ST6Gal I

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PROW 2:23-31(2001)

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OVERVIEW

Summary Sentence

ST6Gal I is a sialyltransferase that transfers sialic acid (Sia) from CMP-Sia to C6 position of terminal galactose forming SiaAlpha2,6Galb1,4GlcNAc-sequence common to many Asparagine(N)-linked oligosaccharides

Abstract

ST6Gal I is an enzyme belonging to the sialyltransferase family {Tsuji_S/Paulson_JC.1996.GLYCO} and forms SiaAlpha2,6Gal linkage on the GlaBeta1,4GlcNAc-sequence present on N-linked glycoproteins. So far, 16 enzymes have been cloned {Tsuji_S.1996.JBT} ; {Lee_YC/Tsuji_S.1999.JBC} ; {Okajima_T/Furukawa_K.1999.JBC} , each of which exhibits unique specificity for its acceptor substrates and forms one of four sialic acid linkages, namely, Neu5Aca2,6Gal, Neu5Aca2,3Gal, Neu5Aca2,6GalNAc, or Neu5Aca2,8Neu5Ac. ST6Gal I forms Neu5Aca2,6Gal linkage. This and other sialyltransferases are localized in the Golgi apparatus {Taatjes_DJ/Shaper_JH.1987.EJCB} and are type II membrane proteins with a short cytoplasmic domain, an N-terminal signal anchor, a "stem" region, and a large luminal domain that confers the catalytic activity. Another structural feature of ST6Gal I that is common among other sialyltransferases despite little homology is the presence of two conserved protein domains, termed, L-(Long) and S-(Short) sialylmotif {Datta_AK/Paulson_JC.1997.IJBB} *. Analysis by site-directed mutagenesis showed that these two motifs are linked by an essential disulfide linkage and important for substrate binding {Datta_AK/Paulson_JC.1995.JBC} ; {Datta_AK/Paulson_JC.1998.JBC} ; {Datta_AK/Paulson_JC.2001.JBC} . In addition, a very small motif of unknown function is found at the C-terminal {Geremia_RA/Delannoy_P.1997.GLYCO} . No structural information, however, is available from X-ray crystallography or NMR studies. The product of this ST6Gal I, Neu5Aca2,6Galb1,4GlcNAc is shown to be the ligand of CD22 , a receptor present on B cells {Powell_LD/Varki_A.1994.JBC} . In vivo functional study using ST6Gal I deficient mice indicated that this sialoside is essential in promoting B lymphocyte activation and immune function {Hennet_T/Marth_JD.1998.PNASU}

Molecular Families

Families in which hST6gal 1 is a member

- hST6gal 1-->sialyltransferase -->glycosyltransferase

Names

- SIAT1 [HUGO gene name]
- hST6gal 1 (STgal 1 , ST6gal 1) [For nomenclature, {Tsuji_S/Paulson_JC.1996.GLYCO}]
- sialyltransferase 1
- beta-galactoside alpha-2,6-sialytransferase (CMP-N-acetylneuraminate beta-galactoside alpha-2,6-sialytransferase)

Major Links

- **Locus Link:** https://www.ncbi.nlm.nih.gov/LocusLink/LocRpt.cgi?l=6480
- **OMIM Link:** https://www.ncbi.nlm.nih.gov/entrez/dispomim.cgi?id=109675
- **PBD Link:**
- **Other Link:** https://www.ncbi.nlm.nih.gov/htbin-post/Entrez/query?uid=P15907&form=6&db=p&Dopt=g

Author's Additional Insights

No information

SYSTEM VIEW

Disease relevance/Function in vivo

ST6Gal I deficient mice showed symptoms of immunosuppression {Hennet_T/Marth_JD.1998.PNASU}

- The symptoms were marked with reduced serum IgM levels with attenuated antibody production to T-independent and T-dependent antigens.
- The absence of the enzyme product did not effect B cell development, however these mice showed impaired B cell proliferation in response to IgM or CD40 crosslinking.
- The deficiency caused an alteration in phosphotyrosine accumulation following cross-linking of the B lymphocyte antigen receptor

