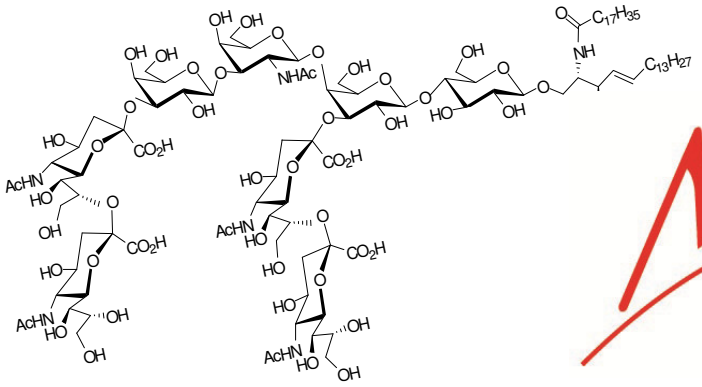


MATREYA LLC

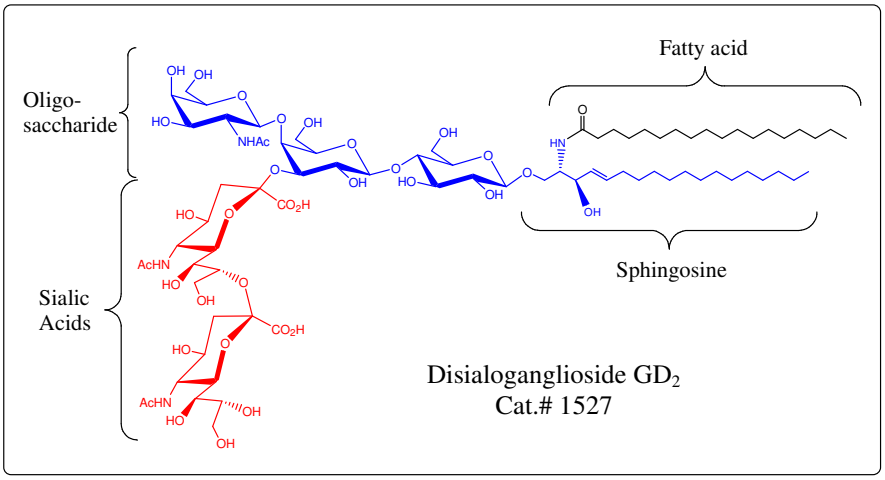
Lipids and Biochemicals

NEWSLETTER FOR GLYCO/SPHINGOLIPID RESEARCH

AUGUST 2017

Ganglioside GD_2 Found to be a New Biomarker for Breast Cancer

Disialoganglioside GD_2 is a sialic acid-containing glycosphingolipid that has important clinical and pathological implications. GD_2 is synthesized in the endoplasmatic reticulum and Golgi apparatus and is then transferred to the outside layer of the plasma membrane. On the cell surface, GD_2 is involved in cell-to-cell adhesion and signal transduction, playing a crucial role both in physiological and in pathological processes by driving proliferation, neoangiogenesis, immune-escape and invasion. It is primarily expressed on the cell surface and is normally found mostly in the central nervous system and in low amounts in peripheral nerves and skin melanocytes. One of GD_2's most important pathological implications is it's presence in elevated amounts in numerous tumor types, including breast cancer cells.



Disialoganglioside GD_2
Cat.# 1527

In malignant cells, GD_2 is uniformly expressed in neuroblastomas and most melanomas and to a variable degree in a variety of other tumors, including bone and soft-tissue sarcomas, small cell lung cancer, and brain tumors. GD_2 is thought to play an important role in the attachment of tumor cells to extracellular matrix proteins, thereby increasing tumorigenesis. Due to its prevalence in various tumor cells, GD_2 can potentially be utilized as a useful biomarker for various cancers. In a recent study, GD_2 has been found to be consistently elevated in a number of breast cancer patients. This finding led the researchers to evaluate its usefulness as a biomarker for breast cancer.

The researchers found a statistically significant correlation of GD_2 with triple-negative breast cancer in comparison to several other breast cancer subtypes, thus confirming that GD_2 may be a good candidate as a biomarker. It was speculated that the elevated GD_2 expression might be related to breast cancer stem cells and to the activation of the process of epithelial-mesenchymal transition.

The researchers were able to conclude that GD_2 immunohistochemical staining was able to be used to show a possible correlation with breast cancer histotypes strongly associated with epithelial-mesenchymal transition. A further study utilizing a larger patient pool is needed to confirm some of the findings of this report; however GD_2 appears to be a new valid biomarker for certain breast cancer subtypes, especially for triple-negative breast cancer which currently lacks any specific marker for diagnostics or targeted therapies.

