Sphingosine-1-phosphate receptor 2, also known as S1PR2 or S1P2, is a human gene which encodes a G protein-coupled receptor which binds the lipid signaling molecule sphingosine 1-phosphate (S1P).

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This protein participates in sphingosine 1-phosphate-induced cell proliferation, survival, and transcriptional activation.

It has also been shown to interact with Nogo-A (RTN4), an neurite outgrowth inhibitor.

S1PR2 is expressed in neuronal and vascular cells and is crucial for the migration and growth of developing and injured neuronal and vascular system.

Growth hormone-secreted pituitary adenoma (GHPA) is a prominent subtype of pituitary adenoma (PA) associated with progressive somatic disfigurement, various complications, and elevated mortality rates. Existing treatment options have limited efficacy, highlighting the urgent need for novel pharmacological interventions. Previous studies have revealed that sphingosine kinase 1 (SphK1)/sphingosine-1-phosphate (S1P)/S1P receptors (S1PRs) signalling have critical roles in the tumour microenvironment, but their role in GHPA remains unclear.

Sun et al. performed integrative analyses including bioinformatics analyses, functional studies, and clinical validation to investigate the pathological roles of SPHK1/S1P and evaluated the effectiveness of the S1P receptor 2 (S1PR2) inhibitor JTE-013 in GHPA treatment.

SPHK1/S1P signalling is abnormally expressed in patients with GHPA. Knockdown of SPHK1 suppresses S1P-mediated cell proliferation in GH3 Cells. Mechanistically, S1P inhibits apoptosis and autophagy while promoting the secretion of Growth Hormone (GH) by binding to the S1P receptor subtype 2 (S1PR2) in GH3 cells. Moreover, the function of S1PR2 in GH3 cells is mediated by the downstream Akt-Creb pathway. They then identify the S1PR2 as a novel target for therapeutic intervention in GHPA. Systemic administration of the potent and selective S1PR2 antagonist, JTE-013, significantly reduces both tumour size and GH secretion. Importantly, they identified preoperative serum S1P levels as a biomarker predicting poor prognosis in GHPA patients at follow-up.

The study shows that blocking SPHK1/S1P/S1PR2 axis can ameliorate the progression of GHPA, providing evidence of a promising therapeutic target for GHPA ¹.

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Sun H, Hu B, Wu C, Jiang T. Targeting the SPHK1/S1P/S1PR2 axis ameliorates GH-secreted pituitary adenoma progression. Eur J Clin Invest. 2023 Oct 27:e14117. doi: 10.1111/eci.14117. Epub ahead of print. PMID: 37888843.

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