Intestinal microbiota: Development, metabolism and functions

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Received 12 January 2011, accepted 10 April 2011.

Abstract
Recent years have witnessed the discovery that intestinal microbiota is not only the important factor for host amino acid and energy metabolism, but are also the crucial determinant for host immunity. Additionally, intestinal microbiota is associated with many diseases. Intestinal microbiota and their metabolites are required for the functions. However, a non-appropriate microbial community composition and their products are pathogenic factors. Thus, an optimal balance among intestinal microbiota in the intestinal tract is crucial for whole body homeostasis. Diet supplementation with one species or mixture of intestinal microorganisms may have beneficial effects on host in keeping an optimal balance of intestinal microbiota, recovering from disturbed microflora, promoting digestion and absorption of food, promoting the development of immune system and killing pathogens. Thus, intestinal microbiota has important functions in host energy metabolism, amino acid nutrition, immunity and health.

Key words: Intestinal microbiota, development, function, metabolism.

Introduction
Intestinal microbiota consists of microorganisms that live in the digestive tracts of animals. The mammalian body is consisted of 100 trillion cells, which carries about ten times as many microorganisms in the intestine. It is estimated that the intestinal microbiota has about one hundred times as many genes in aggregate as there are in the mammalian genome. Bacteria make up most of the intestinal microbiota in the gut, which include 300 to 1000 different species. However, about 99% bacteria belong to 30 or 40 species. Fungi and protozoa also make up a part of the intestinal microbiota, but little is known about their activities.

Recent researches suggest that the relationship between intestinal microbiota and host is not merely commensal, but rather a symbiotic relationship. Though mammal can survive without intestinal microbiota, these bacteria perform a series of important functions, such as keeping energy homeostasis, promoting the development of immune system and gut itself, preventing growth of pathogenic bacteria. At the same time, some bacteria are thought to be capable of causing disease in certain conditions.

The intestinal microbiota forms an essential part of a complex ecosystem that plays an important role in human health and nutrition metabolism. The major objective of this present review is to provide insights into new development in intestinal microbiota research, as well as their implications for both nutrition and health.

Diversity and Development of Mammal Intestinal Microbiota

Diversity of mammal intestinal microbiota: The mammalian intestine hosts a dynamically evolving microbial ecosystem that consists of various bacterial populations. These bacteria are either permanent intestinal residents, for example autochthonous components, or transient inhabitants, for example allochthonous members, introduced from the environment. The relationship between bacteria and host can be regarded as a continuum from commensalism to mutualism to pathogenesis/parasitism. It is presumed that the intestine is colonized by trillions of symbionts and commensals that provide versatile metabolic capabilities for host. Thus, host consequently did not need to develop themselves in many metabolic capabilities. It is believed that intensive selection and co-evolution results in the genetic diversity of the intestine. Horizontal Gene Transfer (HGT) is assumed to function as the principal evolutionary force in shaping the host microbiome.

Mammal intestinal microbiota is characterized by a relatively small number of bacterial and archaeal divisions, compared to other environments such as soil or stromatolite. The 16S rRNA gene sequence analysis revealed that mammal intestinal microbiota is comprised of only nine major bacterial divisions, including Bacteroidetes, Firmicutes, Fusobacteria, Proteobacteria, Verrucomicrobia, Cyanobacteria, Spirochaetes, VadinBE97 and Actinobacteria. Bacteroidetes and Firmicutes constitute the two major bacterial divisions of the mammal intestinal bacteria. Noticeably, proportions and compositions of Bacteroidetes (for example Lactobacillus and Bifidobacteria) were consistently stable within individuals whereas Firmicutes, especially the Clostridium group (for example Clostridium coccoide and Clostridium leptum), showed large inter-individual variation. However, there are different bacterial cells density and bacterial species in the different site along the digestive tract (Fig. 1). Generally, the number and diversity of bacteria flora is increasing from stomach to foregut then to hindgut. The spatial distribution of the piglet intestinal microbiota is also different, which is not random, but rather organized. There are noticeable difference for the intestinal...
microbiota in the mucus and lumen (Fig. 1).

