Anti-Sialosylparagloboside autoantibodies (anti-LM1)

Synonyms Sialosyllactotetraosylceramid

Homologues **Hex-LM1** (Sialosyllactosaminylparagloboside)

Indications
- Guillain Barré syndrome
- Miller Fisher syndrome
- Chronic inflammatory demyelinating polyneuritis (CIDP)
- anti-MAG negative neuropathies in monoclonal gammopathies

see also
- Autoantibodies in peripheral neuropathies

Antigens

LM1 constitutes a glycosphingolipid (GSL) consisting of a hydrophobic ceramide, anchoring within the cytoplasmic membrane, and a glycosidic bond carbohydrate moiety projecting outside the cell membrane (Figure 1). Glycosphingolipids are involved in numerous processes as cell-adhesion to the extracellular matrix, cell protection forming a mechanically stable and chemically resistant outer leaflet of the plasma membrane, cell-cell and cell-substrate interactions. Glycosphingolipids mediate specific functions, such as cell recognition and signal transduction and are situated in cellular microdomains, which therefore have been termed "glycosynapses" (Hakamori 2003). The carbohydrate moieties on the exterior of the cytoplasmic membrane may function as immunoreactive epitopes since their exposed location makes them accessible for circulating autoantibodies. Their composition of a limited number of repetitious carbohydrates (figure 1) may be considered as a cause of the multiple immunological cross reactions seen with this kind of autoantibodies.

Prevalence

Table 1 Disease associations of anti- LM1 autoantibodies

Diseases		Authors
Guillain Barré-syndrome	12,5 % 22 % 5 % mainly IgG3	Kuwahara et al. 2011 Harukawa et al. 2002 Susuki et al. 2002 Yakow et al. 1999 Ilyas et al. 2001
Acute axonal motor neuropathy (AMAN)	26 %	Susuki et al. 2002
Chronic inflammatory demyelinating polyneuritis (CIDP)	3 % 8 % LM1/GM1/GD1b-complex 3 %	Kuwahara et al. 2013 Kuwahara et al. 2011 Yakow et al. 1999
Miller Fisher syndrome	20 % 4 %	Harukawa et al. 2002 Yakow et al. 1999
Motor neuropathy	2 %	Harukawa et al. 2002
Cranial neuropathies		Kunishige et al. 2004
Acute inflammatory demyelinating neuropathy (AIDP)	5 %	Susuki et al. 2002
Paraproteinemic neuropathy	IgA gammopathy	Farrer et al. 1996
Healthy persons	7 %	Harukawa et al. 2002

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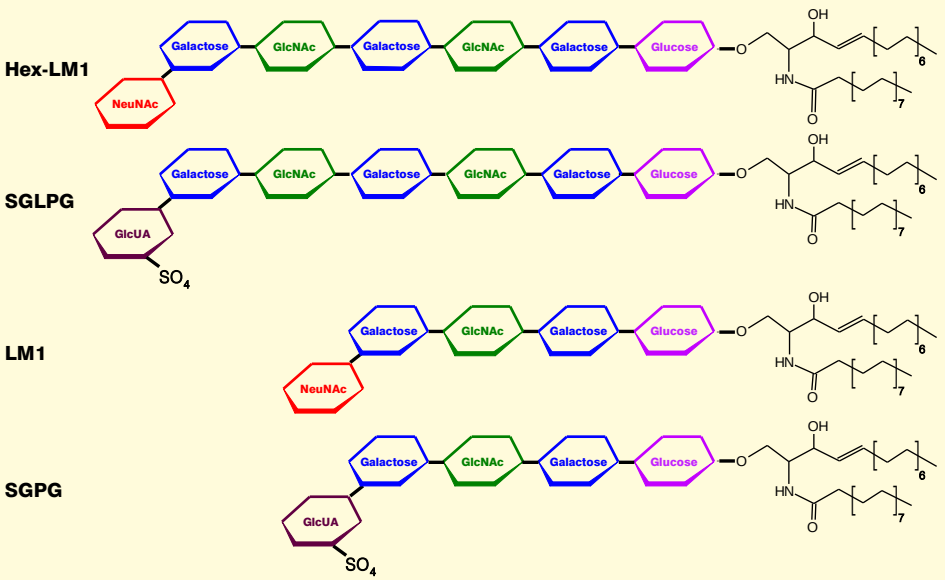

Figure 1 Molecular composition of the acidic glycosphingolipids Hex-LM1, SGLPG, LM1 and SGPG consisting of hydrophobic ceramide- and hydrophilic carbohydrate moieties. Ceramides are composed of sphingosine and fatty acid.

Usually the glycosphingolipids are subdivided in neutral (cerebrosides) and acidic forms, of which the latter ones are further distinguished by their charge bearing residues. Gangliosides contain sialinic acids, sulfatides a sulfate residue.

Hex-LM1	Sialosyllactosaminylparagloboside (ganglioside)
LM1	Sialosylparagloboside (ganglioside)
SGLPG	Sulfuronyllactosaminylparagloboside (sulfatide, sulfoglycosphingolipid)
SGPG	Sulfoglucuronylparagloboside (sulfatide, sulfoglycosphingolipid)
GlcNAc	N-acetylglucosamine
NeuNAc	N-acetylneuraminic acid (acetyl sialic acid)

The myelin of peripheral nerves is abundant in lacto-tetraose and lacto-hexaose gangliosides such as LM1 and Hex-LM1 as well as in the sulfoglucuronyl-glycosphinglipds SGPG and SGLPG (see also autoantibodies anti-SPGP). LM1 is one of the main gangliosdes within peripheral nerve myelin. The substitution of the terminal saccharides of LM1 and Hex-LM1 (sialosyl-lactosaminyl-paragloboside) by a 3-sulfated glucuronic acid results in sulfoglucuronyl-paragloboside (SGPG) and sulfoglucuronyl-lactosaminyl-paragoboside (SGLPG).

Autoantibodies

LM1 as well as Hex-LM1 were figured out as target antigens of autoantibodies in patients with acute and chronic autoimmune neuropathies (table 1). Antibodies against LM1 could be in induced in guinea pigs by immunization with LM1. Irrespective high antibody titers these animals showed only slight neurological symptoms and no histological signs of demyelinisation or inflammation (Gu et al. 2012).

Test methods

Common methods used for detection of antibodies against LM1 and other GSL antigens in sera are ELSA and HPTLC-immunostaining.

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Literature

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