Cellular Function

- ST6Gal I is localized in trans Golgi and trans Golgi network in which it acts to add sialic acid to the oligosaccharide chains of the newly synthesized protein while in transit through Golgi {Roth_J/Paulson_JC.1985.CELL} ; {Taatjes_DJ/Roth_J.1986.EJCB} .
- The dimeric form of this enzyme is inactive and may act as galactose-specific lectin {Ma_J/Colley_KJ.1996.JBC} .
- The enzyme product Sia6LacNAc is a ligand of CD22 , a receptor on B cell and shown to be essential in regulating B lymphocyte activation and immune function {Hennet_T/Marth_JD.1998.PNASU} .
- NeuAc6LacNAc also plays a role in the expression of the biological activity of prolactin/growth hormone family members during rat pregnancy {Manzella_SM/Baenziger_JU.1997.JBC}

TOC

Protein Location

Families in which hST6gal 1 is a member

hST6gal 1 → sialyltransferase → glycosyltransferase

Cellular Expression

Families in which hST6gal 1 is a member

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GENE

Gene sequence links

Families in which hST6gal 1 is a member
hST6gal 1 → sialyltransferase → glycosyltransferase

Chromosomal location

Families in which hST6gal 1 is a member
hST6gal 1 → sialyltransferase → glycosyltransferase

Gene polymorphism

Families in which hST6gal 1 is a member
hST6gal 1 → sialyltransferase → glycosyltransferase

Transcription regulating molecules

Transcription Factor'	Comments	References
Promoter P1	Promoter P1 controls ST6Gal I expression in liver and intestinal epithelium {Wang_X/Lau_JT.1993.JBC} ; {Vertino-Bell_A/Lau_JT.1994.DB} . P1 activity is modulated by liver-enriched transcription factors HNF-1, DBP, and LAP {Svensson_EC/Paulson_JC.1992.JBC} as well as by glucocorticoid {Wang_XC/Lau_JT.1989.JBC}	asdasdasdsad
Promoter P2	Promoter P2 region containing AP2, NF-kB, and TATA transcriptional start sites controls ST6Gal I expression in mature B cells {Lo_NW/Lau_JT.1996.BBRC}	{Lo_NW/Lau_JT.1996.BBRC}
Promoter P3	Promoter P3 was shown to control expression of hST6Gal I gene during HL-60 differentiation. The activity is modulated by Sp-1 and Oct-1 {Taniguchi_A/Matsumoto_K.2000.GLYCO}	{Taniguchi_A/Matsumoto_K.2000.GLYCO}

Gene Annotation

Families in which hST6gal 1 is a member
hST6gal 1 → sialyltransferase → glycosyltransferase

TRANSCRIPT

Transcript Sequence Links

Families in which hST6gal 1 is a member
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Post-transcriptional Modification

Families in which hST6gal 1 is a member
hST6gal 1 → sialyltransferase → glycosyltransferase

Transcript Annotation

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PROTEIN

Biochemical Activity

Families in which hST6gal 1 is a member
hST6gal 1 → sialyltransferase → glycosyltransferase

Protein Sequence Links

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Protein Sequence Annotation

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Protein Polymorphism

Families in which hST6gal 1 is a member
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Protein Physical Properties

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MOLECULAR INTERACTIONS

Molecular Pathways

Families in which hST6gal 1 is a member
hST6gal 1 → sialyltransferase → glycosyltransferase

Enzymes for which this is a Substrate

Families in which hST6gal 1 is a member
hST6gal 1 → sialyltransferase → glycosyltransferase

Substrates

Substrate	Comments	References
Terminal GalBeta1,4GlcNAc containing N-linked glycoproteins	Terminal GalBeta1,4GlcNAc containing N-linked glycoproteins, such as, prolactin	{Manzella_SM/Baenziger_JU.1997.JBC}
lactoferrin	NA	{Coddeville_B/Spik_G.1992.CR}
fat globule membrane CD36	CD36	{Nakata_N/Kobata_A.1993.BIOCH}
HB-6	NA	{Bast_BJ/Tedder_TF.1992.JCB}
CD75s (formerly CDw75 and CDw76)	NA	{Bast_BJ/Tedder_TF.1992.JCB}
Various milk oligosaccharides	NA	{Gyorgy_P/Zilliken_F.1974.EJB}

Other Ligands and Associated Molecules

Families in which hST6gal 1 is a member
hST6gal 1 → sialyltransferase → glycosyltransferase

REAGENTS