonal antibody

Schizophrenia and bipolar disorder

Substantial dysregulation of GAD mRNA expression, coupled with downregulation of reelin, is observed in schizophrenia and bipolar disorder.[37][38] The most pronounced downregulation of GAD_{67} was found in hippocampal stratum oriens layer in both disorders and in other layers and structures of hippocampus with varying degrees.[39]

GAD_{67} is a key enzyme involved in the synthesis of inhibitory neurotransmitter GABA and people with schizophrenia have been shown to express lower amounts of GAD_{67} in the dorsolateral prefrontal cortex compared to healthy controls.[40] The mechanism underlying the decreased levels of GAD_{67} in people with schizophrenia remains unclear.[41] Some have proposed that an immediate early gene, Zif268, which normally binds to the promoter region of GAD_{67} and increases transcription of GAD_{67}, is lower in schizophrenic patients, thus contributing to decreased levels of GAD_{67}.[40] Since the dorsolateral prefrontal cortex (DLPFC) is involved in working memory, and GAD_{67} and Zif268 mRNA levels are lower in the DLPFC of schizophrenic patients, this molecular alteration may account, at least in part, for the working memory impairments associated with the disease.

Parkinson disease

The bilateral delivery of glutamic acid decarboxylase (GAD) by an adeno-associated viral vector into the subthalamic nucleus of patients between 30 and 75 years of age with advanced, progressive, levodopa-responsive Parkinson disease resulted in significant improvement over baseline during the course of a six-month study.[42]

Cerebellar disorders

Intracerebellar administration of GAD autoantibodies to animals increases the excitability of motoneurons and impairs the production of nitric oxide (NO), a molecule involved in learning. Epitope recognition contributes to cerebellar involvement.[43] Reduced GABA levels increase glutamate levels as a consequence of lower inhibition of subtypes of GABA receptors. Higher glutamate levels activate microglia and activation of xc(−) increases the extracellular glutamate release.[44]

Neuropathic pain

Peripheral nerve injury of the sciatic nerve (a neuropathic pain model) induces a transient loss of GAD_{65} immunoreactive terminals in the spinal cord dorsal horn and suggests a potential involvement for these alterations in the development and amelioration of pain behaviour.[45]

Other Anti-GAD-associated neurologic disorders

Antibodies directed against glutamic acid decarboxylase (GAD) are increasingly found in patients with other symptoms indicative of central nervous system (CNS) dysfunction, such as ataxia, progressive encephalomyelitis with rigidity and myoclonus (PERM), limbic encephalitis, and epilepsy.[46] The pattern of anti-GAD antibodies in epilepsy differs from type 1 diabetes and stiff-person syndrome.[47]

Role of glutamate decarboxylase in other organisms

Besides the synthesis of GABA, GAD has additional functions and structural variations that are organism-dependent. In *Saccharomyces cerevisiae*, GAD binds the Ca^{2+} regulatory protein calmodulin (CaM) and is also involved in responding to oxidative stress.[48] Similarly, GAD in plants binds calmodulin as well.[49] This interaction occurs at the 30-50bp CAM-binding domain (CaMBD) in its C terminus and is necessary for proper regulation of GABA production.[50] Unlike vertebrates and invertebrates, the GABA produced by GAD is used in plants to signal abiotic stress by controlling levels of intracellular Ca^{2+} via CaM.

Binding to CaM opens Ca^{2+} channels and leads to an increase in Ca^{2+} concentrations in the cytosol, allowing Ca^{2+} to act as a secondary messenger and activate downstream pathways. When GAD is not bound to CaM, the CaMBD acts as an autoinhibitory domain, thus deactivating GAD in the absence of stress.[50] Interesting, in two plant species, rice and apples, Ca2+ /CAM-independent GAD isoforms have been discovered.[51][52] The C-terminus of these isoforms contain substitutions at key residues necessary to interact with CaM in the CaMBD, preventing the protein from binding to GAD. Whereas CaMBD of the isoform in rice still functions as an autoinhibitory domain,[51] the C-terminus in the isoform in apples does not.[52] Finally, the structure of plant GAD is a hexamer and has pH-dependent activity, with the optimal pH of 5.8 in multiple species.[50][53] but also significant activity at pH 7.3 in the presence of CaM [16]

It is also believed that the control of glutamate decarboxylase has the prospect of improving citrus produce quality post-harvest. In Citrus plants, research has shown that glutamate decarboxylase plays a key role in citrate metabolism. With the increase of glutamate decarboxylase via direct exposure, citrate levels have been seen to significantly increase within plants, and in conjunction post-harvest quality maintenance was significantly improved, and rot rates decreased.[54]

