Identify inflammatory bowel diseases clearly and efficiently

EliA™ Calprotectin – the first fully automated calprotectin stool test
Fecal calprotectin is a very sensitive and specific marker for inflammation in the intestinal tract: as a first line test, a negative result can rule out an inflammatory process while a positive result may prioritize endoscopy in the diagnostic path.\textsuperscript{4}

Fecal calprotectin is an efficient marker for therapeutic effectiveness and mucosal healing since its level correlates well with endoscopic and histological findings in inflammatory bowel diseases.\textsuperscript{2,7} In recent studies it was possible to predict relapse in Crohn’s disease and ulcerative colitis.\textsuperscript{6,8,9}

Fecal calprotectin can now be measured with a fast, fully automated test leading to improved operational efficiency and minimized costs: EliA™ Calprotectin.
EliA™ Calprotectin – fast, fully automated testing

Routine stool extraction samples are processed automatically by the Phadia® Laboratory Systems by reducing the workload for the lab personnel. The four available instruments – Phadia® 100, Phadia® 250, Phadia® 2500 and Phadia® 5000 – are designed to meet the specific needs of the laboratory. EliA™ Calprotectin can easily be performed together with EliA™ serum tests for celiac disease or food allergy, even simultaneously. This provides flexibility, saves costs, and assures a quick delivery of results for improved service quality.

Excellent performance, high predictive values
The outstanding performance of EliA™ Calprotectin is underlined by the high sensitivity and the high specificity of the test (Table 1). Most important, the predictive values and the likelihood ratios give excellent values assuring high clinical usefulness of the test in routine practice.

Identifies IBD clearly
An internal clinical study showed that EliA™ Calprotectin is able to differentiate clearly between inflammatory bowel diseases (IBD), irritable bowel syndrome (IBS) and other functional bowel disorders (BD) (Figure 1).

EliA™ Calprotectin – clear IBD / IBS differentiation

High clinical value

<table>
<thead>
<tr>
<th></th>
<th>EliA™</th>
<th>Supplier 1</th>
<th>Supplier 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>97.7 %</td>
<td>96.7 %</td>
<td>99.2 %</td>
</tr>
<tr>
<td>Specificity</td>
<td>89.8 %</td>
<td>89.8 %</td>
<td>76.3 %</td>
</tr>
<tr>
<td>Positive predictive value (PPV)</td>
<td>0.96</td>
<td>0.96</td>
<td>0.90</td>
</tr>
<tr>
<td>Negative predictive value (NPV)</td>
<td>0.95</td>
<td>0.93</td>
<td>0.98</td>
</tr>
<tr>
<td>Positive likelihood ratio (LR+) *</td>
<td>9.58</td>
<td>9.48</td>
<td>4.19</td>
</tr>
<tr>
<td>Negative likelihood ratio (LR-) *</td>
<td>0.03</td>
<td>0.04</td>
<td>0.01</td>
</tr>
</tbody>
</table>

Table 1: Performance data of EliA™ Calprotectin and tests from two other suppliers (internal study)

* Likelihood Ratios – diagnostic evidence or not
Likelihood ratios use the sensitivity and specificity of a test to determine if the positive or negative result of a diagnostic test changes the probability of the patient actually being afflicted with the disease.

\[ LR+ = \frac{Sensitivity}{1 - Specificity} \]
\[ LR- = \frac{1 - Sensitivity}{Specificity} \]

Diagnostic evidence:
- LR+ 0 - 2 none
- LR+ 2 - 5 weak
- LR+ 5 - 10 moderate
- LR+ > 10 high
- LR- 0.5 none
- LR- 0.2 - 0.5 weak
- LR- 0.1 - 0.2 moderate
- LR- < 0.1 high

The high LR+ value of calprotectin measurement shows the conclusive power of a positive test result for inflammation in the intestine.
Fecal calprotectin – a precise marker for intestinal inflammation: non-invasive, specific, and sensitive

Inflammation is characterized by an increased activity of immune cells (e.g. neutrophil granulocytes) which release pathogen attacking substances such as calprotectin. In intestinal inflammation the barrier function of the intestinal wall is lost and neutrophil granulocytes migrate through the wall into the intestinal lumen. This leads to an elevated calprotectin level in the stool.\(^3\) The level of fecal calprotectin correlates directly to the number of neutrophil granulocytes in the intestinal lumen. As such it is specifically elevated in inflammatory bowel diseases (IBD) such as Crohn's disease and ulcerative colitis and to a much smaller extent in other entities such as neoplasia and polyps. This correlation also makes stool calprotectin a very specific and sensitive marker in indicating intestinal inflammation.\(^3\) The level of calprotectin in feces is approximately 6 times higher than in serum. This makes stool testing more sensitive in addition to its higher specificity for intestinal diseases.\(^4\)

**Recommended as a first line test**

Together with CRP, ESR, and stool culture, the measurement of stool calprotectin is useful as a screening test in all subjects reporting gastrointestinal (GI) problems.\(^4\) Since complaints such as abdominal pain, diarrhea, and bloating are very frequent and are common to several GI diseases which would require different therapeutic approaches, it is crucial to discriminate between inflammatory and non-inflammatory disorders; i.e. between inflammatory bowel diseases (IBD) and non-inflammatory diseases, such as irritable bowel syndrome (IBS). **A negative calprotectin result in a patient without alarm symptoms is reason enough to avoid endoscopy** while a positive result can prioritize invasive and expensive procedures such as endoscopy including intestinal biopsy. The measurement of calprotectin provides an important orientation for the physician in the diagnosis of GI patients.

