

## Common Biostructure of the Fecal Flora in Celiac Disease, Crohn's Disease, and Carcinoid Tumors

To the Editor:

In the April issue of *Inflammatory Bowel Diseases*, West et al<sup>1</sup> reported that carcinoid tumors are 15 times more common in patients with Crohn's disease (CD, 4/111) compared with controls (3/1199). The number of incidental carcinoid tumors in patients who underwent appendectomy was used as a control. The West Midlands Regional Children's Tumor Research Group showed an incidence of 1.0–1.42 cases of appendiceal carcinoid tumors per million children per year from 1957 to 1986, using the childhood population of the West Midlands Health Authority.<sup>2</sup> In their series, 12 carcinoids were found in 24,725 appendectomies, for a detection rate of 0.05%. Although carcinoid tumors of the appendix are rare in children, they are the most common gastrointestinal tumors in this age group. Kortbeek et al<sup>3</sup> reported that by chance alone, 1 carcinoid tumor should only occur every 200 years in the population of patients with inflammatory bowel disease. West et al<sup>1</sup> suggested that the development of carcinoid tumors may be secondary to distant proinflammatory mediators, rather than a local inflammatory effect from the adjacent CD, be-

cause none of the carcinoid tumors developed in areas of CD. Recently, we published a study on the microbial biostructure of feces using sections of paraffin-embedded punched fecal cylinders in healthy subjects ( $n = 32$ ), patients with inflammatory bowel disease (IBD) ( $n = 204$ ), and disease controls ( $n = 227$ ).<sup>4</sup> Fluctuations in spatial distribution of 11 bacterial groups were monitored using fluorescence in situ hybridization (FISH). The microbial biostructure differed in patients with CD, ulcerative colitis, and controls allowing a specific differentiation between the two entities of IBD and other diseases. Most prominent for CD was a depletion of *Faecalibacterium prausnitzii* (Fprau  $< 1 \times 10^9$ /mL). In this first study the depletion of *F. prausnitzii* was found also in untreated celiac disease, but in none of the other disease controls, including diverticulosis, IBS, self-limiting colitis, colonic carcinoma, and adenoma. Since 2006 we have been using FISH investigation of punched fecal cylinders routinely for the surveillance of our gastroenterological outpatients. Since our first study,<sup>4</sup> we have investigated over 4000 fecal cylinders in healthy subjects ( $n = 62$ ) and patients with different gastrointestinal diseases ( $n = 780$ ) and were able to identify a third disease, carcinoid tumors, which is associated with depletion of *F. prausnitzii*. Twelve of 23 patients with carcinoid were positive, while all other disease controls were still negative for this depletion. Brown et al<sup>5</sup> speculated that the coexistence may be more frequent than

the literature suggests. Our data indicate that there is not just a coexistence, but an association between the pathogenesis of carcinoid tumors, celiac disease, and CD. If our assumption is correct, then carcinoids in celiac disease and CD would possibly share unique histomorphologic properties, which are absent in sporadically occurring carcinoid tumors.

It would be interesting to know what pathologists think about such a link, and whether already existing pathomorphologic data may back this hypothesis.

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