



Review Article

Ruminal microbiota–host interaction and its effect on nutrient metabolism



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ABSTRACT

Rumen microbiota has a close and intensive interaction with the ruminants. Microbiota residing in the rumen digests and ferments plant organic matters into nutrients that are subsequently utilized by the host, making ruminants a unique group of animals that can convert plant materials indigestible by humans into high-quality animal protein as meat and milk. Many studies using meta-omics technologies have demonstrated the relationships between rumen microbiome and animal phenotypes associated with nutrient metabolism. Recently, the causality and physiological mechanisms underpinning the host–microbiota interactions have attracted tremendous research interest among researchers. This review discusses the host–microbiota interactions and the factors affecting these interactions in ruminants and provides a summary of the advances in research on animal husbandry. Understanding the microbiota composition, the functions of key bacteria, and the host–microbiota interaction is crucial for the development of knowledge-based strategies to enhance animal productivity and host health.

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1. Introduction

Animal husbandry is an important link during the exchange between humans and nature. The development of animal husbandry not only uninterruptedly provides food for humans but also accounts for a great proportion of the agricultural economy and makes an important contribution to the economy. In addition, animals can use some biomass that cannot be used by humans, which can effectively solve the problem of competition for food between humans and livestock. For example, ruminants can utilize plant cell wall biomass (Dai et al., 2015; He et al., 2019), many by-products of

agriculture and food industry as feed owing to the rumen microbiota (Kimball, 1991; Westendorf, 2000; Malaweera and Wijesundara, 2014). It has been suggested that ruminant livestock farming has the potential to minimize the use of human-edible grains by utilizing available forage resources within a given system (Eisler et al., 2014).

Currently, with the rapid development of animal husbandry, several issues have been raised, such as the low feed conversion efficiency, nitrogen utilization efficiency, product quality and high methane emissions (Nkrumah et al., 2006; Kumar et al., 2013; Wang et al., 2019). The above issues are more prominent for ruminants than for monogastric animals because of their unique digestive system, which needs to be better understood to address the above issues.

The rumen is described as a “black box” due to the multifarious microbes, and the ruminal microbiota is regarded as a new organ consisting of trillions of microbes, and its gene content is hundreds of times that of host cells (Huttenhower et al., 2012). These genes affect host nutrient utilization and health via specific metabolic pathways. Therefore, ruminal microbiota is highly associated with host feed digestion and metabolism. Numerous researchers have

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reported that the feed efficiency, nitrogen digestibility, and methane production in ruminants are affected by one or more groups of ruminal microbiotas (Sasson et al., 2017; Wang et al., 2017; Schären et al., 2018; Elolimy et al., 2018). For example, rumen methanogenic archaea mainly utilize the products of the fermentation pathways to produce methane (CH₄) (Thorpe, 2009; Patra et al., 2017). Furthermore, host health is also affected by the rumen microbiota (Mao et al., 2013). In the metagenomic era, the ruminal microbiota will surely attract much more attention, and the special role of microbiota will be revealed in the future, which may be a key step to search for better methods to improve the production performance.

Rumen epithelial cells are crucial for nutrient absorption, such as volatile fatty acids (VFA) and vitamins. However, our understanding of the host-microbe interactions remains limited. This review summarizes our knowledge of the relationships between ruminal microbes and ruminants' phenotypes, and the impact on the host. The knowledge in this area could assist the development of effective manipulations in enhancing animal productivity and host health.

2. Importance of the rumen microbiota

The rumen in adult ruminants harbors a dense and diverse microbiota, whereas the rumen in newborn calves and lambs has a rather simple microbiota. The rumen is inoculated during lactation, diet ingestion, and contact with the environments so that it is gradually colonized by a large number of diverse microbes that affect the epithelial cell function and gut-associated lymphoid tissue development (Jami et al., 2013). The ruminal microbiota contains bacteria (Firmicutes and Bacteroidetes as the 2 predominant phyla), archaea (such as *Methanobrevibacter smithii* and *Methanosphaera stadtmanae*), fungi and protozoa, among which bacteria are the most predominant and diverse.

