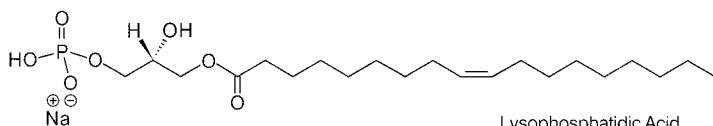
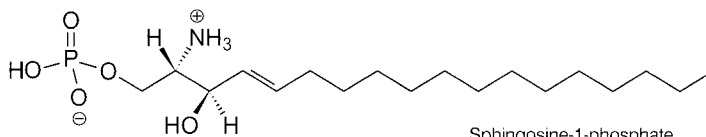


S1P & LPA Activate EDG Receptors

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Lysophosphatidic Acid
Avanti Catalog No. 857130

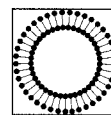


Sphingosine-1-phosphate
Avanti Catalog No. 860492

Recently, a family of G-protein-coupled receptors named endothelial differentiation gene (EDG) receptor family has been identified, which are specifically activated by the two serum lipids, sphingosine-1-phosphate (S1P) and lysophosphatidic acid (LPA). S1P can also act intracellularly to release Ca^{2+} from intracellular stores. Since in several cell types, G-protein-coupled LPA or S1P receptors mobilize Ca^{2+} in the absence of a measurable phospholipase C stimulation, it was analyzed here whether intracellular S1P production was the signalling mechanism used by extracellular S1P for mobilization of stored Ca^{2+} . S1P and the low affinity S1P receptor agonist, sphingosylphosphorylcholine (SPC), induced a rapid, transient and nearly complete pertussis toxin-sensitive Ca^{2+} mobilization in human embryonic kidney (HEK-293) cells. The G-protein-coupled S1P receptors, EDG-1, EDG-3 and EDG-5, were found to be endogenously expressed in these cells. Most interestingly, S1P and SPC did not induce a measurable production of inositol-1,4,5-trisphosphate or accumulation of inositol phosphates. Instead, S1P and SPC induced a rapid and transient increase in production of intracellular S1P with a maximum of about 1.4-fold at 30 s. Stimulation of S1P formation by S1P and SPC was fully blocked by pertussis toxin, indicating that extracellular S1P via endogenously expressed G(i)-coupled receptors induces a stimulation of intracellular S1P production. As S1P- and SPC-induced increases in intracellular Ca^{2+} were blunted by sphingosine kinase inhibitors, this S1P production appears to mediate Ca^{2+} signalling by extracellular S1P and SPC in HEK-293 cells.

Meyer zu Heringdorf, D., H. Lass, I. Kuchar, M. Lipinski, R. Alemany, U. Rumenapp, and K.H. Jakobs. (2001). Stimulation of intracellular sphingosine-1-phosphate production by G-protein-coupled sphingosine-1-phosphate receptors. *Eur J Pharmacol* 414:145-54.

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