GEPHE SUMMARY

Gephebase Gene

CHRNA1 (https://www.gephebase.org/search-criteria?/and+Gene Gephebase=^CHRNA1^#gephebase-summary-title)

GepheID

GP00001686

Entry Status

Published

Main curator

Courtier

PHENOTYPIC CHANGE

Trait Category

Physiology (https://www.gephebase.org/search-criteria?/and+Trait Category=^Physiology^#gephebase-summary-title)

Trait

Xenobiotic resistance (snake venom) (https://www.gephebase.org/search-criteria?/and+Trait=^Xenobiotic resistance (snake venom)^#gephebase-summary-title)

Trait State in Taxon A

sensitive

Trait State in Taxon B

resistant

Ancestral State

Taxon A

Taxonomic Status

Intergeneric or Higher (https://www.gephebase.org/search-criteria?/and+Taxonomic Status=^Intergeneric or Higher^#gephebase-summary-title)

Taxon A

Latin Name

Carnivora (https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=^Carnivora^#gephebase-summary-title)

Common Name

carnivores

Synonyms

carnivores

Rank

order

Lineage

cellular organisms; Eukaryota; Opisthokonta; Metazoa; Eumetazoa; Bilateria; Deuterostomia; Chordata; Craniata; Vertebrata; Gnathostomata; Teleostomi; Euteleostomi; Sarcopterygii; Dipnotetrapodomorpha; Tetrapoda; Amniota; Mammalia; Theria; Eutheria; Boreoeutheria; Laurasiatheria

Parent

Laurasiatheria () - (Rank: superorder) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 314145)

NCBI Taxonomy ID

33554 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 33554)

is Taxon A an Infraspecies?

No

Taxon B

Latin Name

Herpestes ichneumon (https://www.gephebase.org/search-criteria?/and+Taxon and Synonyms=^Herpestes ichneumon^#gephebase-summary-title)

Common Name

Egyptian mongoose

Synonyms

Egyptian mongoose

Rank

species

Lineage

cellular organisms; Eukaryota; Opisthokonta; Metazoa; Eumetazoa; Bilateria; Deuterostomia; Chordata; Craniata; Vertebrata; Gnathostomata; Teleostomi; Euteleostomi; Sarcopterygii; Dipnotetrapodomorpha; Tetrapoda; Amniota; Mammalia; Theria; Eutheria; Boreoeutheria; Laurasiatheria; Carnivora; Feliformia; Herpestidae; Herpestes

Parent

Herpestes () - (Rank: genus) (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 9699)

NCBI Taxonomy ID

9700 (https://www.ncbi.nlm.nih.gov/Taxonomy/Browser/wwwtax.cgi?id= 9700)

is Taxon B an Infraspecies?

No

GENOTYPIC CHANGE

Generic Gene Name

CHRNA1

Synonyms

ACHRA; ACHRD; CHRNA; CMS1A; CMS1B; CMS2A; FCCMS; SCCMS; CHNRA

String

9606.ENSP00000261007 (http://string-db.org/newstring_cgi/show_network_section.pl?identifier=9606.ENSP00000261007)

Sequence Similarities

Belongs to the ligand-gated ion channel (TC 1.A.9) family. Acetylcholine receptor (TC 1.A.9.1) subfamily. Alpha-1/CHRNA1 sub-subfamily.

GO - Molecular Function

GO:0042166 : acetylcholine binding (https://www.ebi.ac.uk/QuickGO/term/GO:0042166)
GO:0015464 : acetylcholine receptor activity (https://www.ebi.ac.uk/QuickGO/term/GO:0015464)
GO:0022848 : acetylcholine-gated cation-selective channel activity (https://www.ebi.ac.uk/QuickGO/term/GO:0022848)
GO:0005216 : ion channel activity (https://www.ebi.ac.uk/QuickGO/term/GO:0005216)

UniProtKB Homo sapiens

P02708 (http://www.uniprot.org/uniprot/P02708)

GenebankID or UniProtKB

()

GO:1904315 : transmitter-gated ion channel activity involved in regulation of postsynaptic membrane potential (https://www.ebi.ac.uk/QuickGO/term/GO:1904315)

