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Leukotriene receptors in GtoPdb v.2023.1

Magnus Bäck[1], Charles Brink[2], Nan Chiang[3], Sven-Erik Dahlén[1], Gordon Dent[4], Jeffrey Drazen[5], Jilly F. Evans[6], Douglas W. P. Hay[7], Motonao Nakamura[8], William Powell[9], Joshua Rokach[10], G. Enrico Rovati[11], Charles N. Serhan[5], Takao Shimizu[8], Mohib Uddin[12] and Takehiko Yokomizo[13]

1. Karolinska Institutet, Sweden
2. Hopital Marie Lannelongue, France
3. Brigham and Women's Hospital, USA
4. Keele University, UK
5. Harvard University, USA
6. PharmAkea, USA
7. GlaxoSmithKline, USA
8. University of Tokyo, Japan
9. McGill University, Canada
10. Florida Institute of Technology, USA
11. University of Milan, Italy
12. AstraZeneca, Sweden
13. Juntendo University, Japan

Abstract

The leukotriene receptors (**nomenclature as agreed by the NC-IUPHAR subcommittee on Leukotriene Receptors [35, 38]**) are activated by the endogenous ligands leukotrienes (LT), synthesized from lipoxygenase metabolism of arachidonic acid. The human BLT_1 receptor is the high affinity LTB_4 receptor whereas the BLT_2 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 [201] and the vanilloid TRPV1 ligand-gated nonselective cation channel [223]. The crystal structure of the BLT_1 receptor was initially determined in complex with selective antagonists [141, 231] and has recently been extended to the cryo-electron microscopy structure of LTB_4-bound human BLT_1 receptor at 2.91 Å resolution [389]. The receptors for the cysteinyl-leukotrienes (*i.e.* LTC_4, LTD_4 and LTE_4) are termed $CysLT_1$ and $CysLT_2$ and exhibit distinct expression patterns in human tissues, mediating for example smooth muscle cell contraction, regulation of vascular permeability, and leukocyte activation. Quite recently, the the crystal structures of both receptors have been solved, the $CysLT_1$ in complex with zafirlukast and pranlukast [203] and the $CysLT_2$ in complex with three dual $CysLT_1$/$CysLT_2$ antagonists [122]. 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 $CysLT_1$ and $CysLT_2$ receptors [38]. Cysteinyl-leukotrienes have also been suggested to signal through the $P2Y_{12}$ receptor [99, 251, 280], GPR17 [60] and GPR99 [173].

Contents

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- $CysLT_2$ receptor
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- OXE receptor
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- FPR2/ALX
  https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=223

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