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Lysophospholipid (LPA) receptors in GtoPdb v.2025.3

Victoria Blaho[1], Jerold Chun[1], Deron R. Herr[2], Yasuyuki Kihara[1], Tony Ngo[1] and Valerie P. Tan[1]

1. Sanford Burnham Prebys Medical Discovery Institute, USA
2. Indiana State University Foundation, USA

Abstract

Lysophosphatidic acid (LPA) receptors (**nomenclature as agreed by the NC-IUPHAR Subcommittee on Lysophospholipid Receptors [67, 27, 96, 151]**) are activated by the endogenous phospholipid LPA. The first receptor, LPA_1, was identified as *ventricular zone gene-1* (*vzg-1*) [52], This discovery represented the beginning of the de-orphanisation of members of the endothelial differentiation gene (edg) family, as other LPA and sphingosine 1-phosphate (S1P) receptors were found. Five additional LPA receptors ($LPA_{2,3,4,5,6}$) have since been identified [96] and their gene nomenclature codified for human *LPAR1, LPAR2, etc*. (HUGO Gene Nomenclature Committee, HGNC) and *Lpar1, Lpar2, etc*. for mice (Mouse Genome Informatics Database, MGI) to reflect species and receptor function of their corresponding proteins. The high-resolution structures of LPA_1 [3, 20, 86, 4] and LPA_6 [31, 135] determined by both X-ray crystallography and cryo-electron microscopy, are solved and indicate that LPA accesses the extracellular binding pocket, consistent with its proposed delivery via autotaxin [20]. These studies have also implicated crosstalk with endocannabinoids *via* phosphorylated intermediates that can also activate these receptors. The binding affinities to LPA_1 of unlabeled, natural LPA and anandamide phosphate (AEAp) were measured using backscattering interferometry (pK_d = 9) [97, 121]. Utilization of this method indicated affinities that were 77-fold lower than when measured using radioactivity-based protocols [150]. Targeted deletion of LPA receptors has clarified signalling pathways and identified physiological and pathophysiological roles. admilparant (BMS-986278) [25], a selective LPA_1 receptor antagonist, is currently in Phase III trials for pulmonary fibrosis. Other LPA_1-targeting drugs such as BMS-986020 were discontinued due to hepatotoxicity [110], while preclinical candidates like PIPE 791 [119] are being explored for neurological and fibrotic diseases. Multiple groups have independently published validation of all six LPA receptors described in these tables, and further validation was achieved using a distinct read-out *via* a novel TGFα "shedding" assay [60]. Moreover, LPA has also been described as an agonist for the transient receptor potential (Trp) ion channels TRPV1 [101] and TRPA1 [70]. 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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References

1. Acton S, O'Donnell MM, Periyasamy K, Dixit B, Eishingdrelo H, Hill C, Paul Ross R and Chesnel L. (2024) LPA3 agonist-producing Bacillus velezensis ADS024 is efficacious in multiple neuroinflammatory disease models. *Brain Behav Immun* **121**: 384-402 [PMID:39147172]
2. Aikawa S, Kano K, Inoue A and Aoki J. (2017) Proliferation of mouse endometrial stromal cells in culture is highly sensitive to lysophosphatidic acid signaling. *Biochem Biophys Res Commun* **484**: 202-208 [PMID:28073697]
3. Akasaka H, Sano FK, Shihoya W and Nureki O. (2024) Structural mechanisms of potent lysophosphatidic acid receptor 1 activation by nonlipid basic agonists. *Commun Biol* **7**: 1444 [PMID:39506093]
4. Akasaka H, Tanaka T, Sano FK, Matsuzaki Y, Shihoya W and Nureki O. (2022) Structure of the active G_i-coupled human lysophosphatidic acid receptor 1 complexed with a potent agonist. *Nat Commun* **13**: 5417 [PMID:36109516]
5. Alioli CA, Demesmay L, Laurencin-Dalacieux S, Beton N, Farlay D, Follet H, Saber A, Duboeuf F, Chun J and Rivera R *et al.*. (2020) Expression of the type 1 lysophosphatidic acid receptor in osteoblastic cell lineage controls both bone mineralization and osteocyte specification. *Biochim Biophys Acta Mol Cell Biol Lipids* **1865**: 158715 [PMID:32330664]
6. Allard J, Barrón S, Diaz J, Lubetzki C, Zalc B, Schwartz JC and Sokoloff P. (1998) A rat G protein-coupled receptor selectively expressed in myelin-forming cells. *Eur J Neurosci* **10**: 1045-53 [PMID:9753172]
7. Amisten S, Braun OO, Bengtsson A and Erlinge D. (2008) Gene expression profiling for the identification of G-protein coupled receptors in human platelets. *Thromb Res* **122**: 47-57 [PMID:17920662]
8. An S, Bleu T, Hallmark OG and Goetzl EJ. (1998) Characterization of a novel subtype of human G protein-coupled receptor for lysophosphatidic acid. *J Biol Chem* **273**: 7906-10 [PMID:9525886]
9. Azeem Z, Jelani M, Naz G, Tariq M, Wasif N, Kamran-Ul-Hassan Naqvi S, Ayub M, Yasinzai M, Amin-Ud-Din M and Wali A *et al.*. (2008) Novel mutations in G protein-coupled receptor gene (P2RY5) in families with autosomal recessive hypotrichosis (LAH3). *Hum Genet* **123**: 515-9 [PMID:18461368]
10. Azhar A, Tariq M, Baig SM, Dahl N and Klar J. (2012) A novel mutation in lysophosphatidic acid receptor 6 gene in autosomal recessive hypotrichosis and evidence for a founder effect. *Eur J Dermatol* **22**: 464-6 [PMID:22531990]
11. Bai R, Pei J, Pei S, Cong X, Chun J, Wang F and Chen X. (2023) LPA_2 Alleviates Septic Acute Lung Injury via Protective Endothelial Barrier Function Through Activation of PLC-PKC-FAK. *J Inflamm Res* **16**: 5095-5109 [PMID:38026263]
