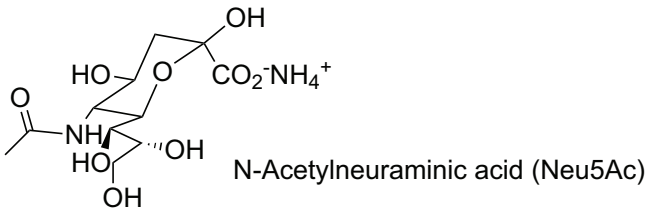
GLYCOLIPID & SPHINGOLIPID RESEARCH DECEMBER 2020
NEWSLETTER

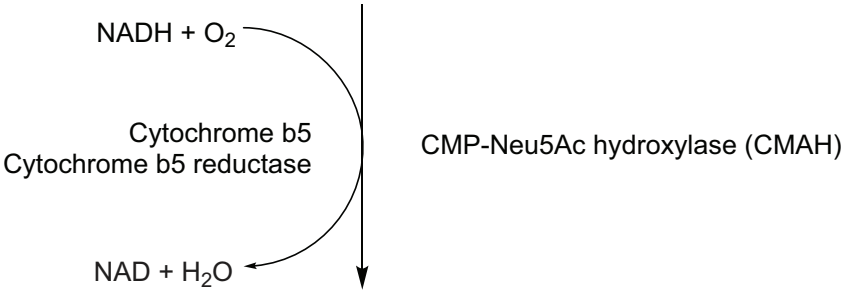
MATREYA LLC
Lipids and Biochemicals
A Cayman Chemical Company

N-Glycolyl-GM$_3$: Cancer Biomarker with Unusual Sialic Acid Content

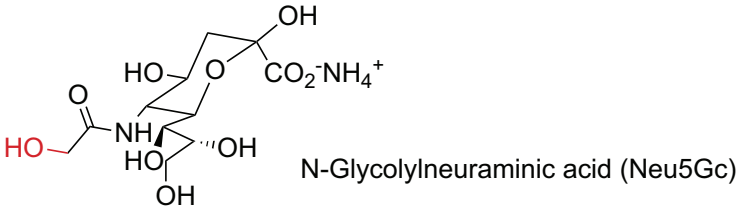
Sialic acids are important for cell-cell recognition and cell-pathogen interactions. They can be found on gangliosides localized to plasma membranes, where sialylated sugar chains protrude out of cells, serving as specific antigens in immune reactions and contacts for glycan binding proteins to mediate cell-cell interactions.[1] N-Acetylneuraminic acid (Neu5Ac) and its hydroxylated form, N-glycolylneuraminic acid (Neu5Gc), are the two major variants of sialic acid found in most mammals.[2] Neu5Gc is mainly derived from Neu5Ac through enzymatic hydroxylation of cytidine-5'-monophospho-NeuAc (CMP-Neu5Ac) but can also be synthesized by hydroxylation of free Neu5Ac or glycoconjugate-linked Neu5Ac. CMP-Neu5Ac hydroxylase, a cytosolic NADH-dependent monooxygenase that requires cytochrome b5 and cytochrome b5 reductase for activity, plays a role in regulating Neu5Gc expression in glycoconjugates by controlling the ratio of Neu5Gc to Neu5Ac.



N-Acetylneuraminic acid (Neu5Ac)



CMP-Neu5Ac hydroxylase (CMAH)



N-Glycolylneuraminic acid (Neu5Gc)

Neu5Gc is generated from Neu5Ac by the enzyme CMP-Neu5Ac hydroxylase (CMAH).

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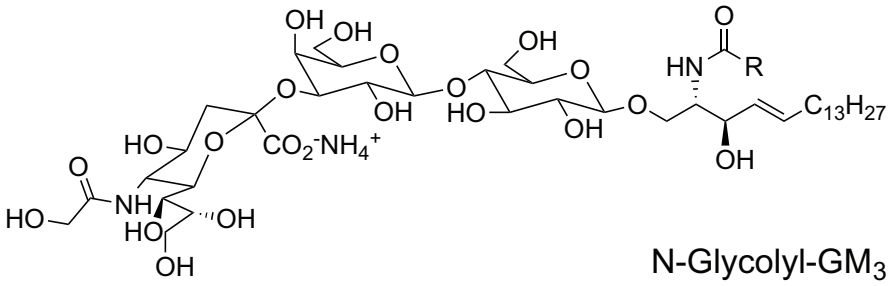
Though Neu5Gc is found in most mammals, its presence in humans is limited due to a partial truncation of the CMP-Neu5Ac hydroxylase gene that renders the biosynthetic enzyme inactive.[3] Therefore, human cells are not capable of synthesizing their own Neu5Gc-sialoconjugates.[4] The possibility that other Neu5Gc-biosynthesis pathways are present in humans has been ruled out since no other biosynthetic enzymes have been identified. However, Neu5Gc can be metabolically incorporated into human cells through diet, primarily from red meat and milk products.[5,6] Neu5Gc is highly immunogenic to humans, and human heterophile antibodies that agglutinate animal erythrocytes, termed Hanganutziu-Deicher (HD) antibodies, detect non-human Neu5Gc.[7] A prolonged antibody reaction to this type of xeno-autoantigen can generate chronic inflammation that leads to cancer or the development of inflammatory or autoimmune diseases.