Just like GAD in plants, GAD in *E. coli* has a hexamer structure and is more active under acidic pH; the pH optimum for *E. coli* GAD is 3.8-4.6. However, unlike plants and yeast, GAD in *E. coli* does not require calmodulin binding to function. There are also two isoforms of GAD, namely GadA and GadB, encoded by separate genes in *E. coli*,[55] although both isoforms are biochemically identical.[56] The enzyme plays a major role in conferring acid resistance and allows bacteria to temporarily survive in highly acidic environments (pH < 2.5) like the stomach.[57] This is done by GAD decarboxylating glutamate to GABA, which requires H+ to be uptaken as a reactant and raises the pH inside the bacteria. GABA can then be exported out of *E. coli* cells and contribute to increasing the pH of the nearby extracellular environments.[16]

References

1. Erlander MG, Tillakaratne NJ, Feldblum S, Patel N, Tobin AJ (July 1991). "Two genes encode distinct glutamate decarboxylases". *Neuron*. **7** (1): 91–100. doi:10.1016/0896-6273(91)90077-D (https://doi.org/10.1016%2F0896-6273%2891%2990077-D). PMID 2069816 (https://pubmed.ncbi.nlm.nih.gov/2069816). S2CID 15863479 (https://api.semanticscholar.org/CorpusID:15863479).
2. Langendorf CG, Tuck KL, Key TL, Fenalti G, Pike RN, Rosado CJ, et al. (January 2013). "Structural characterization of the mechanism through which human glutamic acid decarboxylase auto-activates" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3546353). *Bioscience Reports*. **33** (1): 137–44. doi:10.1042/BSR20120111 (https://doi.org/10.1042%2FBSR20120111). PMC 3546353 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3546353). PMID 23126365 (https://pubmed.ncbi.nlm.nih.gov/23126365).
3. Kim J, Richter W, Aanstoot HJ, Shi Y, Fu Q, Rajotte R, et al. (December 1993). "Differential expression of GAD65 and GAD67 in human, rat, and mouse pancreatic islets". *Diabetes*. **42** (12): 1799–808. doi:10.2337/diab.42.12.1799 (https://doi.org/10.2337%2Fdiab.42.12.1799). PMID 8243826 (https://pubmed.ncbi.nlm.nih.gov/8243826). S2CID 29615710 (https://api.semanticscholar.org/CorpusID:29615710).
4. Krantis A (December 2000). "GABA in the Mammalian Enteric Nervous System". *News in Physiological Sciences*. **15** (6): 284–290. doi:10.1152/physiologyonline.2000.15.6.284 (https://doi.org/10.1152%2Fphysiologyonline.2000.15.6.284). PMID 11390928 (https://pubmed.ncbi.nlm.nih.gov/11390928).

5. Sequerra EB, Gardino P, Hedin-Pereira C, de Mello FG (May 2007). "Putrescine as an important source of GABA in the postnatal rat subventricular zone". *Neuroscience*. **146** (2): 489–93. doi:10.1016/j.neuroscience.2007.01.062 (https://doi.org/10.1016%2Fj.neuroscience.2007.01.062). PMID 17395389 (https://pubmed.ncbi.nlm.nih.gov/17395389). S2CID 43003476 (https://api.semanticscholar.org/CorpusID:43003476).
6. Kim JI, Ganesan S, Luo SX, Wu YW, Park E, Huang EJ, et al. (October 2015). "Aldehyde dehydrogenase 1a1 mediates a GABA synthesis pathway in midbrain dopaminergic neurons" (https://escholarship.org/content/qt6rc4c1hw/qt6rc4c1hw.pdf?t=nw99wr) (PDF). *Science*. **350** (6256): 102–6. Bibcode:2015Sci...350..102K (https://ui.adsabs.harvard.edu/abs/2015Sci...350..102K). doi:10.1126/science.aac4690 (https://doi.org/10.1126%2Fscience.aac4690). PMC 4725325 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4725325). PMID 26430123 (https://pubmed.ncbi.nlm.nih.gov/26430123).
7. Szabo G, Katarova Z, Greenspan R (November 1994). "Distinct protein forms are produced from alternatively spliced bicistronic glutamic acid decarboxylase mRNAs during development" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC359290). *Molecular and Cellular Biology*. **14** (11): 7535–45. doi:10.1128/mcb.14.11.7535 (https://doi.org/10.1128%2Fmcb.14.11.7535). PMC 359290 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC359290). PMID 7935469 (https://pubmed.ncbi.nlm.nih.gov/7935469).
8. Reingold DF, Orlowski M (Mar 1979). "Inhibition of brain glutamate decarboxylase by 2-keto-4-pentenoic acid, a metabolite of allylglycine". *J Neurochem*. **32** (3): 907–13. doi:10.1111/j.1471-4159.1979.tb04574.x (https://doi.org/10.1111%2Fj.1471-4159.1979.tb04574.x). PMID 430066 (https://pubmed.ncbi.nlm.nih.gov/430066). S2CID 31823191 (https://api.semanticscholar.org/CorpusID:31823191).
9. Magri C, Giacopuzzi E, La Via L, Bonini D, Ravasio V, Elhussiny ME, Orizio F, Gangemi F, Valsecchi P, Bresciani R, Barbon A, Vita A, Gennarelli M (Oct 2018). "A novel homozygous mutation in GAD1 gene described in a schizophrenic patient impairs activity and dimerization of GAD67 enzyme" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6195539). *Sci Rep*. **8** (1): 15470. Bibcode:2018NatSR...815470M (https://ui.adsabs.harvard.edu/abs/2018NatSR...815470M). doi:10.1038/s41598-018-33924-8 (https://doi.org/10.1038%2Fs41598-018-33924-8). PMC 6195539 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6195539). PMID 30341396 (https://pubmed.ncbi.nlm.nih.gov/30341396).
10. Giacopuzzi E, Gennarelli M, Minelli A, Gardella R, Valsecchi P, Traversa M, Bonvicini C, Vita A, Sacchetti E, Magri C (Aug 2017). "Exome sequencing in schizophrenic patients with high levels of homozygosity identifies novel and extremely rare mutations in the GABA/glutamatergic pathways" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5546675). *PLOS ONE*. **12** (8): e0182778. Bibcode:2017PLoSO..1282778G (https://ui.adsabs.harvard.edu/abs/2017PLoSO..1282778G). doi:10.1371/journal.pone.0182778 (https://doi.org/10.1371%2Fjournal.pone.0182778). PMC 5546675 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5546675). PMID 28787007 (https://pubmed.ncbi.nlm.nih.gov/28787007).
11. Zhang Y, Vanmeert M, Siekierska A, Ny A, John J, Callewaert G, Lescrinier E, Dehaen W, de Witte PA, Kaminski RM (Aug 2017). "Inhibition of glutamate decarboxylase (GAD) by ethyl ketopentenoate (EKP) induces treatment-resistant epileptic seizures in zebrafish" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5543107). *Sci Rep*. **7** (1): 7195. Bibcode:2017NatSR...7.7195Z (https://ui.adsabs.harvard.edu/abs/2017NatSR...7.7195Z). doi:10.1038/s41598-017-06294-w (https://doi.org/10.1038%2Fs41598-017-06294-w). PMC 5543107 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5543107). PMID 28775328 (https://pubmed.ncbi.nlm.nih.gov/28775328).