Investigators can explore mammal intestinal microbiota using molecular fingerprinting methods. However, such studies have been limited by the relative paucity of sequenced gene fragments, the difference in the relative abundance of intestinal bacteria, and little attention given to potential differences between specific anatomical sites. In addition, variation associated with time, diet, and health status has not been adequately described, nor have the relative importance and contributions of each source. However, new research methods are continuously developed and improved (for example the emerging metagenomic sequencing), by which more detailed and accurate information about the diversity of intestinal microbiota will be obtained to enlarge our knowledge in this area.

Development of mammal intestinal microbiota: Mammalian intestine is assumed to be non-microbial before its birth. Following birth, immediately, bacteria originating from the mother, diet and environment will colonize it. Thus, mammal intestinal microbiota establishes rapidly a microbial population. Then profound changes occur in the intestinal ecosystem when weaning the young mammals onto solid food. During weaning, the composition of intestinal microbiota will become more complex and the diversity will increase dramatically, for example in ileum (Fig. 2a-b). Obligate anaerobes (Streptococcus, Clostridium etc.) increase in number and diversity, especially in the hindgut, and the composition of the microbial varies in different parts of the intestine. The mammals are initiated into an organized and lifelong process of colonization by foreign organisms. The intestine of mammal becomes home to a large bacterial community (including colonization by foreign organisms. The intestine of mammal mammals are initiated into an organized and lifelong process of total number of cells of its host.

Due to the symbiotic relationship between intestinal microbiota and host, young mammal intestine microbiota has to continuously evolve under strong selective pressure acting on both intestinal niche and its bacterial colonizers. Some co-evolved commensal bacteria can be well adapted to occupy the mammal intestinal ecological niche. There is highly significant difference between individuals in the intestinal microbiota during the first couple of days after birth. However, the young mammal is exposed to its environment including the maternal vaginal, fecal, and skin microbiota. Over time, the ecological fitness advantages of specific bacteria will become dominant bacterial groups instead of the initial bacterial colonizers. In addition, the changing environment of intestine (the intrinsic development of intestinal mucosa as well as different dietary intake) and actions elicited by intestinal microbiota themselves may implement the very important selection for the most highly adapted bacteria groups.

Factors influencing the composition of intestinal microbiota: Mammal intestinal microbiota comprises microorganisms (bacteria, archaea, fungi, viruses, and protozoa) that represent superior competitors for a complex intestinal ecosystem. It is generally considered that the genotype of host and the diet are the major factors defining a microbial intestinal niche. However, many other factors also influence mammal intestinal microbiota such as interactions between individual colonizers, as well as transient microorganisms (pathogens and probiotics).

The genotype of the host is considered as a factor influencing variation of intestinal microbiota between individuals, which works through the differential action of the genes that specify and control the immune system. For example, the host immune system modulates the intestinal microbiota composition by restricting microbial penetration through the host mucosal barrier, and by secreting different antimicrobial products such as antimicrobial peptide, as well as antimicrobial enzyme. The genotype of the host determines the availability of specific attachment sites and host-derived resources, which influence the intestinal microbiota. So, monozygotic twins exhibit fewer differences in the intestinal microbiota than their unrelated marital partners. However, there are small differences between the intestinal microbiota of the monozygotic twins, which suggests that maternal transmission is another determining factor. The initial colonizing microbiota influences the eventual microbial composition of the intestine.

It was demonstrated that diet can have an important influence on the composition of intestinal microbiota. Some studies have shown a clear correlation between diet and the presence of specific bacterial groups. For example, a diet rich in inulin and related fibers promote an increase in Bifidobacteria, supplementation with astragalus polysaccharide and related polysaccharide in diet increase the number of Lactobacillus and Bifidobacteria. There are many Lactobacillus salivarius and Lactobacillus mucosae in intestine, when nursing piglet is provided breast milk. However, with the diet transformation from liquid breast milk to solid foods, the two species of Lactobacillus are largely replaced by Lactobacillus amylovorus. In addition, mucin and other host-derived products, as well as the competition and cooperation between bacteria are thought to be important influencing factors of intestinal microbiota.

