PR3s
MPOs
Detect more cases with ANCA-associated vasculitis

- High sensitivity due to indirect coating of the antigens using an anchor technique.

Less false positives

- The specificity of EliA MPO$^S$ and EliA PR3$^S$ is close to 100%.
- A result you can rely on.

Standardized against International Reference

- EliA PR3$^S$ is calibrated against the CDC PR3-ANCA Human Reference Serum #16.
- EliA MPO$^S$ is calibrated against the CDC MPO-ANCA Human Reference Serum #15.
- Results are given in International Units (IU/ml).

Higher clinical value than indirect immunofluorescence (IIF)

- High usefulness for the clinician because of much higher specificity than IIF.
- Only anti-MPO or anti-PR3 are predictive for ANCA-associated vasculitis, while IIF ANCA occur in many other diseases.

EliA PR3$^S$ and EliA MPO$^S$ – the perfect team

- Fast and comfortable: both antibodies can be measured from one sample tube in the same run.
- Two high sensitivity tests playing hand in hand in order to find as many autoimmune vasculitis cases as possible.

Easy and fully automated workup

- Reliable Phadia instruments available for every lab size.
- Objective, operator-independent and quantitative results.
ANCA-Associated Vasculitis (AAV)

Vasculitis is a process caused by inflammation of blood vessel walls and results in a variety of disorders. It may be categorized by the size of the involved blood vessel as large-, medium-, or small-vessel vasculitis. Small-vessel vasculitis may be further classified as ANCA-associated or non-ANCA-associated vasculitis (NAAV). Antineutrophil cytoplasmic antibodies (ANCA) were first described in 1982 in patients with necrotizing and crescentic glomerulonephritis (NCGN) without immune deposits (pauci-immune). Soon it was found that ANCA are not only markers for idiopathic NCGN without signs of extrarenal disease but also for glomerulonephritis associated with systemic vasculitis. ANCA-associated vasculitis may be either Wegener’s granulomatosis (WG), or a form of vasculitis in which small vessels are involved without granuloma formation. The latter condition is called “microscopic polyangiitis (MPA)”. ANCA with MPO-reactivity are also present in patients with the Churg-Strauss syndrome (CSS) characterized by a history of asthma, hypereosinophilia and systemic vasculitis.

The Antigens

ANCA are specific antibodies for antigens in cytoplasmic granules of neutrophils and monocyte lysosomes. These antibodies can be detected with indirect immunofluorescence microscopy, revealing two major patterns of staining: cytoplasmic ANCA (c-ANCA) and perinuclear ANCA (p-ANCA). The major antigen which is targeted by c-ANCA is proteinase 3 (PR3), while for p-ANCA it is mainly anti-myeloperoxidase (MPO). Using antigen-specific immunoassays to characterize ANCA (rather than the pattern of immunofluorescence microscopy) is more specific and more clinically relevant; therefore, the terms anti-PR3 and anti-MPO are used more and more often. Antibodies against other neutrophil antigens might produce ANCA-patterns but are not specific for ANCA-associated vasculitides.

In both EliA PR3 and EliA MPO the antigens are bound to the EliA well using an anchor technique. Such an indirect binding has proven to increase the sensitivity of the assays substantially.

High Clinical Relevance

- EliA PR3 and EliA MPO identify patients with ANCA-associated vasculitides and avoid false positive results

<table>
<thead>
<tr>
<th>EliA PR3 positive &gt; 3.0 IU/ml</th>
<th>EliA MPO positive &gt; 5.0 IU/ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical Sensitivity</td>
<td>79.0 %</td>
</tr>
<tr>
<td>Clinical Specificity (for AAV)</td>
<td>98.0 %</td>
</tr>
<tr>
<td>Positive Predictive Value</td>
<td>77.5 %</td>
</tr>
<tr>
<td>Negative Predictive Value</td>
<td>87.5 %</td>
</tr>
<tr>
<td>Positive likelihood ratio*</td>
<td>39.5</td>
</tr>
<tr>
<td>Negative likelihood ratio**</td>
<td>0.21</td>
</tr>
</tbody>
</table>

Table 1: Clinical performance of EliA PR3 and EliA MPO (in-house data)

The sensitivity of EliA PR3 was calculated using 100 WG-patients and the sensitivity of EliA MPO was calculated using 80 MPA sera. Specificity of both tests was calculated using 150 disease controls.

* A positive likelihood ratio (LR) of 2 to 5 indicates an only limited clinical value, 5 to 10 is modest and above 10 it is of high clinical importance.

** A negative LR of 0.2 to 0.5 indicates an only limited value to exclude the disease, 0.1 to 0.2 is of modest relevance and lower than 0.1 indicates a high clinical importance.
**EliA PR3**: Find Wegener's granulomatosis with an excellent differentiation from non-ANCA related diseases.

