

ALOX15 (Arachidonate 15-Lipoxygenase)

Identity

Note Arachidonate 15-Lipoxygenase (15-LOX-1) is one of several LOX isoforms that oxygenates polyunsaturated fatty acids as well as complex substrates such as biomembranes. Its expression is associated with the development of inflammatory diseases such as atherosclerosis, asthma, cancer and osteoporosis.

Other names

15-LOX

EC 1.13.11.33

arachidonate omega 6-lipoxygenase

LOG15

Hugo

[ALOX15](#)

Location

17p13.3

Genes flanking ALOX15 in centromere to telomere direction on 17p13 are:

Local_order

MYBBP1A 17p13.3 MYB binding protein (P160) 1a.

GGT6 17p13.2 homolog of gamma-glutamyltransferase 6

LOC124974 17p13.2, thioredoxin 1 pseudogene 4.

SMTNL2 17p13.2 smoothelin-like 2

ALOX15 17p13.2 arachidonate 15-lipoxygenase (Homo sapiens)

PELP1 17p13.2 proline, glutamic acid and leucine rich protein 1.

ARRB2 17p13 arrestin, beta 2.

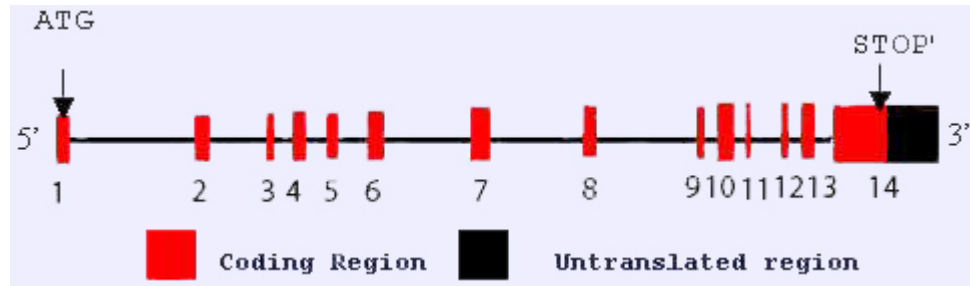
Note

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DNA/RNA

Note

With the exception of [ALOX5](#), all human LOX genes, including ALOX15, are clustered on the short arm of chromosome 17 within a few megabases of each other. ALOX12, which has 86% sequence homology to ALOX15 is in closest proximity (17p13.1). Since chromosome 17 is known for gene duplications, the multiple LOX genes on the same chromosome may be as a result of such duplications.



ALOX15Fig. Diagram of the ALOX15 gene. Exons are represented by red boxes (in scale) untranscribed sequences in black, with exon numbers on the bottom. The arrows show the ATG and the stop codons respectively.

Description ALOX15 gene spans a region of 10.7 kilo bases. and has 14 exons, the sizes being 149, 202, 82, 123, 104, 161, 144, 210, 87, 170, 122, 101, 108 and 859 bps.

Transcription ALOX15 mRNA has 2702 bps.

TH2 cytokines IL-4 ID: 40960 and IL-13 have been shown to transcriptionally upregulate 15-LOX-1 expression via phosphorylation of Signal Transducer and Activator of transcription (STAT) proteins, particularly [STAT-1](#), [STAT-3](#) and STAT-6 and their translocation to the nucleus. Acetylation of histones, which block STAT6 binding at the 15-LOX-1 promoter if they are present as nonacetylated proteins, enables promoter binding of phosphorylated and acetylated STAT6, which in turn may lead to transcriptional activation of the 15-LOX gene.

TRANSCRIPTION NSAIDS have been reported to upregulate 15-LOX-1 expression through GATA-6. Ku70/

ALOX15 mRNA is expressed in bone marrow, spleen, thymus, spinal cord, heart, skeletal muscle, liver, prostate, kidney and lung.

Pseudogene The arachidonate 15-lipoxygenase pseudogene (ALOX15P) is located on 17p13.1.

Protein

Note Two different 15-Lipoxygenases exist, 15-LOX-1 (reticulocyte type) and 15-LOX-2 (epidermis type), differentiated by their tissue expression and a 40% homology at the amino acid level. 15-LOX-1 preferentially oxygenates linoleic acid into 13(S)-hydroxyoctadecadienoic acid (13(S)-HPODE) whereas 15-LOX-2 preferentially metabolizes arachidonic acid (AA) to 15S- hydroperoxyeicosatetraenoic acid (15-HETE) with poor activity with linoleic acid (LA).

Description 15-LOX-1 protein consists of 661 amino acids and is 74.7 kDa. It contains 1 gram atom of non-haem non-sulphur bound iron per mole of the enzyme. Conserved domain search, the presence of a polycystin/lipoxygenase/alpha-toxin (PLAT) domain in the 15-LOX-1 protein allows it access and enables it to catalyze enzymatic lipid peroxidation in complex biological structures via direct dioxygenation of

phospholipids and cholesterol esters of biomembranes and plasma lipoproteins. The membrane binding domain of the rabbit reticulocyte 15-LOX are determined by a concerted action of the N-terminal beta-barrel and the C-terminal catalytic domain.

