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Opinion Article

Short Note on Sphingosine-1-Phosphate and Glucosylceramide

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DESCRIPTION

Sphingosine-1-Phosphate (S1P), like Sph, is made up of a single hydrophobic chain and is soluble enough to cross membranes. Sphingosine kinase phosphorylates sphingosine to generate S1P (SK). S1P phosphatase enzymes can dephosphorylate the product's phosphate group to regenerate sphingosine, or S1P can be broken down to ethanolamine phosphate and hexadecenal by S1P lyase enzymes. Its second messenger function, like Sph, is unknown. S1P, on the other hand, appears to be linked to cell survival, migration, and inflammation. Platelet-Derived Growth Factor (PDGF), Insulin-like Growth Factor (IGF), and Vascular Endothelial Growth Factor (VEGF) are examples of growth-inducing proteins that encourage the synthesis of SK enzymes, resulting in increased levels of S1P. Other factors that cause SK include cytokines, such as Tumour Necrosis Factor (TNF) and interleukin-1 (IL-1), hypoxia, or a shortage of oxygen in the cells, oxidised Low-Density Lipoproteins (oxLDL), and various immunological complexes.

S1P is most likely produced at the plasma membrane's inner leaflet in response to TNF and other agonists that change receptor activity.S1P must interact with high-affinity receptors capable of sensing its low levels because it is present in nanomolar concentrations in the cell. S1P receptors are high-affinity G Protein-Coupled Receptors (GPCRs), commonly known as S1P receptors (S1PRs). To interact with S1PRs and start normal GPCR signalling pathways, S1P must reach the extracellular side (outside leaflet) of the plasma membrane. The zwitterionic headgroup of S1P, on the other hand, renders spontaneous flip-flopping rare. The ATP-Binding Cassette (ABC) transporter C1 (ABCC1) acts as "exit door" for S1P to overcome this barrier. S1P, on the other hand, enters the cell through the Cystic Fibrosis Transmembrane Regulator (CFTR). S1P is linked to albumin and lipoproteins in serum, despite its low intracellular content. S1P can cause calcium release inside the cell without the involvement of S1PRs, albeit the mechanism is unknown. S1P's intracellular molecular targets remain unknown to this day. Multiple functions of the SK1-S1P pathway have been linked to the pro-inflammatory effects of TNF and IL-1. Key enzymes such as S1P lyase and S1P phosphatase have been knocked down in studies. Prostaglandin production increased in tandem with S1P levels. This strongly shows that S1P, not subsequent molecules, is the mediator of SK1 activity. S1P has a critical role in regulating endothelial cell development and motility, according to research done on endothelium and smooth muscle cells.

The ability of a sphingosine analogue, FTY270, to operate as a powerful chemical that changes the activity of S1P receptors has been demonstrated in recent research (agonist). FTY270 was also found to play a function in immunological regulation, such as in the treatment of multiple sclerosis, in clinical trials. This emphasises S1P's significance in lymphocyte function and immune modulation. The majority of S1P research is utilised to learn more about diseases like cancer, arthritis, inflammation, diabetes, immunological function, and neurodegenerative disorders.

CONCLUSION

Glucosylceramides (GluCer) are the most abundant glycosphingolipids in cells, serving as precursors to approximately 200 different glycosphingolipids. GluCer is made by glycosylating ceramide using enzymes called Glucosyl Ceramide Synthase (GCS) or breaking down complex Glyco Sphingo Lipids (GSLs) with specialised hydrolase enzymes in an organelle called the Golgi. Certainglucosidases hydrolyze these lipids and regenerate ceramide as a result.

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