12. Fenalti G, Law RH, Buckle AM, Langendorf C, Tuck K, Rosado CJ, et al. (April 2007). "GABA production by glutamic acid decarboxylase is regulated by a dynamic catalytic loop". *Nature Structural & Molecular Biology*. **14** (4): 280–6. doi:10.1038/nsmb1228 (https://doi.org/10.1038%2Fnsmb1228). PMID 17384644 (https://pubmed.ncbi.nlm.nih.gov/17384644). S2CID 20265911 (https://api.semanticscholar.org/CorpusID:20265911).
13. Langendorf CG, Tuck KL, Key TL, Fenalti G, Pike RN, Rosado CJ, Wong AS, Buckle AM, Law RH, Whisstock JC (Jan 2013). "Structural characterization of the mechanism through which human glutamic acid decarboxylase auto-activates" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3546353). *Biosci Rep*. **33** (1): 137–44. doi:10.1042/BSR20120111 (https://doi.org/10.1042%2FBSR20120111). PMC 3546353 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3546353). PMID 23126365 (https://pubmed.ncbi.nlm.nih.gov/23126365).
14. Kass I, Hoke DE, Costa MG, Reboul CF, Porebski BT, Cowieson NP, Leh H, Pennacchietti E, McCoey J, Kleifeld O, Borri Voltattorni C, Langley D, Roome B, Mackay IR, Christ D, Perahia D, Buckle M, Paiardini A, De Biase D, Buckle AM (Jun 2019). "Cofactor-dependent conformational heterogeneity of GAD65 and its role in autoimmunity and neurotransmitter homeostasis" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4078817). *Proc Natl Acad Sci U S A*. **111** (25): E2524-9. doi:10.1073/pnas.1403182111 (https://doi.org/10.1073%2Fpnas.1403182111). PMC 4078817 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4078817). PMID 24927554 (https://pubmed.ncbi.nlm.nih.gov/24927554).
15. Ellis TM, Atkinson MA (Feb 1996). "The clinical significance of an autoimmune response against glutamic acid decarboxylase". *Nat Med*. **2** (2): 148–53. doi:10.1038/nm0296-148 (https://doi.org/10.1038%2Fnm0296-148). PMID 8574952 (https://pubmed.ncbi.nlm.nih.gov/8574952). S2CID 12788084 (https://api.semanticscholar.org/CorpusID:12788084).
16. Capitani G, De Biase D, Aurizi C, Gut H, Bossa F, Grütter MG (Aug 2003). "Crystal structure and functional analysis of Escherichia coli glutamate decarboxylase" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC175793). *EMBO J*. **22** (16): 4027–37. doi:10.1093/emboj/cdg403 (https://doi.org/10.1093%2Femboj%2Fcdg403). PMC 175793 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC175793). PMID 12912902 (https://pubmed.ncbi.nlm.nih.gov/12912902).
17. Pinal CS, Tobin AJ (1998). "Uniqueness and redundancy in GABA production". *Perspectives on Developmental Neurobiology*. **5** (2–3): 109–18. PMID 9777629 (https://pubmed.ncbi.nlm.nih.gov/9777629).
18. Soghomonian JJ, Martin DL (December 1998). "Two isoforms of glutamate decarboxylase: why?". *Trends in Pharmacological Sciences*. **19** (12): 500–5. doi:10.1016/s0165-6147(98)01270-x (https://doi.org/10.1016%2Fs0165-6147%2898%2901270-x). PMID 9871412 (https://pubmed.ncbi.nlm.nih.gov/9871412).
19. Kaufman DL, Houser CR, Tobin AJ (February 1991). "Two forms of the gamma-aminobutyric acid synthetic enzyme glutamate decarboxylase have distinct intraneuronal distributions and cofactor interactions" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8194030). *Journal of Neurochemistry*. **56** (2): 720–3. doi:10.1111/j.1471-4159.1991.tb08211.x (https://doi.org/10.1111%2Fj.1471-4159.1991.tb08211.x). PMC 8194030 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8194030). PMID 1988566 (https://pubmed.ncbi.nlm.nih.gov/1988566). S2CID 35743434 (https://api.semanticscholar.org/CorpusID:35743434).
20. Kanaani J, Cianciaruso C, Phelps EA, Pasquier M, Brioudes E, Billestrup N, Baekkeskov S (2015). "Compartmentalization of GABA synthesis by GAD67 differs between pancreatic beta cells and neurons" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4315522). *PLOS ONE*. **10** (2): e0117130. Bibcode:2015PLoSO..1017130K (https://ui.adsabs.harvard.edu/abs/2015PLoSO..1017130K). doi:10.1371/journal.pone.0117130 (https://doi.org/10.1371%2Fjournal.pone.0117130). PMC 4315522 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4315522). PMID 25647668 (https://pubmed.ncbi.nlm.nih.gov/25647668).

