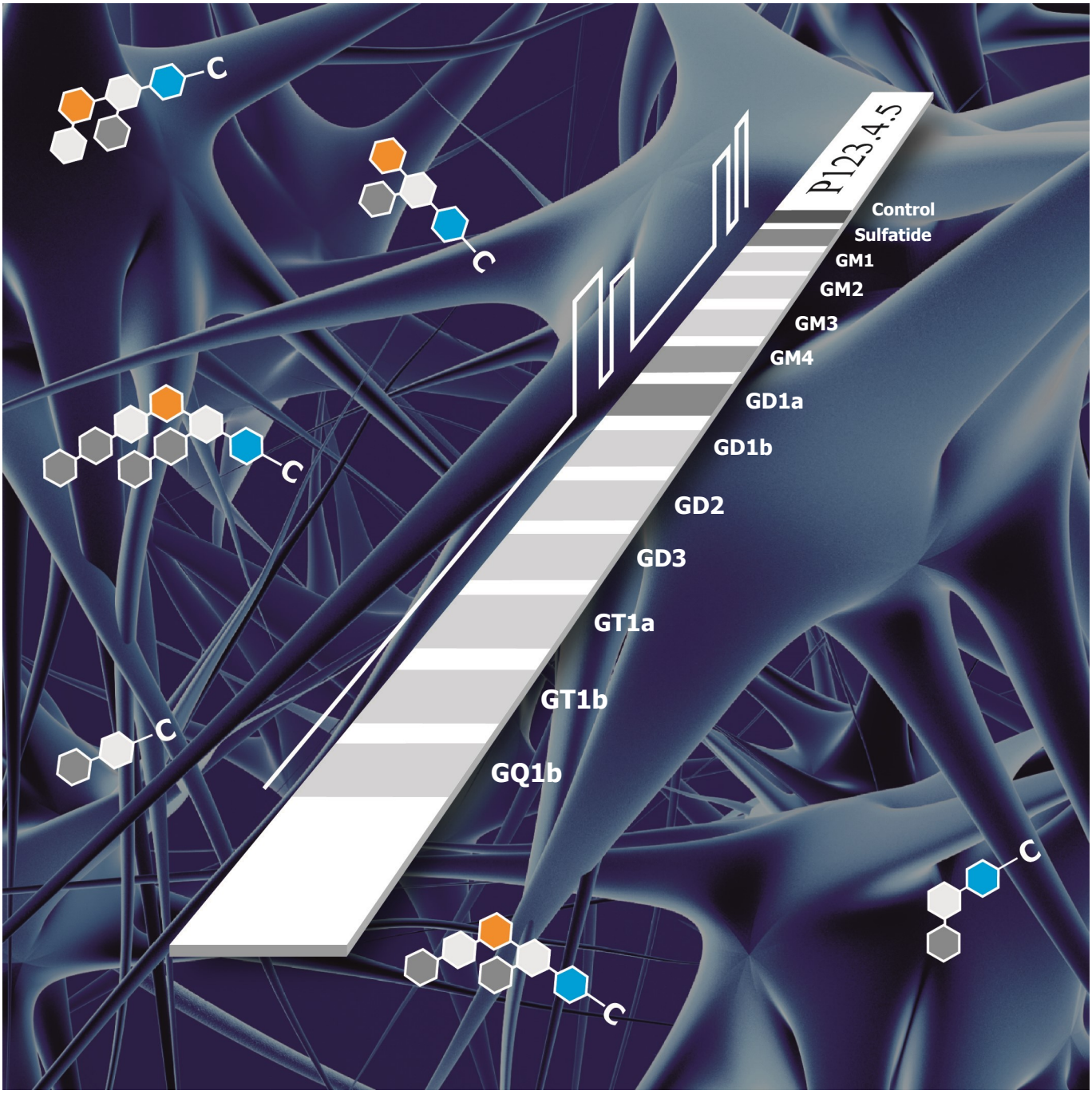
Anti-Ganglioside

12 LINE - Profile Diagnostics (IgG/IgM)



Anti-Gangliosides

Autoimmune Neuropathies

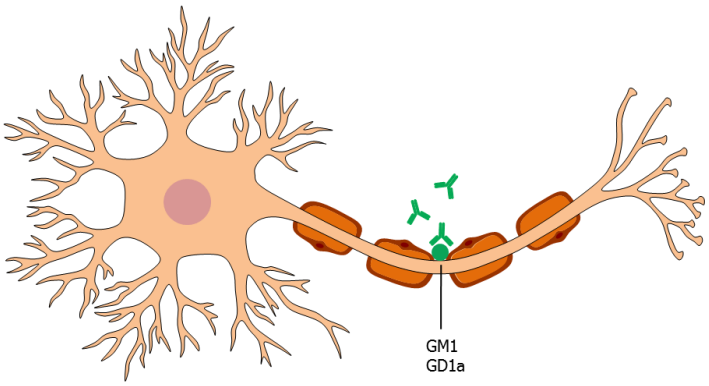
Autoimmune neuropathies are characterized by a number of clinical symptoms, which are however not distinguishable from other neuropathies. Neuropathies with autoimmune pathogenesis (13 % of neuropathies) can therefore be misdiagnosed as being idiopathic and consequently mistreated. The determination of anti-ganglioside antibodies serves not only as opportunity to diagnose autoimmune neuropathies, but also provides therapeutically relevant information regarding the subtype of neuropathic disease:

	Sulf	GM1	GM2	GM3	GM4	GD1a	GD1b	GD2	GD3	GT1a	GT1b	GQ1b
GBS/AIDP		IgG			IgM	IgG	IgG				IgG	
GBS/AMAN & AMSAN	IgM	IgG			IgM	IgG	IgG				IgG	
GBS after CMV-Infection		IgM	IgM			IgM	IgM					
GBS with ataxia							IgG			IgG		IgG
GBS with ONS		IgG				IgG				IgG		IgG
GBS with ophthalmoplegia										IgG		IgG
MFS					IgM		IgG		IgG	IgG	IgG	IgG
Bickerstaff encephalitis										IgG		IgG
CANOMAD				IgM		IgM	IgM	IgM	IgM	IgM	IgM	IgM
MMN		IgM	IgM	IgM	IgM	IgM	IgM					
CIDP	IgM	IgM	IgM	IgM		IgM	IgM					
MN with gammopathy	IgM	IgM					IgM					

