

## GEPHE SUMMARY

<p>CHRNA1 (<a href="https://www.gephebase.org/search-criteria?/and+Gene+Gephebase=^CHRNA1^#gephebase-summary-title">https://www.gephebase.org/search-criteria?/and+Gene+Gephebase=^CHRNA1^#gephebase-summary-title</a>)</p> <p>Published</p>	<p>Gephebase Gene</p> <p>Entry Status</p>	<p>GP00001686</p> <p>Courtier</p>	<p>GepheID</p> <p>Main curator</p>
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## PHENOTYPIC CHANGE

		Trait Category			
		Trait			
		Trait State in Taxon A			
		Trait State in Taxon B			
		Ancestral State			
		Taxonomic Status			
		Taxon A	Taxon B		
		Latin Name	Latin Name		
		Common Name	Common Name		
		Synonyms	Synonyms		
		Rank	Rank		
		Lineage	Lineage		
		Parent	Parent		
		NCBI Taxonomy ID	NCBI Taxonomy ID		
		is Taxon A an Intraspecies?	is Taxon B an Intraspecies?		

## GENOTYPIC CHANGE

<p>CHRNA1</p> <p>ACHRA; ACHRD; CHRNA; CMS1A; CMS1B; CMS2A; FCCMS; SCCMS; CHNRA</p> <p>9606.ENSPO0000261007 (<a href="http://string-db.org/newstring.cgi/show_network_section.pl?identifier=9606.ENSPO0000261007">http://string-db.org/newstring.cgi/show_network_section.pl?identifier=9606.ENSPO0000261007</a>)</p>	<p>Generic Gene Name</p> <p>Synonyms</p> <p>String</p> <p>Sequence Similarities</p> <p>GO - Molecular Function</p>	<p>P02708 (<a href="http://www.uniprot.org/uniprot/P02708">http://www.uniprot.org/uniprot/P02708</a>)</p> <p>()</p>	<p>UniProtKB Homo sapiens</p> <p>GenebankID or UniProtKB</p>
<p>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.</p>		<p>GO:0042166 : acetylcholine binding (<a href="https://www.ebi.ac.uk/QuickGO/term/GO:0042166">https://www.ebi.ac.uk/QuickGO/term/GO:0042166</a>)</p> <p>GO:0015464 : acetylcholine receptor activity (<a href="https://www.ebi.ac.uk/QuickGO/term/GO:0015464">https://www.ebi.ac.uk/QuickGO/term/GO:0015464</a>)</p> <p>GO:0022848 : acetylcholine-gated cation-selective channel activity (<a href="https://www.ebi.ac.uk/QuickGO/term/GO:0022848">https://www.ebi.ac.uk/QuickGO/term/GO:0022848</a>)</p> <p>GO:0005216 : ion channel activity (<a href="https://www.ebi.ac.uk/QuickGO/term/GO:0005216">https://www.ebi.ac.uk/QuickGO/term/GO:0005216</a>)</p>	

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 (AChR) 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 AChR, we chose to study nonclassical muscle AChRs 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

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

Presumptive Null

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

Molecular Type

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

Aberration Type

Nonsynonymous

SNP Coding Change

F189T

Molecular Details of the Mutation

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

Experimental Evidence

	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

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

Presumptive Null

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

Molecular Type

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

Aberration Type

Nonsynonymous

SNP Coding Change

P194L

Molecular Details of the Mutation

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

Experimental Evidence

	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)