Gene Section
Short Communication

ACHE (acetylcholinesterase)

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Identity

Other names: ACEE, ARACHE, N-ACHE, YT
HGNC (Hugo): ACHE
Location: 7q22.1

DNA/RNA

Description

The ACHE gene spans about 6 kilobases on chromosome 7q22.

Transcription

The gene gives rise to multiple alternatively spliced transcripts. These include AChE-Synaptic (AChE-S), AChE-Erythrocyte (AChE-E) and AChE-Read through (AChE-R). AChE-S is the major neuronal transcript. Alternative 3’ splicing gives rise to AChE-E, a dimeric glycosylphosphatidylinositol (GPI)-anchored isoform expressed primarily in erythrocytes. The third variant AChE-R is produced by the inclusion of the normally spliced out intron 4 and is reported to be elevated during stress. In addition, the existence of multiple promoters leads to the production of several variants with extended N-terminal sequences which are transcribed from the alternative promoters although their expression patterns have not yet been well characterized (Soreq and Seidman, 2001; Meshorer and Soreq, 2006).

Pseudogene

None.

Protein

Description

Acetylcholinesterase (AChE) is a 57 kDa protein. AChE can be monomeric (AChE-R), dimeric (AChE-E) or tetrameric (AChE-S). Tetrameric AChE-S can further interact with collagen Q (ColQ), enabling anchorage to neuromuscular junctions (NMJs), and a proline-rich membrane anchor protein (PRIaM) is responsible for the synaptic docking of AChE-S in the brain. AChE-R is a soluble monomer with a unique naturally unfolded C-terminal peptide. Because AChE-E and AChE-R are incapable of anchorage to the NMJ or to synaptic membranes through ColQ or PRIaM, only the AChE-S form of the enzyme is regarded as truly "synaptic" (Massoulié et al., 1993; Taylor et al., 1993; Silman and Sussman, 2008).

Expression

Functional heterogeneity in AChE activity is regulated at the transcriptional, post-transcriptional and post-translational levels, leading to complex expression patterns that reflect tissue and cell-type specificity, differentiation state, physiological condition and response to external stimuli. Recent studies have also looked at regulation of AChE expression by microRNA (Hanin and Soreq, 2011).

Localisation

Intracellular, extracellular, plasma, cerebrospinal fluid.
The human AChE gene is located at q22 of the long arm of chromosome 7. The AChE mRNA has multiple isoforms which arise from both alternative promoter usage in the S' of the gene and alternative splicing of exons 4, 5 and 6.

**Function**

Acetylcholinesterase is a type B hydrolase that rapidly and selectively hydrolyzes the neurotransmitter acetylcholine (ACh) at cholinergic synapses, as well as at neuromuscular junctions (Soreq and Seidman, 2001). In addition to its catalytic function of the hydrolysis of acetylcholine, AChE has been shown to be involved in many non-cholinergic functions, such as cell growth, stem cell differentiation (Sperling et al., 2008; Falugi and Aluigi, 2012), neuritogenesis, cell adhesion (Paraoanu and Layer, 2008), synaptogenesis, activation of dopaminergic neurons, tumorigenesis, amyloid fibril assembly (Inestrosa et al., 1996; Alvarez et al., 1997), haematopoiesis and thrombopoiesis (Greenfield, 1996; Layer, 1996; Small et al., 1996). The role of acetylcholinesterase in modulating the regulation of cholinergic function is still being investigated (Shaked et al., 2009; Schliebs and Arendt, 2011). The role of AChE inhibitors in many neurodegenerative and neurodevelopmental pathologies is also being studied (Hargreaves, 2012; Li et al., 2012).

**Homology**

AChE is widely conserved in the animal kingdom and is found in mammals, Drosophila, C. elegans and Torpedo californica, among others.

**Mutations**

Note

No natural disease-causing mutations have been reported but a number of single nucleotide polymorphisms (SNPs) are known which may affect transcriptional activity and immune properties.

**Implicated in**

**Primary ovarian carcinomas**

Note

Significant amplification and mutagenesis of both the ache and the highly homologous BChE gene were identified in malignant tumors. The frequent co-amplification in ovarian carcinomas of AChE implicates cholinesterases in neoplastic growth and/or proliferation (Zakut et al., 1990).
**Glioblastoma multiforme**

**Note**

AChE mRNA accumulates in primary human astrocytomas in a manner associated with these tumors' grade of aggressiveness (Perry et al., 2002). CREB regulation allows AChE-R-induced, PKA-mediated proliferation of glioblastoma tumors (Perry et al., 2004).

**Leukemia**

**Note**

AChE-S may be a regulator of hematopoiesis, affecting cell fate decisions downstream to the GEMM progenitor cells (Perry et al., 2007). Deletion of the acetylcholinesterase locus at 7q22 is associated with myelodysplastic syndromes (MDS) and acute myeloid leukemia (AML) (Stephenson et al., 1996).

**Breast cancer**

**Note**

In a recent study, amplifications and deletions in the AChE and BChE genes were investigated in sporadic breast tumors using real-time polymerase chain reaction and the relative quantification method and the majority of the tumor tissues showed a notable number of both deletions and amplifications of both the AChE and BChE genes (Bernardi et al., 2010).

**Alzheimer's disease**

**Note**

The loss of cholinergic neurons has long been believed to be an important aspect of Alzheimer's pathology (Oddo and LaFerla, 2006; Schliebs and Arndt, 2011) and increasing the level of acetylcholine by the use of cholinesterase inhibitors is one of the few pharmacological interventions available for the treatment of Alzheimer's disease (Birks, 2006; Shanks et al., 2009). AChE has been identified in the amyloid plaques found in Alzheimer's disease and the isoforms of AChE have different effects on the extent of plaque development (Berson et al., 2008).

**Inflammation**

**Note**

Being a major regulator of acetylcholine levels, AChE may relieve the cholinergic blockade of inflammation (Shaked et al., 2009). Correspondingly, increasing levels of the AChE-targeted microRNA-132, and presumably other AChE-targeted microRNAs can potentiate this blockade (Hanin and Soreq, 2011).

**References**


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