

# Diagnostics of chronic inflammatory bowel diseases.



# Chronic inflammatory bowel diseases (CIBD)

CIBD are characterised by inflammation in different areas of the gastrointestinal tract and occur in episodes.

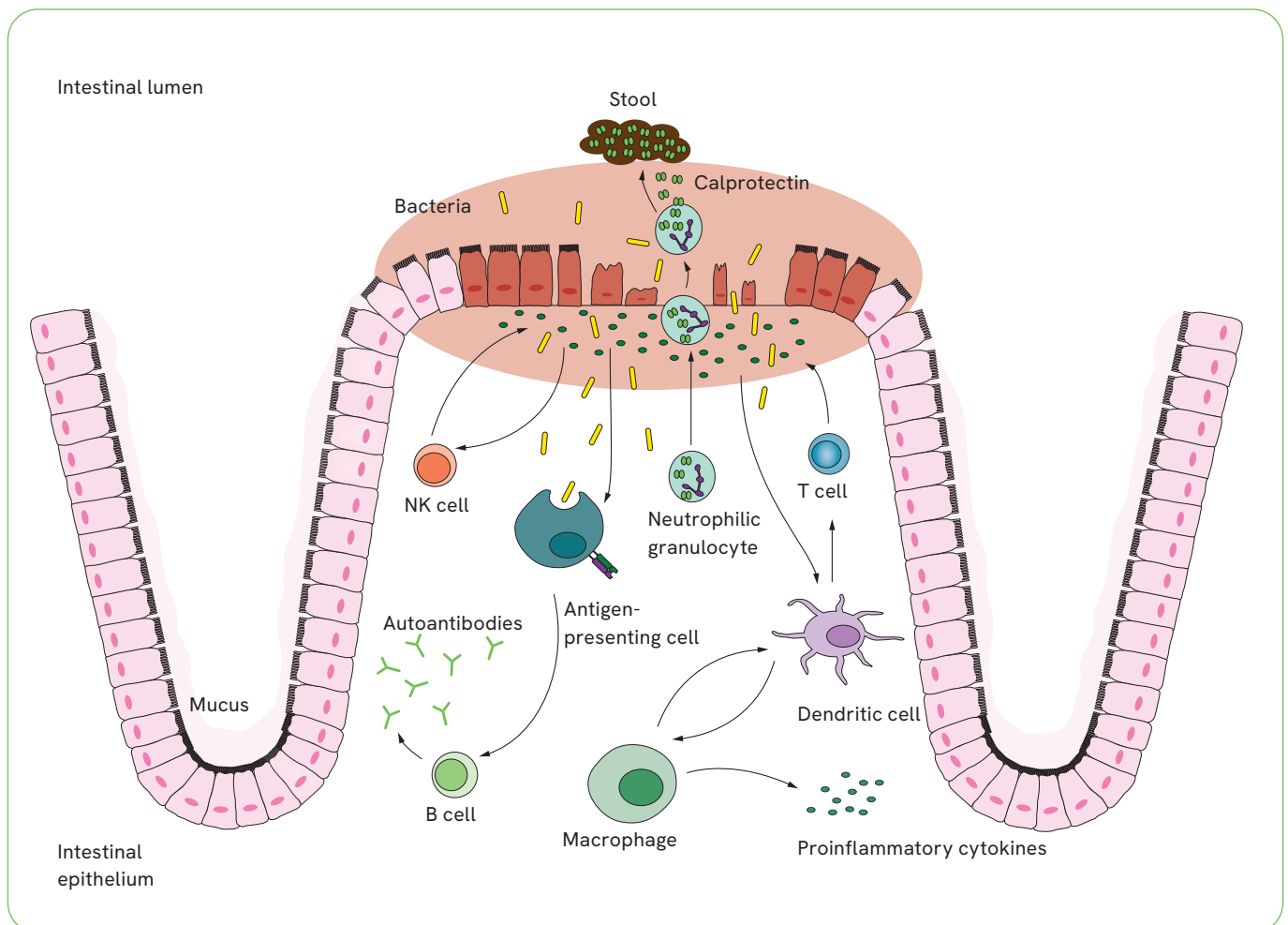
Symptomatic phases alternate with remission phases, in which the disease is inapparent. The severity of the symptoms and the duration of the episodes differ from patient to patient. The aetiology of CIBD is still relatively unknown. However, it is assumed that genetic predisposition and certain environmental factors (antibiotic treatment, smoking, "western diet") can cause the disease.

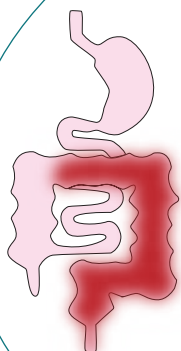
The two most important CIBD forms are **ulcerative colitis (UC)** and **Crohn's disease (CD)**. In around 10% of

cases, a mixed form is observed, which cannot be clearly assigned to either of the diseases (indeterminate colitis).<sup>1</sup>

In both CD and UC there is a dysfunction of the intestinal barrier of mucosa and intestinal epithelium. Thus, pathogenic bacteria may travel from the intestinal lumen to the epithelial cells and trigger an inflammatory response.