N-Glycolyl-GM_3

Despite zero to minimal amounts of Neu5Gc being found in healthy human tissues, higher levels of Neu5Gc have been detected in a variety of tumors and are associated with their progression and metastasis.[8,9] For example, abnormal expression of N-glycolyl-monosialoganglioside GM_3 (N-glycolyl-GM_3), a Neu5Gc-containing ganglioside, is found mostly on the surface of malignant tumors.[10] In breast cancer, both O-acetylated and Neu5Gc-containing gangliosides have been detected.[9] Any alterations to the ceramide portion of these unusual gangliosides could weaken its anchor in the cell membrane, enabling them to be actively shed and taken up by other cells.[4] In both pediatric and adult sarcomas, N-glycolyl-GM_3 expression was increased by 59.3-100%.[10] Another study conducted on 27 cases of neuroectodermal tumors found 85% were reported to have N-glycolyl-GM_3.[11] These 23 N-glycolyl-GM_3-positive tumors were more aggressive than those in the other four cases. The most aggressive urinary bladder tumors and malignant gliomas also contain N-glycolyl-GM_3. Reports of reduced survival have been linked to colon adenocarcinomas and non-small cell lung cancer (NSCLC) cells bearing N-glycolyl-GM_3.[10]

Because N-glycolyl-GM_3 is easily detected on the surface of malignant cells, and this expression is minimal in healthy cells, the presence of these tumor-associated antigens provides a basis for early (and potentially pre-malignant) immunological localization and diagnosis. These antigens also serve as an excellent target for immunotherapy to suppress tumor growth through macrophage activation or antibody-dependent cytotoxicity. At least two vaccines, racotumomab and NGcGM3/VSSP, that specifically target Neu5Gc tumor antigens are being developed to fight breast tumors, melanoma, and NSCLC.[12-14] Both of these vaccines have been found to improve the survival of patients with an immune response to the N-glycolyl-GM_3 antigen.

As gangliosides are minor components in human tissues, sensitive methods for their quantitative isolation and analysis are needed. Matreya's scientists have developed a high-quality standard for N-glycolyl-GM_3 detection to advance this research.

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Related Ganglioside Cancer Biomarkers

Biomarker	Source	Catalog No(s).	Associated Cancer Type(s)	Formula Weight	Purity
Monosialoganglioside GM_1	Bovine; ovine; porcine	1061; 1544; 1545	Breast, renal	1547 + NH_3	98+%
Fucosylated monosialoganglioside GM_1	Porcine	1526	Small cell lung cancer	1693 + NH_3	98+%
Monosialoganglioside GM_2	Bovine; human	1542; 1502	Melanomas, gliomas, neuroblastomas, breast	1385 + NH_3	98+%
Monosialoganglioside GM_3	Bovine	1503	Breast, gliomas	1252 + NH_3	98+%
N-Glycolyl-monosialoganglioside GM_3	Bovine	1553	Non-small cell lung cancer, bladder, gliomas, neuroectodermal tumors, colon adenocarcinomas	1268 + NH_3	98+%
Disialoganglioside GD_{1b}	Bovine; porcine	1501; 1547	Gliomas, astrocytomas	1838 + $2NH_3$	98+%
Disialoganglioside GD_2	Rabbit	1527	Melanomas, gliomas, neuroblastomas, breast, bladder	1676 + $2NH_3$	98+%
Disialoganglioside GD_3	Bovine	1504	Melanomas, gliomas, neuroblastomas, breast, ovarian	1543 + $2NH_3$	98+%
Trisialoganglioside GT_{1b}	Bovine; porcine	1063; 1548	Metastatic brain tumors, Ehrlich ascites carcinoma	2129 + $3NH_3$	98+%

View Matreya's full list of Gangliosides and Ganglioside Reference Mixtures at www.matreya.com