**Non-invasive testing with high clinical value**

Stool calprotectin measurement is an easy, non-invasive first line test which clearly differentiates IBD from IBS and other functional disorders. It has been shown to be the most sensitive and most specific test for this discrimination **clearly outperforming blood tests such as CRP or ESR** (Figure 2).\(^5\) The high positive and negative predictive value of fecal calprotectin provides valuable help in the diagnostic process.\(^5\) Furthermore, stool calprotectin correlates with disease activity and allows the prediction of relapses in IBD.\(^6\) This makes calprotectin useful for both the diagnosis and the monitoring of IBD patients.

**Definition of fecal calprotectin**

Calprotectin is an abundant protein in pathogen defense. The calcium- and zinc-binding protein is predominantly present in the cytoplasm of cells involved in pathogen defense such as neutrophil granulocytes, monocytes, and macrophages. Calprotectin shows bacteriostatic and fungistatic properties in vitro which underline its function in pathogen attack. In neutrophil granulocytes it accounts for as much as 60% of the cytosolic protein.\(^1,2\)

**Crohn’s disease**

Skip lesions

**Ulcerative colitis**

Continuous colonic involvement beginning in rectum

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Figure 2, 3: Crohn's disease and ulcerative colitis (UC)

Location of inflammatory changes: Crohn's disease can affect any part of the gastrointestinal tract, from mouth to anus (skip lesions). The majority of cases start in the terminal ileum. UC is restricted to the colon and the rectum.
Crohn’s disease / IBS – fecal calprotectin minimizes false positives

Fecal Calprotectin is more effective
Fecal calprotectin is more effective in terms of diagnostic accuracy than the standard tests ESR and CPR currently used for distinguishing IBD from IBS. Fecal calprotectin minimizes the number of false positive results and reduces the number of unnecessary biopsies.

Figure 4: Receiver operator characteristic analysis of the ability of calprotectin, C reactive protein (CRP), and erythrocyte sedimentation rate (ESR) to discriminate between patients with Crohn’s disease and irritable bowel syndrome (modified after Tibble et al 2000).

Your Advantages with EliA™ Calprotectin:

- clear differentiation between IBD and IBS
- early diagnostic guidance
- completely automated and efficient testing
- reducing the workload for your lab personnel
- add-on to the EliA™ gastro panel on Phadia® Laboratory Systems

References:
EliA™ Calprotectin: technical data

EliA™ Calprotectin offers a complete solution: from stool extraction to automated sample measurement.

Coating: Mouse monoclonal antibodies to calprotectin

Dilution: 1:100

Sample material: Human stool

Standardization: Six point calibration curve; results in mg/kg

Cut-off / measuring range:

<table>
<thead>
<tr>
<th>Cut-off / Measuring Range</th>
<th>Negative</th>
<th>Positive</th>
<th>Measuring Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 50 mg/kg</td>
<td>&gt; 50 mg/kg</td>
<td>15 – ≥ 3000 mg/kg</td>
<td></td>
</tr>
</tbody>
</table>

Normal distribution:

- 27.3 mg/kg / 43.6 mg/kg
  (95% / 99% percentile)

Reproducibility:

- Intra-run variance*: 2.8 - 7.0%
- Inter-run variance*: 1.9 - 7.3%
  * for details see directions for use

Ordering information:

<table>
<thead>
<tr>
<th>EliA™ Calprotectin Well</th>
<th>4 x 12 wells</th>
<th>14-5610-01</th>
</tr>
</thead>
<tbody>
<tr>
<td>EliA™ Calprotectin Calibrator Well</td>
<td>4 x 12 wells</td>
<td>14-5618-01</td>
</tr>
<tr>
<td>EliA™ Calprotectin Extraction Buffer</td>
<td>6 x 24 tests</td>
<td>83-1068-01</td>
</tr>
<tr>
<td>Fecal Extraction Device</td>
<td>50 devices</td>
<td>14-5619-01</td>
</tr>
</tbody>
</table>

Reagents for Phadia® 100:

| EliA™ Calprotectin Calibrators | 6 vials for 1 curve | 83-1058-01 |
| EliA™ Calprotectin Curve Control | 6 vials for 6 runs | 83-1059-01 |
| EliA™ Calprotectin Conjugate | 2 x 48 tests | 83-1060-01 |
| EliA™ Calprotectin Conjugate | 6 x 48 tests | 83-1061-01 |
| EliA™ Calprotectin Positive Control 100 | 6 vials for 12 tests | 83-1066-01 |
| EliA™ Calprotectin Negative Control 100 | 6 vials for 12 tests | 83-1067-01 |

Reagents for Phadia® 250/2500/5000:

| EliA™ Calprotectin Calibrator Strips | 5 strips for 5 curves | 83-1062-01 |
| EliA™ Calprotectin Curve Control Strips | 5 strips for 30 runs | 83-1063-01 |
| EliA™ Calprotectin Conjugate 50 | 6 x 50 tests | 83-1064-01 |
| EliA™ Calprotectin Conjugate 200 | 6 x 200 tests | 83-1065-01 |
| EliA™ Calprotectin Conjugate Positive Control 250 | 6 vials for 12 tests | 83-1083-01 |
| EliA™ Calprotectin Conjugate Positive Control 50 | 6 vials for 12 tests | 83-1084-01 |
| EliA™ Calprotectin Conjugate Positive Control 250/5000 | 6 vials for 12 tests | 83-1085-01 |
| EliA™ Calprotectin Conjugate Negative Control 250/5000 | 6 vials for 12 tests | 83-1086-01 |

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