Association of intestinal and systemic inflammatory responses with microbial bile acid deconjugation and hydrogen sulfide production in high fat-fed mice

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Recent studies in mice have demonstrated that consumption of a diet enriched in fat representative of a typical Western diet induces colonic inflammation potentially mediated by the microbiome. In this context, we have examined microbial metabolism of sulfated compounds and bile acid deconjugation, which produce inflammatory end-products. We tested the hypothesis that a high fat diet rich in saturated fatty acids stimulates sulfate- and sulfite-reducing bacteria (SRB) and 7 alpha-dehydroxylating bacteria (7ADB) producing, respectively, hydrogen sulfide and secondary bile acids, and that these increases correlate with inflammatory responses and disruption of gut barrier function. Forty, 3 wk-old C57BL/6J male mice were fed a low fat (LF: 10% of kcals; n=20) or high fat diet (HF: 60% of kcals; n=20) for 6 or 20 weeks. Mucosa and digesta samples were collected from the ileum, cecum and colon and used for microbial DNA extraction. Matching intestinal samples and visceral and subcutaneous white adipose tissue (WAT) depots were used to measure mRNA abundance for candidate inflammatory genes using qRT-PCR. Functional gene based and 16S rRNA gene qPCR assays were performed to quantify SRB (dissimilatory sulfite reductase (dsrAB) gene of SRB and 16S rRNA genes of Desulfovibrio, Desulfobulbus, Desulfobacter and Desulfotomaculum), the taurine-degrading, sulfite-reducing Bilophila wadsworthia and 7ADB. Overall, the functional genes for SRB, B. wadsworthia and 7ADB were significantly more abundant in samples from HF-fed mice after 20 weeks and this increase was detected for SRB and 7ADB after 6 weeks. More specifically, the increase was generally more marked in digesta samples. The most significant increases, including the genes cited previously and the SRB genera, were observed in cecal and colonic digesta as well as distal colonic mucosa but were not observed for proximal colon. Although high fat feeding did not increase markers of intestinal inflammation at 6 weeks, the expression of markers of macrophage infiltration (e.g., MCP-1, CD11c) and inflammation (e.g., TLR-4) were significantly more abundant in the ileum at 20 weeks. High fat feeding reduced the abundance of the tight junction protein, ZO-1, at the apical area of the ileal epithelium at 6 and 20 weeks. Genes encoding multiple markers of macrophage inflammation (e.g., MCP-1, CD11c, F4/80 (Emr1), TNFα) were also upregulated in visceral WAT after 6 and 20 weeks of high fat feeding. These data indicate that long term consumption of a HF diet has a distinct effect on the composition and function of the intestinal microbiome and associated inflammatory responses. These results contribute to a mechanistic model linking the consumption of a high fat diet with pathways of microbial metabolism that potentially contribute to chronic intestinal and systemic inflammation.