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**Dietary whey protein protects against Crohn's disease via the gut phageome and bacteriome**

Su R, Wen W, Jin Y, *et al.* Dietary whey protein protects against Crohn's disease by orchestrating cross-kingdom interaction between the gut phageome and bacteriome. Gut 2025; 74(8): 1246-1260. doi: 10.1136/gutjnl-2024-334516.

Dietary influence on the development and/or propagation of Crohn’s disease remains a key interest. Diet is a potent modulator of the gut microbiome (community of microorganisms in the gut), which in turn impacts intestinal inflammation. However, less is known about the gut phageome that refers to the viral component of the microbiome, made up of bacteriophages that influence bacterial populations and microbial diversity. In this article, Su et al. explore the impact of diet on the gut phageome by obtaining terminal ileal biopsy samples to assess the mucosal microbiome from 140 patients (70 Crohn’s, 70 healthy controls) alongside dietary data. They initially identified that Whey Protein (WP) significantly impacts the gut phageome. When extrapolating this new information to data from the IBD UK Biobank, they found that consumers (versus non-consumers) showed higher differences in alpha-diversity of the phageome (i.e., more variety and balance), particularly against pathogenic bacteria, without differences to the bacteriome. Su *et al.* then conducted a series of in vivo murine experiments to prove that WP is causally associated with reduced intestinal inflammation. First, WP-fed mice were protected from dextran sulphate sodium-induced inflammation (toxic to intestinal epithelium). Second, WP-fed mice had higher upregulation of genes related to immune protection. Third, by looking at the faecal microbiome at different timepoints, WP appeared to temporally reshape both the phageome and bacteriome towards populations that help resist intestinal inflammation. This final point was confirmed by faecal transplantation from the WP-fed mice to unfed recipients that led to an attenuated inflammatory response. These effects appeared to be mediated by recusing the inhibitory effects of A. muciniphila on S. thermophilus through phage-mediated lysis in a series of further experiments to investigate this proposed phage-bacteria-inflammatory cascade. Take collectively, Su *et al.* provide important evidence into the role of diet and cross-kingdom interaction for the maintenance of gut health.