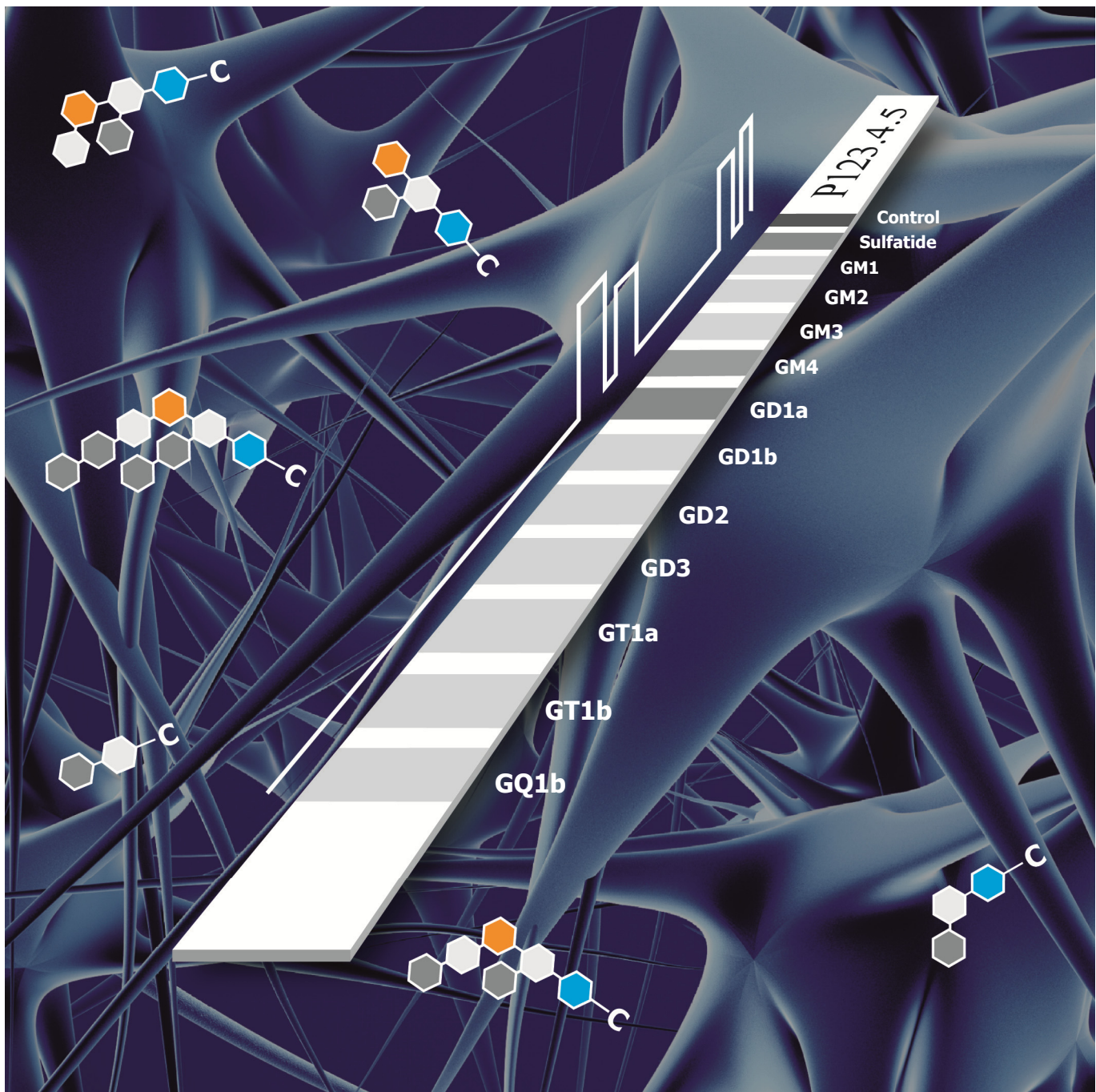


# Anti-Ganglioside Dot

12 LINE - Profile Diagnostics (IgG/IgM)



# Anti-Ganglioside Dot

## Autoimmune Neuropathies

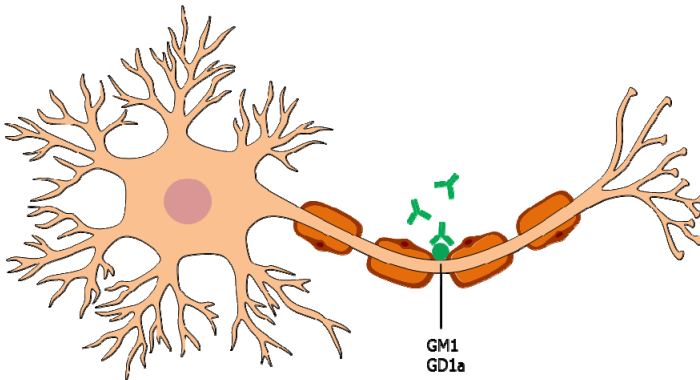
Autoimmune neuropathies are characterized by a number of clinical symptoms, which are however not distinguishable from other neuropathies. Neuropathies with autoimmune pathogenesis (13 % of neuropathies) can therefore be misdiagnosed as being idiopathic and consequently mistreated. The determination 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
<b>GBS/AIDP</b>		IgG			IgM	IgG	IgG				IgG	
<b>GBS/AMAN &amp; AMSAN</b>	IgM	IgG			IgM	IgG	IgG				IgG	