GO - Biological Process

GO:0007165 : signal transduction (https://www.ebi.ac.uk/QuickGO/term/GO:0007165)
GO:0007268 : chemical synaptic transmission (https://www.ebi.ac.uk/QuickGO/term/GO:0007268)
GO:0007271 : synaptic transmission, cholinergic (https://www.ebi.ac.uk/QuickGO/term/GO:0007271)
GO:0034220 : ion transmembrane transport (https://www.ebi.ac.uk/QuickGO/term/GO:0034220)
GO:0046716 : muscle cell cellular homeostasis (https://www.ebi.ac.uk/QuickGO/term/GO:0046716)
GO:0050881 : musculoskeletal movement (https://www.ebi.ac.uk/QuickGO/term/GO:0050881)
GO:0050877 : nervous system process (https://www.ebi.ac.uk/QuickGO/term/GO:0050877)
GO:0007528 : neuromuscular junction development (https://www.ebi.ac.uk/QuickGO/term/GO:0007528)
GO:0050905 : neuromuscular process (https://www.ebi.ac.uk/QuickGO/term/GO:0050905)
GO:0007274 : neuromuscular synaptic transmission (https://www.ebi.ac.uk/QuickGO/term/GO:0007274)
GO:0070050 : neuron cellular homeostasis (https://www.ebi.ac.uk/QuickGO/term/GO:0070050)
GO:0019228 : neuronal action potential (https://www.ebi.ac.uk/QuickGO/term/GO:0019228)
GO:0042391 : regulation of membrane potential (https://www.ebi.ac.uk/QuickGO/term/GO:0042391)
GO:0035094 : response to nicotine (https://www.ebi.ac.uk/QuickGO/term/GO:0035094)
GO:0003009 : skeletal muscle contraction (https://www.ebi.ac.uk/QuickGO/term/GO:0003009)
GO:0048630 : skeletal muscle tissue growth (https://www.ebi.ac.uk/QuickGO/term/GO:0048630)

GO - Cellular Component

GO:0005886 : plasma membrane (https://www.ebi.ac.uk/QuickGO/term/GO:0005886)
GO:0005887 : integral component of plasma membrane (https://www.ebi.ac.uk/QuickGO/term/GO:0005887)
GO:0030054 : cell junction (https://www.ebi.ac.uk/QuickGO/term/GO:0030054)
GO:0043005 : neuron projection (https://www.ebi.ac.uk/QuickGO/term/GO:0043005)
GO:0045211 : postsynaptic membrane (https://www.ebi.ac.uk/QuickGO/term/GO:0045211)
GO:0045202 : synapse (https://www.ebi.ac.uk/QuickGO/term/GO:0045202)
GO:0005892 : acetylcholine-gated channel complex (https://www.ebi.ac.uk/QuickGO/term/GO:0005892)
GO:0009986 : cell surface (https://www.ebi.ac.uk/QuickGO/term/GO:0009986)
GO:0099060 : integral component of postsynaptic specialization membrane (https://www.ebi.ac.uk/QuickGO/term/GO:0099060)
GO:0031594 : neuromuscular junction (https://www.ebi.ac.uk/QuickGO/term/GO:0031594)

Mutation #1

Presumptive Null

No (https://www.gephebase.org/search-criteria?/and+Presumptive Null=^No^#gephebase-summary-title)

Molecular Type

Coding (https://www.gephebase.org/search-criteria?/and+Molecular Type=^Coding^#gephebase-summary-title)

Aberration Type

SNP (https://www.gephebase.org/search-criteria?/and+Aberration Type=^SNP^#gephebase-summary-title)

SNP Coding Change

Nonsynonymous

Molecular Details of the Mutation

W187N

Experimental Evidence

Candidate Gene (https://www.gephebase.org/search-criteria?/and+Experimental Evidence=^Candidate Gene^#gephebase-summary-title)

	Taxon A	Taxon B	Position
Codon	-	-	-
Amino-acid	Trp	Asn	187

Main Reference

How the mongoose can fight the snake: the binding site of the mongoose acetylcholine receptor. (1992) (https://pubmed.ncbi.nlm.nih.gov/1380164)

Authors

Barchan D; Kachalsky S; Neumann D; Vogel Z; Ovadia M; Kochva E; Fuchs S

Abstract

The ligand binding site of the nicotinic acetylcholine receptor (AcChoR) is within a short peptide from the alpha subunit that includes the tandem cysteine residues at positions 192 and 193. To elucidate the molecular basis of the binding properties of the AcChoR, we chose to study nonclassical muscle AcChoRs from animals that are resistant to alpha-neurotoxins. We

have previously reported that the resistance of snake AcChoR to alpha-bungarotoxin (alpha-BTX) may be accounted for by several major substitutions in the ligand binding site of the receptor. In the present study, we have analyzed the binding site of AcChoR from the mongoose, which is also resistant to alpha-neurotoxins. It was shown that mongoose AcChoR does not bind alpha-BTX in vivo or in vitro. cDNA fragments of the alpha subunit of mongoose AcChoR corresponding to codons 122-205 and including the presumed ligand binding site were cloned, sequenced, and expressed in Escherichia coli. The expressed protein fragments of the mongoose, as well as of snake receptors, do not bind alpha-BTX. The mongoose fragment is highly homologous (greater than 90%) to the respective mouse fragment. Out of the seven amino acid differences between the mongoose and mouse in this region, five cluster in the presumed ligand binding site, close to cysteines 192 and 193. These changes are at positions 187 (Trp----Asn), 189 (Phe----Thr), 191 (Ser----Ala), 194 (Pro----Leu), and 197 (Pro----His). The mongoose like the snake AcChoR has a potential glycosylation site in the binding site domain. Sequence comparison between species suggests that substitutions at positions 187, 189, and 194 are important in determining the resistance of mongoose and snake AcChoR to alpha-BTX. In addition, it was shown that amino acid residues that had been reported to be necessary for acetylcholine binding are conserved in the toxin-resistant animals as well.