21. Jin H, Wu H, Osterhaus G, Wei J, Davis K, Sha D, et al. (April 2003). "Demonstration of functional coupling between gamma -aminobutyric acid (GABA) synthesis and vesicular GABA transport into synaptic vesicles" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC153086). *Proceedings of the National Academy of Sciences of the United States of America*. **100** (7): 4293–8. Bibcode:2003PNAS..100.4293J (https://ui.adsabs.harvard.edu/abs/2003PNAS..100.4293J). doi:10.1073/pnas.0730698100 (https://doi.org/10.1073%2Fpnas.0730698100). PMC 153086 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC153086). PMID 12634427 (https://pubmed.ncbi.nlm.nih.gov/12634427).
22. Wei J, Davis KM, Wu H, Wu JY (May 2004). "Protein phosphorylation of human brain glutamic acid decarboxylase (GAD)65 and GAD67 and its physiological implications". *Biochemistry*. **43** (20): 6182–9. doi:10.1021/bi0496992 (https://doi.org/10.1021%2Fbi0496992). PMID 15147202 (https://pubmed.ncbi.nlm.nih.gov/15147202).
23. Battaglioli G, Liu H, Martin DL (August 2003). "Kinetic differences between the isoforms of glutamate decarboxylase: implications for the regulation of GABA synthesis". *Journal of Neurochemistry*. **86** (4): 879–87. doi:10.1046/j.1471-4159.2003.01910.x (https://doi.org/10.1046%2Fj.1471-4159.2003.01910.x). PMID 12887686 (https://pubmed.ncbi.nlm.nih.gov/12887686). S2CID 23640198 (https://api.semanticscholar.org/CorpusID:23640198).
24. Ueno H (October 2000). "Enzymatic and structural aspects on glutamate decarboxylase". *Journal of Molecular Catalysis B: Enzymatic*. **10** (1–3): 67–79. doi:10.1016/S1381-1177(00)00114-4 (https://doi.org/10.1016%2FS1381-1177%2800%2900114-4).
25. Feldblum S, Erlander MG, Tobin AJ (April 1993). "Different distributions of GAD65 and GAD67 mRNAs suggest that the two glutamate decarboxylases play distinctive functional roles". *Journal of Neuroscience Research*. **34** (6): 689–706. doi:10.1002/jnr.490340612 (https://doi.org/10.1002%2Fjnr.490340612). PMID 8315667 (https://pubmed.ncbi.nlm.nih.gov/8315667). S2CID 19314092 (https://api.semanticscholar.org/CorpusID:19314092).
26. Fatemi SH, Halt AR, Stary JM, Kanodia R, Schulz SC, Realmuto GR (October 2002). "Glutamic acid decarboxylase 65 and 67 kDa proteins are reduced in autistic parietal and cerebellar cortices". *Biological Psychiatry*. **52** (8): 805–10. doi:10.1016/S0006-3223(02)01430-0 (https://doi.org/10.1016%2FS0006-3223%2802%2901430-0). PMID 12372652 (https://pubmed.ncbi.nlm.nih.gov/12372652). S2CID 30140735 (https://api.semanticscholar.org/CorpusID:30140735).
27. Baekkeskov S, Aanstoot HJ, Christgau S, Reetz A, Solimena M, Cascalho M, Folli F, Richter-Olesen H, De Camilli P, Camilli PD (September 1990). "Identification of the 64K autoantigen in insulin-dependent diabetes as the GABA-synthesizing enzyme glutamic acid decarboxylase". *Nature*. **347** (6289): 151–6. Bibcode:1990Natur.347..151B (https://ui.adsabs.harvard.edu/abs/1990Natur.347..151B). doi:10.1038/347151a0 (https://doi.org/10.1038%2F347151a0). PMID 1697648 (https://pubmed.ncbi.nlm.nih.gov/1697648). S2CID 4317318 (https://api.semanticscholar.org/CorpusID:4317318).
28. Kaufman DL, Erlander MG, Clare-Salzler M, Atkinson MA, Maclaren NK, Tobin AJ (January 1992). "Autoimmunity to two forms of glutamate decarboxylase in insulin-dependent diabetes mellitus" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC442846). *The Journal of Clinical Investigation*. **89** (1): 283–92. doi:10.1172/JCI115573 (https://doi.org/10.1172%2FJCI115573). PMC 442846 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC442846). PMID 1370298 (https://pubmed.ncbi.nlm.nih.gov/1370298).
29. Tisch R, Yang XD, Singer SM, Liblau RS, Fugger L, McDevitt HO (November 1993). "Immune response to glutamic acid decarboxylase correlates with insulitis in non-obese diabetic mice". *Nature*. **366** (6450): 72–5. Bibcode:1993Natur.366...72T (https://ui.adsabs.harvard.edu/abs/1993Natur.366...72T). doi:10.1038/366072a0 (https://doi.org/10.1038%2F366072a0). PMID 8232539 (https://pubmed.ncbi.nlm.nih.gov/8232539). S2CID 4273636 (https://api.semanticscholar.org/CorpusID:4273636).