For differentiation between the different CIBD and for discrimination of these from irritable bowel syndrome, targeted differential diagnostics are of great importance.<sup>2,3</sup>





### Ulcerative colitis

Incidence: 3.0-24 per 100,000<sup>4</sup>

Prevalence: 90-500 per 100,000<sup>4</sup>

Manifestation before age 18: 20-30% of patients<sup>4</sup>

Latency period until diagnosis: 1.2 years<sup>6</sup>

Colectomy necessary in 10-30% of patients<sup>7</sup>

### Indeterminate colitis

### Crohn's disease

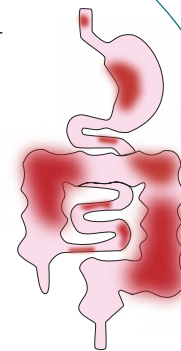
Incidence: up to 12.7 per 100,000<sup>5</sup>

Prevalence: up to 322 per 100,000<sup>5</sup>

Manifestation before age 18: approx. 25% of patients<sup>5</sup>

Latency period until diagnosis: 7.7 years<sup>6</sup>

Intestinal surgery necessary in 80% of patients<sup>7</sup>



### Symptoms of UC:

- The inflammation is often limited to the colon.
- It starts at the anus and spreads further along the colon.
- Only the intestinal mucosa is inflamed.
- Typical symptoms are bloody diarrhoea (mostly at night and postprandial) with pus or slimy discharge and severe abdominal cramps during defaecation.
- The most severe complications include toxic megacolon, which is defined by extreme dilatation of the colon and potential bursting.

### Symptoms of CD:

- The inflammation can affect the entire gastrointestinal tract - from the mouth to the anus.
- Patches of inflamed intestinal sections alternate with healthy patches, with the terminal ileum being most frequently affected.
- The symptoms often depend on the disease locus and resemble those of UC.
- The inflammation may permeate all the layers of the intestinal wall and spread even further. This can lead to the formation of fistulas and abscesses.
- Scarred and swollen intestinal tissue can also lead to intestinal stenosis.

### Our test systems for the determination of faecal and serological markers for CIBD diagnostics:

- Calprotectin ELISA - Secure differentiation between chronic inflammatory and functional bowel diseases
- IFA CIBD mosaics - Screening tests to support differential diagnostics of UC and CD
- Anti-Saccharomyces cerevisiae ELISA - Provides useful information on the severity of the diseases
- EUROLINE Autoimmune Gastrointestinal Diseases - Discrimination of CD from coeliac disease and autoimmune gastritis

# Faecal and serological CIBD markers

The diagnosis of CIBD is based on the clinical picture as well as on a combination of laboratory, endoscopic, histological and radiological tests.

The faecal inflammation marker calprotectin is an important parameter in laboratory testing. In addition to early diagnosis, it enables discrimination of CIBD from functional bowel diseases such as irritable bowel syndrome. The additional detection of CIBD-associated

autoantibodies (IgA and IgG) in serum can further secure the diagnosis and support differential diagnostics of UC and CD.

Euroimmun offers indirect immunofluorescence assays (IFA), ELISAs, ChLIAs and immunoblot tests with suitable automation solutions for the detection of faecal and serological markers.

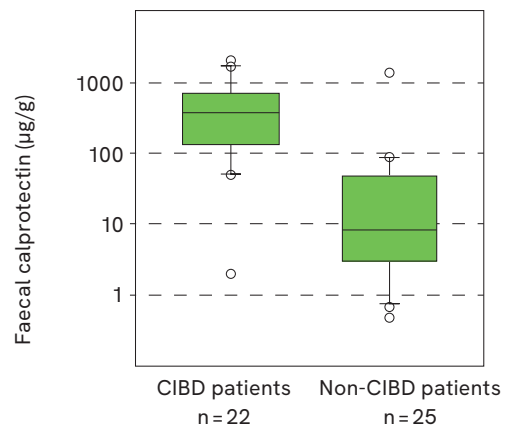
## Calprotectin – a faecal CIBD marker

Calprotectin is a calcium- and zinc-binding protein complex, which is produced by neutrophilic granulocytes and monocytes. In case of an inflammatory intestinal disease, neutrophils move into the gut lumen and release

calprotectin, which is secreted with stool. In CIBD diagnostics, **faecal calprotectin (FC)** is the ideal marker for various reasons.

