Atlas of Genetics and Cytogenetics in Oncology and Haematology

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Gene Section
Mini Review

ADD3 (adducin 3)

José Luis Vizmanos

Departamento de Genética, Facultad de Ciencias, Universidad de Navarra, Pamplona, Spain (JLV)

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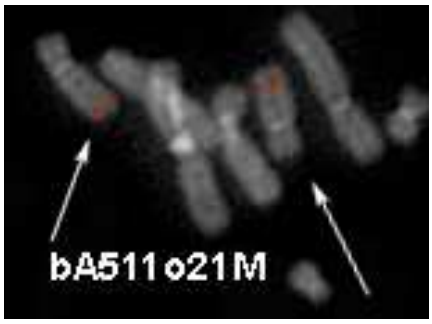
Identity

Other names: ADDL; Adducin-like; adducin 3 (gamma); gamma adducin (adducin-like protein 70)

HGNC (Hugo): ADD3

Location: 10q25.1-q25.2

Local order: MXI1 (MAX-interacting protein 1) is more telomeric. XPNPEP1 (X-prolylaminopeptidase 1) is more telomeric.



Probe(s) - Courtesy Mariano Rocchi, Resources for Molecular Cytogenetics.

DNA/RNA

Description

15 exons spanning 129.52 Kb on 10q25.1-10q25.2. Transcription is from centromere to telomere.

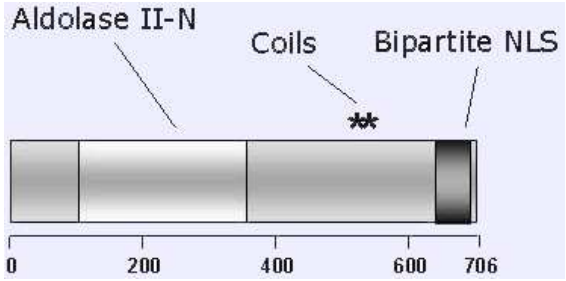
Transcription

2 alternative transcripts:
Variant 1 includes an in-frame alternate coding exon and encodes a longer protein isoform (isoform a) compared to transcript variant 2.
Variant 2 lacks an in-frame alternate coding exon and exon 13 and encodes a shorter protein (isoform b) compared to transcript variant 1.
3 alternative transcripts corresponding to variant 1 and 2.

Genomic structure of ADD3. Black boxes indicate exons.

Protein

Note
Adducin 3 (adducin-like).



Schematic representation of ADD3. AldolaseII-N: domain belonging to aldolase class I family, adducin subfamily N-terminal, Coils: coiled-coil domain, Bipartite NLS: Bipartite nuclear localization signal.

Description

is membrane-cytoskeleton-associated protein that promotes the assembly of the spectrin-actin network and binds to calmodulin. Adducins are heteromeric proteins composed of different subunits referred to as adducin alpha, beta and gamma encoded by distinct genes and belong to a family of membrane skeletal proteins involved in the assembly of spectrin-actin network in erythrocytes and at sites of cell-cell contact in epithelial tissues. Structurally, each subunit is comprised of two distinct domains. The amino-terminal region is protease resistant and globular in shape, while the carboxy-terminal region is protease sensitive. The latter contains multiple phosphorylation sites for protein kinase C, the binding site for calmodulin, and is required for association with spectrin and actin. Alternatively spliced adducin gamma transcripts encoding different isoforms have been described. The functions of the different isoforms are not known.

Expression

Ubiquitous. Heart only expresses isoform 1 or a.

Localisation

Membrane skeleton.

Function

Adducins are membrane skeletal proteins involved in the assembly of spectrin-actin network in erythrocytes and at sites of cell-cell contact in epithelial tissues. Adducin is a heterodimeric cytoskeleton protein and consists of an [alpha]-subunit (Mr 103 kDa) and either a [beta]- (Mr 97 kDa) or [gamma]-subunit (Mr 90kDa). Three genes (ADD1, ADD2, and ADD3, respectively) that map to different chromosomes encode these subunits. Adducin promotes the organization of the spectrin-actin lattice by favoring the spectrin-actin binding and controlling the rate of actin polymerization as an end-capping actin protein. Its function is calcium- and calmodulin-dependent. It is phosphorylated by protein kinases A and C, tyrosine, and [rho]-kinases.10 It is a member of the myristoylated alanine-rich C kinase substrate protein family, which is involved in signal transduction, cell-to-cell contact formation, and cell migration. Non-silent polymorphisms resulting in subunits alpha and beta have been associated with the regulation of blood pressure in an animal model of hypertension.

Homology

It presents homology in various species. It also belongs to ADDUCIN protein family (3 members ADD1, ADD2 and ADD3).

Mutations

Germinal

It has been shown that the interaction of ADD1 and ADD3 gene variants in humans is statistically associated with variation in blood pressure, suggesting the presence of epistatic effects among these loci.

Somatic

t(10;11)(q25;p15) 5' NUP98-ADD3 3' fusion in a T-cell acute lymphoblastic leukemia with biphenotipic characteristics (T/myeloid).

