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# Normal Light-Dark and Short-Light Cycles Regulate Intestinal Inflammation, Circulating Short-chain Fatty Acids and Gut Microbiota in *Period2* Gene Knockout Mice

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Regular environmental light–dark (LD) cycle-regulated period circadian clock 2 (*Per2*) gene expression is essential for circadian oscillation, nutrient metabolism, and intestinal microbiota balance. Herein, we combined environmental LD cycles with *Per2* gene knockout to investigate how LD cycles mediate *Per2* expression to regulate colonic and cecal inflammatory and barrier functions, microbiome, and short-chain fatty acids (SCFAs) in the circulation. Mice were divided into knockout (KO) and wild type (CON) under normal light–dark cycle (NLD) and short-light (SL) cycle for 2 weeks after 4 weeks of adaptation. The concentrations of SCFAs in the serum and large intestine, the colonic and cecal epithelial circadian rhythm, SCFAs transporter, inflammatory and barrier-related genes, and Illumina 16S rRNA sequencing were measured after euthanasia during 10:00–12:00. KO decreased the feeding frequency at 0:00–2:00 but increased at 12:00–14:00 both under NLD and SL. KO upregulated the expression of *Per1* and *Rev-erbα* in the colon and cecum, while it downregulated *Clock* and *Bmal1*. In terms of inflammatory and barrier functions, KO increased the expression of *Tnf-α*, *Tlr2*, and *Nf-κb p65* in the colon and cecum, while it decreased *Claudin* and *Occludin-1*. KO decreased the concentrations of total SCFAs and acetate in the colon and cecum, but it increased butyrate, while it had no impact on SCFAs in the serum. KO increased the SCFAs transporter because of the upregulation of *Nhe1*, *Nhe3*, and *Mct4*. Sequencing data revealed that KO improved bacteria α-diversity and increased Lachnospiraceae and Ruminococcaceae abundance, while it downregulated *Erysipelatoclostridium*, *Prevotellaceae UCG_001*, *Olsenella*, and *Christensenellaceae R-7* under NLD in KO mice. Most of the differential bacterial genus were enriched in amino acid and carbohydrate metabolism pathways. Overall, *Per2* knockout altered circadian oscillation in the large intestine, KO improved intestinal microbiota diversity, the increase in Clostridiales abundance led to the reduction in