Short-chain Fatty Acids Regulate the Immune Responses via G Protein Coupled Receptor 41 in Bovine Rumen Epithelial Cells

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The rumen immune system often suffers when challenging antigens from lysis of dead microbiota cells in the rumen. However, the rumen epithelium innate immune system can actively respond to the infection. Previous studies have demonstrated G protein-coupled receptors 41 (GPR41) as receptors for short chain fatty acids (SCFAs) in human. We hypothesized that SCFAs, the most abundant microbial metabolites in rumen, may regulate the immune responses by GPR41 in bovine rumen epithelial cells (BRECs). Therefore, the objective of study was to firstly establish an immortal BRECs line and investigate the regulatory effects of SCFAs and GPR41 on innate immunity responses in BRECs. These results showed that long-term BRECs cultures were established by SV40T-induced immortalization. The concentrations of 20 mM SCFAs significantly enhanced the levels of GPR41, IL1β, TNFα, chemokines, and immune barrier genes by transcriptome analysis. Consistent with transcriptome results, the expression of GPR41, IL1β, TNFα, and chemokines were markedly upregulated in BRECs treated with 20 mM SCFAs by qRT-PCR compared with control BRECs. Remarkably, the GPR41 knockdown (GPR41KD) BRECs treated with 20 mM SCFAs significantly enhanced the proinflammatory cytokines IL1β and TNFα expression compared with wild type BRECs treated with 20 mM SCFAs, but reduced the expression of CCL20, CXCL2, CXCL3, CXCL5, CXCL8, CXCL14, Occludin, and ZO-1. Moreover, GPR41 mRNA expression is positively correlated with CCL20, CXCL2, CXCL3, CXCL8, CXCL14, and ZO-1. These findings revealed that SCFAs regulate GPR41-mediated levels of genes involved in immune cell recruitment and epithelial immune barrier and thereby mediate protective innate immunity in BRECs.