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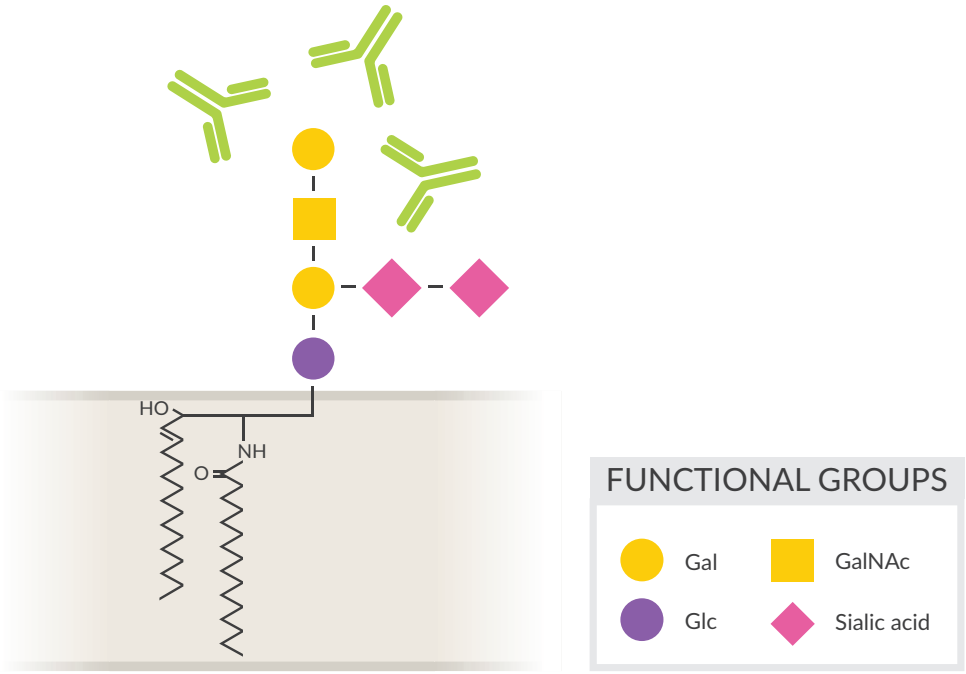
Ganglioside Antibodies

Several gangliosides, particularly GD_{1b}, GD_2, GD_3, GM_2, and GM_3, have been identified as tumor-associated antigens and exhibit elevated expression in tumor cells. As a result, an investigational therapeutic approach that is showing great potential is the use of ganglioside antibodies to target cancer cells that express these gangliosides. Matreya's ganglioside antibodies are directed against the carbohydrate chains of key glycolipids and are useful in the identification of gangliosides. All antibodies are quality tested by ELISA and TLC-based immunoblotting analysis.



Ganglioside GD_{1b} residing in a glycolipid raft (additional lipids not depicted) of a cell membrane is detected by antibodies.

Available from Matreya

Catalog No.	Antibody	Source	Applications	Size
1954	Anti-ganglioside GM_1 (polyclonal antibody)	Rabbit	ELISA, TLC immunoblotting	100 µl
1950	Anti-ganglioside asialo GM_1 (polyclonal antibody)	Rabbit	ELISA, TLC immunoblotting	100 µl
1951	Anti-ganglioside asialo GM_2 (polyclonal antibody)	Rabbit	ELISA, TLC immunoblotting	50 µl
1964	Anti-ganglioside GD_{1b} (polyclonal antibody)	Rabbit	ELISA, TLC immunoblotting	50 µl
1963	Anti-ganglioside GD_2 (polyclonal antibody)	Rabbit	ELISA, TLC immunoblotting	50 µl
1977	Anti-ganglioside GD_3 (monoclonal antibody)	Mouse	ELISA, TLC immunoblotting	50 µl

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IN MEMORIAM

Dr. Subramania Ramachandran
January 8, 1938 - August 10, 2020

The Matreya family is deeply saddened by the recent passing of our esteemed researcher, Dr. Subramania Ramachandran. He began his academic journey at The Ohio State University where he earned two doctoral degrees (Biochemistry, Organic Chemistry). He started his career at Applied Science, Inc. before founding his own fine chemicals company. Dr. Ramachandran joined Matreya where he served as Director of Research and Development for the past twelve years. Dr. Ramachandran was passionate about his work in the laboratory, which continued until his passing. The energy and dedication he brought to work with him each day cannot be easily replaced. He also contributed to many articles published in the Matreya newsletter. He will be sorely missed by both his colleagues and the research community.

We wanted to take a moment to let you know...
how thankful we are to have customers like you.

In 2020, we successfully delivered custom synthesis projects, optimized our methods to make research reagents more affordable, and expanded our catalog offering. During the holiday season, our thoughts turn gratefully to those who have made our success possible. It is in this spirit that we say thank you and send best wishes for the holidays and New Year.