<b>GBS after CMV-Infection</b>		IgM	IgM			IgM	IgM					
<b>GBS with ataxia</b>							IgG			IgG		IgG
<b>GBS with ONS</b>		IgG				IgG				IgG		IgG
<b>GBS with ophthalmoplegia</b>										IgG		IgG
<b>MFS</b>					IgM		IgG		IgG	IgG	IgG	IgG
<b>Bickerstaff encephalitis</b>										IgG		IgG
<b>CANOMAD</b>				IgM		IgM	IgM	IgM	IgM	IgM	IgM	IgM
<b>MMN</b>		IgM	IgM	IgM	IgM	IgM	IgM					
<b>CIDP</b>	IgM	IgM	IgM	IgM		IgM	IgM					
<b>MN with gammopathy</b>	IgM	IgM					IgM					

AIDP - acute inflammatory 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 inflammatory 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

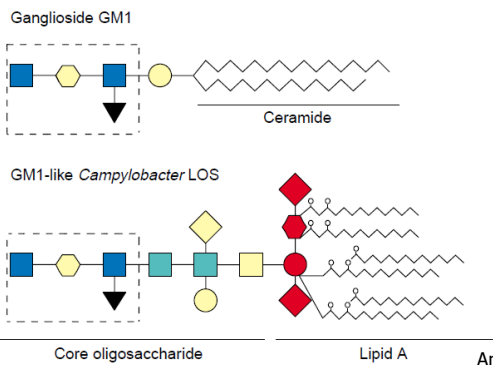
## An Example for Immunopathogenesis - GBS/AMAN