AIDP - acute inflammatoric demyelinating polyneuropathy, AMAN - acute motor axonal neuropathy, AMSAN - acute motor and sensory axonal neuropathy, CANOMAD - chronic ataxic neuropathy ophthalmoplegia IgM paraprotein cold agglutinins disialosyl antibodies, CIDP - chronic inflammatoric demyelinating polyneuropathy, CMV - *cytomegalovirus*, GBS - Guillain-Barré syndrome, MFS - Miller Fisher syndrome, MMN - multifocal motor neuropathy with conduction blocks, MN - motor neuropathy, ONS - acute paralysis of the oropharyngeal neck and shoulder muscles

adapted from Conrad et al. 2011

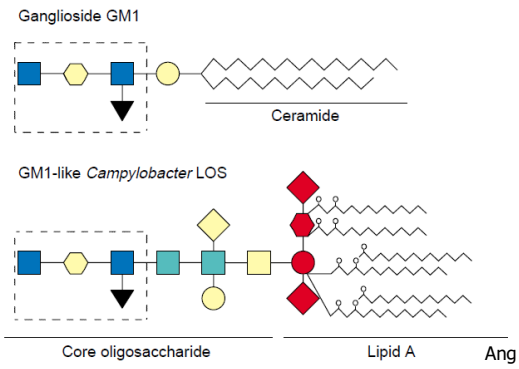
An Example for Immunpathogenesis - GBS/AMAN



Gangliosides GM1 and GD1a are strongly expressed at the nodes of Ranvier of myelinated axons, where the voltage-gated sodium (Nav) channels are localized. IgG anti-GM1 or anti-GD1a autoantibodies bind to the nodal axolemma, leading to membrane attack complex (MAC) formation. This results in the disappearance of Nav clusters and the detachment of paranodal myelin, which can lead to nerve-conduction failure and muscle weakness. Axonal degeneration may follow at a later stage. Macrophages subsequently invade from the nodes into the periaxonal space, scavenging the injured axons.