- Calprotectin is produced at the onset of the intestinal inflammation and therefore allows early diagnosis.
- Increased FC values exclusively reflect inflammatory processes in the gastrointestinal tract. FC is therefore a much better marker for CIBD diagnostics than systemic markers such as C-reactive protein (CRP) or erythrocyte sedimentation rate (ESR).
- A positive FC result is used to discriminate CIBD from a functional disease such as irritable bowel syndrome. Concentrations  $>50 \mu\text{g/g}$  should be considered conspicuous and monitored. Suspected cases should be clarified by endoscopy. Endoscopic evaluation of the inflammation status is indicated in case of very high concentrations. The determination of FC cannot be used to differentiate between CD and UC.

- The FC concentration is proportional to the number of neutrophilic granulocytes in the intestinal lumen – and thus to the severity of the inflammation – and correlates with the activity of the CIBD (relapse or remission). FC determination therefore supports assessment of the severity of the disease and may reduce the number of costly and unpleasant endoscopies and biopsies – an particular advantage in paediatrics.



All current guidelines on CIBD diagnostics recommend the detection of FC for establishing a diagnosis. Especially the good correlation of the faecal marker with the inflamma-

tion activity is emphasised. Moreover, FC levels can support the prediction of relapses.

| Calprotectin in international guidelines on CIBD diagnostics |                  |                   |                   |                    |                   |                   |                   |
|--|------------------|-------------------|-------------------|--------------------|-------------------|-------------------|-------------------|
| Year   | 2015             | 2018              |                   |                    | 2019              | 2021              | 2025              |
| Organisation   | WGO <sup>8</sup> | JSGE <sup>9</sup> | ACG <sup>10</sup> | ECCO <sup>11</sup> | BSG <sup>12</sup> | DGVS <sup>3</sup> | DGVS <sup>2</sup> |
| Country / Region   | Worldwide        | JP                | USA               | EU                 | UK                | D                 | D                 |
| Disease  | CIBD             | CIBD              | CD                | CIBD               | CIBD              | CD                | UC                |
| Differential diagnostics for CIBD/IBS                        | ●                | ●                 | ●                 | ●                  | ●                 | ●                 | ●                 |
| Correlation with disease activity                            |                  |                   |                   | ●                  | ●                 | ●                 | ●                 |
| Prognosis of a relapse                                       |                  |                   |                   | ●                  | ●                 | ●                 | ●                 |
| Marker of mucosal healing                                    |                  |                   |                   | ●*                 |                   |                   | ●                 |
| Marker of post-operative relapse                             |                  |                   |                   | ●                  | ●                 | ●                 |                   |

● recommended; ○ mentioned; \* only UC

## Our test systems for FC determination

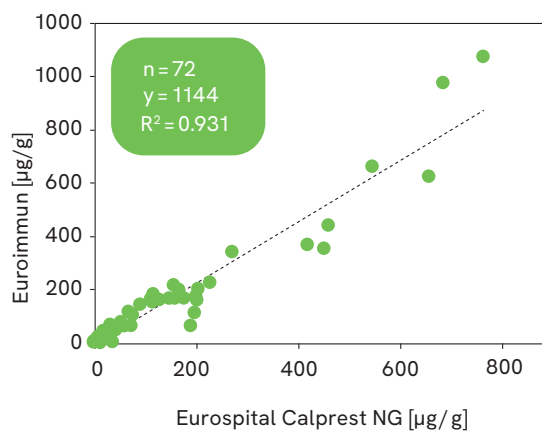
### Quantitative determination with ELISA or ChLIA

Euroimmun offers ELISA and ChLIA for reliable measurement of FC in stool samples. The tests allow non-invasive, quantitative determination of FC.

Stool dosage tubes and the IDS Calprotectin Extraction Device<sup>a</sup> are available for simple sample extraction. Manual processing of the ELISA is fast (approx. 75 min) and simple. Automated processing on all open ELISA platforms is also possible. For the ChLIAs there are different automation solutions available, suited for different laboratory requirements.

The test systems have a comprehensive measurement interval (Calprotectin ELISA: 1.9–2100 µg/g; IDS Calprotectin<sup>a</sup>: 20.0–2000.0 µg/g) including subsequent dilution from 1:10 or 1:3 in fully automated processing).

When compared with other established assays such as the Eurospital Calprotectin ELISA, the Calprotectin ELISA (see below) and the ChLIA IDS Calprotectin showed a good correlation.