30. Kaufman DL, Clare-Salzler M, Tian J, Forsthuber T, Ting GS, Robinson P, Atkinson MA, Sercarz EE, Tobin AJ, Lehmann PV (November 1993). "Spontaneous loss of T-cell tolerance to glutamic acid decarboxylase in murine insulin-dependent diabetes" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8216222). *Nature*. **366** (6450): 69–72. Bibcode:1993Natur.366...69K (https://ui.adsabs.harvard.edu/abs/1993Natur.366...69K). doi:10.1038/366069a0 (https://doi.org/10.1038%2F366069a0). PMC 8216222 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8216222). PMID 7694152 (https://pubmed.ncbi.nlm.nih.gov/7694152). S2CID 4370149 (https://api.semanticscholar.org/CorpusID:4370149).
31. Tian J, Clare-Salzler M, Herschenfeld A, Middleton B, Newman D, Mueller R, Arita S, Evans C, Atkinson MA, Mullen Y, Sarvetnick N, Tobin AJ, Lehmann PV, Kaufman DL (December 1996). "Modulating autoimmune responses to GAD inhibits disease progression and prolongs islet graft survival in diabetes-prone mice". *Nature Medicine*. **2** (12): 1348–53. doi:10.1038/nm1296-1348 (https://doi.org/10.1038%2Fnm1296-1348). PMID 8946834 (https://pubmed.ncbi.nlm.nih.gov/8946834). S2CID 27692555 (https://api.semanticscholar.org/CorpusID:27692555).
32. Ludvigsson J, Faresjö M, Hjorth M, Axelsson S, Chéramy M, Pihl M, Vaarala O, Forsander G, Ivarsson S, Johansson C, Lindh A, Nilsson NO, Aman J, Ortqvist E, Zerhouni P, Casas R (October 2008). "GAD treatment and insulin secretion in recent-onset type 1 diabetes" (https://doi.org/10.1056%2FNEJMoa0804328). *The New England Journal of Medicine*. **359** (18): 1909–20. doi:10.1056/NEJMoa0804328 (https://doi.org/10.1056%2FNEJMoa0804328). PMID 18843118 (https://pubmed.ncbi.nlm.nih.gov/18843118).
33. "Diamyd announces completion of type 1 diabetes vaccine trial with long term efficacy demonstrated at 30 months" (http://www.diamyd.com/docs/pressClip.aspx?section=investor&ClipID=420). *Press Release*. Diamyd Medical AB. 2008-01-28. Retrieved 2010-01-13.
34. Brophy, Sinead; Davies, Helen; Mannan, Sopna; Brunt, Huw; Williams, Rhys (2011-09-07). "Interventions for latent autoimmune diabetes (LADA) in adults" (https://doi.org/10.1002/14651858.CD006165.pub3). *Cochrane Database of Systematic Reviews*. **2011** (9): CD006165. doi:10.1002/14651858.cd006165.pub3 (https://doi.org/10.1002%2F14651858.cd006165.pub3). ISSN 1465-1858 (https://www.worldcat.org/issn/1465-1858). PMC 6486159 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6486159). PMID 21901702 (https://pubmed.ncbi.nlm.nih.gov/21901702).
35. Dalakas MC, Fujii M, Li M, Lutfi B, Kyhos J, McElroy B (December 2001). "High-dose intravenous immune globulin for stiff-person syndrome". *The New England Journal of Medicine*. **345** (26): 1870–6. doi:10.1056/NEJMoa01167 (https://doi.org/10.1056%2FNEJMoa01167). PMID 11756577 (https://pubmed.ncbi.nlm.nih.gov/11756577).
36. Chang T, Alexopoulos H, McMenamin M, Carvajal-González A, Alexander SK, Deacon R, Erdelyi F, Szabó G, Gabor S, Lang B, Blaes F, Brown P, Vincent A (September 2013). "Neuronal surface and glutamic acid decarboxylase autoantibodies in Nonparaneoplastic stiff person syndrome" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6055982). *JAMA Neurology*. **70** (9): 1140–9. doi:10.1001/jamaneurol.2013.3499 (https://doi.org/10.1001%2Fjamaneurol.2013.3499). PMC 6055982 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6055982). PMID 23877118 (https://pubmed.ncbi.nlm.nih.gov/23877118).
37. Guidotti, Alessandro; Auta, James; Davis, John M.; Gerevini, Valeria DiGiorgi; Dwivedi, Yogesh; Grayson, Dennis R.; Impagnatiello, Francesco; Pandey, Ghanshyam; Pesold, Christine; Sharma, Rajiv; Uzunov, Doncho; Costa, Erminio (2000). "Decrease in reelin and glutamic acid decarboxylase$_{67}$ (GAD$_{67}$) expression in schizophrenia and bipolar disorder: a postmortem brain study". *Archives of General Psychiatry*. **57** (11): 1061–1069. doi:10.1001/archpsyc.57.11.1061 (https://doi.org/10.1001%2Farchpsyc.57.11.1061). PMID 11074872 (https://pubmed.ncbi.nlm.nih.gov/11074872).