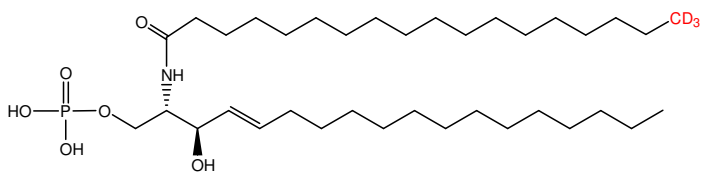
Reference:

G. Orsi et al. Oncotarget, (2017) 8:19, 31592-31600

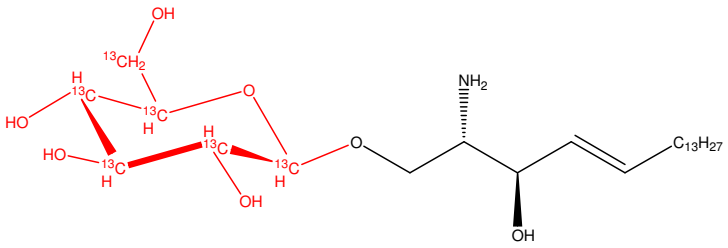
INSIDE THIS ISSUE

Stable Isotope Labeled Sphingolipids as Highly Specific Mass Spectrometry Standards

Deuterium Labeled Ceramide-1-Phosphate, Cat.# 2206



13C Labeled Glucosylsphingosine, Cat.# 2209



Over the past several decades sphingolipids have gained enormous recognition as vital and complex components of biological systems. For many years lipids in general, and sphingolipids in particular, have received far less attention than their critical functions deserve. Many reasons contributed to this oversight including the difficulty of extraction and analysis as well as their tremendous diversity in structure and function.[1,2] Another problem was the very limited availability of appropriate natural and synthetic sphingolipid standards. Recently there has been a welcome advance in making standards available, as well as methods which allow for the relatively quick extraction and analysis of whole classes of sphingolipids from small samples. This advance has greatly accelerated the approach known as sphingolipidomics and has tremendously increased the understanding and classification of these important biomolecules.

Sphingolipidomics is the determination of the complete sphingolipid profile of a given system and the metabolism and pathways of those sphingolipids. It is the sphingolipid subfield of the greater lipidomic discipline and began to appear as a distinct entity around 2005.[3,4] There are tens of thousands of possible naturally occurring sphingolipids that vary in their polar head groups, acyl chains, and sphingoid bases. The metabolic pathway of these sphingolipids has been extensively studied in an attempt to understand and treat diseases related to sphingolipids and to use sphingolipids to correct various diseases. Many of these sphingolipids are present in only picomole to nanomole amounts, making detection difficult. However, with the incorporation of soft ionization techniques in mass spectrometry the detection of very small amounts of sphingolipids has been accomplished. The two major approaches of sphingolipidomic studies are the LC-MS based methods and the shotgun lipidomics approach[1]. In both methods internal standards for each individual sphingolipid detected would be ideal. However, due to the vast number of possible sphingolipids in a system this is currently impractical. Therefore, the preferred method is to use internal standards for each class of sphingolipid expected to be found in a sample. To meet the need for standards in sphingolipidomic studies, sphingolipids that are modified on either the oligosaccharide head, ceramide acyl chain, or the sphingosine tail have been synthesized. These standards are usually stable isotope labeled, unusual chain length modified, or fluorescent sphingolipids.[5,6,7]

One of the most preferred internal standards for LC-MS and shotgun lipidomic studies are stable isotope labeled standards. These standards can be easily detected by mass spectrometry while demonstrating nearly identical physical properties as compared to natural sphingolipids. This is very important to ensure similar extraction properties between the analytes and the internal standards [1]. Most commonly, deuterium or carbon-13 atoms are introduced in the acyl chain of the ceramide. However, the label can also be introduced into the sphingosine tail or oligosaccharide head group, allowing for lyso-sphingolipids to be produced. Another useful internal standard is one that has an acyl or sphingosine chain that has been modified to a length not commonly found in nature, usually C_{17} or C_{19}, or the use of fluorescent tags on the lipid.[8,9]

In addition to the internal standards mentioned above there is a need for natural sphingolipid standards that can be compared to the analytes detected in samples. Methods have been developed to both synthesize these compounds and to extract them from natural sources. Matreya has over 25 years of experience working with lipids and offers an extensive selection of both labeled and