Figure adapted from Yuki & Hartung 2012

Molecular Mimicry: a Possible Cause for



Ang et al. 2004

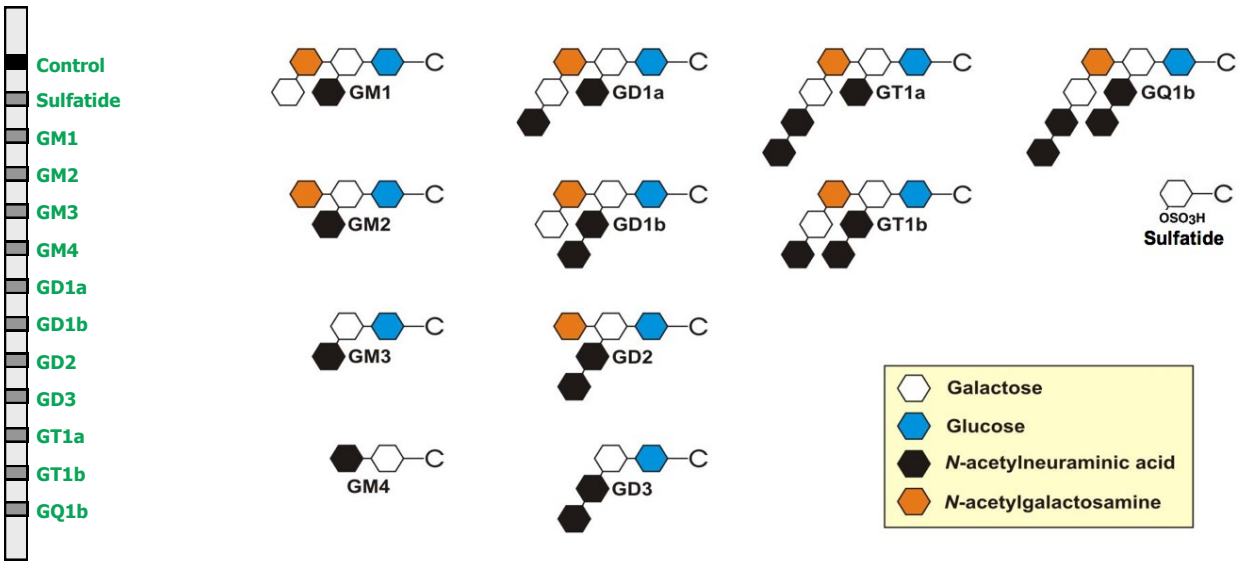
Glycolipid-mimicking structures identified on neuropathy associated microorganisms

Microorganism	Glycolipid mimicked
Campylobacter jejuni	GM1, GM1b, GD1a, GalNAc-GD1a, GD3, GT1a, GQ1b
Haemophilus influenzae	GM1, GT1a
Mycoplasma pneumoniae	Galactocerebroside
Cytomegalovirus	GM2

Table adapted from Willison & Yuki 2002

Anti-Ganglioside Assays

Dot with the highest number of antigens (12)



