IUPHAR/BPS Guide to Pharmacology CITE
https://doi.org/10.2218/gtopdb/F35/2025.3

Leukotriene receptors in GtoPdb v.2025.3

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Abstract

The leukotriene receptors (**nomenclature as agreed by the NC-IUPHAR subcommittee on Leukotriene Receptors [36, 39]**) are activated by the endogenous ligands leukotrienes (LT), synthesized from lipoxygenase metabolism of arachidonic acid. The human BLT1 receptor is the high affinity LTB_4 receptor whereas the BLT2 receptor in addition to being a low-affinity LTB_4 receptor also binds several other lipoxygenase-products, such as 12S-HETE, 12S-HPETE, 15S-HETE, and the thromboxane synthase product 12-hydroxyheptadecatrienoic acid. The BLT receptors mediate chemotaxis and immunomodulation in several leukocyte populations and are in addition expressed on non-myeloid cells, such as vascular smooth muscle and endothelial cells. In addition to BLT receptors, LTB_4 has been reported to bind to the peroxisome proliferator activated receptor (PPAR) α [206] and the vanilloid TRPV1 ligand-gated nonselective cation channel [228]. The crystal structure of the BLT1 receptor was initially determined in complex with selective antagonists [145, 236] and extended to the cryo-electron microscopy structure of LTB_4-bound human BLT1 receptor at 2.91 Å resolution [402]. The receptors for the cysteinyl-leukotrienes (*i.e.* LTC_4, LTD_4 and LTE_4) are termed CysLT1 and CysLT2 and exhibit distinct expression patterns in human tissues, mediating for example smooth muscle cell contraction, regulation of vascular permeability, and leukocyte activation. The crystal structures of both receptors have been solved; CysLT1 in complex with zafirlukast and pranlukast [208] and CysLT2 in complex with three dual CysLT1/CysLT2 antagonists [126]. There is also evidence in the literature for additional CysLT receptor subtypes, derived from functional *in vitro* studies, radioligand binding and in mice lacking both CysLT1 and CysLT2 receptors [39]. Cysteinyl-leukotrienes have also been suggested to signal through the P2Y12 receptor [101, 256, 286], GPR17 [60] and the oxoglutarate receptor OXGR1 (previously referred to as GPR99) [177].

Contents

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