Concise Commentary: Calling in Your Marker—Rectal CD30-Positive Cells Differentiate Ulcerative Colitis from Crohn’s Disease

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In both children and adults, the diagnosis of Crohn’s disease (CD) and ulcerative colitis (UC) relies on a combination of clinical, biological, radiological, endoscopic, and histological features. While in many cases, e.g., penetrating disease, distinguishing between these two inflammatory bowel diseases (IBDs) is straightforward, 10–20% of IBD cases affecting the colon remain unclassified, even in the era of molecular pathology and multimodal diagnostic approaches [1–3]. Since most of the pathological features observed in colonic biopsies are shared between CD and UC, new tools are being explored to help the pathologist and the clinician to reach an accurate diagnosis. For many years, cluster-of-differentiation (CD)30 has been proposed as a potential marker differentially expressed between UC and CD [4]. More recently, Flores et al. studied whether CD30 immunostaining in affected colonic segments could be an efficient tool to discriminate between UC and CD in adults. A cutoff of fifteen CD30-positive cells/high power field (HPF) yielded a sensitivity of 97.4% and a specificity of 97.4% [6].

In this issue of *Digestive Diseases and Sciences*, Fabian et al. explored the value of CD30 staining in a pediatric population of IBD studying 74 patients including 33 CD, 30 UC, and 11 IBD-undetermined [5]. They assessed the number of CD30-positive cells in intestinal and colonic segments from the terminal ileum to the rectum, confirming the results previously published in the adult population [6]. Although the median number of CD30-positive cells differed in most segments between UC and CD patients, rectal assessment alone was sufficient to discriminate between CD and UC. They determined that 2.5 positive cells/HPF was the most accurate with a sensitivity of ~83% and a specificity of 90%. Interestingly, they found that the number of CD30-positive

cells was not dependent on the intensity of endoscopic or microscopic inflammation. Since the main caveat of their study was that CD30 counts may depend on the presence of inflammation and that about half of CD patients did not have rectal inflammation, this observation convincingly addressed this concern.

Overall, their study opens to the use of a new easily applicable method in clinical practice. CD30 staining could be optimally used in the context of mild colonic IBD when the clinical and pathological picture does not correspond obviously to CD or UC. For the pathologist, it brings an additional feature that could be used in combination with the “classical signs” such as basal plasmacytosis and eosinophilia.

Regarding the bigger picture of the specific pathogenesis of UC, CD30 could be the starting point of fundamental research studying its contribution to intestinal inflammation. CD30 is a plasma membrane protein that belongs to the tumor necrosis factor receptor family which although expressed on several cell types, has been primarily studied in T and B cells and as a marker of some neoplastic diseases such as Hodgkin lymphoma. Although in T cells, CD30 expression is linked to the interleukin (IL)-4 expressing, interferon (IFN)- γ non-expressing CD4 cells that define T helper (Th)2-like cells [7], the biological function of CD30 expressing cells is highly variable, not restricted to a single effect or a unique cell type. Its complex biological functions that are likely to reflect the interplay of many immune subsets could provide fascinating clues to the pathogenesis of IBD.

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