

# Gut Bacterial DNA Translocation is an Independent Risk Factor of Flare at Short Term in Patients With Crohn's Disease

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- OBJECTIVES:** We aimed at evaluating bacterial DNA (bactDNA) presence in blood of Crohn's disease (CD) patients in remission as an independent risk factor of flare at 6 months.
- METHODS:** This is a prospective, multicenter study on CD patients with Crohn's disease activity index (CDAI)<150. The primary end point was time-to-relapse as evaluated by CDAI>150 in the following 6 months. BactDNA in blood, the nucleotide-binding oligomerization domain containing 2 (NOD2) genotype, and serum cytokine levels were determined at baseline.
- RESULTS:** A total of 288 patients were included. BactDNA was detected in 98 patients (34.0%). A variant-NOD2 genotype was identified in 114 patients (39.6%). Forty patients (14%) relapsed during follow-up. Multivariate survival analysis identified bactDNA as an independent risk factor of flare (hazard ratio (HR) 8.75 (4.02–19.06) 95% confidence interval (CI)). Hospitalization, surgery, switch of treatment, initiation and escalation of anti-tumor necrosis factor (TNF) therapy, steroids initiation, and increased fecal calprotectin levels at 6 months were associated with bactDNA at baseline. A logistic regression analysis showed bactDNA as an independent and significant predictive factor of hospitalization (odds ratio (OR) 11.9 (3.4–42.3);  $P<0.001$ ), steroids startup (OR 8.5 (2.7–27.1);  $P<0.001$ ), and switch of treatment (OR 3.5 (1.6–7.7);  $P=0.002$ ) at 6 months. No relationship was observed between bactDNA and mucosal lesions in patients with colonoscopy at admission. Serum pro-inflammatory cytokines were significantly increased in patients with bactDNA or a variant-NOD2 genotype. The combination of both factors induced decreased anti-TNF- $\alpha$  levels and a higher percentage of patients on intensified anti-TNF therapy.
- CONCLUSIONS:** BactDNA is an independent risk factor of relapse at 6 months in CD patients. BactDNA is also independently associated with an increased risk of hospitalization, switch of treatment, and steroids initiation.

**SUPPLEMENTARY MATERIAL** is linked to the online version of the paper at <http://www.nature.com/ajg>

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## INTRODUCTION

The translocation of bacterial genomic fragments (bactDNA) into blood is a frequent event arising in up to 40% of patients with Crohn's disease (CD) (1,2). The multifactorial etiology of the disease includes partial genetic susceptibility and immunological

interactions between the host and commensal bacteria (3–6). An impaired host–microbe immune relationship, probably driven by allelic variants in these predisposition-associated genes, has been associated with the development of inflammatory bowel disease (7) and may contribute for the translocation of bacterial antigenic

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