12. Balogh A, Shimizu Y, Lee SC, Norman DD, Gangwar R, Bavaria M, Moon C, Shukla P, Rao R and Ray R *et al.*. (2015) The autotaxin-LPA2 GPCR axis is modulated by γ-irradiation and facilitates DNA damage repair. *Cell Signal* **27**: 1751-62 [PMID:26027517]
13. Bandoh K, Aoki J, Hosono H, Kobayashi S, Kobayashi T, Murakami-Murofushi K, Tsujimoto M, Arai H and Inoue K. (1999) Molecular cloning and characterization of a novel human G-protein-coupled receptor, EDG7, for lysophosphatidic acid. *J Biol Chem* **274**: 27776-85 [PMID:10488122]
14. Bandoh K, Aoki J, Taira A, Tsujimoto M, Arai H and Inoue K. (2000) Lysophosphatidic acid (LPA) receptors of the EDG family are differentially activated by LPA species. Structure-activity

relationship of cloned LPA receptors. *FEBS Lett* **478**: 159-65 [PMID:10922489]
15. Beck HP, Kohn T, Rubenstein S, Hedberg C, Schwandner R, Hasslinger K, Dai K, Li C, Liang L and Wesche H *et al.*. (2008) Discovery of potent LPA2 (EDG4) antagonists as potential anticancer agents. *Bioorg Med Chem Lett* **18**: 1037-41 [PMID:18178086]
16. Buneman P, Christie G, Davies JA, Dimitrellou R, Harding SD, Pawson AJ, Sharman JL and Wu Y. (2020) Why data citation isn't working, and what to do about it *Database* **2020** [PMID:32367113]
17. Chen WM, Chiang JC, Lin YC, Lin YN, Chuang PY, Chang YC, Chen CC, Wu KY, Hsieh JC and Chen SK *et al.*. (2020) Lysophosphatidic acid receptor LPA_3 prevents oxidative stress and cellular senescence in Hutchinson-Gilford progeria syndrome. *Aging Cell* **19**: e13064 [PMID:31714004]
18. Cheng PTW, Kaltenbach 3rd RF, Zhang H, Shi J, Tao S, Li J, Kennedy LJ, Walker SJ, Shi Y and Wang Y *et al.*. (2021) Discovery of an Oxycyclohexyl Acid Lysophosphatidic Acid Receptor 1 (LPA_1) Antagonist BMS-986278 for the Treatment of Pulmonary Fibrotic Diseases. *J Med Chem* **64**: 15549-15581 [PMID:34709814]
19. Choi JW, Herr DR, Noguchi K, Yung YC, Lee CW, Mutoh T, Lin ME, Teo ST, Park KE, Mosley AN and Chun J. (2010) LPA receptors: subtypes and biological actions. *Annu Rev Pharmacol Toxicol* **50**: 157-86 [PMID:20055701]
20. Chrencik JE, Roth CB, Terakado M, Kurata H, Omi R, Kihara Y, Warshaviak D, Nakade S, Asmar-Rovira G and Mileni M *et al.*. (2015) Crystal Structure of Antagonist Bound Human Lysophosphatidic Acid Receptor 1. *Cell* **161**: 1633-43 [PMID:26091040]
21. Chun J, Hla T, Lynch KR, Spiegel S and Moolenaar WH. (2010) International Union of Basic and Clinical Pharmacology. LXXVIII. Lysophospholipid receptor nomenclature. *Pharmacol Rev* **62**: 579-87 [PMID:21079037]
22. Contos JJ and Chun J. (1998) Complete cDNA sequence, genomic structure, and chromosomal localization of the LPA receptor gene, lpA1/vzg-1/Gpcr26. *Genomics* **51**: 364-78 [PMID:9721207]
23. Contos JJ and Chun J. (2000) Genomic characterization of the lysophosphatidic acid receptor gene, lp(A2)/Edg4, and identification of a frameshift mutation in a previously characterized cDNA. *Genomics* **64**: 155-69 [PMID:10729222]
24. Contos JJ, Fukushima N, Weiner JA, Kaushal D and Chun J. (2000) Requirement for the lpA1 lysophosphatidic acid receptor gene in normal suckling behavior. *Proc Natl Acad Sci USA* **97**: 13384-9 [PMID:11087877]
25. Corte TJ, Lancaster L, Swigris JJ, Maher TM, Goldin JG, Palmer SM, Suda T, Ogura T, Minnich A and Zhan X *et al.*. (2021) Phase 2 trial design of BMS-986278, a lysophosphatidic acid receptor 1 (LPA_1) antagonist, in patients with idiopathic pulmonary fibrosis (IPF) or progressive fibrotic interstitial lung disease (PF-ILD). *BMJ Open Respir Res* **8** [PMID:34969771]
26. Dancs PT, Ruisanchez É, Balogh A, Panta CR, Miklós Z, Nüsing RM, Aoki J, Chun J, Offermanns S and Tigyi G *et al.*. (2017) LPA_1 receptor-mediated thromboxane A_2 release is responsible for lysophosphatidic acid-induced vascular smooth muscle contraction. *FASEB J* **31**: 1547-1555 [PMID:28069828]
27. Davenport AP, Alexander SP, Sharman JL, Pawson AJ, Benson HE, Monaghan AE, Liew WC, Mpamhanga CP, Bonner TI and Neubig RR *et al.*. (2013) International Union of Basic and Clinical Pharmacology. LXXXVIII. G protein-coupled receptor list: recommendations for new pairings with cognate ligands. *Pharmacol Rev* **65**: 967-86 [PMID:23686350]
28. de Souza CO, Paschoal VA, Sun X, Vishvanath L, Zhang Q, Shao M, Onodera T, Chen S, Joffin N and Bueno LM *et al.*. (2022) GPR92 activation in islet macrophages controls β cell function in a diet-induced obesity model. *J Clin Invest* **132** [PMID:36066975]
29. Diao H, Aplin JD, Xiao S, Chun J, Li Z, Chen S and Ye X. (2011) Altered spatiotemporal expression of collagen types I, III, IV, and VI in Lpar3-deficient peri-implantation mouse uterus. *Biol Reprod* **84**: 255-65 [PMID:20864640]
30. Diez-Roux G, Banfi S, Sultan M, Geffers L, Anand S, Rozado D, Magen A, Canidio E, Pagani M and Peluso I *et al.*. (2011) A high-resolution anatomical atlas of the transcriptome in the mouse embryo. *PLoS Biol* **9**: e1000582 [PMID:21267068]
31. Duan Y, Xu Z, Hao B, Zhang A, Guo C and He Y. (2025) Molecular mechanism of ligand recognition and activation of lysophosphatidic acid receptor LPAR6. *Proc Natl Acad Sci U S A* **122**: e2415426122 [PMID:39847322]
32. Dubin AE, Bahnson T, Weiner JA, Fukushima N and Chun J. (1999) Lysophosphatidic acid stimulates neurotransmitter-like conductance changes that precede GABA and L-glutamate in early, presumptive cortical neuroblasts. *J Neurosci* **19**: 1371-81 [PMID:9952414]