100 % Sensitivity and Specificity

Immune-mediated peripheral neuropathies	Number of samples	Anti-ganglioside autoantibody profiles detected by in-house immunodot	Number of positive samples using minimal positivity criteria*				
			Ih T	T1	T2	T3	T4
AMAN and AMSAN	6	IgG antibodies against GM1 > GD1b	6	6	3	1	6
Miller Fisher syndrome	4	IgG antibodies against GQ1b	4	4	2	3	3
GBS with ophthalmoplegia	1	IgG antibodies against GD1a, GQ1b	1	1	0	0	0
GBS with ophthalmoplegia	1	IgG antibodies against GD1a, GD1b, GT1b, GQ1b	1	1	0	0	1
GBS post CMV infection	2	IgM antibodies against GM2	2	2	2	2	2
Axonal motor GBS post CJ infection	1	IgG and IgM antibodies against GM1 and GD1b	1	1	0	0	1
Total of acute PN	15		15	15	7	6	13
CANOMAD syndrome	12	M-IgM antibodies against GD1b, GD3, GT1b, GQ1b	12	12	6	5	7
Chronic motor neuropathy	3	M-IgM antibodies against GM1 and GD1b	3	3	2	1	3
Chronic motor neuropathy with lymphoma	1	M-IgM antibodies against GD1a and GT1b	1	1	1	1	1
Chronic sensory neuropathy	1	M-IgM antibodies against sulfatides > GD1b > GM1	1	1	1	1	1
MMN	1	IgM antibodies against GM1 > GD1b	1	1	0	0	1
Total of chronic PN	18		18	18	10	8	13
Total of PN	33		33	33	17	14	26

Comparison with other commercial assays (Caudie et al. 2013)

Specific antibody profiles obtained in 15 patients with acute peripheral neuropathies and 18 patients with chronic peripheral neuropathies as obtained by in-house immunodot assay and by 4 commercial assays (see table).

CJ - *Campylobacter jejuni,* M-IgM - Monoclonal IgM antibodies, PN - peripheral neuropathies, IhT: In-house Test, T - Test, see left for other abbreviations
* The 5 immunodominant gangliosides present on each test are GM1, GM2, GD1a, GD1b, and GQ1b.

Sensitivity

IgG:	**T1 = GA**	**100 % (15/15)**
	T2 = Zentech	47 % (7/15)
	T3 = Euroimmun	40 % (6/15)
	T4 = Bühlmann	87 % (13/15)
IgM:	**T1 = GA**	**100 % (18/18)**
	T2 = Zentech	55 % (10/18)
	T3 = Euroimmun	44 % (8/18)
	T4 = Bühlmann	72 % (13/18)

Specificity

100 % for all tests

(10 non-autoimmune neuropathies)

Anti-Ganglioside Dot

Product Specifications

Conjugate:	Anti-human-IgG-HRP, anti-human-IgM-HRP
Format:	Membranes with 12 different gangliosides (purified human antigens)
Sample:	10 µl undiluted serum
Substrate:	TMB

Manual

Classic version with manual processing and visual or automated suevaluation through scan software pport (DotBlot Analyzer).

Automated

Fully automatic processing and evaluation of the results with the DotDiver2.0 device.

Order No.		Product	Results	Determinations	Time (h)	Tempera-ture (°C)
5003		Anti-Gangliosid Dot	Qualitative, Semi-Quantitative	20 x 12	3:10	4
50301		**DotDiver** Anti-Gangliosid Screen (IgGM)	Semi-Quantitative	20 x 12	2	RT
50381		**DotDiver** Anti-Gangliosid IgG	Semi-Quantitative	20 x 12	2	RT
50391		**DotDiver** Anti-Gangliosid IgM	Semi-Quantitative	20 x 12	2	RT

Literature

1. Conrad K, Schößler W, Hiepe F, Fritzler MJ Autoantibodies in organ specific autoimmune diseases - a diagnostic reference. Autoantigens, Autoantibodies, Autoimmunity 2011, Volume 8
2. Yuki N & Hartung HP. Guillain-Barré syndrome. N Engl J Med. 2012;366(24):2294-304.
3. Ang CW, Jacobs BC, Laman JD. The Guillain-Barré syndrome: a true case of molecular mimicry. Trends Immunol. 2004;25(2):61-6.
4. Willison HJ & Yuki N. Peripheral neuropathies and anti-glycolipid antibodies. Brain. 2002;125(Pt 12):2591-625.
5. Caudie C, Quittard Pinon A, Bouhour F, Vial C, Garnier L, Fabien N. Comparison of commercial tests for detecting multiple anti-ganglioside autoantibodies in patients with well-characterized immune-mediated peripheral neuropathies. Clin Lab. 2013;59(11-12):1277-87.

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