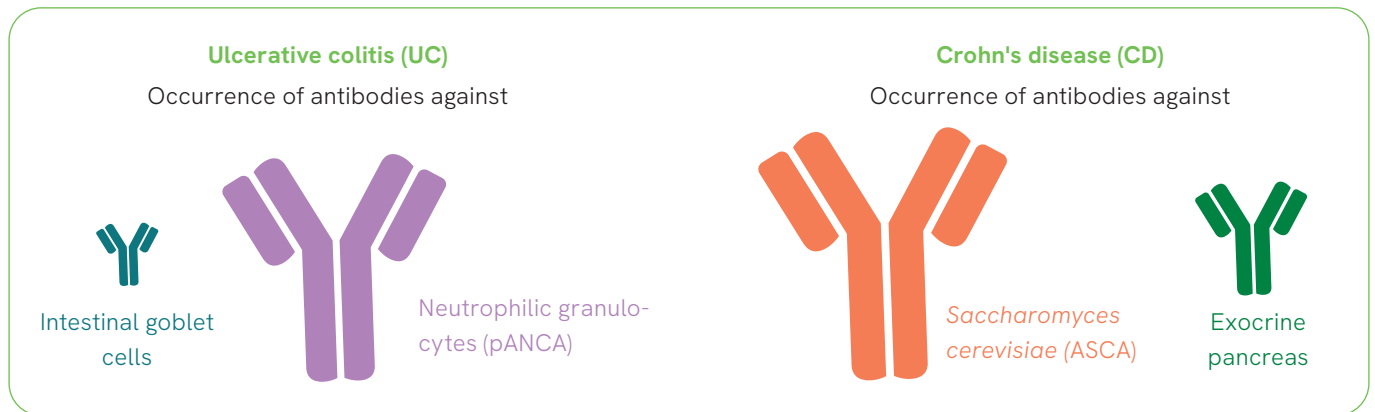


<sup>a</sup> Manufactured by Immunodiagnostic Systems Limited (IDS)

# Serological markers for CIBD diagnostics

Chronic inflammatory bowel diseases can be diagnosed in most patients by serological testing for various pathognomonic antibodies. Determination of these antibodies supports differential diagnosis and allows

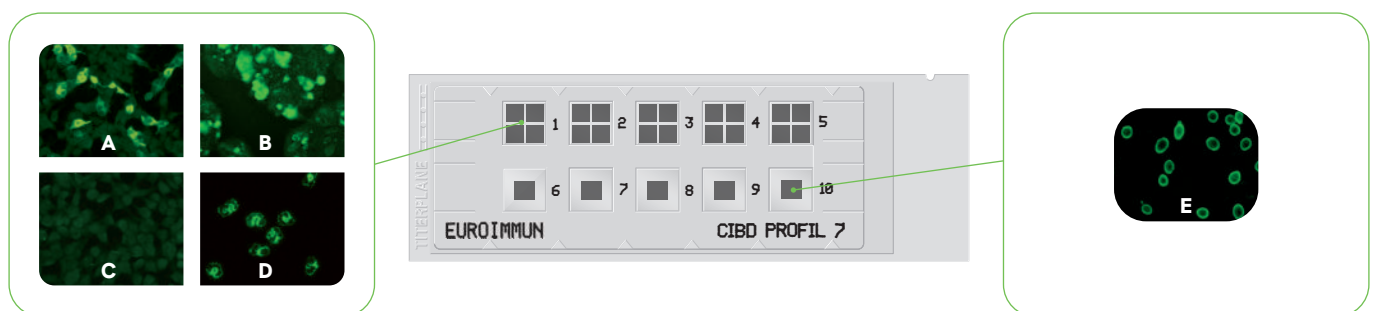
conclusions to be drawn with respect to the presence of UC or CD (in the following figure, the proportions of the antibodies represent the different frequencies of occurrence).



## Indirect immunofluorescence assay (IFA):

Euroimmun produces BIOCHIP combinations with various IFA substrates, which are used to detect specific autoantibodies against intestinal goblet cells and exocrine pancreas, as well as anti-neutrophil cytoplasmic

antibodies (ANCA) and antibodies against *Saccharomyces cerevisiae* (ASCA). The slides for the IFA Mosaics (e.g. CIBD profiles) can be flexibly equipped with different BIOCHIPS. As an example, the CIBD Profile 7 is depicted:



A: Autoantibodies against exocrine pancreas antigens: rPAg1 (CUZD1)/rPAg2 (GP2); B: Antibodies against goblet cells; C: Control-transfected cells; D: Anti-neutrophil cytoplasmic antibodies, perinuclear type (pANCA); E: Antibodies against *Saccharomyces cerevisiae*.

## Antibodies against intestinal goblet cells

Autoantibodies directed against intestinal goblet cells are pathognomonic for UC and occur in 11 % of patients.<sup>13,14</sup> The relevant target antigen has not yet been identified. The BIOCHIP uses a primate intestinal cell line consisting of cells that differentiate spontaneously into goblet cells

under defined culture conditions. In case of a positive reaction in the IFA, the substrate shows a cloudy fluorescence with fuzzy borders. When both antibodies against goblet cells and pANCA are investigated, the combined detection rate for UC amounts to 82 %.