33. Dubin AE, Herr DR and Chun J. (2010) Diversity of lysophosphatidic acid receptor-mediated intracellular calcium signaling in early cortical neurogenesis. *J Neurosci* **30**: 7300-9 [PMID:20505096]
34. Durgam GG, Virag T, Walker MD, Tsukahara R, Yasuda S, Liliom K, van Meeteren LA, Moolenaar WH, Wilke N and Siess W *et al.*. (2005) Synthesis, structure-activity relationships, and biological evaluation of fatty alcohol phosphates as lysophosphatidic acid receptor ligands,

activators of PPARgamma, and inhibitors of autotaxin. *J Med Chem* **48**: 4919-30 [PMID:16033271]
35. Estivill-Torrús G, Llebrez-Zayas P, Matas-Rico E, Santín L, Pedraza C, De Diego I, Del Arco I, Fernández-Llebrez P, Chun J and De Fonseca FR. (2008) Absence of LPA1 signaling results in defective cortical development. *Cereb Cortex* **18**: 938-50 [PMID:17656621]
36. Fells JI, Tsukahara R, Fujiwara Y, Liu J, Perygin DH, Osborne DA, Tigyi G and Parrill AL. (2008) Identification of non-lipid LPA3 antagonists by virtual screening. *Bioorg Med Chem* **16**: 6207-17 [PMID:18467108]
37. Fells JI, Tsukahara R, Liu J, Tigyi G and Parrill AL. (2009) Structure-based drug design identifies novel LPA3 antagonists. *Bioorg Med Chem* **17**: 7457-64 [PMID:19800804]
38. Fischer DJ, Nusser N, Virag T, Yokoyama K, Wang Da, Baker DL, Bautista D, Parrill AL and Tigyi G. (2001) Short-chain phosphatidates are subtype-selective antagonists of lysophosphatidic acid receptors. *Mol Pharmacol* **60**: 776-84 [PMID:11562440]
39. Fukushima N, Ishii I, Habara Y, Allen CB and Chun J. (2002) Dual regulation of actin rearrangement through lysophosphatidic acid receptor in neuroblast cell lines: actin depolymerization by Ca(2+)-alpha-actinin and polymerization by rho. *Mol Biol Cell* **13**: 2692-705 [PMID:12181339]
40. Fukushima N, Kimura Y and Chun J. (1998) A single receptor encoded by vzg-1/lpA1/edg-2 couples to G proteins and mediates multiple cellular responses to lysophosphatidic acid. *Proc Natl Acad Sci USA* **95**: 6151-6 [PMID:9600933]
41. Fukushima N, Shano S, Moriyama R and Chun J. (2007) Lysophosphatidic acid stimulates neuronal differentiation of cortical neuroblasts through the LPA1-G(i/o) pathway. *Neurochem Int* **50**: 302-7 [PMID:17056154]
42. Fukushima N, Weiner JA and Chun J. (2000) Lysophosphatidic acid (LPA) is a novel extracellular regulator of cortical neuroblast morphology. *Dev Biol* **228**: 6-18 [PMID:11087622]
43. Fukushima N, Weiner JA, Kaushal D, Contos JJ, Rehen SK, Kingsbury MA, Kim KY and Chun J. (2002) Lysophosphatidic acid influences the morphology and motility of young, postmitotic cortical neurons. *Mol Cell Neurosci* **20**: 271-82 [PMID:12093159]
44. Garozzo R, Zuccarini M, Giuliani P, Di Liberto V, Mudò G, Caciagli F, Ciccarelli R, Ciruela F, Di Iorio P and Condorelli DF. (2022) Guanine inhibits the growth of human glioma and melanoma cell lines by interacting with GPR23. *Front Pharmacol* **13**: 970891 [PMID:36199684]
45. Gnocchi D, Kapoor S, Nitti P, Cavalluzzi MM, Lentini G, Denora N, Sabbà C and Mazzocca A. (2020) Novel lysophosphatidic acid receptor 6 antagonists inhibit hepatocellular carcinoma growth through affecting mitochondrial function. *J Mol Med (Berl)* **98**: 179-191 [PMID:31863151]
46. González-Gil I, Zian D, Vázquez-Villa H, Hernández-Torres G, Martínez RF, Khiar-Fernández N, Rivera R, Kihara Y, Devesa I and Mathivanan S *et al.*. (2020) A Novel Agonist of the Type 1 Lysophosphatidic Acid Receptor (LPA_1), UCM-05194, Shows Efficacy in Neuropathic Pain Amelioration. *J Med Chem* **63**: 2372-2390 [PMID:31790581]
47. Guillot E, Le Bail JC, Paul P, Fourgous V, Briand P, Partiseti M, Cornet B, Janiak P and Philippo C. (2020) Lysophosphatidic Acid Receptor Agonism: Discovery of Potent Nonlipid Benzofuran Ethanolamine Structures. *J Pharmacol Exp Ther* **374**: 283-294 [PMID:32409422]
48. Hama K, Aoki J, Inoue A, Endo T, Amano T, Motoki R, Kanai M, Ye X, Chun J and Matsuki N *et al.*. (2007) Embryo spacing and implantation timing are differentially regulated by LPA3-mediated lysophosphatidic acid signaling in mice. *Biol Reprod* **77**: 954-9 [PMID:17823089]
49. Hasegawa Y, Erickson JR, Goddard GJ, Yu S, Liu S, Cheng KW, Eder A, Bandoh K, Aoki J and Jarosz R *et al.*. (2003) Identification of a phosphothionate analogue of lysophosphatidic acid (LPA) as a selective agonist of the LPA3 receptor. *J Biol Chem* **278**: 11962-9 [PMID:12554733]
50. Hata E, Sasaki N, Takeda A, Tohya K, Umemoto E, Akahoshi N, Ishii S, Bando K, Abe T and Kano K *et al.*. (2016) Lysophosphatidic acid receptors LPA4 and LPA6 differentially promote lymphocyte transmigration across high endothelial venules in lymph nodes. *Int Immunol* **28**: 283-92 [PMID:26714589]
51. Heasley BH, Jarosz R, Lynch KR and Macdonald TL. (2004) Initial structure-activity relationships of lysophosphatidic acid receptor antagonists: discovery of a high-affinity LPA1/LPA3 receptor antagonist. *Bioorg Med Chem Lett* **14**: 2735-40 [PMID:15125924]
52. Hecht JH, Weiner JA, Post SR and Chun J. (1996) Ventricular zone gene-1 (vzg-1) encodes a lysophosphatidic acid receptor expressed in neurogenic regions of the developing cerebral cortex. *J Cell Biol* **135**: 1071-83 [PMID:8922387]
53. Heise CE, Santos WL, Schreihofer AM, Heasley BH, Mukhin YV, Macdonald TL and Lynch KR. (2001) Activity of 2-substituted lysophosphatidic acid (LPA) analogs at LPA receptors: discovery of a LPA1/LPA3 receptor antagonist. *Mol Pharmacol* **60**: 1173-80 [PMID:11723223]