**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 Neuropathies



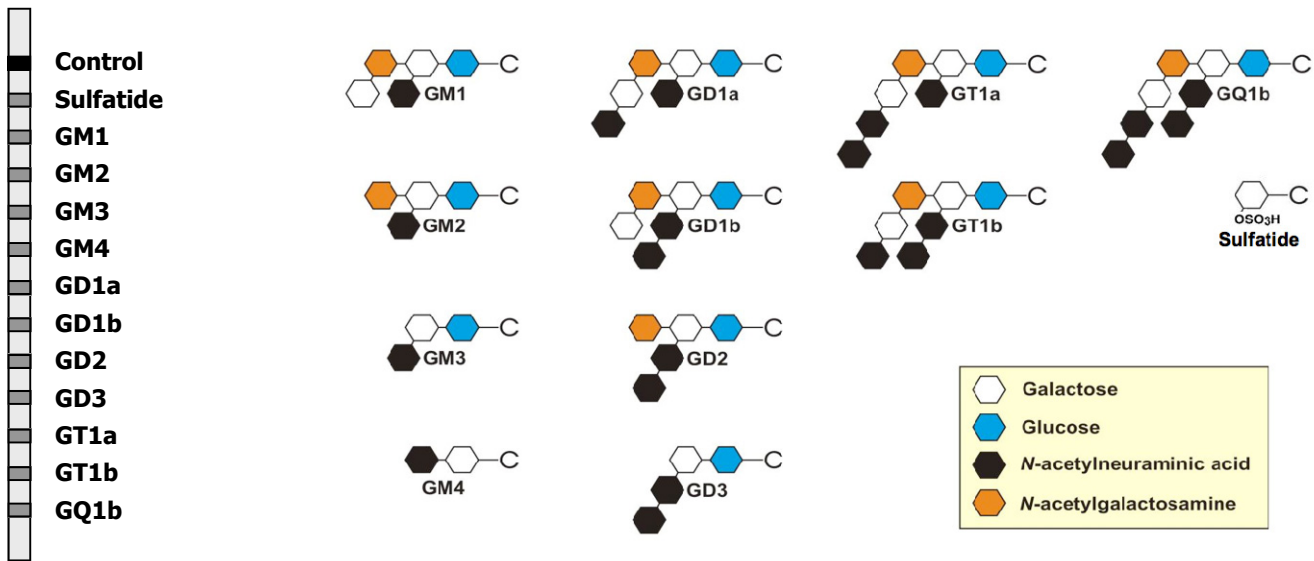
## Glycolipid-mimicking structures identified on neuropathy associated microorganisms

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

Table adapted from Willison & Yuki 2002

# Anti-Ganglioside Dot

## 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
<b>Total of acute PN</b>	<b>15</b>		<b>15</b>	<b>15</b>	<b>7</b>	<b>6</b>	<b>13</b>
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
<b>Total of chronic PN</b>	<b>18</b>		<b>18</b>	<b>18</b>	<b>10</b>	<b>8</b>	<b>13</b>
<b>Total of PN</b>	<b>33</b>		<b>33</b>	<b>33</b>	<b>17</b>	<b>14</b>	<b>26</b>

## 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 (in-house = 100 %)

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

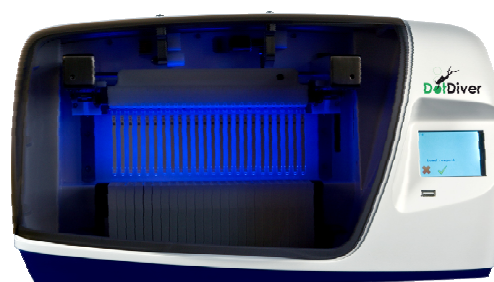
## Product Specifications





Conjugate:	Anti-human-IgG-HRP, anti-human-IgM-HRP
Format:	Membranes with 12 different gangliosides (purified human antigens)
Incubation time:	3 h 10 min (4 °C, RT)
Sample:	10 µl undiluted serum
Substrate:	TMB

DotBlot Analyzer Software and Scanner are additionally for semi-quantitative evaluation available.

## Automation

Automated processing using **DotDiver** instrument and DrDot software is also possible.



Order No.		Product	Results	Determinations
5003		Anti-Gangliosid Dot	Qualitative, Semi-Quantitative	20 x 12
5030		<b>DotDiver</b> Anti-Gangliosid Screen (IgGM)	Semi-Quantitative	20 x 12
5038		<b>DotDiver</b> Anti-Gangliosid IgG	Semi-Quantitative	20 x 12
5039		<b>DotDiver</b> Anti-Gangliosid IgM	Semi-Quantitative	20 x 12

## Literature

1. Conrad K, Schöbler 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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