## Anti-neutrophil cytoplasm antibodies (ANCA)

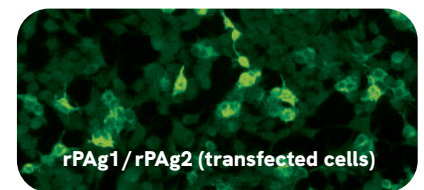
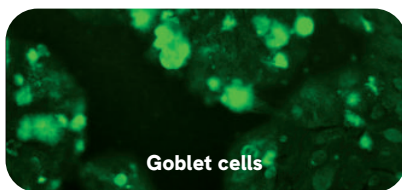
ANCA of the perinuclear type (pANCA) are not only of major importance in serological diagnostics of various forms of vasculitis, but also in CIBD differential diagnostics. They occur in the majority of patients with UC (67%), but can also be found in some CD patients (7%).<sup>15</sup> Patients with CIBD produce a pANCA pattern on ethanol-fixed granulocytes, whereas formalin-fixed cells do not react. This form of ANCA is called atypical ANCA (or DNA-ANCA, aANCA or xANCA in the literature).

## Antibodies against exocrine pancreas

Autoantibodies against exocrine pancreas are directed against acinar cells. They can be found in 39% of patients with CD, while they are only present in around 2% of UC patients. They are therefore characteristic of CD.<sup>16,17</sup> In CD,

the target antigens of the autoantibodies are the protoglycans CUZD1 (PAg1) and GP2 (rPAg2) in the pancreas secretion.<sup>17</sup> The prevalence of IgG autoantibodies against CUZD1 and GP2 is on average 40%, in CD of a duration of more than two years even 50%.

These antigens are detected using transfected cells, which ensure reproducibility of the results. Antibodies against rPAg1 cause a broad granular fluorescence in the cytoplasm, the cell nuclei are only weakly stained. Anti-rPAg2 antibodies stain the cytoplasm with a smooth to fine-granular fluorescence that is mainly located in the nucleus. By investigating autoantibodies against pancreas antigens as well as ASCA in CD diagnostics, the detection rate for CD can be increased to 80%.<sup>18,19</sup>



### Study:

Autoantibodies against the pancreas antigens CUZD1 and GP2 have a high specificity for the diagnosis of CD. In a study based on 224 CD and 136 UC patients, Michaels et al. showed that each of these autoantibodies is associated with a specific clinical phenotype.<sup>20</sup>

Autoantibodies against GP2 and CUZD1 were both found significantly more often in CD than in UC patients. Generally, antibodies against these two antigens were associated with an earlier disease onset, the presence of ASCA and the necessity of immunosuppressive therapy. Patients with autoantibodies against CUZD1 suffered significantly more often from ileocolic and perianal diseases. In patients with anti-GP2 antibodies, intestinal strictures were especially frequently observed.

| n = 360               | Antibodies against pancreatic glycoproteins |                   |
|-----------------------|---|-------------------|
|                       | Antibody-positive                           | Antibody-negative |
| Ileocolic disease     | 44.1%                                       | 23.4%             |
| Perianal disease      | 48.6%                                       | 31.1%             |
| ASCA                  | 43.1%                                       | 29.6%             |
| Immunosuppressives    | 43.6%                                       | 30.0%             |
|                       | Anti-CUZD1 antibodies                       |                   |
| Age at onset          | 19.5 years                                  | 27.5 years        |
| Ileocolic disease     | 30.3%                                       | 15.6%             |
| Perianal disease      | 37.8%                                       | 18.9%             |
|                       | Anti-GP2 antibodies                         |                   |
| Age at onset          | 20 years                                    | 26 years          |
| Intestinal strictures | 25.3%                                       | 12.2%             |



## Anti-Saccharomyces cerevisiae antibodies (ASCA)

ASCA mostly occur in CD patients. ASCA of classes IgA and IgG together have a prevalence of around 73%.<sup>19</sup> In UC patients, ASCA occur less frequently with a prevalence

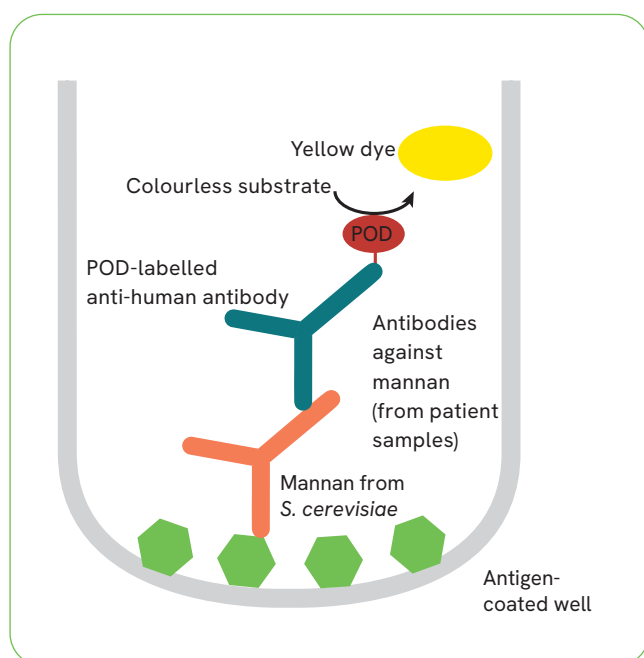
of around 18%.<sup>13</sup> The detection of ASCA can support differential diagnostics.<sup>2</sup>

