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Lysophospholipid (LPA) receptors (version 2020.5) in the IUPHAR/BPS Guide to Pharmacology Database

Victoria Blaho[1], Jerold Chun[1], Danielle Jones[1], Deepa Jonnalagadda[1], Yasuyuki Kihara[1], Wouter Moolenaar[2], Tony Ngo[1], Manisha Ray[1] and Valerie Tan[1]

1. Sanford Burnham Prebys Medical Discovery Institute, USA
2. Netherlands Cancer Institute, The Netherlands

Abstract

Lysophosphatidic acid (LPA) receptors (**nomenclature as agreed by the NC-IUPHAR Subcommittee on Lysophospholipid Receptors [54, 18, 80, 125]**) are activated by the endogenous phospholipid LPA. The first receptor, LPA_1, was identified as *ventricular zone gene-1* (*vzg-1*) [39], leading to deorphanisation of members of the endothelial differentiation gene (*edg*) family as other LPA receptors along with sphingosine 1-phosphate (S1P) receptors. Additional LPA receptor GPCRs were later identified. Gene names have been codified as *LPAR1*, *etc*. to reflect the receptor function of proteins. The crystal structure of LPA_1 was solved and demonstrates extracellular LPA access to the binding pocket, consistent with proposed delivery *via* autotaxin [12]. These studies have also implicated cross-talk with endocannabinoids *via* phosphorylated intermediates that can also activate these receptors. The identified receptors can account for most, although not all, LPA-induced phenomena in the literature, indicating that a majority of LPA-dependent phenomena are receptor-mediated. Binding affinities of unlabeled, natural LPA and AEAp to LPA_1 were measured using backscattering interferometry (pK_d = 9) [81, 102]. Binding affinities were 77-fold lower than than values obtained using radioactivity [124]. Targeted deletion of LPA receptors has clarified signalling pathways and identified physiological and pathophysiological roles. Independent validation by multiple groups has been reported in the peer-reviewed literature for all six LPA receptors described in the tables, including further validation using a distinct read-out *via* a novel TGFα "shedding" assay [47]. LPA LPA has been proposed to be a ligand for GPCR35 [92], supported by a recent study revealing that LPA modulates macrophage function through GPR35 [53]. However CXCL17 is reported to be a ligand for GPR35/CXCR8 [74]. Moreover, LPA has also been described as an agonist for the transient receptor potential (Trp) ion channel TRPV1 [85] and TRPA1 [57]. All of these proposed non-GPCR receptor identities require confirmation and are not currently recognized as *bona fide* LPA receptors.

Contents

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LPA_2 receptor

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LPA_6 receptor

https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=163

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