- Expression** 15-LOX-1 was first purified in rabbit reticulocytes and was subsequently found to be specifically expressed or induced in mast cells, eosinophils, activated monocytes or dendritic cells, and bronchial epithelial cells.
- Localisation** Located in the cytoplasm.
- Function** 15-LOX-1 is a member of the inflammatory leukotriene biosynthesis pathway where, in presence of molecular oxygen, it converts arachidonic acid to(15-HETE). Also acts on C-12 of arachidonate forming products (12-HETE) at a ratio of 12:1 (15-HETE:12-HETE). Preferentially converts linoleic acid to 13(S)-HODE.
- Homology** C. familiaris LOC4894581 similar to Arachidonate 15-lipoxygenase; R. norvegicus: Alox15 arachidonate 12-lipoxygenase; M. musculus: Alox15 arachidonate 15-lipoxygenase (12/15LOX); A. thaliana: F12B7.11, F12B7_111 iron ion binding / lipoxygenase;

Mutations

- Note** No mutations have been reported for ALOX15 that cause congenital anomalies. Single nucleotide polymorphism (SNP) studies have revealed that a C-to-T base exchange (-292C/T) enhances the transcriptional activity of the ALOX15 promoter in macrophages through the generation of a novel [SPI1](#) transcription factor binding site. In addition, a G to A base exchange (-5229G/A) in the ALOX15 promoter region has been associated with low bone mineral density.

Implicated in

- Entity** Prostate cancer
- Note** Genechip study of the mRNA levels of key enzymes involved in the LA and AA pathways in 18 human donor (normal) prostates compared to 60 prostate tumours showed a lower level of 15-LOX-1 expression (the key enzyme in the LA pathway) in contrast to a higher 15-lipoxygenase-2 expression in donor (normal) prostates. On the other hand, significantly high levels of 15-LOX-1 and low levels of 15-LOX-2/ALOX15B were observed in prostate carcinoma tissues.
- Entity** Colorectal cancer
- Note** The role of 15-LOX-1 in colorectal cancer is controversial with some researchers claiming a mitogenic role through up-regulation of the EGF signaling pathway as well as activation of ERK and down regulation of anti-inflammatory PPAR-gamma transcriptional activity. Its upregulation by mutant [TP53](#) has been reported. On the other hand, in recent years others have shown that 15-LOX-1 expression is reduced in colorectal cancer and implicated 13(S)-HPODE in the pro-apoptotic functions of 15-LOX-1. 15-LOX-1 expression was shown to be down-regulated in colorectal adenomas (compared with non neoplastic epithelial mucosa) in 87% (13 of 15) of patients with familial adenomatous polyposis

resulting in an escape from apoptosis. Ectopic restoration of 15-LOX-1 expression re-established apoptosis in Caco-2 colon cancer cells. A proapoptotic function ascribed to 15-LOX-1 and 15-LOX-2 in colon cancer is said to be through the activation of the anti-tumorigenic PPAR-gamma and down-regulation of the pro-tumorigenic PPAR-delta/beta. In addition, the apoptotic functions of NSAIDS are reported to be via an upregulation of 15-LOX-1.

Entity [Breast cancer](#)

Note An immunoblot analysis of metastatic human breast carcinoma cells with antibodies to 15-LOX-1 and 15-LOX-2 indicated that it is the 15(S)-LOX-2 isoform that generates 15-HETE and activates specific growth factor receptor-related signalling pathways, thereby initiating signal transduction events resulting in enhanced cell adhesion to the extracellular matrix. However, a second study indicated that both 15-LOX-2 and 15-LOX-1 were expressed at significantly lower levels in metastatic tumours and in patients who died of breast cancer related causes. This reduction is correlated with the disease progression of breast cancer and a poor clinical outcome.

Entity Atherosclerosis

Disease Atherosclerosis is a chronic proliferative disease of the arterial wall that is associated with aberrant immune reactions. A proatherogenic activity of 12/15LOX via oxidation of low density lipoproteins and formation of foam cells in various rodent atherosclerosis models has been shown. A similar extrapolation to humans has not been convincingly proven, particularly since significantly lower expression of 15-LOX-1 was detected in diseased and normal human arteries when compared to 5-LOX.

Entity Asthma

Disease Patients with severe asthma with persistent airway eosinophils have been shown to manifest high levels of 15(S)-HETE in bronchoalveolar lavage (BALF), which may be associated with airway fibrosis. In addition, IL-4-induced apoptosis via upregulation of 15-LOX-1 and PPAR-gamma may contribute to severe loss of alveolar structures and infiltration of eosinophils, mononuclear phagocytes, etc., into the lung tissue of chronic asthma patients.

