Letter to the Editor

Gut Microbiota-Derived Propionate Production May Explain Beneficial Effects of Intermittent Fasting in Experimental Colitis

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Dear Editor,

We read with interest the article by Bajic et al. entitled ‘Gut microbiota-derived propionate regulates the expression of reg3 mucosal lectins and ameliorates experimental colitis in mice’. The role of short chain fatty acid (SFAC)-producing gut bacteria is attracting widespread attention with regard to its potential usefulness in the prevention of inflammatory bowel disease, both from patients and from healthcare professionals. The study by Bajic et al. does an admirable job in exploring the effects of such important microbiota-derived SCFAs on the regulation of regenerating islet-derived protein type 3 [Reg3] lectins in a dextran-sodium sulphate colitis model, with respect to preclinical work on the potential of these gut bacterial metabolites for constraining experimental colitis. Intriguingly, the authors found that the Reg3–propionate axis may be an important mediator of gut epithelial regeneration in colitis.

Although in the gnotobiotic experimental model employed by the authors propionate production is mediated by Clostridia, in the human intestine propionate is mainly secreted through the bacterium Akkermansia muciniphila, which may become more dominant in the intestinal flora upon fasting. Intriguingly, we recently performed a microbiome study in two cohorts of intermittently fasting volunteers (a cohort of young males and cohort of middle-aged males), characterizing the remodelling of gut microbiota during and following a 1-month period of intermittent fasting. In view of the data presented by Bajic et al. and the known association between propionate production and A. muciniphila, we revisited our data specifically looking for changes in levels of this bacterium during intermittent fasting (Figure 1). We observed that in both volunteer cohorts A. muciniphila was indeed increased as a consequence of intermittent fasting. Importantly, a high-profile study in Cell Reports recently linked intermittent fasting to intestinal regeneration and reduction of inflammatory bowel disease pathology, effects being concordant with those seen by Bajic et al. following induction of propionate production. We thus propose that the beneficial effects of intermittent fasting in experimental colitis can at least be partly attributed to increased levels of A. muciniphila and subsequent propionate-mediated induction of Reg3 lectins in the epithelial compartment.

Conflict of Interest

The authors declare that they have no competing interests.

Author Contributions

M.P.P., H.B. and J.S. wrote the paper. M.P.P. and H.B. had the original idea for the paper. All authors reviewed and approved the final draft of the paper.

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Figure 1. Intermittent fasting increased the level of *Akkermansia municiphila* in two independent cohorts. The figure shows the relative abundance of *A. municiphila* in faecal samples obtained in two volunteer cohorts undergoing intermittent fasting (for details, see reference 3). [A] Results from a cohort of young adult males. Faecal samples were collected before (day 0; *n* = 30), during (day 15; *n* = 30) and at the end of intermittent fasting (day 30; *n* = 30). [B] Results from a middle-aged male cohort. Faecal samples were collected before intermittent fasting (day 0; *n* = 27), at the end of intermittent fasting (day 30; *n* = 27) and 30 days following cessation of intermittent fasting (day 60; *n* = 23). 16S rRNA gene sequencing was applied to calculate the abundance of *A. municiphila* at each time point.