Sphingosine 1-phosphate turnover (version 2019.4) in the IUPHAR/BPS Guide to Pharmacology Database

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Abstract

S1P (sphingosine 1-phosphate) is a bioactive lipid which, after release from cells via certain transporters, acts as a ligand for a family of five S1P-specific G protein-coupled receptors (S1P1-5). However, it also has a number of intracellular targets. S1P is formed by the ATP-dependent phosphorylation of sphingosine, catalysed by two isoforms of sphingosine kinase (EC 2.7.1.91). It can be dephosphorylated back to sphingosine by sphingosine 1-phosphate phosphatase (EC 3.1.3) or cleaved into phosphoethanolamine and hexadecenal by sphingosine 1-phosphate lyase (EC 4.1.2.27). Recessive mutations in the S1P lyase (SPL) gene underlie a recently identified sphingolipidosis: SPL Insufficiency Syndrome (SPLIS). In general, S1P promotes cell survival, proliferation, migration, adhesion and inhibition of apoptosis. Intracellular S1P affects epigenetic regulation, endosomal processing, mitochondrial function and cell proliferation/senescence. S1P has myriad physiological functions, including vascular development, lymphocyte trafficking and neurogenesis. However, S1P is also involved in a number of diseases such as cancer, inflammation and fibrosis. Therefore, its GPCRs and enzymes of synthesis and degradation are a major focus for drug discovery.

Contents

This is a citation summary for Sphingosine 1-phosphate turnover in the Guide to Pharmacology database (GtoPdb). It exists purely as an adjunct to the database to facilitate the recognition of citations to and from the database by citation analyzers. Readers will almost certainly want to visit the relevant sections of the database which are given here under database links.

GtoPdb is an expert-driven guide to pharmacological targets and the substances that act on them. GtoPdb is a reference work which is most usefully represented as an on-line database. As in any publication this work should be appropriately cited, and the papers it cites should also be recognized. This document provides a citation for the relevant parts of the database, and also provides a reference list for the research cited by those parts.

Please note that the database version for the citations given in GtoPdb are to the most recent preceding version in which the family or its subfamilies and targets were substantially changed. The links below are to the current version. If you need to consult the cited version, rather than the most recent version, please contact the GtoPdb curators.

Database links

Sphingosine 1-phosphate turnover
Sphingosine kinase

Enzymes

SPHK1(sphingosine kinase 1)
http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=2204

SPHK2(sphingosine kinase 2)
http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=2205

Sphingosine 1-phosphate phosphatase

Enzymes

SGPP1(sphingosine-1-phosphate phosphatase 1)
http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=2523

SGPP2(sphingosine-1-phosphate phosphatase 2)
http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=2524

Sphingosine 1-phosphate lyase

Enzymes

sphingosine-1-phosphate lyase 1
http://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=2522

References

1. Bagdanoff JT, Donoviel MS, Nouraldeen A, Carlsen M, Jessop TC, Tarver J, Aleem S, Dong L, Zhang H and Boteju L et al. (2010) Inhibition of sphingosine 1-phosphate lyase for the treatment of rheumatoid arthritis: discovery of (E)-1-(4-((1R,2S,3R)-1,2,3,4-tetrahydroxybutyl)-1H-imidazol-2-yl)ethanone oxime (LX2931) and (1R,2S,3R)-1-(2-(isoxazol-3-yl)-1H-imidazol-4-yl)butane-1,2,3,4-tetraol (LX2932). J. Med. Chem. 53: 8650-62 [PMID:21090716]