### Anti-Saccharomyces cerevisiae IIFT (IgA, IgG)

A yeast smear is used as the IFA substrate. The main antigen of ASCA is phosphopeptidomannan, which is a 200 kDA glycoprotein from the yeast cell wall. Antibodies against *Saccharomyces cerevisiae* cause a broad to edge-accentuated fluorescence of the yeast cells.



### Anti-Saccharomyces cerevisiae ELISA (IgA, IgG)



ASCA can also be reliably detected by means of ELISA. With the Euroimmun Anti-Saccharomyces cerevisiae ELISA (IgA, IgG) they can be investigated in serum or plasma. The break-off microplate wells of the test system are coated with mannan, a carbohydrate from the yeast cell wall. In positive samples, specific IgA or IgG antibodies bind to the antigens. To make ASCA visible, the samples are then incubated with a peroxidase (POD)-labelled anti-human antibody. POD catalyses a colour reaction, which can be measured using a photometer.

The prevalence of ASCA in a clinically precharacterised cohort of 67 CD patients was 43.3% for IgA and 31.3% for IgG antibodies. The Anti-Saccharomyces cerevisiae ELISA yielded a specificity of 100% in a precharacterised UC control cohort (n = 47).

## Studies

In a study with 115 CD patients, Kim et. al investigated whether the presence of ASCA is associated with a specific disease course.<sup>21</sup> CD patients exhibiting ASCA showed the following characteristics:

- increased fibrostenosis and intestinal ruptures (according to the Vienna classification),
- more frequent hospitalisation,
- increased values according to the Harvey-Bradshaw index (a scale for quantification of the disease activity in CIBD).

Moreover, steroids and immunosuppressives for treatment were used more frequently. In CD, ASCA may therefore indicate a severe disease course, which requires more aggressive therapy. A prospective study by Kovacs et al. investigated whether there is an association between ASCA and the activity of UC.<sup>13</sup> A total of 187 clinically diagnosed UC patients (origin: Hungary), 17.6 % of them positive for ASCA, were monitored over a period of 135 months. ASCA IgA-positive patients had an increased risk of requiring long-term immunosuppressive therapy.

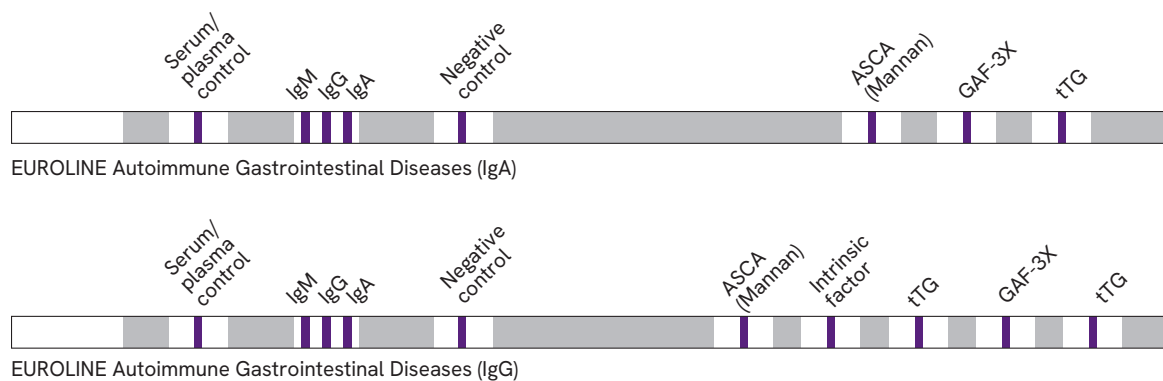
## Immunoblot test systems

### EUROLINE Autoimmune Gastrointestinal Diseases

Differentiation between CD and other autoimmune diseases of the gastrointestinal tract such as coeliac disease and autoimmune gastritis (AIG) or pernicious anaemia (PA) is difficult due to the unspecific clinical symptoms. Serological determination of disease-specific antibodies is particularly useful in these cases for efficient diagnostics. Antibodies against tissue transglutaminase (tTG) occur in coeliac disease with a prevalence of almost 100%, whereas they are virtually absent in healthy persons and patients with other intestinal diseases. Furthermore, patients with coeliac disease form very specific antibodies against deamidated gliadin fragments. In the blood of AIG

or PA patients, antibodies against intrinsic factor (IF) and parietal cell antigens (PCA) are present.