In animal husbandry, milk, milk replacer (MR), and MR with starters (MR + S) are usually fed to calves, piglets and other livestock during the weaning transition period to promote gastrointestinal growth and microbiota development (Meale et al., 2017). Researchers reported that the regulation of immune responses could be dictated by the activation or suppression of Toll-like receptor (TLR) caused by microbial signals in humans (Spiljar et al., 2017). Thus, we speculate that rumen microbes are essential for the development and regulation of the neonates' immune system and that rumen microbes play a key role in maintaining life-long health and high productivity. Malmuthuge et al. (2013) found that gut microbiota and mucosal immune functions differed during the weaning transition of calves fed MR or MR + S. These authors also showed that the expression of *TLR6* was up-regulated in the MR + S group compared with that in the MR, and the expression of peptidoglycan recognition protein 1 and tight junction-regulating genes claudin-4 and occludin were affected differentially by the 2 types of diets. For ruminants, in the early days of the postnatal period, the initial microbial sources and the profiles may be critical to determine the microbe-immune system interaction and its implication in adulthood health. To date, this type of research is lacking in ruminants. When the regulatory mechanism of the immune system by specific microbes in the gastrointestinal tract (GIT) is sufficiently understood, more microbial vaccines can be developed for the prevention of diseases. In brief, early colonization of GIT microbes is affected particularly by dietary composition and critical for the expression of host genes that encode the mucosal immune responses and epithelial barriers during the postnatal period and weaning transition period for ruminants and mono-gastric mammals.

Compared with the reticulum, omasum, and abomasum, the adult rumen plays a most vital role in the degradation of dietary organic materials due to the various microbes therein. Rumen microbes can ferment dietary carbohydrates to VFA, which contribute up to 80% of the total energy required by ruminants (Wolin, 1979). Some rumen microbes also synthesize their own proteins for growth (referred to microbial crude protein, MCP) utilizing the energy and nitrogen acquired from the feed. The MCP are digested in the small intestine and absorbed by the host, thereby contributing to the host's nutrition and health (Russell and Rychlik, 2001; Hall and Huntington, 2008). Moreover, some microbes can produce vitamins, such as vitamins B and K. Rumen microbes have many enzymes involved in the de novo synthesis of vitamin B₁₂, which is not found in the GIT microbiome of humans (Seshadri et al., 2018). The main advantage of rumen microbes is their ability to use plant polysaccharides and non-protein-nitrogen in a diet, which cannot be digested and utilized by the host.

Several microbes in the rumen can secrete cellulase, which is a key enzyme to use plant cell wall materials by ruminants. Therefore, cellulolytic bacteria are focused by many researchers. The application of omics technologies reveals more and more cellulolytic bacteria. Studies using metatranscriptomics found that the rumen microbiome in Hu sheep (a local breed in China) encoded a repertoire of new cellulases (He et al., 2019). Cellulases enable the utilization of low-quality roughage (e.g., corn stover) and can be used to digest roughage for ruminants. Our laboratory has studied the effect of sequential addition of fibrolytic enzymes on the degradation of corn stover, and our results showed that the best enzyme use sequence was hemicellulase-cellulase-pectinase-laccase (Diaby, 2019). On the contrary, methanogens in the rumen produce methane via a series of redox reactions, and methane is a powerful greenhouse gas (Patra et al., 2017). Thus, rumen microbes possess great potential contributions to animal husbandry, and some of them can be applied in animal production (McCann et al., 2017).