References:
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3. M. Maceyka et al., Prostaglandins Other Lipid Mediat. (2005) 77, 15–22
4. A. Merrill et al., Methods (2005) 36, 207–224
5. J. Huang et al., Mol Ther Methods Clin Dev. (2017) 12:5, 241-258
6. S. Kleinecke et al., eLife. (2017), 6, e23332
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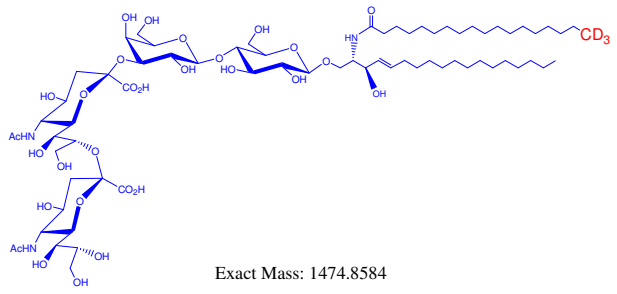
Stable Isotope Labeled Sphingolipids	Catalog #	Amount	Purity
D-*erythro*-sphingosine, D_9	2079	1 mg	98$^+$%
N-*omega*-CD_3-Octadecanoyl-D-*erythro*-sphingosine	2201	1 mg	98$^+$%
N-*omega*-CD_3-Octadecanoyl-D-*erythro*-dihydrosphingosine	2202	1 mg	98$^+$%
N-1-^{13}C-Hexadecanoyl-D-*erythro*-sphingosylphosphorylcholine	2200	1 mg	98$^+$%
N-Octadecanoyl-D_3-D-*erythro*-sphingosine-1-phosphate, deuterated	2206	1 mg	98$^+$%
N-Octadecanoyl-D_{35}-psychosine	1914	5 mg	98$^+$%
$^{13}C_6$-Glucosylsphingosine	2209	1 mg	98$^+$%
N-*omega*-CD_3-Hexadecanoyl-glucopsychosine	1533	1 mg	98$^+$%
N-*omega*-CD_3-Octadecanoyl-sulfatide	1536	1 mg	98$^+$%
N-*omega*-CD_3-Hexadecanoyl-lactosylceramide	1534	1 mg	98$^+$%
N-*omega*-CD_3-Octadecanoyl-ceramide trihexoside	1537	500 µg	98$^+$%
N-*omega*-CD_3-Octadecanoyl monosialoganglioside GM_1	2050	500 µg	98$^+$%
N-*omega*-CD_3-Octadecanoyl monosialoganglioside GM_2	2051	250 µg	98$^+$%
N-*omega*-CD_3-Octadecanoyl monosialoganglioside GM_3	2052	250 µg	98$^+$%
N-*omega*-CD_3-Octadecanoyl disialoganglioside GD_3 **(NEW)**	2091	500 µg	98$^+$%

Deuterated GD_3 as a New Mass Spectrometry Ganglioside Standard

To effectively study the effects and pathologies of the highly versatile group of lipids known as gangliosides, it is important to have an arsenal of suitable and well defined standards. In response to requests from numerous researchers, Matreya's chemists have worked on producing ganglioside standards for the highly specific research that is currently underway. With the use of Matreya's natural and stable isotope labeled ganglioside standards, researchers have been able to probe the mechanisms of ganglioside functions and metabolism. Matreya is proud to now introduce stable isotope labeled GD_3 as a new mass spectrometry internal standard for ganglioside studies.

N-*omega*-CD_3-Octadecanoyl disialoganglioside GD_3
Cat.# 2091



Exact Mass: 1474.8584

Gangliosides are acidic glycosphingolipids that accumulate in lipid domains in the outer leaflet of the cell plasma membrane, especially in neuronal cells in the central nervous system.[1,2] These highly versatile lipids participate in numerous processes including cellular proliferation, differentiation, adhesion, signal transduction, cell-to-cell interactions, tumorigenesis, and metastasis. The accumulation of gangliosides has also been linked to several diseases, among which are Tay-Sachs, Sandhoff disease and gangliosidosis.

Ganglioside GD_3 is predominantly expressed during neuronal development and becomes very limited in adult tissues,

although it has been found to be critical in maintaining the self-renewal capacity of postnatal neural stem cells.[3] Over expression of GD_3 can lead to apoptosis by recruiting mitochondria to apoptotic pathways and suppressing NF-κB activation and subsequent κB-dependent gene induction.[4] Increased levels of GD_3 have also been found to be associated with proliferative diseases, such as atherosclerosis. GD_3 expression is unusually high in basal cell carcinomas and malignant melanomas and is considered to be a tumor associated antigen.[5] Although GD_3 is not immunogenic it has been investigated as a tool for immunotargeting human melanoma cells due to it's unusually high presence.[6]

Recent evidence has implicated gangliosides in the pathogenesis of several neurodegenerative diseases. In addition, it has been shown that interventions which simultaneously increase the neuroprotective GM_1 ganglioside and decrease the pro-apoptotic GD_3 ganglioside are neuroprotective in vitro and in a number of preclinical models. A recent study has demonstrated that inhibition of GD_3 synthase, thereby decreasing levels of GD_3, has neuroprotective properties in a Parkinson's model and may warrant further investigation as a therapeutic target.[7]

Product Name	Catalog #	Amount	Purity
N-*omega*-CD_3-Octadecanoyl disialoganglioside GD_3	2091	500 µg	98^+%

References:

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Matreya's Online Resources

Be sure to check out Matreya's helpful information found online at www.matreya.com. On our website you can: download COA's and SDS's, find dealers in your country, read past newsletters, find product data sheets, and more. Be sure to check the online catalog or download the PDF version for up to date product information and prices. Get expert advice on Matreya's products using our technical support form, or find out about an order status from the customer service link. We strive to provide you with useful information to help your research become a success with our products and services. If you can't find what you're looking for give us a call or send us an email. We're always delighted to help. You can even send us suggestions online, through email, or by phone on how we can improve our service to you or what new products you would like to see added to Matreya's product list.

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