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Short focus on short-chain fatty acids

Intestinal microbes and/or their metabolites are key determinants of gut health. Of the microbial metabolites, short-chain fatty acids (SCFA) represent major products of microbial fermentation of carbohydrates, and include acetate, propionate and butyrate. Protein fermentation can also contribute to the intestinal SCFA pool but typically results in branched-chain fatty acids (e.g. isobutyrate, 2-methylbutyrate, and isovalerate). Although SCFA are often used for food/feed hygiene (Broom, 2015), here we will focus specifically on effects within the intestine.

Intestinal SCFA concentrations generally increase distally and primarily reflect microbe composition (dominant metabolic pathway(s)), density and substrate availability. In the proximal intestinal lumen, (total) SCFA concentrations are typically <10 mM, which may increase to >100 mM in the distal intestine (Koh et al., 2016; Rehman et al., 2007). The concentrations of SCFA could be particularly relevant for the host cell receptor-mediated biological effects mentioned below (Koh et al., 2016).

SCFA can have strong antimicrobial activity, which is thought to be principally mediated by undissociated forms of the acids diffusing freely across the microbial cell membrane before dissociating into protons and anions that disrupt cell physiology (Cherrington et al., 1991). Oral administration of organic acids has been reported to influence intestinal bacterial populations (Broom, 2015). The antimicrobial efficacy of SCFA is, however, dependent on the local, extracellular pH (Boyen et al., 2008), as less of the acid is undissociated at higher pH. In addition, SCFA can also affect virulence of intestinal pathogens, although exposure to acid may induce an acid tolerance response (ATR) in some microbes (Sun and O'Riordan, 2013).

More recently, attention has turned to the specific effects of SCFA on host cells. Butyrate is the preferred energy source for colonocytes and is the SCFA that has been investigated the most. SCFA can influence cell function by inhibiting histone deacetylase activity, and thus gene expression regulation, or through binding to, and activation of, G-protein coupled receptors (GPRs), which are sensors of metabolites (Macia et al., 2015). Butyrate and propionate bind GPR41 (free fatty acid receptor (FFAR)3), acetate and propionate bind GPR43 (FFAR2), and butyrate binds GPR109A (hydroxy carboxylic acid (HCA) receptor 2). GPR are expressed by various host, including immune, cells and studies have shown that mice deficient in GPR are more susceptible to loss of intestinal homeostasis and inflammation in experimental models (Koh et al., 2016). In addition, activation of GPR43 and GPR109A in the gut epithelium, and downstream activation of the NLRP3 inflammasome pathway, have been shown to promote intestinal homeostasis (Macia et al., 2015).

Conclusion

Through control of microbes in food and feed, modulation of intestinal populations and/or influencing host cell function, SCFA have been demonstrated to be important in the context of gut (and host) health. Questions remain regarding optimal intestinal concentrations of SCFA and how these relate to activation of GPR. Much work has been done in mice and humans and it will be interesting to see whether all these concepts are directly transferrable to farmed animal species. The effects of SCFA may also be context (e.g. cell/environment) specific and may be influenced by other microbial metabolites (Koh et al., 2016). Although lactate that is produced in the gut is typically considered an intermediate (as it is thought to be readily converted to other SCFA (e.g. butyrate)), lactate is recognised for having bioactive properties and is a ligand for GPR81, and thus influences intracellular signalling (e.g. lipolysis) (Garrote et al., 2015). These observations could be important for benefits derived from lactic acid-producing bacteria. There are clear links between microbial metabolites and intestinal homeostasis, which are, at least in part, connected to the host's metabolite sensing capability. Research continues to highlight the profound importance of gut microbes and their metabolites on intestinal health.

References

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