3. Ruminal microbes and nutrient metabolism

The microbes that reside in the rumen influence the host metabolism by degrading the dietary materials, although these microbes are not considered as one of the specific tissues of the host. This microbiota participates in the digestion of the diet by their own secreted enzymes. It has been demonstrated that the rumen microbiome plays a critical role in feed efficiency, milk yield, and components in dairy cows (Schären et al., 2018). Recently, many studies have reported strong correlations between feed efficiency and rumen microbial profiles. For example, some ruminal microbes, their genes, and related pathways are closely linked to feed efficiency in dairy cows (Li, 2017; Paz et al., 2018). One study showed that under certain conditions a less sophisticated but more specialized rumen microbiome of dairy cows was able to support the host energy requirements (Shabat et al., 2016). Additionally, an analysis of microbiome genes and species could accurately predict the host feed efficiency phenotype (Shabat et al., 2016). *Megasphaera elsdenii* and its genes were enriched in certain microbiomes, resulting in high energy availability for the host. Moreover, the acrylate metabolic pathway was also enriched in high-efficiency cows, but methanogenic archaea and the methanogenesis pathway were less prevalent (Shabat et al., 2016). However, the abundance of archaeal genes involved in methanogenesis was greater in high methane emitters than in low methane emitters, and lower emissions were correlated with higher *Succinivibrionaceae* abundance and less changes in acetate and hydrogen production (Wallace et al., 2015, 2017; Roehe et al., 2016). These observations emphasize the significant role of specific metabolic

pathways in the rumen microbiota and for the host to acquire nutrients from the feed. Methane emissions not only cause global warming but also reduce feed utilization efficiency in the host. Future research is needed to explore direct-feeding microbes to improve animal productivity.

The balance between carbohydrate and nitrogen metabolism in the host is crucial for efficient utilization of dietary nutrients. Nitrogen sources in the intestine exert constraints on the microbial competition for carbohydrates, affect microbiota assembly, and shape the host–microbiome interactions (Holmes et al., 2017; Abdelmegeid et al., 2018). For example, monosaccharide content can be increased due to the role of microbial enzyme activities (Ibrahim and Anishetty, 2012). Digestion of nitrogen and fiber contributes substantially to feed efficiency and it is also related to rumen microbes that produce MCP and VFA for the host (McDonald, 1954; Hall and Huntington, 2008). One research has shown that *Fibrobacter succinogenes*, *Butyrivibrio fibrisolvens*, and *Ruminococcus* sp._HUN007 are the most critical ruminal bacterial species in terms of utilization of nitrogen by the host (Wang et al., 2019). The secretion of metabolites by some microbes may affect the amino acid pool and nitrogen turnover in the host by binding to GIT receptors, thereby regulating the nitrogen utilization efficiency of the host. For example, TLR in the epithelium can sense lipopolysaccharide and lipoprotein degradation products from the bacteria (Wells et al., 2011). When lipopolysaccharide activates TLR4, TLR5, and TLR9, the host secretes bacterial flagellin and other bioactive substances (such as cholecystokinin), which further influence the digestion and absorption of dietary nitrogen. One previous study showed that repeated inoculation of the cattle rumen with a sample of the contents of the bison rumen could increase protein digestibility and nitrogen retention and alter the proportion of VFA (Ribeiro et al., 2017). However, the microbial species responsible for the observed outcomes remain to be identified, and further research is warranted. Moreover, a study found that apparent nitrogen digestibility was positively correlated with the total rumen protozoal number and the relative abundance of the bacterial family Christensenellaceae, but negatively correlated with the relative abundance of the BS11 gut group of bacteria. Thus, in addition to bacteria, rumen protozoa also play a key role in ruminal nitrogen and carbohydrate metabolism (Williams and Coleman, 1997).