54. Herr KJ, Herr DR, Lee CW, Noguchi K and Chun J. (2011) Stereotyped fetal brain disorganization is induced by hypoxia and requires lysophosphatidic acid receptor 1 (LPA1) signaling. *Proc Natl Acad Sci USA* **108**: 15444-9 [PMID:21878565]
55. Horev L, Saad-Edin B, Ingber A and Zlotogorski A. (2010) A novel deletion mutation in

P2RY5/LPA(6) gene cause autosomal recessive woolly hair with hypotrichosis. *J Eur Acad Dermatol Venereol* **24**: 858-9 [PMID:20015179]
56. Hu J, Oda SK, Shotts K, Donovan EE, Strauch P, Pujanauski LM, Victorino F, Al-Shami A, Fujiwara Y and Tigyi G *et al.*. (2014) Lysophosphatidic acid receptor 5 inhibits B cell antigen receptor signaling and antibody response. *J Immunol* **193**: 85-95 [PMID:24890721]
57. Igarashi H, Akahoshi N, Ohto-Nakanishi T, Yasuda D and Ishii S. (2015) The lysophosphatidic acid receptor LPA4 regulates hematopoiesis-supporting activity of bone marrow stromal cells. *Sci Rep* **5**: 11410 [PMID:26090649]
58. Im DS. (2010) Pharmacological tools for lysophospholipid GPCRs: development of agonists and antagonists for LPA and S1P receptors. *Acta Pharmacol Sin* **31**: 1213-22 [PMID:20729877]
59. Im DS, Heise CE, Harding MA, George SR, O'Dowd BF, Theodorescu D and Lynch KR. (2000) Molecular cloning and characterization of a lysophosphatidic acid receptor, Edg-7, expressed in prostate. *Mol Pharmacol* **57**: 753-9 [PMID:10727522]
60. Inoue A, Ishiguro J, Kitamura H, Arima N, Okutani M, Shuto A, Higashiyama S, Ohwada T, Arai H and Makide K *et al.*. (2012) TGFα shedding assay: an accurate and versatile method for detecting GPCR activation. *Nat Methods* **9**: 1021-9 [PMID:22983457]
61. Ishii I, Contos JJ, Fukushima N and Chun J. (2000) Functional comparisons of the lysophosphatidic acid receptors, LP(A1)/VZG-1/EDG-2, LP(A2)/EDG-4, and LP(A3)/EDG-7 in neuronal cell lines using a retrovirus expression system. *Mol Pharmacol* **58**: 895-902 [PMID:11040035]
62. Jongsma M, Matas-Rico E, Rzadkowski A, Jalink K and Moolenaar WH. (2011) LPA is a chemorepellent for B16 melanoma cells: action through the cAMP-elevating LPA5 receptor. *PLoS ONE* **6**: e29260 [PMID:22195035]
63. Kano K, Arima N, Ohgami M and Aoki J. (2008) LPA and its analogs-attractive tools for elucidation of LPA biology and drug development. *Curr Med Chem* **15**: 2122-31 [PMID:18781939]
64. Kano K, Matsumoto H, Inoue A, Yukiura H, Kanai M, Chun J, Ishii S, Shimizu T and Aoki J. (2019) Molecular mechanism of lysophosphatidic acid-induced hypertensive response. *Sci Rep* **9**: 2662 [PMID:30804442]
65. Kawamoto Y, Seo R, Murai N, Hiyama H and Oka H. (2018) Identification of potent lysophosphatidic acid receptor 5 (LPA5) antagonists as potential analgesic agents. *Bioorg Med Chem* **26**: 257-265 [PMID:29208511]
66. Khiar-Fernández N, Zian D, Vázquez-Villa H, Martínez RF, Escobar-Peña A, Foronda-Sainz R, Ray M, Puigdomenech-Poch M, Cincilla G and Sánchez-Martínez M *et al.*. (2022) Novel Antagonist of the Type 2 Lysophosphatidic Acid Receptor (LPA_2), UCM-14216, Ameliorates Spinal Cord Injury in Mice. *J Med Chem* **65**: 10956-10974 [PMID:35948083]
67. Kihara Y, Maceyka M, Spiegel S and Chun J. (2014) Lysophospholipid receptor nomenclature review: IUPHAR Review 8. *Br J Pharmacol* **171**: 3575-94 [PMID:24602016]
68. Kingsbury MA, Rehen SK, Contos JJ, Higgins CM and Chun J. (2003) Non-proliferative effects of lysophosphatidic acid enhance cortical growth and folding. *Nat Neurosci* **6**: 1292-9 [PMID:14625558]
69. Kiss GN, Fells JI, Gupte R, Lee SC, Liu J, Nusser N, Lim KG, Ray RM, Lin FT and Parrill AL *et al.*. (2012) Virtual screening for LPA2-specific agonists identifies a nonlipid compound with antiapoptotic actions. *Mol Pharmacol* **82**: 1162-73 [PMID:22968304]
70. Kittaka H, Uchida K, Fukuta N and Tominaga M. (2017) Lysophosphatidic acid-induced itch is mediated by signalling of LPA_5 receptor, phospholipase D and TRPA1/TRPV1. *J Physiol (Lond.)* **595**: 2681-2698 [PMID:28176353]
71. Kotarsky K, Boketoft A, Bristulf J, Nilsson NE, Norberg A, Hansson S, Owman C, Sillard R, Leeb-Lundberg LM and Olde B. (2006) Lysophosphatidic acid binds to and activates GPR92, a G protein-coupled receptor highly expressed in gastrointestinal lymphocytes. *J Pharmacol Exp Ther* **318**: 619-28 [PMID:16651401]
72. Kozian DH, Evers A, Florian P, Wonerow P, Joho S and Nazare M. (2012) Selective non-lipid modulator of LPA5 activity in human platelets. *Bioorg Med Chem Lett* **22**: 5239-43 [PMID:22801643]
73. Kritikou E, van Puijvelde GH, van der Heijden T, van Santbrink PJ, Swart M, Schaftenaar FH, Kröner MJ, Kuiper J and Bot I. (2016) Inhibition of lysophosphatidic acid receptors 1 and 3 attenuates atherosclerosis development in LDL-receptor deficient mice. *Sci Rep* **6**: 37585 [PMID:27883026]
74. Kuo B, Szabó E, Lee SC, Balogh A, Norman D, Inoue A, Ono Y, Aoki J and Tigyi G. (2018) The LPA_2 receptor agonist Radioprotectin-1 spares Lgr5-positive intestinal stem cells from radiation injury in murine enteroids. *Cell Signal* **51**: 23-33 [PMID:30063964]
75. Ledein L, Léger B, Dees C, Beyer C, Distler A, Vettori S, Boukaiba R, Bidouard JP, Schaefer M and Pernerstorfer J *et al.*. (2020) Translational engagement of lysophosphatidic acid receptor 1 in skin fibrosis: from dermal fibroblasts of patients with scleroderma to tight skin 1 mouse. *Br J Pharmacol* **177**: 4296-4309 [PMID:32627178]

