Fucosyl-GM₁ is a Tumor-Associated Antigen

Fucosyl-GM₁ is a sphingolipid monosialoganglioside and tumor-associated antigen with a high prevalence in certain cancers while its expression is minimal in most normal tissue. A highly specific anti-fucosyl-GM₁ was found to bind to fucosyl-GM₁ on small cell lung cancer (SCLC) cells and activate antibody-dependent cellular cytotoxicity, complement-dependent cytotoxicity, and antibody-mediated phagocytosis. Dose-dependent antitumor activity was observed in a panel of SCLC xenograft models with tumor regressions occurring at doses greater than 0.3 mg/kg against tumors. Combination therapy of anti-fucosyl-GM₁ with standard of care chemotherapy resulted in significantly enhanced antitumor activity compared to monotherapy alone. Finally, studies conducted with this antibody in combination with anti-CD137 antibody resulted in significant improvement in efficacy.¹

Hepatocellular carcinoma (HCC) is one of the most common human malignancies. Serum concentrations of anti-disialosyl galactosyl globoside (DSGG), anti-fucosyl-GM₁ and anti-Gb2 were significantly higher in patients with HCC than in chronic HBV infection individuals. Overall, the biomarker candidates DSGG, fucosyl-GM₁, and Gb2 of cancer-associated carbohydrate antigens achieved better predictive sensitivity than the current clinical biomarker serum a-fetoprotein.²

References:
O-Acetyl Gangliosides are Expressed in Tumor Cells

Gangliosides are sialic acid containing glycosphingolipids that play important roles in cell adhesion, cell recognition, signal transduction, and neural development. O-Acetylation of hydroxyl groups on the sialic acid is one of the most common modifications of gangliosides and can exist acetylated to the C-4, 7, 8 and 9 hydroxyl groups. This causes major changes in their physiological properties, resistance to sialidase hydrolysis, and lectin binding. Acetylated gangliosides have especially been correlated with various cancers.\(^{(1)}\)

While an accumulation of the ganglioside GD\(_3\) is known to induce apoptosis, acetylation to 9-O-acetyl-GD\(_3\) renders it unable to trigger this important function. Because of this, there is a critical ratio between GD\(_3\) and 9-O-acetyl GD\(_3\) which promotes tumor survival in glioblastoma cell cultures. In glioblastoma cells, cleaving the acetyl group of 9-O-acetyl-GD\(_3\) restores normal GD\(_3\), resulting in a reduction in tumor cell viability while normal astrocytes remain unaffected.\(^{(2)}\)

The O-acetylated-derivative of GD\(_2\) has recently received attention as a novel antigen to target GD\(_2\)-positive cancers. The absence of O-acetyl-GD\(_2\) expression on nerve fibers and the lack of allogenic properties of anti-GD\(_2\) antibodies, which are believed to play a major role in mediating anti-GD\(_2\) therapeutic antibody’s dose-limiting side effects, provide an important rationale for the clinical application of immunotherapeutic strategies in patients with O-acetyl-GD\(_2\)-expressing tumors.\(^{(3)}\)

Expression of 9-O-acetyl GD\(_3\) increases in Schwann cells (SC) following infection with *Mycobacterium leprae* (ML), the etiologic agent of leprosy. Immunoblockage of 9-O-acetyl GD\(_3\) in *vitro* significantly reduces adhesion of ML to SC surfaces.\(^{(1)}\)

### Stability of 9-O-Acetyl Gangliosides:

9-O-Acetyl gangliosides readily revert to their non-acetylated form. They have a shelf-life of approximately 3 months when stored at \(-20^\circ\text{C}\). Long term storage of these compounds will result in a mixture of the acetylated and non-acetylated gangliosides. Therefore Matreya produces and purifies 9-O-acetyl gangliosides on a custom basis, to ensure the highest purity of the acetylated product. Please contact us for a free quote.

### References:


### Product Table

| Product Name                        | Catalog #   | Purity  
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New Products from Matreya

- N-Hexanoyl-biotin-sulfatide  cat. 2207
- N-Hexanoyl-biotin-disialoganglioside GD₃  cat. 2055
  - Biotin labeled lipids are useful for ELISA studies and for studying lipid/protein interactions

- lyso-Lactosylceramide, synthetic  cat. 2088
- N-Octadecanoyl-sulfated-lactosylceramide  cat. 1540
- N-Tetracosanoyl-D-erythro-dihydrosphingosine  cat. 2093
  - Synthetic lipids are well defined standards for analysis and cellular studies

- N-(32-Linoleoyloxy-dotriacontanoyl)-sphingosine-D₉  cat. 2208
  - Omega-Esterified ceramides are vital components of the skin's water barrier. Stable isotope labeled standards are critical for analytical studies.

- N-Glycinated-glucosylsphingosine  cat. 2089
- N-Glycinated lactosylsphingosine  cat. 2090
- N-Glycinated lyso-sulfatide  cat. 2092
  - Glycinated lyso-sphingolipids are highly useful as mass spectrometry internal standards with the glycine providing a unique mass without changing the important physical properties of the free amine.

- Methyl punicate  cat. 1240
- Methyl jacarate  cat. 1234
- Methyl stearidonate  cat. 1277
  - Conjugated linolenic acids are found in very high amounts in various oils and exhibit some very powerful physiological effects.

- ¹³C₆-Glucosylsphingosine  cat. 2209
- N-omega-CD₃-Octadecanoyl disialoganglioside GD₃  cat. 2054
- N-omega-CD₃-Octadecanoyl-phytosphingosine  cat. 2210
  - Stable isotope labeled standards are critical for analytical studies.