The presence of ASCA, however, is indicative of CD. Thus, parallel detection of these antibodies provides important information for differential diagnosis. For this purpose, Euroimmun offers two EUROLINE test systems. The test strips are coated with recombinant tTG, recombinant gliadin-analogue fusion peptide (GAF-3X) and mannan from *S. cerevisiae*. Additionally, the EUROLINE Autoimmune Gastrointestinal Diseases (IgG) contains recombinant IF as well as native PCA:





## In a nutshell:

- For CIBD diagnostics, endoscopic, histological and radiological examinations should be supplemented by laboratory and serological tests.
- The determination of calprotectin in stool allows early diagnosis and differentiation between CIBD and irritable bowel syndrome. Normal calprotectin values largely exclude CIBD.
- According to current guidelines, calprotectin levels are a valuable aid in monitoring the disease activity and therapy control. Calprotectin values correlate with the clinical result from endoscopy or biopsy. The determination is a non-invasive examination method and favourable especially in paediatric patients.
- The investigation of patient serum by IFA supports reliable discrimination of CD from UC. It is non-invasive and less costly than other methods.
- Specific markers for UC diagnostics are antibodies against intestinal goblet cells and pANCA. Antibodies against exocrine pancreas antigens and ASCA may point towards CD.
- The combination of different IFA substrates in one mosaic increases the detection rate in differential CIBD diagnostics.
- In a study by Michaels et al., antibodies against CUZD1 were associated with ileocolic and perianal diseases, and antibodies against GP2 with intestinal strictures.<sup>20</sup> Both antibodies were accompanied by ASCA and the necessity of immunosuppressive therapy.
- The presence of ASCA indicates a severe course of CD. In UC patients, they are associated with an increased risk of requiring long-term therapy with immunosuppressives.
- For exclusion of other autoimmune gastrointestinal diseases, such as coeliac disease and autoimmune gastritis, antibodies that are highly relevant in differential diagnostics are investigated: antibodies against tTG, deamidated gliadin fragments, IF and PCA.

## Order information

| Tests and accessories for the determination of faecal calprotectin |  |                                    |                |
|--|--|------------------------------------|----------------|
| Test system  | Product name   | Substrate                          | Order number   |
| ELISA  | Calprotectin ELISA   | antibody-coated microplate wells   | EQ 6831-9601 W |
| ChLIA <sup>b</sup>   | Faecal Calprotectin ChLIA  | antibody-coated magnetic particles | LQ 6831-0100 W |
|  | Control set Faecal Calprotectin ChLIA <sup>c</sup>                                   | -                                  | LR 6831-0160 W |
|  | IDS Calprotectin <sup>a</sup>  | antibody-coated magnetic particles | IS-AI26000     |
|  | IDS Calprotectin Control Set <sup>a,d</sup>  | -                                  | IS-AI26030     |
|  | IDS Calprotectin Calibrator Set <sup>a,d</sup>                                       | -                                  | IS-AI26020     |
| Stool extraction   | Stool dosage tubes (SDT), prefilled with extraction buffer, 45 pieces <sup>e</sup>   | -                                  | ZE 6010-4501-2 |
|  | Stool dosage tubes (SDT), not filled with extraction buffer, 100 pieces <sup>e</sup> | -                                  | ZE 6010-0100-3 |
|  | IDS Calprotectin Extraction Device <sup>a,d</sup>                                    | -                                  | IS-AI26040     |

<sup>a</sup> Manufactured by Immunodiagnostic Systems Limited (IDS); IDS-i10, IDS-iSYS, IDS i20 are trademarks of IDS.

<sup>b</sup> All ChLIAs are processed automatically on the IDS-i10<sup>a</sup>, the IDS-iSYS<sup>a</sup> or the IDS i20<sup>a</sup>. The required product or lot-specific information is provided via QR code.

<sup>c</sup> For use with the Faecal Calprotectin ChLIA

<sup>d</sup> For use with the IDS Calprotectin<sup>b</sup>

<sup>e</sup> For use with the Calprotectin ELISA or Faecal Calprotectin ChLIA

| Tests for the determination of serological CIBD markers |   |   |  |                                  |
|---|---|---|--|----------------------------------|
| Test system   | Test name   | Antibodies against                          | Substrate  | Order number                     |
| IFA   | CIBD mosaics  | intestinal goblet cells                     | goblet cells (culture)                                 | FA 1391-1005-3<br>FA 1391-1005-7 |
|   |   | pancreas antigens rPAG1 (CUZD1)/rPAG2 (GP2) | transfected cells                                      |                                  |
|   |   | pANCA                                       | granulocytes (EOH)                                     |                                  |
|   |   | <i>S. cerevisiae</i>                        | fungal smear   |                                  |
|   | Anti-Saccharomyces cerevisiae IIFT (IgA, IgG)       | <i>S. cerevisiae</i>                        | gliadin (GAF-3X)                                       | FV 2841-1010 A/G                 |
| ELISA   | Anti-Saccharomyces cerevisiae ELISA (IgA, IgG)      | <i>S. cerevisiae</i>                        | purified mannan from <i>S. cerevisiae</i> cell wall    | EV 2841-9601 A/G                 |
| EUROLINE  | EUROLINE Autoimmune Gastrointestinal Diseases (IgA) | tTG, GAF-3X, mannan                         | tTG, GAF-3X, mannan from <i>S. cerevisiae</i>          | DL 1360-1601 A                   |
|   | EUROLINE Autoimmune Gastrointestinal Diseases (IgG) | tTG, GAF-3X, PCA, IF, mannan                | tTG, GAF-3X, PCA, IF, mannan from <i>S. cerevisiae</i> | DL 1360-1601 G                   |