76. Lee CW, Rivera R, Dubin AE and Chun J. (2007) LPA(4)/GPR23 is a lysophosphatidic acid (LPA) receptor utilizing G(s)-, G(q)/G(i)-mediated calcium signaling and G(12/13)-mediated Rho activation. *J Biol Chem* **282**: 4310-7 [PMID:17166850]
77. Lee CW, Rivera R, Gardell S, Dubin AE and Chun J. (2006) GPR92 as a new G12/13- and Gq-coupled lysophosphatidic acid receptor that increases cAMP, LPA5. *J Biol Chem* **281**: 23589-97 [PMID:16774927]
78. Lee M, Choi S, Halldén G, Yo SJ, Schichnes D and Aponte GW. (2009) P2Y5 is a G(alpha)i, G(alpha)12/13 G protein-coupled receptor activated by lysophosphatidic acid that reduces intestinal cell adhesion. *Am J Physiol Gastrointest Liver Physiol* **297**: G641-54 [PMID:19679818]
79. Lee Z, Cheng CT, Zhang H, Subler MA, Wu J, Mukherjee A, Windle JJ, Chen CK and Fang X. (2008) Role of LPA4/p2y9/GPR23 in negative regulation of cell motility. *Mol Biol Cell* **19**: 5435-45 [PMID:18843048]
80. Lescop C, Birker M, Brotschi C, Bürki C, Morrison K, Froidevaux S, Delahaye S, Nayler O and Bolli MH. (2024) Discovery of the Novel, Orally Active, and Selective LPA1 Receptor Antagonist ACT-1016-0707 as a Preclinical Candidate for the Treatment of Fibrotic Diseases. *J Med Chem* **67**: 2397-2424 [PMID:38349250]
81. Li Q, Schachter JB, Harden TK and Nicholas RA. (1997) The 6H1 orphan receptor, claimed to be the p2y5 receptor, does not mediate nucleotide-promoted second messenger responses. *Biochem Biophys Res Commun* **236**: 455-60 [PMID:9240460]
82. Liliom K, Tsukahara T, Tsukahara R, Zelman-Femiak M, Swiezewska E and Tigyi G. (2006) Farnesyl phosphates are endogenous ligands of lysophosphatidic acid receptors: inhibition of LPA GPCR and activation of PPARs. *Biochim Biophys Acta* **1761**: 1506-14 [PMID:17092771]
83. Lin ME, Rivera RR and Chun J. (2012) Targeted deletion of LPA5 identifies novel roles for lysophosphatidic acid signaling in development of neuropathic pain. *J Biol Chem* **287**: 17608-17 [PMID:22461625]
84. Lin S, Yeruva S, He P, Singh AK, Zhang H, Chen M, Lamprecht G, de Jonge HR, Tse M, Donowitz M, Hogema BM, Chun J, Seidler U and Yun CC. (2010) Lysophosphatidic acid stimulates the intestinal brush border Na(+)/H(+) exchanger 3 and fluid absorption via LPA(5) and NHERF2. *Gastroenterology* **138**: 649-58 [PMID:19800338]
85. Lin YN, Audira G, Malhotra N, Ngoc Anh NT, Siregar P, Lu JH, Lee H and Hsiao CD. (2020) A Novel Function of the Lysophosphatidic Acid Receptor 3 (LPAR3) Gene in Zebrafish on Modulating Anxiety, Circadian Rhythm Locomotor Activity, and Short-Term Memory. *Int J Mol Sci* **21** [PMID:32325720]
86. Liu S, Paknejad N, Zhu L, Kihara Y, Ray M, Chun J, Liu W, Hite RK and Huang XY. (2022) Differential activation mechanisms of lipid GPCRs by lysophosphatidic acid and sphingosine 1-phosphate. *Nat Commun* **13**: 731 [PMID:35136060]
87. Lu Y, Wang Z, Li CM, Chen J, Dalton JT, Li W and Miller DD. (2010) Synthesis, in vitro structure-activity relationship, and in vivo studies of 2-arylthiazolidine-4-carboxylic acid amides as anticancer agents. *Bioorg Med Chem* **18**: 477-95 [PMID:20056548]
88. Lummis NC, Sánchez-Pavón P, Kennedy G, Frantz AJ, Kihara Y, Blaho VA and Chun J. (2019) $LPA_{1/3}$ overactivation induces neonatal posthemorrhagic hydrocephalus through ependymal loss and ciliary dysfunction. *Sci Adv* **5**: eaax2011 [PMID:31633020]
89. Lundequist A and Boyce JA. (2011) LPA5 is abundantly expressed by human mast cells and important for lysophosphatidic acid induced MIP-1β release. *PLoS ONE* **6**: e18192 [PMID:21464938]
90. Mahmoudi H, Tug E, Parlak AH, Atasoy HI, Ludwig M, Polat M, Pasternack SM and Betz RC. (2012) Identification of an Alu-mediated 12.2-kb deletion of the complete LPAR6 (P2RY5) gene in a Turkish family with hypotrichosis and woolly hair. *Exp Dermatol* **21**: 469-71 [PMID:22621192]
91. Masago K, Kihara Y, Yanagida K, Hamano F, Nakagawa S, Niwa M and Shimizu T. (2018) Lysophosphatidic acid receptor, LPA_6, regulates endothelial blood-brain barrier function: Implication for hepatic encephalopathy. *Biochem Biophys Res Commun* **501**: 1048-1054 [PMID:29778535]
92. Matas-Rico E, García-Diaz B, Llebrez-Zayas P, López-Barroso D, Santín L, Pedraza C, Smith-Fernández A, Fernández-Llebrez P, Tellez T and Redondo M *et al.*. (2008) Deletion of lysophosphatidic acid receptor LPA1 reduces neurogenesis in the mouse dentate gyrus. *Mol Cell Neurosci* **39**: 342-55 [PMID:18708146]
93. Mathew D, Kremer KN, Strauch P, Tigyi G, Pelanda R and Torres RM. (2019) LPA_5 Is an Inhibitory Receptor That Suppresses CD8 T-Cell Cytotoxic Function via Disruption of Early TCR Signaling. *Front Immunol* **10**: 1159 [PMID:31231367]
94. McGiffert C, Contos JJ, Friedman B and Chun J. (2002) Embryonic brain expression analysis of lysophospholipid receptor genes suggests roles for s1p(1) in neurogenesis and s1p(1-3) in angiogenesis. *FEBS Lett* **531**: 103-8 [PMID:12401212]
95. Mirendil H, Thomas EA, De Loera C, Okada K, Inomata Y and Chun J. (2015) LPA signaling initiates schizophrenia-like brain and behavioral changes in a mouse model of prenatal brain

hemorrhage. *Transl Psychiatry* **5**: e541 [PMID:25849980]
96. Mizuno H and Kihara Y. (2020) Druggable Lipid GPCRs: Past, Present, and Prospects. *Adv Exp Med Biol* **1274**: 223-258 [PMID:32894513]
97. Mizuno H, Kihara Y, Kussrow A, Chen A, Ray M, Rivera R, Bornhop DJ and Chun J. (2019) Lysophospholipid G protein-coupled receptor binding parameters as determined by backscattering interferometry. *J Lipid Res* **60**: 212-217 [PMID:30463988]