Implicated in

t(10;11)(q25;p15)

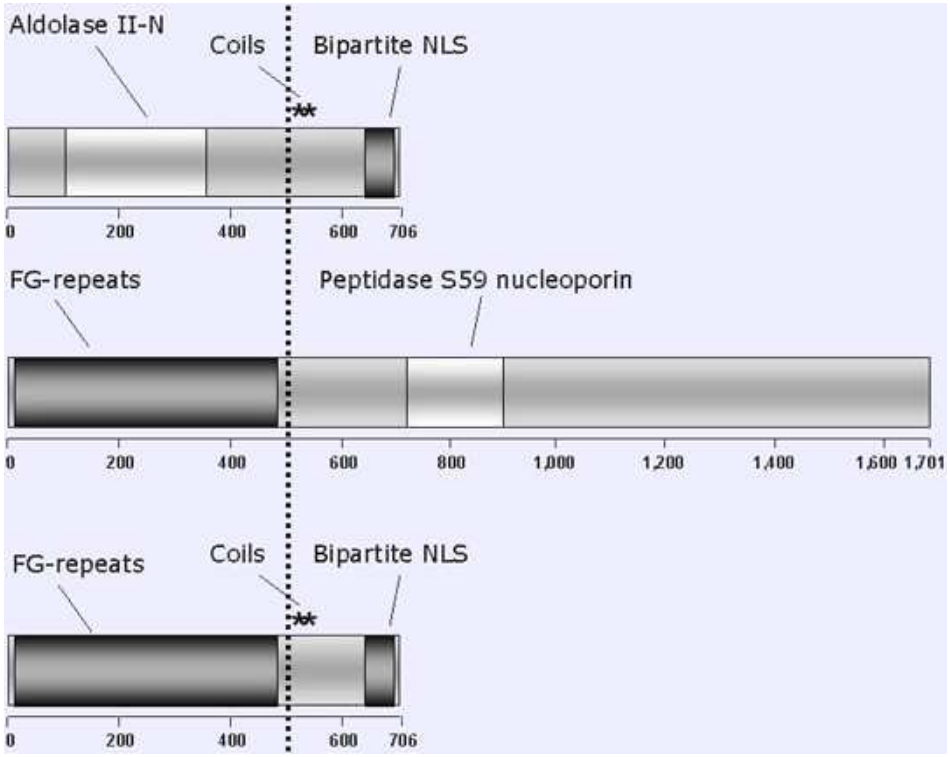
Disease
T-cell acute lymphoblastic leukemia with biphenotipic characteristics (T/myeloid).

Prognosis
Bad.

Cytogenetics
t(10;11)(q25;p15) (cryptic).

Hybrid/Mutated gene
5' NUP98 - ADD3 3'.

Abnormal protein
NUP98-ADD3.



Schematic representation of the fusion NUP98-ADD3 consecuence of the t(10;11)(q25;p15) in a T-cell acute lymphoblastic leukemia with biphenotipic characteristics. From up to down: ADD3, NUP98 and the putative chimeric NUP98-ADD3 structure. FG-repeats, phenilalanine-glycine repeats; bipartite NLS, bipartite nuclear localization signal. Coiled coil domains on ADD3 and NUP98-ADD3 are indicated with asterisks.

References

Katagiri T, Ozaki K, Fujiwara T, Shimizu F, Kawai A, Okuno S, Suzuki M, Nakamura Y, Takahashi E, Hirai Y. Cloning, expression and chromosome mapping of adducin-like 70 (ADDL), a human cDNA highly homologous to human erythrocyte adducin. Cytogenet Cell Genet. 1996;74(1-2):90-5

Kuhlman PA, Hughes CA, Bennett V, Fowler VM. A new function for adducin. Calcium/calmodulin-regulated capping of the barbed ends of actin filaments. J Biol Chem. 1996 Apr 5;271(14):7986-91

Citterio L, Azzani T, Duga S, Bianchi G. Genomic organization of the human gamma adducin gene. Biochem Biophys Res Commun. 1999 Dec 9;266(1):110-4

Matsuoka Y, Li X, Bennett V. Adducin: structure, function and regulation. Cell Mol Life Sci. 2000 Jun;57(6):884-95

Yang H, Francis SC, Sellers K, DeBarros M, Sun C, Sumners C, Ferrario CM, Katovich MJ, Muro AF, Raizada MK. Hypertension-linked decrease in the expression of brain gamma-adducin. Circ Res. 2002 Oct 4;91(7):633-9

Lahortiga I, Vizmanos JL, Agirre X, Vázquez I, Cigudosa JC, Larrayoz MJ, Sala F, Gorosquieta A, Perez-Equiza K, Calasanz MJ, Odero MD. NUP98 is fused to adducin 3 in a patient with T-cell acute lymphoblastic leukemia and myeloid markers, with a new translocation t(10;11)(q25;p15). Cancer Res. 2003 Jun 15;63(12):3079-83

Yang H, Reaves PY, Katovich MJ, Raizada MK. Decrease in hypothalamic gamma adducin in rat models of hypertension. Hypertension. 2004 Feb;43(2):324-8

Bianchi G, Ferrari P, Staessen JA. Adducin polymorphism: detection and impact on hypertension and related disorders. Hypertension. 2005 Mar;45(3):331-40

Lanzani C, Citterio L, Jankaricova M, Sciarrone MT, Barlassina C, Fattori S, Messaggio E, Serio CD, Zagato L, Cusi D, Hamlyn JM, Stella A, Bianchi G, Manunta P. Role of the adducin family genes in human essential hypertension. J Hypertens. 2005 Mar;23(3):543-9

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