Editorial

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Biomarkers of inflammatory bowel disease: ready for prime time?

DOI 10.1515/cclm-2015-0918

Inflammatory bowel disease (IBD), a multifactorial disorder which results, in genetically predisposed individuals, from a dysregulated immune response to environmental stimuli and to host intestinal microflora. IBD consists of two major clinical conditions, ulcerative colitis (UC) and Crohn's disease (CD), which are characterized by appreciably distinctive pathogenetic and clinical features. The epidemiologic burden of IBD has increased considerably over the past decades, and recent data suggests that the overall prevalence may be as high as 200:100,000 persons for both UC and CD, with highest incidence being recorded in northern Europe [1]. A similar trend has also been described for pediatric IBD, now exhibiting a sex- and age-standardized incidence of 2.8 per 10 person-years for UC and 9.2 per 10 person-years for CD, respectively [2]. Even more importantly, patients with these conditions pose a substantial burden to society and healthcare systems, since a diagnosis of IBD is associated on average with 20 years of life lost (YLL) and 7.0 disability-adjusted life years (DALYs) [3]. The clinical manifestations of IBD, which depend on disease type (UC or CD), on the area of the intestinal tract that has been involved, and on disease activity, may remain not specific for this condition for months (e.g. fatigue, anemia, weight loss, fever, diarrhea, constipation, abdominal cramps and pain, vomiting, fistulas and perianal disease). Occasionally additional extraintestinal manifestations may be present in up to 10%–20% of cases, and noticeably include arthritis, uveitis or liver disease.

According to the recent indications of the World Gastroenterology Organization (WGO), the diagnosis of IBD entails a combination of physical examination, patient history as well as a number of diagnostic tests including laboratory analyses, stool examination, endoscopy, biopsy and imaging studies [4]. More specifically, a detailed diagnostic strategy has been put forward, including (in sequential steps) physical examination, stool tests for infection and occult blood, complete blood count (CBC), serum albumin, ferritin, C-reactive protein (CRP), flexible sigmoidoscopy or colonoscopy, abdominal ultrasound scan and computed tomography (or, when available, magnetic resonance imaging) scan of the abdomen [4]. Besides blood and stool testing, the diagnostic work-up thus entails techniques and procedures that are variably invasive (e.g. sigmoidoscopy, colonoscopy, biopsy), or which may be associated with substantial future health risks (e.g. those attributable to radiation exposure). The introduction of reliable and accurate laboratory tests that would contribute to limit the number of unnecessary further investigations should hence be regarded as a foremost perspective for safeguarding patients health and lowering healthcare expenditures. These considerations are even more relevant for IBD patients monitoring.

Among the various (noninvasive) biomarkers that have been proposed over the past few years, fecal calprotectin has gained a prominent role. A meta-analysis of eight studies totaling 1062 subjects recently concluded that a patient with a fecal calprotectin value ≤ 40 μg/g has a 1% probability of having IBD and a 84.1% probability of being healthy [5], thus exhibiting better diagnostic performance than C-reactive protein, erythrocyte sedimentation rate and fecal lactoferrin for ruling out this condition. Despite some analytical and preanalytical drawbacks remain [6–9], encouraging data has also been recently published about the clinical efficacy of this biomarker for monitoring disease activity, response to treatment and relapse [10, 11].

In this issue of *Clinical Chemistry and Laboratory Medicine*, Dumoulin et al. [12] describe the results of an interesting study about the measurement of leukocyte esterase activity in fecal extracts. The analytical performance of the technique was adequate for routine diagnostics, and the correlation with fecal calprotectin was found to be acceptable. Some advantages over fecal calprotectin testing were also emphasized, namely a higher sensitivity and a lower vulnerability against proteolysis, two aspects that seemingly make leukocyte esterase a highly stable, reliable and more affordable biomarker for diagnosis and monitoring of IDB.

Although further studies are needed to translate these preliminary results into clinical practice, it seems

reasonable to hypothesize that prime time for noninvasive biomarkers of IBD may not be too late.

Author contributions: All the authors have accepted responsibility for the entire content of this submitted manuscript and approved submission.
Financial support: None declared.
Employment or leadership: None declared.
Honorarium: None declared.
Competing interests: The funding organization(s) played no role in the study design; in the collection, analysis, and interpretation of data; in the writing of the report; or in the decision to submit the report for publication.

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