98. Mukherjee A, Ma Y, Yuan F, Gong Y, Fang Z, Mohamed EM, Berrios E, Shao H and Fang X. (2015) Lysophosphatidic Acid Up-Regulates Hexokinase II and Glycolysis to Promote Proliferation of Ovarian Cancer Cells. *Neoplasia* **17**: 723-34 [PMID:26476080]
99. Murai N, Hiyama H, Kiso T, Sekizawa T, Watabiki T, Oka H and Aoki T. (2017) Analgesic effects of novel lysophosphatidic acid receptor 5 antagonist AS2717638 in rodents. *Neuropharmacology* **126**: 97-107 [PMID:28859883]
100. Nakamura M and Tokura Y. (2009) Congenital woolly hair without P2RY5 mutation. *Dermatoendocrinol* **1**: 58-9 [PMID:20046591]
101. Nieto-Posadas A, Picazo-Juárez G, Llorente I, Jara-Oseguera A, Morales-Lázaro S, Escalante-Alcalde D, Islas LD and Rosenbaum T. (2012) Lysophosphatidic acid directly activates TRPV1 through a C-terminal binding site. *Nat Chem Biol* **8**: 78-85 [PMID:22101604]
102. Noguchi K, Ishii S and Shimizu T. (2003) Identification of p2y9/GPR23 as a novel G protein-coupled receptor for lysophosphatidic acid, structurally distant from the Edg family. *J Biol Chem* **278**: 25600-6 [PMID:12724320]
103. Oda SK, Strauch P, Fujiwara Y, Al-Shami A, Oravecz T, Tigyi G, Pelanda R and Torres RM. (2013) Lysophosphatidic acid inhibits CD8 T cell activation and control of tumor progression. *Cancer Immunol Res* **1**: 245-55 [PMID:24455753]
104. Oh DY, Yoon JM, Moon MJ, Hwang JI, Choe H, Lee JY, Kim JI, Kim S, Rhim H, O'Dell DK, Walker JM, Na HS, Lee MG, Kwon HB, Kim K and Seong JY. (2008) Identification of farnesyl pyrophosphate and N-arachidonylglycine as endogenous ligands for GPR92. *J Biol Chem* **283**: 21054-64 [PMID:18499677]
105. Ohashi T and Yamamoto T. (2015) Antifibrotic effect of lysophosphatidic acid receptors LPA1 and LPA3 antagonist on experimental murine scleroderma induced by bleomycin. *Exp Dermatol* **24**: 698-702 [PMID:25959255]
106. Ohta H, Sato K, Murata N, Damirin A, Malchinkhuu E, Kon J, Kimura T, Tobo M, Yamazaki Y, Watanabe T, Yagi M, Sato M, Suzuki R, Murooka H, Sakai T, Nishitoba T, Im DS, Nochi H, Tamoto K, Tomura H and Okajima F. (2003) Ki16425, a subtype-selective antagonist for EDG-family lysophosphatidic acid receptors. *Mol Pharmacol* **64**: 994-1005 [PMID:14500756]
107. Ohuchi H, Hamada A, Matsuda H, Takagi A, Tanaka M, Aoki J, Arai H and Noji S. (2008) Expression patterns of the lysophospholipid receptor genes during mouse early development. *Dev Dyn* **237**: 3280-94 [PMID:18924241]
108. Okusa MD, Ye H, Huang L, Sigismund L, Macdonald T and Lynch KR. (2003) Selective blockade of lysophosphatidic acid LPA3 receptors reduces murine renal ischemia-reperfusion injury. *Am J Physiol Renal Physiol* **285**: F565-74 [PMID:12770838]
109. Olianas MC, Dedoni S and Onali P. (2020) Antidepressants induce profibrotic responses via the lysophosphatidic acid receptor LPA_1. *Eur J Pharmacol* **873**: 172963 [PMID:32007501]
110. Palmer SM, Snyder L, Todd JL, Soule B, Christian R, Anstrom K, Luo Y, Gagnon R and Rosen G. (2018) Randomized, Double-Blind, Placebo-Controlled, Phase 2 Trial of BMS-986020, a Lysophosphatidic Acid Receptor Antagonist for the Treatment of Idiopathic Pulmonary Fibrosis. *Chest* **154**: 1061-1069 [PMID:30201408]
111. Pasternack SM, Murugusundram S, Eigelshoven S, Müller M, Kruse R, Lehmann P and Betz RC. (2009) Novel mutations in the P2RY5 gene in one Turkish and two Indian patients presenting with hypotrichosis and woolly hair. *Arch Dermatol Res* **301**: 621-4 [PMID:19529952]
112. Pasternack SM, von Kügelgen I, Aboud KA, Lee YA, Rüschendorf F, Voss K, Hillmer AM, Molderings GJ, Franz T, Ramirez A, Nürnberg P, Nöthen MM and Betz RC. (2008) G protein-coupled receptor P2Y5 and its ligand LPA are involved in maintenance of human hair growth. *Nat Genet* **40**: 329-34 [PMID:18297070]
113. Pasternack SM, von Kügelgen I, Müller M, Oji V, Traupe H, Sprecher E, Nöthen MM, Janecke AR and Betz RC. (2009) In vitro analysis of LIPH mutations causing hypotrichosis simplex: evidence confirming the role of lipase H and lysophosphatidic acid in hair growth. *J Invest Dermatol* **129**: 2772-6 [PMID:19536142]
114. Pedraza C, Sánchez-López J, Castilla-Ortega E, Rosell-Valle C, Zambrana-Infantes E, García-Fernández M, Rodriguez de Fonseca F, Chun J, Santín LJ and Estivill-Torrús G. (2014) Fear extinction and acute stress reactivity reveal a role of LPA(1) receptor in regulating emotional-like behaviors. *Brain Struct Funct* **219**: 1659-72 [PMID:23775489]
115. Pei J, Cai L, Wang F, Xu C, Pei S, Guo H, Sun X, Chun J, Cong X and Zhu W *et al.*. (2022) LPA_2 Contributes to Vascular Endothelium Homeostasis and Cardiac Remodeling After Myocardial Infarction. *Circ Res* **131**: 388-403 [PMID:35920162]
116. Pei S, Xu C, Pei J, Bai R, Peng R, Li T, Zhang J, Cong X, Chun J and Wang F *et al.*. (2022)

Lysophosphatidic Acid Receptor 3 Suppress Neutrophil Extracellular Traps Production and Thrombosis During Sepsis. *Front Immunol* **13**: 844781 [PMID:35464399]

117. Petukhova L, Sousa Jr EC, Martinez-Mir A, Vitebsky A, Dos Santos LG, Shapiro L, Haynes C, Gordon D, Shimomura Y and Christiano AM. (2008) Genome-wide linkage analysis of an autosomal recessive hypotrichosis identifies a novel P2RY5 mutation. *Genomics* **92**: 273-8 [PMID:18692127]
