

Lipoxygenases (E.C. 1.13.11.-)

Overview: The lipoxygenases (LOXs) are a structurally related family (ENSFM00250000000705) of non-heme iron dioxygenases that function in the production, and in some cases metabolism, of fatty acid hydroperoxides. In humans there are five LOXs, the 5S-(arachidonate : oxygen 5-oxidoreductase), 12R-(arachidonate 12-lipoxygenase, 12R-type), 12S-(arachidonate : oxygen 12-oxidoreductase), and two distinct 15S-(arachidonate : oxygen 15-oxidoreductase) LOXs that oxygenate arachidonic acid in different positions along the carbon chain and form the corresponding 5S-, 12S-, 12R-, or 15S-hydroperoxides, respectively. The sixth LOX member, epidermal lipoxygenase 3 (E-LOX), metabolises the product from the 12R-lipoxygenase (12R-HPETE) to a specific epoxyalcohol compound (Yu *et al.*, 2003). Some general LOX inhibitors are NDGA and esculetin.

Nomenclature	5-LOX	12R-LOX	12S-LOX
E.C.	1.13.11.34	1.13.11.-	1.13.11.31
Other names	ALOX5	ALOX12B, epidermis-type lipoxygenase 12	ALOX12, platelet-type 12-lipoxygenase
Ensembl ID	ENSG00000012779	ENSG00000179477	ENSG00000108839
Substrates	Arachidonic acid	Methyl arachidonate	Arachidonic acid
Activators	FLAP	–	–
Selective inhibitors	Zileuton, CJ13610 (Fischer <i>et al.</i> , 2004)	–	–

The crystal structure of FLAP has been described (Ferguson *et al.*, 2007).

Nomenclature	15-LOX-1	15-LOX-2	E-LOX
E.C.	1.13.11.33	1.13.11.33	1.13.11.-
Other names	ALOX15, arachidonate ω -6 lipoxygenase	ALOX15B	Epidermis type LOX 3
Ensembl ID	ENSG00000161905	ENSG00000179593	ENSG00000179148
Substrates	Linoleic acid, arachidonic acid	Arachidonic acid	12R-HPETE

An 8-LOX (EC 1.13.11.40, arachidonate : oxygen 8-oxidoreductase) may be the mouse orthologue of 15-LOX-2 (Furstenberger *et al.*, 2002). Zileuton and caffeic acid are used as 5-lipoxygenase inhibitors, while baicalein and CDC are 12-lipoxygenase inhibitors. The specificity of these inhibitors has not been rigorously assessed with all LOX forms: baicalein, along with other flavonoids, such as fisetin and luteolin, also inhibits 15-LOX-1 (Sadik *et al.*, 2003).

Abbreviations: CDC, cinnamyl-3,4-dihydroxy- α -cyanocinnamate; **CJ13610**, 1-carboxamido-1-(3-S-[4-[2-methylimidazole]-thiophenyl])-4-cyclopentylether; **esculetin**, 6,7-dihydroxycoumarin; **12R-HPETE**, 12R-hydroperoxyeicosatetraenoic acid; **FLAP**, 5-lipoxygenase-activating protein, also known as MK-886-binding protein (ENSG00000132965); **NDGA**, nordihydroguaiaretic acid

Further Reading

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