

## Lysophospholipid (S1P) receptors (version 2019.4) in the IUPHAR/BPS Guide to Pharmacology Database

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### Abstract

Sphingosine 1-phosphate (S1P) receptors (**nomenclature as agreed by the NC-IUPHAR Subcommittee on Lysophospholipid receptors [70]**) are activated by the endogenous lipid [sphingosine 1-phosphate](#) (S1P). Originally cloned as orphan members of the endothelial differentiation gene (*edg*) family, current gene names have been designated as S1P<sub>1</sub>R through S1P<sub>5</sub>R [52]. S1PRs, particularly S1P<sub>1</sub>, are expressed throughout all mammalian organ systems. Ligand delivery occurs *via* two known carriers (or "chaperones"): albumin and HDL-bound apolipoprotein M (ApoM), the latter of which elicits biased agonist signaling by S1P<sub>1</sub> in multiple cell types [15, 39]. The five S1PRs, two chaperones, and active cellular metabolism have complicated analyses of receptor ligand binding in native systems. Signaling pathways and physiological roles have been characterized through radioligand binding in heterologous expression systems, targeted deletion of the different S1PRs, and most recently, mouse models that report *in vivo* S1P<sub>1</sub>R activation [74, 76]. A crystal structure of an S1P<sub>1</sub>-T4 fusion protein confirmed aspects of ligand binding, specificity, and receptor activation determined previously through biochemical and genetic studies [48, 14]. [fingolimod](#) (FTY720), the first drug to target any of the lysophospholipid receptors, binds to four of the five S1PRs, and was the first oral therapy for multiple sclerosis [26]. The mechanisms of action of fingolimod and other S1PR modulating drugs in development include binding S1PRs in multiple organ systems, *e.g.*, immune and nervous systems, although the precise nature of their receptor interactions requires clarification [107, 28, 43, 44].

### Contents

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##### S1P<sub>5</sub> receptor

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