118. Plastira I, Bernhart E, Goeritzer M, Reicher H, Kumble VB, Kogelnik N, Wintersperger A, Hammer A, Schlager S and Jandl K *et al.*. (2016) 1-Oleyl-lysophosphatidic acid (LPA) promotes polarization of BV-2 and primary murine microglia towards an M1-like phenotype. *J Neuroinflammation* **13**: 205 [PMID:27565558]
119. Poon MM, Lorrain KI, Stebbins KJ, Edu GC, Broadhead AR, Lorenzana AO, Paulson BE, Baccei CS, Roppe JR and Schrader TO *et al.*. (2024) Discovery of a brain penetrant small molecule antagonist targeting LPA1 receptors to reduce neuroinflammation and promote remyelination in multiple sclerosis. *Sci Rep* **14**: 10573 [PMID:38719983]
120. Qian L, Xu Y, Simper T, Jiang G, Aoki J, Umezu-Goto M, Arai H, Yu S, Mills GB and Tsukahara R *et al.*. (2006) Phosphorothioate analogues of alkyl lysophosphatidic acid as LPA3 receptor-selective agonists. *ChemMedChem* **1**: 376-83 [PMID:16892372]
121. Ray M, Nagai K, Kihara Y, Kussrow A, Kammer MN, Frantz A, Bornhop DJ and Chun J. (2020) Unlabeled lysophosphatidic acid receptor binding in free solution as determined by a compensated interferometric reader. *J Lipid Res* **61**: 1244-1251 [PMID:32513900]
122. Rivera RR, Lin ME, Bornhop EC and Chun J. (2020) Conditional Lpar1 gene targeting identifies cell types mediating neuropathic pain. *FASEB J* **34**: 8833-8842 [PMID:32929779]
123. Sánchez-Marín L, Jiménez-Castilla V, Flores-López M, Navarro JA, Gavito A, Blanco-Calvo E, Santín LJ, Pavón-Morón FJ, Rodríguez de Fonseca F and Serrano A. (2025) Sex-specific alterations in emotional behavior and neurotransmitter systems in LPA_1 receptor-deficient mice. *Neuropharmacology* **268**: 110325 [PMID:39864586]
124. Santos WL, Heasley BH, Jarosz R, Carter KM, Lynch KR and Macdonald TL. (2004) Synthesis and biological evaluation of phosphonic and thiophosphoric acid derivatives of lysophosphatidic acid. *Bioorg Med Chem Lett* **14**: 3473-6 [PMID:15177455]
125. Sattikar A, Dowling MR and Rosethorne EM. (2017) Endogenous lysophosphatidic acid (LPA1) receptor agonists demonstrate ligand bias between calcium and ERK signalling pathways in human lung fibroblasts. *Br J Pharmacol* **174**: 227-237 [PMID:27864940]
126. Schmitz K, Brunkhorst R, de Bruin N, Mayer CA, Häussler A, Ferreiros N, Schiffmann S, Parnham MJ, Tunaru S and Chun J *et al.*. (2017) Dysregulation of lysophosphatidic acids in multiple sclerosis and autoimmune encephalomyelitis. *Acta Neuropathol Commun* **5**: 42 [PMID:28578681]
127. Shimomura Y, Garzon MC, Kristal L, Shapiro L and Christiano AM. (2009) Autosomal recessive woolly hair with hypotrichosis caused by a novel homozygous mutation in the P2RY5 gene. *Exp Dermatol* **18**: 218-21 [PMID:18803659]
128. Shimomura Y, Wajid M, Ishii Y, Shapiro L, Petukhova L, Gordon D and Christiano AM. (2008) Disruption of P2RY5, an orphan G protein-coupled receptor, underlies autosomal recessive woolly hair. *Nat Genet* **40**: 335-9 [PMID:18297072]
129. Simon MF, Daviaud D, Pradère JP, Grès S, Guigné C, Wabitsch M, Chun J, Valet P and Saulnier-Blache JS. (2005) Lysophosphatidic acid inhibits adipocyte differentiation via lysophosphatidic acid 1 receptor-dependent down-regulation of peroxisome proliferator-activated receptor gamma2. *J Biol Chem* **280**: 14656-62 [PMID:15710620]
130. Southern C, Cook JM, Neetoo-Isseljee Z, Taylor DL, Kettleborough CA, Merritt A, Bassoni DL, Raab WJ, Quinn E and Wehrman TS *et al.*. (2013) Screening β-Arrestin Recruitment for the Identification of Natural Ligands for Orphan G-Protein-Coupled Receptors. *J Biomol Screen* **18**: 599-609 [PMID:23396314]
131. Spencer SA, Suárez-Pozos E, Soto-Verdugo J, Wang H, Afshari FS, Li G, Manam S, Yasuda D, Ortega A and Lister JA *et al.*. (2022) Lysophosphatidic acid signaling via LPA_6 : A negative modulator of developmental oligodendrocyte maturation. *J Neurochem* **163**: 478-499 [PMID:36153691]
132. Sumida H, Noguchi K, Kihara Y, Abe M, Yanagida K, Hamano F, Sato S, Tamaki K, Morishita Y and Kano MR *et al.*. (2010) LPA4 regulates blood and lymphatic vessel formation during mouse embryogenesis. *Blood* **116**: 5060-70 [PMID:20713964]
133. Swaney JS, Chapman C, Correa LD, Stebbins KJ, Broadhead AR, Bain G, Santini AM, Darlington J, King CD and Baccei CS *et al.*. (2011) Pharmacokinetic and pharmacodynamic characterization of an oral lysophosphatidic acid type 1 receptor-selective antagonist. *J Pharmacol Exp Ther* **336**: 693-700 [PMID:21159750]
134. Swaney JS, Chapman C, Correa LD, Stebbins KJ, Bundey RA, Prodanovich PC, Fagan P, Baccei CS, Santini AM and Hutchinson JH *et al.*. (2010) A novel, orally active LPA(1) receptor antagonist inhibits lung fibrosis in the mouse bleomycin model. *Br J Pharmacol* **160**: 1699-713 [PMID:20649573]

135. Taniguchi R, Inoue A, Sayama M, Uwamizu A, Yamashita K, Hirata K, Yoshida M, Tanaka Y, Kato HE and Nakada-Nakura Y *et al.*. (2017) Structural insights into ligand recognition by the lysophosphatidic acid receptor LPA_6. *Nature* **548**: 356-360 [PMID:28792932]
136. Tariq M, Ayub M, Jelani M, Basit S, Naz G, Wasif N, Raza SI, Naveed AK, ullah Khan S and Azeem Z *et al.*. (2009) Mutations in the P2RY5 gene underlie autosomal recessive hypotrichosis in 13 Pakistani families. *Br J Dermatol* **160**: 1006-10 [PMID:19292720]
137. Terakado M, Suzuki H, Hashimura K, Tanaka M, Ueda H, Kohno H, Fujimoto T, Saga H, Nakade S and Habashita H *et al.*. (2016) Discovery of ONO-7300243 from a Novel Class of Lysophosphatidic Acid Receptor 1 Antagonists: From Hit to Lead. *ACS Med Chem Lett* **7**: 913-918 [PMID:27774128]