A previous study found that some bacteria hindered the digestibility of neutral detergent fiber (NDF) in goats (Liu et al., 2019). Also, several bacterial phyla such as Proteobacteria, Tenericutes, and TM7 and a few bacterial genera, including *Anaeroplasma*, *Campylobacter*, and *Clostridium*, are correlated with apparent crude fiber digestibility in pigs (Niu et al., 2015). Cellulolytic microbes are among the most prominent bacteria in the rumen, they affect the host fiber digestibility by secreting the cellulase and regulating the production and profile of VFA. And, VFA can both provide energy and modulate the intestinal barrier function of the host. One study showed that changing the intestinal microbial populations in mice could affect the yield and profile of VFA (Fredrik et al., 2007). Another study found that ruminal bacteria were positively correlated with the gene expression level of ruminal epithelial cells and the amount of VFA in adult beef cattle (Chen et al., 2011). Furthermore, changing VFA also plays a key role in the expression of genes in rumen epithelial cells (Lu et al., 2014). However, ruminal VFA and the microbiota exhibit disparity across different individuals (Chung et al., 2012; Cox et al., 2014), which is also found in other species (Goodrich et al., 2014; Carthage et al., 2015). These observations indicate that the influence of microbiota on the host is not one-directional, and the host also plays a key role in regulating GIT microbiota. However, the causality and physiological mechanisms underpinning the host–microbiota interactions are still unclear.

Meta-omics technologies have provided new perspectives on understanding nutrient metabolism, generating an ever-expanding and integrated microbial database, and revealed an in-depth symbiotic relationship between the host and rumen/gut microbiota. In the future, specific microbes should be identified and explored to modulate feed and nutrient utilization efficiency in animals. These microbial products can significantly improve the efficiency of animal production and enhance food security.

4. Factors influencing the microbiota–host interaction

The rumen microbiota responds to changes in its environments by altering its composition and function. Many researchers have investigated the factors that could affect the rumen microbiota over the past decades. Different technologies have been applied, ranging from community fingerprint technologies to high throughput sequencing technologies. Diet, environment, age, and health status of the host are found to be important in shaping the rumen microbiota (Table 1). However, further researches that use integrated and comprehensive technologies are needed to elucidate the specific causes that lead to the change of rumen microbiota.

The productivity of ruminants relies heavily on rumen function, which can be regulated by interactions between host genes and the environment (e.g., diet, management), leading to the alteration of rumen microbial ecology. In particular, the type of diet can strongly influence rumen function by altering the microbial populations and fermentation activities (Bevans et al., 2005; Auffret et al., 2017; Liu et al., 2017; Pandit et al., 2018). Roughage has a significant impact on rumen development and expression of the genes involved in VFA absorption in the rumen epithelial cells. Therefore, diet, which is regarded as one of the most significant factors, has been modified in large feeding operations of ruminants to improve feed efficiency.

During evolution over millions of years, ruminants have evolved a digestive system able to digest roughages. When ruminants are fed high-grain or fiber-deficient rations, rapid degradation of readily fermentable carbohydrates produces a large quantity of VFA, resulting in a decline of the ruminal pH and occurrence of acidosis, which can alter the microbial ecology and disrupt the physiological homeostasis (Russell and Rychlik, 2001; Bevans et al., 2005). Besides forage-to-concentrate ratio, different types of roughages can markedly influence the ruminal metabolome and fermentation. Dairy cows fed a mixture of alfalfa hay, *Leymus chinensis* hay, and corn silage produce high levels of acetate, valerate, hydrocinnamate, and methylamine, and low level of glucose, glycine, propionate, and isovalerate, than dairy cows fed corn stover (Zhao et al., 2014). Furthermore, the rumen papilla width, thickness of the stratum granulosum, stratum spinosum, stratum basale, and stratum corneum vary with roughage types (Weng et al., 2013). The change of dietary components also influences the expression of TLR genes (Malmuthuge et al., 2013). Several studies have shown that dietary compositions and types can affect ruminal microbiota, rumen epithelial tissue morphology, and receptors. Detailed elucidation of the interactive mechanism of rumen microbes and the rumen epithelial cells is likely to prove useful for manipulating ruminant farming by dietary interventions.