Additional References

Two subsites in the binding domain of the acetylcholine receptor: an aromatic subsite and a proline subsite. (1995) (https://pubmed.ncbi.nlm.nih.gov/7479887)

Mutation #2

Presumptive Null

No (https://www.gephebase.org/search-criteria?/and+Presumptive Null=^No^#gephebase-summary-title)

Molecular Type

Coding (https://www.gephebase.org/search-criteria?/and+Molecular Type=^Coding^#gephebase-summary-title)

Aberration Type

SNP (https://www.gephebase.org/search-criteria?/and+Aberration Type=^SNP^#gephebase-summary-title)

SNP Coding Change

Nonsynonymous

Molecular Details of the Mutation

F189T

Experimental Evidence

Candidate Gene (https://www.gephebase.org/search-criteria?/and+Experimental Evidence=^Candidate Gene^#gephebase-summary-title)

	Taxon A	Taxon B	Position
Codon	-	-	-
Amino-acid	Phe	Thr	189

Main Reference

Two subsites in the binding domain of the acetylcholine receptor: an aromatic subsite and a proline subsite. (1995) (https://pubmed.ncbi.nlm.nih.gov/7479887)

Authors

Kachalsky SG; Jensen BS; Barchan D; Fuchs S

Abstract

The ligand binding site of the nicotinic acetylcholine receptor (AcChoR) is localized in the alpha-subunit within a domain containing the tandem Cys-192 and -193. By analyzing the binding-site region of AcChoR from animal species that are resistant to alpha-neurotoxins, we have previously shown that four residues in this region, at positions 187, 189, 194, and 197, differ between animals sensitive (e.g., mouse) and resistant (e.g., mongoose and snake) to alpha-bungarotoxin (alpha-BTX). In the present study, we performed site-directed mutagenesis on a fragment of the mongoose AcChoR alpha-subunit (residues 122-205) and exchanged residues 187, 189, 194, and 197, either alone or in combination, with those present in the mouse alpha-subunit sequence. Only the mongoose fragment in which all four residues were mutated to the mouse ones exhibited alpha-BTX binding similar to that of the mouse fragment. The mongoose double mutation in which Leu-194 and His-197 were replaced with proline residues, which are present at these positions in the mouse AcChoR and in all other toxin binders, bound alpha-BTX to approximately 60% of the level of binding exhibited by the mouse fragment. In addition, replacement of either Pro-194 or -197 in the mouse fragment with serine and histidine, respectively, markedly decreased alpha-BTX binding. All other mutations resulted in no or just a small increase in alpha-BTX binding. These results have led us to propose two subsites in the binding domain for alpha-BTX: the proline subsite, which includes Pro-194 and -197 and is critical for alpha-BTX binding, and the aromatic subsite, which includes amino acid residues 187 and 189 and determines the extent of alpha-BTX binding.

Additional References

How the mongoose can fight the snake: the binding site of the mongoose acetylcholine receptor. (1992) (https://pubmed.ncbi.nlm.nih.gov/1380164)

Mutation #3

Presumptive Null

No (https://www.gephebase.org/search-criteria?/and+Presumptive Null=^No^#gephebase-summary-title)

Molecular Type

Coding (https://www.gephebase.org/search-criteria?/and+Molecular Type=^Coding^#gephebase-summary-title)

Aberration Type

SNP (https://www.gephebase.org/search-criteria?/and+Aberration Type=^SNP^#gephebase-summary-title)

SNP Coding Change

Nonsynonymous

Molecular Details of the Mutation

P194L

Experimental Evidence

Candidate Gene (https://www.gephebase.org/search-criteria?/and+Experimental Evidence=^Candidate Gene^#gephebase-summary-title)

	Taxon A	Taxon B	Position
Codon	-	-	-
Amino-acid	Pro	Leu	194

Main Reference

Two subsites in the binding domain of the acetylcholine receptor: an aromatic subsite and a proline subsite. (1995) (https://pubmed.ncbi.nlm.nih.gov/7479887)