138. Ueda H, Neyama H and Matsushita Y. (2020) Lysophosphatidic Acid Receptor 1- and 3-Mediated Hyperalgesia and Hypoalgesia in Diabetic Neuropathic Pain Models in Mice. *Cells* **9** [PMID:32824296]
139. Virag T, Elrod DB, Liliom K, Sardar VM, Parrill AL, Yokoyama K, Durgam G, Deng W, Miller DD and Tigyi G. (2003) Fatty alcohol phosphates are subtype-selective agonists and antagonists of lysophosphatidic acid receptors. *Mol Pharmacol* **63**: 1032-42 [PMID:12695531]
140. von Kügelgen I. (2006) Pharmacological profiles of cloned mammalian P2Y-receptor subtypes. *Pharmacol Ther* **110**: 415-32 [PMID:16257449]
141. Wang F, Liu S, Pei J, Cai L, Liu N, Liang T, Dong X, Cong X, Chun J and Chen J *et al.*. (2020) LPA_3-mediated lysophosphatidic acid signaling promotes postnatal heart regeneration in mice. *Theranostics* **10**: 10892-10907 [PMID:33042260]
142. Webb TE, Kaplan MG and Barnard EA. (1996) Identification of 6H1 as a P2Y purinoceptor: P2Y5. *Biochem Biophys Res Commun* **219**: 105-10 [PMID:8619790]
143. Weiner JA and Chun J. (1999) Schwann cell survival mediated by the signaling phospholipid lysophosphatidic acid. *Proc Natl Acad Sci USA* **96**: 5233-8 [PMID:10220449]
144. Weiner JA, Fukushima N, Contos JJ, Scherer SS and Chun J. (2001) Regulation of Schwann cell morphology and adhesion by receptor-mediated lysophosphatidic acid signaling. *J Neurosci* **21**: 7069-78 [PMID:11549717]
145. Williams JR, Khandoga AL, Goyal P, Fells JI, Perygin DH, Siess W, Parrill AL, Tigyi G and Fujiwara Y. (2009) Unique ligand selectivity of the GPR92/LPA5 lysophosphatidate receptor indicates role in human platelet activation. *J Biol Chem* **284**: 17304-19 [PMID:19366702]
146. Wu C, Rakhshandehroo T, Wettersten HI, Campos A, von Schalscha T, Jain S, Yu Z, Tan J, Mose E and Childers BG *et al.*. (2023) Pancreatic cancer cells upregulate LPAR4 in response to isolation stress to promote an ECM-enriched niche and support tumour initiation. *Nat Cell Biol* **25**: 309-322 [PMID:36646789]
147. Xu Y, Aoki J, Shimizu K, Umezu-Goto M, Hama K, Takanezawa Y, Yu S, Mills GB, Arai H and Qian L *et al.*. (2005) Structure-activity relationships of fluorinated lysophosphatidic acid analogues. *J Med Chem* **48**: 3319-27 [PMID:15857137]
148. Yanagida K, Igarashi H, Yasuda D, Kobayashi D, Ohto-Nakanishi T, Akahoshi N, Sekiba A, Toyoda T, Ishijima T and Nakai Y *et al.*. (2018) The Gα12/13-coupled receptor LPA4 limits proper adipose tissue expansion and remodeling in diet-induced obesity. *JCI Insight* **3** [PMID:30568036]
149. Yanagida K, Ishii S, Hamano F, Noguchi K and Shimizu T. (2007) LPA4/p2y9/GPR23 mediates rho-dependent morphological changes in a rat neuronal cell line. *J Biol Chem* **282**: 5814-24 [PMID:17172642]
150. Yanagida K, Masago K, Nakanishi H, Kihara Y, Hamano F, Tajima Y, Taguchi R, Shimizu T and Ishii S. (2009) Identification and characterization of a novel lysophosphatidic acid receptor, p2y5/LPA6. *J Biol Chem* **284**: 17731-41 [PMID:19386608]
151. Yanagida K and Valentine WJ. (2020) Druggable Lysophospholipid Signaling Pathways. *Adv Exp Med Biol* **1274**: 137-176 [PMID:32894510]
152. Yang AH, Ishii I and Chun J. (2002) In vivo roles of lysophospholipid receptors revealed by gene targeting studies in mice. *Biochim Biophys Acta* **1582**: 197-203 [PMID:12069829]
153. Yang L, Kraemer M, Fang XF, Angel PM, Drake RR, Morris AJ and Smyth SS. (2019) LPA receptor 4 deficiency attenuates experimental atherosclerosis. *J Lipid Res* **60**: 972-980 [PMID:30796085]
154. Yasuda D, Kobayashi D, Akahoshi N, Ohto-Nakanishi T, Yoshioka K, Takuwa Y, Mizuno S, Takahashi S and Ishii S. (2019) Lysophosphatidic acid-induced YAP/TAZ activation promotes developmental angiogenesis by repressing Notch ligand Dll4. *J Clin Invest* **129**: 4332-4349 [PMID:31335323]
155. Ye X, Hama K, Contos JJ, Anliker B, Inoue A, Skinner MK, Suzuki H, Amano T, Kennedy G and Arai H *et al.*. (2005) LPA3-mediated lysophosphatidic acid signalling in embryo implantation and spacing. *Nature* **435**: 104-8 [PMID:15875025]
156. Ye X, Skinner MK, Kennedy G and Chun J. (2008) Age-dependent loss of sperm production in mice via impaired lysophosphatidic acid signaling. *Biol Reprod* **79**: 328-36 [PMID:18448840]
157. Yukiura H, Kano K, Kise R, Inoue A and Aoki J. (2015) LPP3 localizes LPA6 signalling to non-

contact sites in endothelial cells. *J Cell Sci* **128**: 3871-7 [PMID:26345369]
158. Yung YC, Mutoh T, Lin ME, Noguchi K, Rivera RR, Choi JW, Kingsbury MA and Chun J. (2011) Lysophosphatidic acid signaling may initiate fetal hydrocephalus. *Sci Transl Med* **3**: 99ra87 [PMID:21900594]
159. Yung YC, Stoddard NC and Chun J. (2014) LPA receptor signaling: pharmacology, physiology, and pathophysiology. *J Lipid Res* **55**: 1192-1214 [PMID:24643338]
160. Zhang D, Decker AM, Woodhouse K, Snyder R, Patel P, Harris DL, Tao YX, Li JX and Zhang Y. (2022) Isoquinolone derivatives as lysophosphatidic acid receptor 5 (LPA5) antagonists: Investigation of structure-activity relationships, ADME properties and analgesic effects. *Eur J Med Chem* **243**: 114741 [PMID:36126387]
161. Zhang H, Xu X, Gajewiak J, Tsukahara R, Fujiwara Y, Liu J, Fells JI, Perygin D, Parrill AL and Tigyi G *et al*.. (2009) Dual activity lysophosphatidic acid receptor pan-antagonist/autotaxin inhibitor reduces breast cancer cell migration in vitro and causes tumor regression in vivo. *Cancer Res* **69**: 5441-9 [PMID:19509223]