External links

Nomenclature

[Hugo](#)

[ALOX15](#)

[GDB](#)

[ALOX15](#)

[Entrez_Gene](#)

[ALOX15 246](#) arachidonate 15-lipoxygenase

Cards

Atlas	ALOX15ID42986ch17p13
GeneCards	ALOX15
Ensembl	ALOX15
Genatlas	ALOX15
GeneLynx	ALOX15
eGenome	ALOX15
euGene	246

Genomic and cartography

GoldenPath	ALOX15 - 17p13.3 chr17:4480970-4491709 - 17p13.2 (hg18-Mar_2006)
Ensembl	ALOX15 - 17p13.2 [CytoView]
NCBI	Genes Cyto Gene Seq [Map View - NCBI]
OMIM	Disease map [OMIM]
HomoloGene	ALOX15

Gene and transcription

Genbank	BC029032 [ENTREZ]
Genbank	M23892 [ENTREZ]
Genbank	M95923 [ENTREZ]
Genbank	XM_001131480 [ENTREZ]
Genbank	XM_001131480 [ENTREZ]
RefSeq	NM_001140 [SRS] NM_001140 [ENTREZ]
RefSeq	NC_000017 [SRS] NC_000017 [ENTREZ]
RefSeq	NT_010718 [SRS] NT_010718 [ENTREZ]
AceView	ALOX15 AceView - NCBI
TRASER	ALOX15 Traser - Stanford
Unigene	Hs.73809 [SRS] Hs.73809 [NCBI] HS73809 [spliceNest]

Protein : pattern, domain, 3D structure

SwissProt	P16050 [SRS] P16050 [EXPASY] P16050 [INTERPRO]
Prosit	PS00711 LIPOXYGENASE_1 [SRS] PS00711 LIPOXYGENASE_1 [Expasy]
Prosit	PS00081 LIPOXYGENASE_2 [SRS] PS00081 LIPOXYGENASE_2 [Expasy]
Prosit	PS50095 PLAT [SRS] PS50095 PLAT [Expasy]
Interpro	IPR008976 Lipase LipOase [SRS] IPR008976 Lipase LipOase [EBI]
Interpro	IPR000907 LipOase [SRS] IPR000907 LipOase [EBI]
Interpro	IPR001024 LipOase LH2 [SRS] IPR001024 LipOase LH2 [EBI]
Interpro	IPR001885 Mammal lipOase [SRS] IPR001885

	Mammal lipOase [EBI]
CluSTr	P16050
Pfam	PF00305 Lipoygenase [SRS] PF00305 Lipoygenase [Sanger] pfam00305 [NCBI-CDD]
Pfam	PF01477 PLAT [SRS] PF01477 PLAT [Sanger] pfam01477 [NCBI-CDD]
Smart Blocks	SM00308 LH2 [EMBL]
HPRD	P16050
Protein Interaction databases	
DIP	P16050
IntAct	P16050
Polymorphism : SNP, mutations, diseases	
OMIM	152392 [map]
GENECLINICS	152392
SNP	ALOX15 [dbSNP-NCBI]
SNP	NM_001140 [SNP-NCI]
SNP	ALOX15 [GeneSNPs - Utah] ALOX15 [HGBASE - SRS]
HAPMAP	ALOX15 [HAPMAP]
General knowledge	
Family Browser	ALOX15 [UCSC Family Browser]
SOURCE	NM_001140
SMD	Hs.73809
SAGE	Hs.73809
Enzyme	1.13.11.33 [Enzyme-SRS] 1.13.11.33 [Brenda-SRS] 1.13.11.33 [KEGG] 1.13.11.33 [WIT]
Amigo	iron ion binding [Amigo] iron ion binding [EGO-EBI]
Amigo	plasma membrane [Amigo] plasma membrane [EGO-EBI]
Amigo	electron transport [Amigo] electron transport [EGO-EBI]
Amigo	lipid metabolism [Amigo] lipid metabolism [EGO-EBI]
Amigo	inflammatory response [Amigo] inflammatory response [EGO-EBI]
Amigo	lipoxygenase activity [Amigo] lipoxygenase activity [EGO-EBI]
Amigo	lipoxygenase activity [Amigo] lipoxygenase activity [EGO-EBI]
Amigo	oxidoreductase activity [Amigo] oxidoreductase activity [EGO-EBI]
Amigo	leukotriene biosynthesis [Amigo] leukotriene biosynthesis [EGO-EBI]
Amigo	metal ion binding [Amigo] metal ion binding [EGO-EBI]
Amigo	arachidonate 15-lipoxygenase activity [Amigo] arachidonate 15-lipoxygenase activity [EGO-EBI]

[KEGG](#) [Prostaglandin and Leukotriene Metabolism](#)

[PubGene](#) [ALOX15](#)

Other databases

Probes

[Probe](#) [ALOX15 Related clones \(RZPD - Berlin\)](#)

PubMed

[PubMed](#) [44 Pubmed reference\(s\) in LocusLink](#)

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Contributor(s)

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