The age of the host is another factor that affects rumen microbes. For example, the dominant rumen bacteria are different among newborn, 2-month-old, 6-month-old, and 2-year-old cows (Jami et al., 2013). This is partially due to differences in diets (colostrum, milk, milk-supplemented rations for calves, and total mixed rations for adult cows). However, the growth of the host also has a decisive role in the changes of GIT microbiota (Li et al., 2012) because microbiota varies with the age of cows fed the same diet. It is probably due to the changes in the rumen and metabolites as animals grow over time. These results indicate that the maturity process

Table 1
Factors influencing the rumen microbiota.

Factor	Model	Treatment	Technology	Results	Explanation	References
Age	Bovine	1 day, 3 days, 2 months, 6 months, 2 years old	454 tag-encoded amplicon pyrosequencing	Diversity and within-group similarity increase with age, and each group has its own distinct microbiota		Jami et al. (2013)
	Calf	14 days, 42 days old	16S rRNA gene sequencing, whole-genome shotgun approach	Rumen microbiota of pre-ruminant calves displays compositional heterogeneity, but functional classes between the 2 age groups are similar	GIT development seemingly has an impact on microbial diversity	Li et al. (2012)
Diet	Goat	Complete feed all forages	16S rDNA sequencing	The richness of fiber-, protein-, and fat-digesting bacteria is affected by diet		Liu et al. (2017)
	Holstein dairy cows	Mixture of corn stover And alfalfa hay, <i>Leymus chinensis</i> hay, and corn silage	Metabolomics	Roughage type can significantly influence the ruminal microbial metabolome, especially organic acids, amines, and amino acids	Ruminal bacteria are increased with increasing associated substrates	Zhao et al. (2014)
	Dairy calves	MR, MR + S	DGGE	Feeding solid feed affects bacterial diversity, expression of <i>TLR</i> , β -defensin, <i>PGLYRP1</i> , claudin-4, and occluding		Malmuthuge et al. (2013)
Genetic	Cattle bison	Transfer of rumen contents from bison to cattle	16S rRNA gene sequencing	Inoculation with bison rumen contents alters the cattle rumen microbiome and metabolism	The rumen microbiome in cattle and bison is distinct	Ribeiro et al. (2017)
	Dairy cows	Forty-severn animals are used to estimate genotypic, 78 Holstein-Friesian dairy cows are used to assess rumen microbiota.	SNP-based heritability estimates and 16S rRNA gene sequencing	Host genetic variation is associated with specific microbes		Sasson et al. (2017)
	Bovine	2 × 2 factorial analysis of breed types and diets	Metagenomics	Host genetics shapes the microbiome		Roehe et al. (2016)
Feed efficiency	Milking cows	Feed-efficient, feed-inefficient	16S rRNA gene sequencing, shotgun DNA sequencing	Inoculation with bison rumen contents alters the cattle rumen microbiome and metabolism <i>Megasphaera elsdenii</i> is enriched in the rumen of the feed-efficient group; <i>Methanobrevibacter</i> was diminished	Microbial-related genes and metabolic pathways affect host feed efficiency	Shabat et al. (2016)
	Beef cattle	Feed-efficient, feed-inefficient	Metatranscriptomics	<i>Lachnospiraceae</i> , <i>Lactobacillaceae</i> , and <i>Veillonellaceae</i> are more abundant in low-feed-efficiency animals; <i>Methanomassiliicoccales</i> was diminished		Chen et al. (2011)

GIT = gastrointestinal tract; MR = milk replacer; MR + S = milk replacer + calf starter; DGGE = denaturing gradient gel electrophoresis; *TLR* = Toll-like receptors; *PGLYRP1* = peptidoglycan recognition protein 1; SNP = single nucleotide polymorphism.

of the host can lead to alteration of the rumen microbiome. Yet, in-depth understanding is lacking and more research is needed to investigate how rumen microbiota and the hosts interact at different ages and provide the knowledge that can be used to develop new strategies to improve animal productivity at various stages.

