

Lysophospholipid (LPA) receptors (version 2019.4) in the IUPHAR/BPS Guide to Pharmacology Database

Victoria Blaho¹, Jerold Chun¹, Aaron Frantz¹, Timothy Hla², Danielle Jones³, Deepa Jonnalagadda¹, Yasuyuki Kihara¹, Hirotaka Mizuno¹, Wouter Moolenaar⁴, Chido Mpamhanga⁵, Sarah Spiegel⁶, Valerie Tan¹ and Yun C. Yung¹

1. Sanford Burnham Prebys Medical Discovery Institute, USA
2. Cornell University, USA
3. Scripps Research Institute, USA
4. Netherlands Cancer Institute, The Netherlands
5. LifeArc, UK
6. Virginia Commonwealth University, USA

Abstract

Lysophosphatidic acid (LPA) receptors (**nomenclature as agreed by the NC-IUPHAR Subcommittee on Lysophospholipid Receptors [50, 18]**) are activated by the endogenous phospholipid LPA. The first receptor, LPA₁, was identified as *ventricular zone gene-1 (vzg-1)* [38], 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 LPA₁ 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 LPA₁ were measured using backscattering interferometry ($pK_d = 9$) [73]. Binding affinities were 77-fold lower than than values obtained using radioactivity [111]. 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 TGF α "shedding" assay [45]. LPA has also been described as an agonist for the transient receptor potential (Trp) ion channel TRPV1 [76] and TRPA1 [53]. LPA was originally proposed to be a ligand for

View metadata, citation and similar papers at CORE.  receptor identities require confirmation and are not currently recognized as bona fide LPA receptors.

Contents

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Receptors

LPA₁ receptor

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LPA₂ receptor

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LPA₃ receptor

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LPA₆ receptor

<http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=163>

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