**GanglioCombi ELISA**

Screening Tests for Autoimmune–Neuropathies

**The Expert’s Choice**

GanglioCombi: IgG/IgM Mix conjugate for classic initial screening

GanglioCombi–GM: Individual conjugates for IgG and IgM – differential diagnosis of acute and chronic diseases

GanglioCombi–Light-GM: Anti-Gangliosid antibody profiles for the clinically most relevant Gangliosides

Quantitative: Clinically defined titer categories
anti-Ganglioside Autoantibodies

Introduction
The diagnosis of peripheral Neuropathies increasingly is relying on the use of anti-Ganglioside antibody tests. Conditions such as Guillain–Barré Syndrome (GBS) and its variants and a variety of sensory and motor neuropathy syndromes can now be defined in terms of immunologic profiles. Detection of these autoantibodies indicates an immune-mediated origin of the peripheral nerve disturbances and that immune suppressive therapy may be beneficial.

Gangliosides and anti-Ganglioside Autoantibodies
Elevated antibody titers may occur as monoclonal IgMs or polyclonal IgGs. There is a large number of gangliosides which differ in terms of its number and position of hexoses and sialic acid residues (Figure 1). Consequently, there are many targets giving rise to various antibodies each of which differs in its specificity. There are differences in structure, quantity and distribution of different gangliosides in the nervous system. For example motor nerves are particularly rich in GM1 or GD1b, whereas in sensory nerves polysialo-gangliosides are predominant.

Figure 1. The most important and clinically relevant gangliosides.

Clinical Syndrome Antibody

<table>
<thead>
<tr>
<th>Clinical Syndrome</th>
<th>Antibody</th>
<th>Isotype</th>
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</thead>
<tbody>
<tr>
<td>Chronic sensori-motor demyelinating Neuropathy</td>
<td>SGPG, MAG</td>
<td>IgM</td>
</tr>
<tr>
<td>CANOMAD</td>
<td>GD1b, Q1b</td>
<td>IgM*</td>
</tr>
<tr>
<td>MMN</td>
<td>(asialo)–GM1, GD1b, GM2</td>
<td>IgM</td>
</tr>
<tr>
<td>AMAN(S)AN</td>
<td>GM1, GD1a</td>
<td>IgG</td>
</tr>
<tr>
<td>MFS</td>
<td>GQ1b</td>
<td>IgG</td>
</tr>
</tbody>
</table>

Table 1. Clinical Syndromes associated with specific and clinically most relevant anti-glycolipid antibodies. Abbreviations footnotes:

-asca present as IgM monoclonal gangliosidese; SGPG: sulphated glucuronyl paragloboside; MAG: Myelid Associated Glycoprotein; CANOMAD: chronic ataxic neuropathy with ophthalmoplegia, M-protein, Agglutinin and Disialoglcycolipid antibodies; AMAN: acute motor axonal neuropathy, MFS: Miller–Fisher Syndrome.

Acute Neuromuscular Paralysis – IgG
Anti-ganglioside antibodies of IgG class are detected in some acute forms of polyradiculoneuritis. The most important one is a pure motor form of the Guillain–Barré Syndrome (GBS) with axonal damage (e.g. AMAN, acute motor axonal neuropathy). It is characterized by very high titers of anti-ganglioside antibodies, mainly directed against GM1 and GD1b. The Miller–Fisher syndrome (MFS) is associated with the paralysis of oculomotor nerves and ataxia. It is characterized by the occurrence of anti-GQ1b antibodies.

The occurrence of these antibodies may be explained with molecular mimicry: Campylobacter jejuni strains contain sugar determinants very similar to some gangliosides. In addition, other infectious agents might be involved in the pathogenesis.

Anti-Ganglioside Antibody Profiles
Considering the diversity of anti-ganglioside antibodies, the measurement of the appropriate and clinical relevant anti-ganglioside antibody panels is important to maximize the detection of neuropathy-associated anti-ganglioside antibodies. Furthermore, a differential analysis of IgG and IgM class antibodies is important, particularly as IgG antibodies are associated with acute diseases, whereas the occurrence of IgM antibodies is typical for chronic conditions.

Frequency of anti-Ganglioside Antibodies
In a study in which n=124 post-infectious GBS patients have been included, the most commonly implicated anti-ganglioside antibodies were GM1 (38%), GD1a (12%), GM2 (23%), GQ1b (9%) and GD1b (9%), (PhD thesis, D. Taravel, 2008).

Detection of anti-Ganglioside Antibodies
The quantitative ELISA technique is recommended as the method of choice for anti-ganglioside autoantibodies analysis. BÜHLMANN offers a panel of quantitative GanglioCombi formats for comprehensive and basic screening. The results are reported in clinically defined titer categories.

Differentiation between acute and chronic disease: GanglioCombi–GM; Differentiation of sensory and motor neuropathies: GanglioCombi; Differentiation of particular neuropathies: GanglioCombi–Light–GM.