## References

1. Deutsche Morbus Crohn/Colitis ulcerosa Vereinigung (DCCV e.V.); [www.dccv.de](http://www.dccv.de).
2. Blumenstein I, et al. Aktualisierte S3-Leitlinie Colitis ulcerosa (Version 7.0). (2025).
3. Sturm A, et al. Aktualisierte S3-Leitlinie – „Diagnostik und Therapie des Morbus Crohn“ der Deutschen Gesellschaft für Gastroenterologie, Verdauungs- und Stoffwechselkrankheiten (DGVS). *Z Gastroenterol.* 60:332-418 (2022).
4. Conrad K, et al. Diagnosis and classification of ulcerative colitis. *Autoimmun Rev.* 13:436-466 (2014).
5. Laass M, et al. Diagnosis and classification of Crohn's disease. *Autoimmun Rev.* 13:467-471 (2014).
6. Pimentel M, et al. Identification of a prodromal period in Crohn's disease but not ulcerative colitis. *Am J Gastroenterol* 95:3458-3462 (2000).
7. Cosnes J, et al. Epidemiology and natural history of inflammatory bowel disease. *Gastroenterology* 140:1785-1794 (2011).
8. Bernstein C, et al. World gastroenterology organisation global guidelines inflammatory bowel disease: Update August 2015. *J Clin Gastroenterol* 50:803-818 (2016).
9. Matsuoka K, et al. Evidence-based clinical practice guidelines for inflammatory bowel disease. *J Gastroenterol* 53:305-353 (2018).
10. Lichtenstein GR, et al. ACG Clinical Guideline: Management of Crohn's Disease in Adults. *Am J Gastroenterol* 113:481-517 (2018).
11. Maaser C, et al. ECCO-ESGAR Guideline for Diagnostic Assessment in IBD Part 1: Initial diagnosis, monitoring of known IBD, detection of complications. *J Crohns Colitis* 13(2):144-164 (2019).
12. Lamb CA, et al. British Society of Gastroenterology consensus guidelines on the management of inflammatory bowel disease in adults. *Gut* 68: s1-s106 (2019).
13. Kovacs G, et al. Significance of serological markers in the disease course of ulcerative colitis in a prospective clinical cohort of patients. *PLoS ONE* 13:e0194166 (2018).
14. Homsak E, et al. Autoantibodies pANCA, GAB and PAB in inflammatory bowel disease: prevalence, characteristics and diagnostic value. *Wien Klin Wochenschr* 122:19-25 (2010).
15. Stöcker W, et al. Autoantibodies to granulocytes in chronic inflammatory bowel disease are not correlated with antibodies to intestinal goblet cells in ulcerative colitis and to pancreatic juice in Crohn's disease. *Immunobiology* 186:96 (1992).
16. Stöcker W, et al. Autoimmunity to pancreatic juice in Crohn's disease. Results of an autoantibody screening in patients with chronic inflammatory bowel disease. *Scand J Gastroenterol* 139:41-52 (1987).
17. Komorowski L, et al. Autoantibodies against exocrine pancreas in Crohn's disease are directed against two antigens: The glycoproteins CUZD1 and GP2. *Journal of Crohn's and Colitis* 7:780-790 (2013).
18. Teegen B, et al. Prevalence of antibodies against *Saccharomyces cerevisiae* in the diagnosis of chronic-inflammatory bowel disease. *J Lab Med* 24:494 (2000).
19. Kovacs M, et al. Pancreatic autoantibodies and autoantibodies against goblet cells in pediatric patients with inflammatory bowel disease. *JPGN* 55:429-435 (2012).
20. Michaels MA, et al. Pancreatic autoantibodies against CUZD1 and GP2 are associated with distinct clinical phenotypes of Crohn's disease. *Inflamm Bowel Dis* 21:2864-2872 (2015).
21. Kim BC, et al. Clinical significance of anti-*Saccharomyces cerevisiae* antibody (ASCA) in Korean patients with Crohn's disease and its relationship to the disease clinical course. *Dig Liver Dis* 39:610-616 (2007).

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