Sialyltransferases and Other Enzymes Involved in the Biosynthesis of Gangliosides

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Introduction

The sialyltransferases involved in the biosynthesis of gangliosides were summarized in Table 1. The simplest sialosylglycolipid is GM3 except for GM4 (sialylgalactosyl ceramide). GM3 is located at the starting point of all ganglio-series glycolipids, extending to a-series, b-series and c-series gangliosides. GM3 synthase is called ST3Gal-V (Tsuji et al. 1996; Furukawa et al. 2007). GD3 synthase is the key enzyme for the synthesis of b-series and c-series gangliosides (GT3 synthase, Nakayama et al. 1996). GD3 synthase is called ST8Sia-I (Tsuji et al. 1996; Furukawa et al. 2007). After extending ganglio-core chain by GM2/GD2/GA2 synthase (Furukawa et al. 2007) and GM1/GD1b/GA1 synthase (Furukawa et al. 2007), GD1a/GT1b/GM1b synthase adds NeuAc to Gal at the non-reducing end (Tsuji et al. 1996). Then GT1a/GQ1b/GD1c synthase catalyzes biosynthesis of GT1a, GQ1b, or GD1c from GD1a, GT1b, or GM1b, respectively (Tsuji et al. 1996).

In addition, α-series gangliosides are also synthesized by ST6GalNAc-III (Sjoberg et al. 1996; Furukawa et al. 2007), ST6GalNAc-V (Furukawa et al. 2007), and ST6GalNAc-VI (Furukawa et al. 2007). ST6GalNAc-V synthesizes GD1α in brain tissues, and ST6GalNAc-VI synthesizes GT1aα and GQ1bα from GM1b or GD1a and GT1b, respectively. This enzyme also produces GD1α.

Besides ganglioside-series gangliosides, sialyl-glycolipids are generated with globo-series and lacto/neolacto-series glycolipids. All these structures are synthesized via common precursors, such as Glc-Cer and lactosylceramide. In globo-series, MSGG (monosialyl-galactosylgloboside) and DSGG (disialyl-galactosylgloboside) are synthesized via Gb3/CD77, Gb4, and Gb5. MSGG is synthesized by ST3Gal-II (Saito et al. 2003), and DSGG is synthesized by ST6GalNAc-VI (Senda et al. 2007). In lacto/neolacto-series, sialyl-paragloboside (Furukawa et al. 2007), sialyl-Lewis a, or sialyl-Lewis x are synthesized via the biosynthesis of amino-CTH synthase, β3/4-galactosyltransferase, α2.3-sialyltransferase, and α1,3/4-fucosyltransferase. Recently identified disialyl-Lewis a is synthesized by ST6GalNAc-VI (α2,6-sialyl-transferase) (Furukawa et al. 2007).

List

In Table 1, sialyltransferases and other glycosyltransferases, responsible for the synthesis of ganglio-series gangliosides, are summarized first. Sialyltransferaess involved in the biosynthesis of gangliosides with globo-core are then listed. As for sialyltransferases

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Table I Sialyltransferases involved in the biosynthesis of gangliosides

Gene name	Anonyms	Enzyme	Accession No.**	EC	References
GM3 synthase	ST3 Sia-V, SAT-I	alpha2,3Sia-T	NM_003896 NP_003887	2.4.99.9	Furukawa et al. 2007
GD3 synthase	ST8Sia-I, SAT-II	alpha2,8Sia-T	NM_003034 NP_003025	2.4.99.8	Furukawa et al. 2007
GT3 synthase	ST8Sia-I	alpha2,8Sia-T	NM_003034	2.4.99.8	Nakayama et al. 1996
GM2/GD2 synthase	Beta4GalNAcT-I	beta,4-GalNAc-T	NM_001478	2.4.1.92	Furukawa et al. 2007
GM1/GD1b/GA1 synthase	Beta3GalT-IV	beta3-Gal-T	NM_017420 (M) NP_062293	2.4.1.62	Furukawa et al. 2007
GD1a/GT1b/GM1b synthase	SAT-IV, ST3Gal-II	alpha2,3Sia-T	U63090 Q16842	2.4.99.2	Tsuji 1996
GQ1b/GT1a/GD1c synthase	ST8Sia-V, SAT-V	alpha2,8Sia-T	NM_013305 NP_037437		Tsuju 1996
ST6GalNAcIII	STY, ST6O-II	alpha2,6Sia-T	NM_152996 NP_694541		Sjoberg et al. 1996
ST6GalNAcV	GD1α synthase	alpha2,6Sia-T	NM_030965 Q9BVH7		Furukawa et al. 2007
ST6GAlNAcVI	GD1α/GT1aα/GQ1bα synthase	alpha2,6Sia-T	NM_013443 NP_038471		Furukawa et al. 2007
	Disialy1-Lewis a synthase				Furukawa et al. 2007
	DSGG synthase*				Senda M et al. 2007
Sialy-Gb5 synthase	α3SiaTII, MSGG synthase, SATIV	alpha2,3Sia-T	U63090 Q16842	2.4.99.2	Saito S et al. 2003

*Disialyl-galactosylgloboside synthase

**Unless otherwise mentioned, human gene or proteins are shown

involved in the synthesis of lacto/neolacto-series gangliosides, only a newly defined sialyltransferase responsible for the synthesis of disialyl-Lewis a was listed.

References

Furukawa K, Tsuchida A, Furukawa K (2007) Biosynthesis of glycolipids. In: Kamerling JP (ed.) Comprehensive glycoscience. Elsevier, Oxford, UK, pp 105–114

Nakayama J, Fukuda NM, Hirabayashi Y et al. (1996) Expression cloning of a human GT3 synthase, GD3 AND GT3 are synthesized by a single enzyme. J Biol Chem 271:3684–3691

Saito S, Aoki H, Ito A et al. (2003) Human alpha2,3-sialyltransferase (ST3Gal II) is a stage-specific embryonic antigen-4 synthase. J Biol Chem 278:26474–26479

Senda M, Ito A, Tsuchida A et al. (2007) Identification and expression of a sialyltransferase responsible for the synthesis of disialylgalactosylgloboside in normal and malignant kidney cells: downregulation of ST6GalNAc VI in renal cancers. Biochem J 402:459–470

Sjoberg ER, Kitagawa H, Glushka J et al. (1996) Molecular cloning of a developmentally regulated N-acetylgalactosamine alpha2,6-sialyltransferase specific for sialylated glycoconjugates. J Biol Chem 271:7450–7459

Tsuji S (1996) Molecular cloning and functional analysis of sialyltransferases. J Biochem (Tokyo) 120:1–13