- Sterculic acid  cat. 1235
- Methyl sterculate  cat. 1236
- Methyl malvalate  cat. 1238
  - Cyclopropene fatty acids inhibit Δ9-desaturase and can cause carcinogenicity and acute and chronic toxicity.
lyso-Sphingomyelin as a Sensitive and Specific Biomarker for Niemann-Pick Disease

Niemann-Pick disease is a lysosomal storage disorder that results in the accumulation of various lipids. Several biomarkers are currently used to diagnose and monitor this disease but none have proven to be ideal. lyso-Sphingomyelin (Sphingosylphosphorylcholine, lyso-SPM) has recently been identified as a highly sensitive and specific biomarker for Niemann-Pick disease.

Niemann–Pick disease type B (NPD-B) is caused by a partial deficiency of acid sphingomyelinase activity and results in the accumulation of lysosomal sphingomyelin (SPM), predominantly in macrophages. Notably, SPM is not significantly elevated in the plasma, whole blood, or urine of NPD-B patients. However, lyso-SPM is elevated approximately 5-fold in dried blood spots (DBS) from NPD-B patients and has no overlap with normal controls, making it a potentially useful biomarker.\(^1\)

SPM levels have been shown to be significantly elevated in the livers and spleens of NPD-B patients while SPM levels in plasma have been found to overlap with those of normal controls. A recent LC/MS/MS analysis of dried blood spots showed that lyso-SPM levels from NPD-B patients were substantially elevated when compared to normal controls, with no overlap in values. lyso-SPM has the potential to be an NPD-B biomarker for diagnosis or disease monitoring.\(^1\)

lyso-SPM has also been shown to be a precise and specific biomarker for Niemann-Pick Type C with a sensitivity of 100.0% and specificity of 91.0%. lyso-SPM analysis is relatively quick and easy to perform from blood plasma samples, making it useful in a clinical setting.\(^2\)

References:

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Please visit www.matreya.com for a full list of sphingomyelin products
Lysosomal storage diseases (LSDs) are a heterogeneous group of disorders caused by lysosomal enzyme dysfunction. Gaucher disease (GD) is the most common of these lysosomal storage disorders and has recently warranted much research due to the debilitating effects of excess lipid storage in Gaucher cells. A lack of activity in the lysosomal enzyme β-glucosidase, or occasionally in its activator protein saposin C, causes an accumulation of glucosylceramide, glucosylsphingosine, and other glycosphingolipids in macrophage cells, especially in the liver, spleen, lung, and bone marrow. These lipid heavy cells are commonly known as “Gaucher cells” and can result in hepatosplenomegaly, cytopenia, skeletal disfunctions, lung disorders, and neuronal degradation. In lipid storage disorders such as GD, it is very important to diagnose and treat patients as early as possible. One very effective method of diagnosis is the use of biomarkers.

Chitotriosidase is the most well-established biomarker for GD. However, it is not specific for GD and may give a false negative in a significant percentage of patients due to a particular mutation. Chitotriosidase also reflects the changes in the course of the disease belatedly. Furthermore, a significant percentage of the population, 6%, are deficient in the chitotriosidase gene. Due to these limitations a more specific biomarker is needed for GD.

A recent report demonstrated that glucosylsphingosine can be used as a promising, reliable, and specific biomarker for GD and for measuring the effectiveness of enzyme replacement therapy. Evaluation of the sensitivity and specificity of glucosylsphingosine during enzyme replacement therapy showed significant decreased levels of glucosylsphingosine in both new patients and patients that had previously been treated. The quantitation of glucosylsphingosine was demonstrated to serve as a direct indicator of disease intensity and response to enzyme replacement therapy.

Taking advantage of glucosylsphingosine as a biomarker, M. Fuller et al. have developed a quick and reproducible method for the determination of abnormally high glucosylsphingosine levels from 0.01 mL of plasma. The plasma is spiked with N-palmitoyl-d3-lactosylceramide as an internal standard, extracted with chloroform/methanol, and centrifuged to remove the insoluble protein precipitates. The sample is then ready to be analyzed by LC/ESI-MS/MS. Recovery of the glucosylsphingosine was found to be >90% as calculated from the quality control samples and the calibration curve was linear over the entire relevant range. The assay was described as “accurate, reproducible, robust, and easy to perform in routine laboratory settings”. This method found that glucosylsphingosine was elevated in all GD patients compared to unaffected controls and patients with other metabolic disorders. These results have validated the effectiveness of glucosylsphingosine in diagnosing Gaucher disease and in monitoring the results of enzyme replacement therapy.

Matreya is pleased to now offer $^{13}$C$_6$ Glucosylsphingosine and N-glycinated

![Glucosylsphingosine](image-url)
Glucosylsphingosine as new, highly specific, glucosylsphingosine internal standards. 13C6-Glucosylsphingosine contains six carbon-13 units on the glucose moiety while N-Glycinated glucosylsphingosine contains a glycine attached to the amine of sphingosine, preserving its primary amine. These sphingolipids are ideal for use as internal standards in the extraction and mass spectrometry analysis of samples. The free amine group of glycine gives very similar physical characteristics to the natural sphingolipid while the glycine adds an additional 57 units to the molecule, making it easy to detect by mass spectrometry methods.\(^{(4)}\)

References:


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Please visit [www.matreya.com](http://www.matreya.com) for a full list of glucosylceramide products