The external living environment, such as the climate, temperature, humidity, geography, and herd management also affect the rumen microbiota–host interaction. One study revealed the importance of the living environment in determining the comparison of the ruminal microbiome of cattle and bison (Ribeiro et al., 2017). Consequently, microbial genomes in the GIT gradually alter when host living environments change. When the host becomes ill, its gut microbes and the microbial functions may differ from those in healthy individuals (Clavel et al., 2017). Unfortunately, it is difficult to identify the specific causes for the alterations in microbial diversity and to quantitate the host–microbiota interaction

due to the complexity of the GIT environment. Based on the analysis of the published literature (Liu et al., 2017), the diet has the most significant influence on the ruminal microbiota, but comparative studies across species are needed. Empowered by the contemporary omics technologies, scientists would rapidly reveal the microbial composition, the functions in the GIT, the host–microbe interactions, and the factors affecting GIT microbiota. Future research should focus on the mechanisms of the host–microbe interrelation, especially the quantification of dietary effects on GIT microbiota and the epithelial cells and their coordinated variation.

5. Regulation of host–microbiota interaction

The tight and constant interaction between the host and rumen microbiota is a vital prerequisite for ensuring host health and

optimal productivity. The rumen provides a permissive residence for the microbes, and the rumen microbes can secrete special enzymes that aid feed digestion in the host. If any 1 of these 2 factors becomes abnormally, the regular metabolic mechanism will be interrupted in ruminants. Therefore, regulating the host–microbiota interaction may bring benefits to the host. Prospective studies can focus on these approaches to improve animal productive performance and host health under harmonious host–microbiota interactions.

Diet is the key factor determining and maintaining the host–microbiota interaction. It is a universal means to reach the genetic potential of the animals by providing a properly matched diet. Researchers have proved that the ruminal microbiome–host crosstalk stimulates the development of the ruminal epithelium (Lin et al., 2019). It was shown that the abundances of genes involved in sugar degradation decreased in the rumen of lambs fed starter, but the abundance of glycoside hydrolase family 13 encoding α -amylase increased; simultaneously, the expression of the genes involved in cell growth modules, such as *MAPK1*, *PIK3CB*, *TNFSF10*, *ITGA6*, *SNAI2*, *SAV1*, and *DLG*, were up-regulated, whereas the genes encoding the proapoptotic protein BAD's promotion of cell death was down-regulated in the rumen epithelial cells (Lin et al., 2019). If the same results are present in goats, sheep, and cows, it will emphasize the importance of diet in the regulation of host growth. Firmicutes and Bacteroidetes are the dominant bacterial phyla of the rumen microbiota irrespective of host species, and both participate in fiber degradation and produce VFA (Sandra and Macfarlane, 2003). The various species in these 2 phyla have their special niches, and they can be influenced by dietary types. Specific fiber sources can alter the rumen microbiota, modulate innate immune systems, and affect intestinal mucosa barrier integrity and colon pH, ultimately improving the absorption of nutrients. It may be an effective way to maintain high efficiency between cellulolytic bacteria and host gut health by changing the type and amount of fiber in the diet. Formulating appropriate composite diets can stimulate the development of the immune system during not only the early life but also the adulthood, which may have an impact on the economic return in animal farming.