Authors

Kachalsky SG; Jensen BS; Barchan D; Fuchs S

Abstract

The ligand binding site of the nicotinic acetylcholine receptor (AcChoR) is localized in the alpha-subunit within a domain containing the tandem Cys-192 and -193. By analyzing the binding-site region of AcChoR from animal species that are resistant to alpha-neurotoxins, we have previously shown that four residues in this region, at positions 187, 189, 194, and 197, differ between animals sensitive (e.g., mouse) and resistant (e.g., mongoose and snake) to alpha-bungarotoxin (alpha-BTX). In the present study, we performed site-directed mutagenesis on a fragment of the mongoose AcChoR alpha-subunit (residues 122-205) and exchanged residues 187, 189, 194, and 197, either alone or in combination, with those present in the mouse alpha-subunit sequence. Only the mongoose fragment in which all four residues were mutated to the mouse ones exhibited alpha-BTX binding similar to that of the mouse fragment. The mongoose double mutation in which Leu-194 and His-197 were replaced with proline residues, which are present at these positions in the mouse AcChoR and in all other toxin binders, bound alpha-BTX to approximately 60% of the level of binding exhibited by the mouse fragment. In addition, replacement of either Pro-194 or -197 in the mouse fragment with serine and histidine, respectively, markedly decreased alpha-BTX binding. All other mutations resulted in no or just a small increase in alpha-BTX binding. These results have led us to propose two subsites in the binding domain for alpha-BTX: the proline subsite, which includes Pro-194 and -197 and is critical for alpha-BTX binding, and the aromatic subsite, which includes amino acid residues 187 and 189 and determines the extent of alpha-BTX binding.

Additional References

How the mongoose can fight the snake: the binding site of the mongoose acetylcholine receptor. (1992) (https://pubmed.ncbi.nlm.nih.gov/1380164)

Mutation #4

Presumptive Null

No (https://www.gephebase.org/search-criteria?/and+Presumptive Null=^No^#gephebase-summary-title)

Molecular Type

Coding (https://www.gephebase.org/search-criteria?/and+Molecular Type=^Coding^#gephebase-summary-title)

Aberration Type

SNP (https://www.gephebase.org/search-criteria?/and+Aberration Type=^SNP^#gephebase-summary-title)

SNP Coding Change

Nonsynonymous

Molecular Details of the Mutation

H197P

Experimental Evidence

Candidate Gene (https://www.gephebase.org/search-criteria?/and+Experimental Evidence=^Candidate Gene^#gephebase-summary-title)

	Taxon A	Taxon B	Position
Codon	-	-	-
Amino-acid	His	Pro	197

Main Reference

Two subsites in the binding domain of the acetylcholine receptor: an aromatic subsite and a proline subsite. (1995) (https://pubmed.ncbi.nlm.nih.gov/7479887)

Authors

Kachalsky SG; Jensen BS; Barchan D; Fuchs S

Abstract

The ligand binding site of the nicotinic acetylcholine receptor (AcChoR) is localized in the alpha-subunit within a domain containing the tandem Cys-192 and -193. By analyzing the binding-site region of AcChoR from animal species that are resistant to alpha-neurotoxins, we have previously shown that four residues in this region, at positions 187, 189, 194, and 197, differ between animals sensitive (e.g., mouse) and resistant (e.g., mongoose and snake) to alpha-bungarotoxin (alpha-BTX). In the present study, we performed site-directed mutagenesis on a fragment of the mongoose AcChoR alpha-subunit (residues 122-205) and exchanged residues 187, 189, 194, and 197, either alone or in combination, with those present in the mouse alpha-subunit sequence. Only the mongoose fragment in which all four residues were mutated to the mouse ones exhibited alpha-BTX binding similar to that of the mouse fragment. The mongoose double mutation in which Leu-194 and His-197 were replaced with proline residues, which are present at these positions in the mouse AcChoR and in all other toxin binders, bound alpha-BTX to approximately 60% of the level of binding exhibited by the mouse fragment. In addition, replacement of either Pro-194 or -197 in the mouse fragment with serine and histidine, respectively, markedly decreased alpha-BTX binding. All other mutations resulted in no or just a small increase in alpha-BTX binding. These results have led us to propose two subsites in the binding domain for alpha-BTX: the proline subsite, which includes Pro-194 and -197 and is critical for alpha-BTX binding, and the aromatic subsite, which includes amino acid residues 187 and 189 and determines the extent of alpha-BTX binding.

Additional References

How the mongoose can fight the snake: the binding site of the mongoose acetylcholine receptor. (1992) (https://pubmed.ncbi.nlm.nih.gov/1380164)

RELATED GEPHE

Related Genes

No matches found.

Related Haplotypes

4 (https://www.gephebase.org/search-criteria?/or+Gene Gephebase=^CHRNA1^/and+Taxon ID=^33554^/or+Gene Gephebase=^CHRNA1^/and+Taxon ID=^9700^#gephebase-summary-title)

EXTERNAL LINKS

COMMENTS

@SeveralMutationsWithEffect ; Parallel changes in a 3rd lineage thought to be venom resistant (pigs)