38. Akbarian, Schahram; Huang, Hsien-Sung (2006). "Molecular and cellular mechanisms of altered GAD1/GAD67 expression in schizophrenia and related disorders". *Brain Research Reviews*. **52** (2): 293–304. doi:10.1016/j.brainresrev.2006.04.001 (https://doi.org/10.1016%2Fj.brainresrev.2006.04.001). PMID 16759710 (https://pubmed.ncbi.nlm.nih.gov/16759710). S2CID 25771139 (https://api.semanticscholar.org/CorpusID:25771139).
39. Benes FM, Lim B, Matzilevich D, Walsh JP, Subburaju S, Minns M (June 2007). "Regulation of the GABA cell phenotype in hippocampus of schizophrenics and bipolars" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1888575). *Proceedings of the National Academy of Sciences of the United States of America*. **104** (24): 10164–9. Bibcode:2007PNAS..10410164B (https://ui.adsabs.harvard.edu/abs/2007PNAS..10410164B). doi:10.1073/pnas.0703806104 (https://doi.org/10.1073%2Fpnas.0703806104). PMC 1888575 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1888575). PMID 17553960 (https://pubmed.ncbi.nlm.nih.gov/17553960).
40. Kimoto S, Bazmi HH, Lewis DA (September 2014). "Lower expression of glutamic acid decarboxylase 67 in the prefrontal cortex in schizophrenia: contribution of altered regulation by Zif268" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4376371). *The American Journal of Psychiatry*. **171** (9): 969–78. doi:10.1176/appi.ajp.2014.14010004 (https://doi.org/10.1176%2Fappi.ajp.2014.14010004). PMC 4376371 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4376371). PMID 24874453 (https://pubmed.ncbi.nlm.nih.gov/24874453).
41. Georgiev, Danko; Yoshihara, Toru; Kawabata, Rika; Matsubara, Takurou; Tsubomoto, Makoto; Minabe, Yoshio; Lewis, David A.; Hashimoto, Takanori (2016). "Cortical gene expression after a conditional knockout of 67 kDa glutamic acid decarboxylase in parvalbumin neurons" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4903066). *Schizophrenia Bulletin*. **42** (4): 992–1002. doi:10.1093/schbul/sbw022 (https://doi.org/10.1093%2Fschbul%2Fsbw022). PMC 4903066 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4903066). PMID 26980143 (https://pubmed.ncbi.nlm.nih.gov/26980143). S2CID 24197087 (https://api.semanticscholar.org/CorpusID:24197087).
42. LeWitt PA, Rezai AR, Leehey MA, Ojemann SG, Flaherty AW, Eskandar EN, Kostyk SK, Thomas K, Sarkar A, Siddiqui MS, Tatter SB, Schwalb JM, Poston KL, Henderson JM, Kurlan RM, Richard IH, Van Meter L, Sapan CV, During MJ, Kaplitt MG, Feigin A (April 2011). "AAV2-GAD gene therapy for advanced Parkinson's disease: a double-blind, sham-surgery controlled, randomised trial". *The Lancet. Neurology*. **10** (4): 309–19. doi:10.1016/S1474-4422(11)70039-4 (https://doi.org/10.1016%2FS1474-4422%2811%2970039-4). PMID 21419704 (https://pubmed.ncbi.nlm.nih.gov/21419704). S2CID 37154043 (https://api.semanticscholar.org/CorpusID:37154043).
43. Manto MU, Hampe CS, Rogemond V, Honnorat J (February 2011). "Respective implications of glutamate decarboxylase antibodies in stiff person syndrome and cerebellar ataxia" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3042903). *Orphanet Journal of Rare Diseases*. **6** (3): 3. doi:10.1186/1750-1172-6-3 (https://doi.org/10.1186%2F1750-1172-6-3). PMC 3042903 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3042903). PMID 21294897 (https://pubmed.ncbi.nlm.nih.gov/21294897).
44. Mitoma H, Manto M, Hampe CS (2017-03-12). "Pathogenic Roles of Glutamic Acid Decarboxylase 65 Autoantibodies in Cerebellar Ataxias" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5366212). *Journal of Immunology Research*. **2017**: 2913297. doi:10.1155/2017/2913297 (https://doi.org/10.1155%2F2017%2F2913297). PMC 5366212 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5366212). PMID 28386570 (https://pubmed.ncbi.nlm.nih.gov/28386570).