The micro-ecological environment of GIT is another important factor affecting the metabolism and health of the host by regulating the host–microbiota interaction. Species of bacteria with specific functions may be identified, cultured/enriched, manufactured, and used as feed additives. Using direct-fed microbes is an efficient method to provide some functional microbes to the host. Yet, it remains a challenge to identify the specific function of microbes and to acquire the microbes of interest. Currently, researchers focus on microbial transplantation to enhance feed efficiency, productivity, and host health. For example, Hu et al. (2018) reported that fecal microbiota transplantation from diarrhea-resistant pigs to susceptible piglets significantly prevented early weaning stress-induced diarrhea in Landrace \times Yorkshire crossbred piglets. *Lactobacillus gasseri* LA39 and *Lactobacillus frumenti* were confirmed as 2 bacterial species mediating diarrhea resistance in pigs. Gasserin A, a bacterial secretory circular peptide, was found to play a vital role in diarrhea resistance via a mechanism involving keratin 19 (KRT19) on the plasma membrane of intestinal epithelial cells, which reduces the levels of cyclic adenosine monophosphate (cAMP) and cyclic guanosine monophosphate (cGMP), contributing to diarrhea resistance by promoting intestinal epithelial fluid absorption and reducing fluid secretion (Hu et al., 2018). These observations suggest that *L. gasseri* LA39 and *L. frumenti* could have a practical value for preventing diarrhea in piglets and may be used to support early weaning and pig raising. To improve feed efficiency in beef cattle, the rumen contents from high and low feed efficiency cattle were exchanged, and the results showed that the brief

substitution of the content was not an effective strategy to improve feed efficiency (Zhou et al., 2018). Thus, it is necessary to identify the key microbes that are associated with feed efficiency. Moreover, future research is needed for the successful establishment of the transplanted microbiota in recipient animals.

Many researchers have revealed that some ruminal microbes are influenced by host genetics (Li et al., 2019a, 2019b). The variations in host genetics can further induce performance differences. These findings highlighted a potential to explore desirable and efficient rumen microbiota by genetic selection of individual animals. In the future, rumen microbiota may become a potential marker for breeding and selection for important animal traits, such as feed efficiency, optimize rumen fermentation, and gut health.

6. Conclusions and future directions

The rumen microbiota plays an essential role in the nutrient acquisition and utilization of ruminants. The ruminal microbial fermentation provides VFA, MCP, and vitamins by degrading plant fibers, non-protein-nitrogen, and other organic matters in the diet. The gut microbiota interplays with intestinal epithelial cell metabolism and influences nutrient utilization, immune function, and health of the host. Although some bacterial species have received particular attention, the roles of most microbes in the rumen remain undefined. For improving animal productions, the microbiota features and function should be characterized firstly. In this regard, metatranscriptomics can provide new perspectives at the transcriptional level and reveal the potential function of microbes. Continuous research is needed to identify and characterize, both taxonomically and biochemically, ruminal microbes so that they can be explored for application in livestock production.

The host-microbe interaction, in general, is bidirectional, complex, and wide-ranging, making it challenging to distinguish between the causality relationship and the roles in host nutrition and diseases. Additionally, there are many gaps in knowledge about the interaction among different members of the ruminal microbiota and how these interactions affect the host metabolism. Recently, many researchers have focused on the role of individual bacteria, but the synergism and antagonism between 2 or more bacteria have been ignored, because one metabolite is probably secreted by more than one bacterium and the bacterial metabolites are the key factors stimulating the host. More research is needed to elucidate the various interplay mechanisms. However, it is not easy to explore the change of rumen epithelial barrier function and microbes. A better understanding of the rumen microbiome-host interaction can provide novel insights that inform the development of applicable approaches to improve animal production and health. Future studies need to also focus on specific microbes or metabolites that are linked to particular pathophysiological processes.

Author contributions

Yangdong Zhang and Kaizhen Liu provided concepts of the paper; Kaizhen Liu wrote the manuscript; Guoxin Huang, Qingbiao Xu, and Shengguo Zhao revised the manuscript; Zhongtong Yu made a major contribution to the revision of the manuscript, including the concept, structure, and language; Nan Zheng and Jiaqi Wang revised the language and checked the manuscript.

Conflict of Interest

We declare that we have no financial or personal relationships with other people or organizations that might inappropriately

influence our work. There is no professional or other personal interest of any nature or kind in any product, service, and/or company that could be construed as influencing the content of this paper.

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