**EliA MPO**: Find microscopic polyangiitis and other ANCA-related diseases with highest specificity.

**Standardization**

Growing evidence for the relevance of quantitative results of antibodies against PR3 and MPO for the diagnosis but also for the monitoring of AAV increased the call for a better standardization of these tests. Finally, international efforts led to the implementation of the CDC references in 2008. Both, EliA PR3 and EliA MPO are calibrated against the new CDC ANCA references: CDC PR3-ANCA Human Reference Serum #16 and CDC MPO-ANCA Human Reference Serum #15. Results are given in International Units (IU/ml).
Almost 30% of disease controls gave an ANCA pattern in IIF

Clinical value matters — EliA PR3\(^{\text{S}}\) and EliA MPO\(^{\text{S}}\) versus IIF

An ANCA pattern was found in 63.2% of ANCA-associated vasculitides (AAV) and in 29.3% of controls, resulting in a specificity of only 70.7%. On the other hand, only 2 out of 150 disease control samples were positive in EliA PR3\(^{\text{S}}\) and EliA MPO\(^{\text{S}}\) (specificity of 98.7%). The classical c-ANCA and p-ANCA patterns occur less often in AAV than anti-PR3 and anti-MPO, respectively. Only when all ANCA patterns are considered, also the atypical ones, the sensitivity is higher than that of EliA. However, at the same time the specificity is so much lower that the clinical utility of a positive ANCA is questionable. The clinical utility can be expressed in positive likelihood ratio (LR). In this serum panel, the positive LR of IIF is only 2.22 while EliA receives a positive LR of more than 48. Therefore, an IIF result alone is not indicative for any disease or disease group while a positive anti-PR3 or anti-MPO result gives a strong indication for AAV such as Wegener's granulomatosis or microscopic polyangiitis.

Easy and Comfortable: Fully Automated Tests

EliA PR3\(^{\text{S}}\) and EliA MPO\(^{\text{S}}\) are fully automated tests which are run on the Phadia Laboratory Systems (Phadia 100, Phadia 250 and the high-capacity instruments Phadia 2500 and Phadia 5000). Anti-PR3 and anti-MPO tests can be done from one sample tube in the same run. Of course, also all other EliA parameters such as antinuclear antibodies (ANA) can be measured in parallel on the same sample, as well as anti-GBM, which may be positive in ANCA-positive sera and give important clinical information. A stored IgG standard curve makes ANCA testing cost-efficient, even if you run only very few samples. With the STAT function, results of urgent samples can be obtained in short time. EliA PR3\(^{\text{S}}\) and EliA MPO\(^{\text{S}}\) provide quantitative results, given in International Units, which are objective and reproducible and independent of the operator.

Leave the routine to the instruments and improve your efficiency!
Technical Data

- **Products**
  - EliA™ PR3<sup>®</sup>
  - EliA™ MPO<sup>®</sup>

- **Antigens**
  - EliA™ PR3: proteinase 3, purified from human granulocytes
  - EliA™ MPO: myeloperoxidase, purified from human granulocytes

- **Standardization**
  - 6 point standard curve for IgG;
  - calibrated against the CDC PR3-ANCa Human Reference Serum #16 and CDC MPO-ANCa Human Reference Serum #15

- **Cut-off / measuring range**

<table>
<thead>
<tr>
<th>EliA™ PR3&lt;sup&gt;®&lt;/sup&gt;</th>
<th>negative</th>
<th>equivocal</th>
<th>positive</th>
<th>measuring range</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;2.0 IU/ml</td>
<td>2.0–3.0 IU/ml</td>
<td>&gt; 3.0 IU/ml</td>
<td>0.2 – 177 IU/ml</td>
</tr>
<tr>
<td>EliA™ MPO&lt;sup&gt;®&lt;/sup&gt;</td>
<td>&lt;3.5 IU/ml</td>
<td>3.5–5.0 IU/ml</td>
<td>&gt; 5.0 IU/ml</td>
<td>0.2 – 134 IU/ml</td>
</tr>
</tbody>
</table>

- **Dilution**
  - EliA™ PR3<sup>®</sup>: 1:100 (automated)
  - EliA™ MPO<sup>®</sup>: 1:50 (automated)

- **Sample Material**
  - Serum, Plasma (EDTA, citrate, heparin)

- **Normal Distribution**

<table>
<thead>
<tr>
<th>EliA™ PR3&lt;sup&gt;®&lt;/sup&gt;</th>
<th>mean</th>
<th>95% percentile</th>
<th>99% percentile</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.3 IU/ml</td>
<td>0.6 IU/ml</td>
<td>0.7 IU/ml</td>
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</table>

<table>
<thead>
<tr>
<th>EliA™ MPO&lt;sup&gt;®&lt;/sup&gt;</th>
<th>mean</th>
<th>95% percentile</th>
<th>99% percentile</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0.6 IU/ml</td>
<td>0.9 IU/ml</td>
<td>1.5 IU/ml</td>
</tr>
</tbody>
</table>

- **Reproducibility**
  - EliA™ PR3<sup>®</sup>: Intra-run CV* 3.9–10.5 %
  - EliA™ MPO<sup>®</sup>: Intra-run CV* 2.5–6.1 %
  - Inter-run CV* 0.0–7.0 %
  - Inter-run CV* 1.9–4.9 %

*for details see Directions For Use

Ordering Information

- **EliA™ PR3<sup>®</sup> Well**
  - 4 x 12 determinations
  - Article No. 14-5536-01

- **EliA™ MPO<sup>®</sup> Well**
  - 4 x 12 determinations
  - Article No. 14-5537-01

**EliA™ Controls**

- **EliA™ ANCA/GBM Positive Control 100**
  - 6 vials for single use
  - Article No. 83-1039-01

- **EliA™ ANCA/GBM Positive Control 250**
  - 6 vials for single use
  - Article No. 83-1034-01

- **EliA™ IgG/IgM/IgA Negative Control 100**
  - 6 vials for single use
  - Article No. 83-1042-01

- **EliA™ IgG/IgM/IgA Negative Control 250**
  - 6 vials for single use
  - Article No. 83-1037-01

For EliA™ specific reagents and general reagents please refer to the Phadia product catalogue.