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Distinct involvement of plasma cells and monocytes/macrophages in ileal and colonic ulcer formation in patients with Crohn's disease

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Background: Despite its interest for the development of personalised medicine, the pathophysiological distinctions between ileal and colonic Crohn's disease (CD) have been poorly characterised. This study aims to search for immunological differences between ileal and colonic CD.

Methods: We reanalysed our proteomic dataset[1] to extract non-exploited immunological information. Using mass spectrometry-based proteomics, we previously compared the proteome of ulcer edges and adjacent normal mucosa (paired design) in the ileum (n=16 biopsies) and colon (n=16 biopsies) of 16 CD patients (Figure 1). A total of 4,428 and 5,204 proteins were screened in the ileum and colon, respectively. To identify proteins specific to particular immune cell populations, we searched in the Human Proteome Atlas and literature.

Results: We identified markers specific to plasma cells (IgA1, IgM, IgG1, IgG2, IgG3, IgG4, immunoglobulin J chain [IGJ], and immunoglobulin lambda-like polypeptide 5 [IGLL5]), monocytes/macrophages (cluster of differentiation 14 [CD14]), and mast cells (chymase [CMA1], mast cell carboxypeptidase A [CPA3], and tryptase alpha/beta-1 [TPSAB1]). No specific markers were identified for the other immune cells. The number of increased plasma cell markers (ulcer edges vs adjacent normal mucosa) was higher in the ileum (IgA1, IgM, IgG1, IgG2, IgG3, IGLL5, and IGJ) than in the colon (IgG3) (Figure 2). Of note, immune exclusion markers (IgM, IgA1, IGJ) were increased in the ileum, but not the colon (ulcer edges vs adjacent normal mucosa). The marker of monocytes/macrophages CD14 was increased in the colon, but not in the ileum (ulcer edges vs adjacent normal mucosa) (Figure 2). Mast cells markers (CMA1, CPA3, and TPSAB1) showed no significant change in the ileum or colon (ulcer edges vs adjacent normal mucosa) (Figure 2).

Conclusion: Plasma cells and monocytes/macrophages may play distinct roles in the formation of ileal and colonic ulcers in patients with CD, suggesting further investigations.

References:

1. Pierre N, Salée C, Massot C, Blétard N, Mazzucchelli G, Smargiasso N, et al. Proteomics Highlights Common and Distinct Pathophysiological Processes Associated with Ileal and Colonic Ulcers in Crohn's Disease. J Crohns Colitis 2020;14(2):205–15.

Figure 1. Patients' characteristics

	Patients with ileal ulcers	Patients with colonic ulcers
Patient, n (m/f)	8 (1/7)	8 (4/4)
Age, median years (min-max)	37.5 (30-68)	38.0 (30-43)
Disease duration, median years (min-max)	9 (1-41)	12.5 (0-34)
Smoking		
Yes	4	4
Former	3	2
No	1	2
Disease location at the time of the endoscopy		
Ileal	5	0
Colonic	0	3
Ileocolonic	3	5
Medication*		
Anti-TNFα	3	1
Anti-α4β7 integrin	0	2
Antimetabolites	2	1
Antibiotics	0	0
Corticoids	2	3
None	3	4

*Some patients may have several medications

Figure(s)/Table(s): see next page