45. Lorenzo LE, Magnussen C, Bailey AL, St Louis M, De Koninck Y, Ribeiro-da-Silva A (September 2014). "Spatial and temporal pattern of changes in the number of GAD65-immunoreactive inhibitory terminals in the rat superficial dorsal horn following peripheral nerve injury" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4164746). *Molecular Pain*. **10** (1): 1744-8069–10-57. doi:10.1186/1744-8069-10-57 (https://doi.org/10.1186%2F1744-8069-10-57). PMC 4164746 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4164746). PMID 25189404 (https://pubmed.ncbi.nlm.nih.gov/25189404).
46. Dayalu P, Teener JW (November 2012). "Stiff Person syndrome and other anti-GAD-associated neurologic disorders". *Seminars in Neurology*. **32** (5): 544–9. doi:10.1055/s-0033-1334477 (https://doi.org/10.1055%2Fs-0033-1334477). PMID 23677666 (https://pubmed.ncbi.nlm.nih.gov/23677666). S2CID 35562171 (https://api.semanticscholar.org/CorpusID:35562171).
47. Liimatainen S, Honnorat J, Pittock SJ, McKeon A, Manto M, Radtke JR, Hampe CS (April 2018). "GAD65 autoantibody characteristics in patients with co-occurring type 1 diabetes and epilepsy may help identify underlying epilepsy etiologies" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5892043). *Orphanet Journal of Rare Diseases*. **13** (1): 55. doi:10.1186/s13023-018-0787-5 (https://doi.org/10.1186%2Fs13023-018-0787-5). PMC 5892043 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5892043). PMID 29636076 (https://pubmed.ncbi.nlm.nih.gov/29636076).
48. Coleman ST, Fang TK, Rovinsky SA, Turano FJ, Moye-Rowley WS (Jan 2001). "Expression of a glutamate decarboxylase homologue is required for normal oxidative stress tolerance in Saccharomyces cerevisiae" (https://doi.org/10.1074%2Fjbc.M007103200). *J Biol Chem*. **276** (1): 244–50. doi:10.1074/jbc.M007103200 (https://doi.org/10.1074%2Fjbc.M007103200). PMID 11031268 (https://pubmed.ncbi.nlm.nih.gov/11031268).
49. Baum G, Lev-Yadun S, Fridmann Y, Arazi T, Katsnelson H, Zik M, Fromm H (Jun 1996). "Calmodulin binding to glutamate decarboxylase is required for regulation of glutamate and GABA metabolism and normal development in plants" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC450240). *EMBO J*. **15** (12): 2988–96. doi:10.1002/j.1460-2075.1996.tb00662.x (https://doi.org/10.1002%2Fj.1460-2075.1996.tb00662.x). PMC 450240 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC450240). PMID 8670800 (https://pubmed.ncbi.nlm.nih.gov/8670800).
50. Baum G, Chen Y, Arazi T, Takatsuji H, Fromm H (Sep 1993). "A plant glutamate decarboxylase containing a calmodulin binding domain. Cloning, sequence, and functional analysis" (https://doi.org/10.1016%2FS0021-9258%2819%2936560-3). *J Biol Chem*. **268** (26): 19610–7. doi:10.1016/S0021-9258(19)36560-3 (https://doi.org/10.1016%2FS0021-9258%2819%2936560-3). PMID 8366104 (https://pubmed.ncbi.nlm.nih.gov/8366104).
51. Akama K, Akihiro T, Kitagawa M, Takaiwa F (Dec 2001). "Rice (Oryza sativa) contains a novel isoform of glutamate decarboxylase that lacks an authentic calmodulin-binding domain at the C-terminus". *Biochim Biophys Acta*. **1522** (3): 143–50. doi:10.1016/s0167-4781(01)00324-4 (https://doi.org/10.1016%2Fs0167-4781%2801%2900324-4). PMID 11779628 (https://pubmed.ncbi.nlm.nih.gov/11779628).
52. Trobacher CP, Zarei A, Liu J, Clark SM, Bozzo GG, Shelp (Sep 2013). "Calmodulin-dependent and calmodulin-independent glutamate decarboxylases in apple fruit" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3849887). *BMC Plant Biol*. **144** (13): 144. doi:10.1186/1471-2229-13-144 (https://doi.org/10.1186%2F1471-2229-13-144). PMC 3849887 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3849887). PMID 24074460 (https://pubmed.ncbi.nlm.nih.gov/24074460).
53. Zik M, Arazi T, Snedden WA, Fromm H (Aug 1998). "Two isoforms of glutamate decarboxylase in Arabidopsis are regulated by calcium/calmodulin and differ in organ distribution". *Plant Mol Biol*. **37** (6): 967–75. doi:10.1023/a:1006047623263 (https://doi.org/10.1023%2Fa%3A1006047623263). PMID 9700069 (https://pubmed.ncbi.nlm.nih.gov/9700069). S2CID 28501096 (https://api.semanticscholar.org/CorpusID:28501096).

