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Zinc-Alpha-2-Glycoprotein in Inflammatory Bowel Disease

To the Editors,

Zinc-Alpha-2-Glycoprotein (ZAG), a 40 kDa soluble protein present in various body fluids (serum, urine, seminal fluid, saliva, and milk), controls adipose tissue mobilization in the context of cachexia.¹⁻³ Inflammatory Bowel Diseases (IBD), including Crohn's disease (CD) and ulcerative colitis (UC), have been historically associated with cachexia and malnutrition. Furthermore, a recent connection between ZAG and Th17 lymphocyte, a subpopulation of adaptive immune cell involved in both mucosal homeostatic microbial protection and IBD occurring inflammation has been made, suggesting a vicious cycle worsening inflammation and metabolic disorder in systemic inflammatory disease.⁴ We thus explored the potential role of ZAG in IBD.

We first measured serum levels of ZAG using ELISA in IBD patients, UC (n = 70) and CD (n = 109), enrolled in the "Nancy IBD cohort" and healthy controls (n = 105). ZAG levels are significantly increased in patients with UC ($31,4 \pm 8 \mu\text{g/ml}$ vs $27,6 \pm 3,8 \mu\text{g/ml}$; $P = 0.0019$), whereas no statistical difference is observed in patients with CD ($28,2 \pm 6,5 \mu\text{g/ml}$) (Fig. 1A). This prompted us to look in the animal model of colitis. We thus induced dextran sodium sulfate (DSS) colitis in ZAG^{-/-} mice (n = 12) and wild-type animals (n = 11). Severity of colitis, measured by disease activity score (Fig. 1B), daily fecal lipocalin2 dosage (not shown), and final histological examination (not shown) revealed no difference between wild-type and ZAG deficient mice.

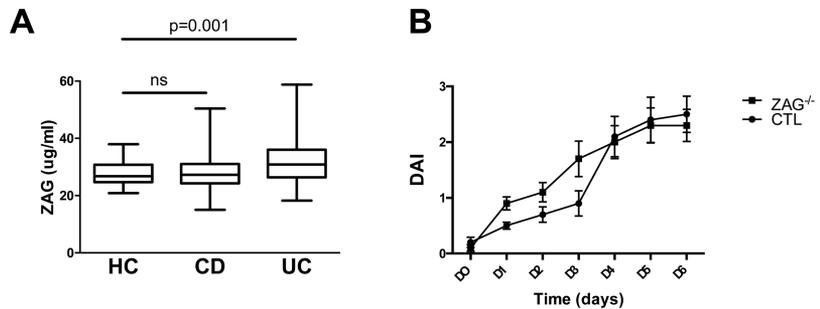


FIGURE 1. A, ZAG protein level is elevated in UC patients. Plasmatic levels of ZAG were measured by ELISA in UC (n = 70), CD (n = 109), and healthy controls (n = 105). **B, DSS occurrence and severity is not altered in ZAG deficient mice.** DSS Colitis was induced by administration of 3% DSS (Colitis grade MW 36-50kDa) (MPBiomedicals) in drinking water for 6 days in control and ZAG deficient mice. Daily, the severity of colitis was evaluated by the disease activity index (DAI). The DAI was calculated with the body weight loss (0 = no weight loss, 1 = 0%-5% weight loss, 2 = 5%-10% weight loss, 3 = 10%-20% weight loss, 4 = more than 20% weight loss); feces consistency (0 = normal, 2 = loose stools, 4 = diarrhea); and the presence of blood in the feces (0 = negative, 2 = positive, 4 = important presence of blood in the feces).

Taken together, these data suggest that ZAG might only reflect inflammation occurring in patients with UC, as animal data are not in favor of a direct role in IBD pathophysiology.

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Conflicts of Interest: Authors have no conflict of interest to declare.

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