54. Sheng L, Shen D, Luo Y, Sun X, Wang J, Luo T, Zeng Y, Xu J, Deng X, Cheng Y (February 2017). "Exogenous γ-aminobutyric acid treatment affects citrate and amino acid accumulation to improve fruit quality and storage performance of postharvest citrus fruit". *Food Chemistry*. **216**: 138–45. doi:10.1016/j.foodchem.2016.08.024 (https://doi.org/10.1016%2Fj.foodchem.2016.08.024). PMID 27596402 (https://pubmed.ncbi.nlm.nih.gov/27596402).
55. Smith DK, Kassam T, Singh B, Elliott JF (Sep 1992). "Escherichia coli has two homologous glutamate decarboxylase genes that map to distinct loci" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC207112). *J Bacteriol*. **174** (18): 5820–6. doi:10.1128/jb.174.18.5820-5826.1992 (https://doi.org/10.1128%2Fjb.174.18.5820-5826.1992). PMC 207112 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC207112). PMID 1522060 (https://pubmed.ncbi.nlm.nih.gov/1522060).
56. De Biase D, Tramonti A, John RA, Bossa F (Dec 1996). "Isolation, overexpression, and biochemical characterization of the two isoforms of glutamic acid decarboxylase from Escherichia coli". *Protein Expr Purif*. **8** (4): 430–8. doi:10.1006/prep.1996.0121 (https://doi.org/10.1006%2Fprep.1996.0121). PMID 8954890 (https://pubmed.ncbi.nlm.nih.gov/8954890).
57. Lin J, Lee IS, Frey J, Slonczewski JL, Foster JW (Jul 1995). "Comparative analysis of extreme acid survival in Salmonella typhimurium, Shigella flexneri, and Escherichia coli" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC177142). *J Bacteriol*. **177** (14): 4097–104. doi:10.1128/jb.177.14.4097-4104.1995 (https://doi.org/10.1128%2Fjb.177.14.4097-4104.1995). PMC 177142 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC177142). PMID 7608084 (https://pubmed.ncbi.nlm.nih.gov/7608084).

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- Media related to Glutamate decarboxylase at Wikimedia Commons
- Genetics, Expression Profiling Support GABA Deficits in Schizophrenia (https://web.archive.org/web/20070815162255/http://www.schizophreniaforum.org/new/detail.asp?id=1358) - Schizophrenia Research Forum, 25 June 2007.
- Overview of all the structural information available in the PDB for UniProt: *Q99259 (https://www.ebi.ac.uk/pdbe/pdbe-kb/proteins/Q99259)* (Glutamate decarboxylase 1) at the PDBe-KB.
- Overview of all the structural information available in the PDB for UniProt: *Q05329 (https://www.ebi.ac.uk/pdbe/pdbe-kb/proteins/Q05329)* (Glutamate decarboxylase 2) at the PDBe-KB.