Finally, age, antibiotic and probiotic have crucial influences on the mammal intestinal microbiota. It is noted that the effect differs between antibiotics or probiotics. Age, in fact, is an important determinant. The composition of intestinal microbiota in adult has generally been considered to be stable as long as the host is not subjected to stressful circumstances. Some studies reported,
However, that the elderly subjects have fewer bifidobacteria and more fungi and enterobacteria colonized in intestine compared to the younger subjects. *Clostridium difficile* has the greater frequency of isolation in elderly mammals than in young subjects.

**Intestinal microbiota influences host metabolism:** Intestinal microbiota constitutes a complex and dynamic ecosystem which constantly interacts with host metabolism. The microbiota provides crucial trophic and protective functions for mammals, and exerts great impact on the host’s energy metabolism, facilitating the absorption of complex carbohydrates (cellulose, hemicellulose, gums etc.) and modulating amino acids homeostasis. In addition, the microbiota synthesizes essential vitamins such as vitamin K and group B vitamins. In total, the mammalian symbiotic superorganism has been shown to be closely connected with host evolution and take control of many metabolic functions result in host genome reduction. Mammal microbiota also influence the metabolism of many drugs and nutrients, modifying their bioavailability and metabolic fate.

**Microbial amino acid synthesis and utilization in mammalian intestine:** It is considered that intestine microbial protein is of no nutritional importance to non-ruminants, because the greatest microbial population is concentrated in cecum and colon, whereas the major site of amino acid absorption is the small intestine. In fact, small intestine has strong microbial activity too. The microbiota has significant impact on amino acid synthesis and utilization in both ruminants and non-ruminants.

The supplementation with non-specific nitrogen in low protein diet can improve nitrogen balance and be incorporated into amino acids. The metabolic basis of these observations is not well clarified. A possible reason is that the intestinal microbiota makes the absorption and utilization of essential amino acids 25-27. In addition, the microbiota synthesizes essential vitamins such as vitamin K and group B vitamins. In total, the mammalian symbiotic superorganism has been shown to be closely connected with host evolution and take control of many metabolic functions result in host genome reduction. Mammal microbiota also influences the metabolism of many drugs and nutrients, modifying their bioavailability and metabolic fate.

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**Figure 2a.** Unrooted phylogenetic tree was based on the combination of the six individual 16S rRNA sequences from bacteria in the ileum digesta of sucking piglets on Day 28. Clones represented by 1–194 were generated from sucking piglets on Day 28. The similarity to the existing database sequences of 16S rRNA genes and the total number of clones are shown in parentheses.
Amino acids and protein synthesized by the intestinal microbiota, in order to be utilized by host, must be produced in regions of the intestine where amino acid absorption occurs or proximate to these segments, or recycled by reverse peristalsis or coprophagy. Torrhallmoda 14 kept young pigs in cages to prevent coprophagy. These pigs were given the diet that included both $^{15}$N ammonium chloride and $^{14}$C poly-glucose (a substrate resistant to mammalian digestive enzymes but fermentable by the intestinal microbiota). After 10 days, the pigs were killed and the $^{14}$C-specific radioactivity of amino acid in carcasses were found in all the amino acids examined (lysine, valine, leucine, isoleucine, tyrosine, phenylalanine and histidine). In another experiment, ileal digesta from pigs given a diet supplemented with $^{15}$N ammonium chloride was quantitatively infused into cecum of similar pigs.

Figure 2b. Unrooted phylogenetic tree was based on the combination of the six individual 16S rRNA sequences from bacteria in the ileum digesta of weaned piglets on Day 28. Clones represented by 1–169w28 were generated from weaned piglets on Day 28. The similarity to the existing database sequences of 16S rRNA genes and the total number of clones are shown in parentheses.

<table>
<thead>
<tr>
<th>Clones</th>
<th>Sequence Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>1w28(98%, 1clone)</td>
<td>Lactobacillus acidophilus (M82434)</td>
</tr>
<tr>
<td>11w28(99%, 1clone)</td>
<td>Lactobacillus acidophilus (M82434)</td>
</tr>
<tr>
<td>15w28(99%, 1clone)</td>
<td>Lactobacillus acidophilus (M82434)</td>
</tr>
<tr>
<td>22w28(98%, 1clone)</td>
<td>Lactobacillus acidophilus (M82434)</td>
</tr>
<tr>
<td>111w28(99%, 1clone)</td>
<td>Lactobacillus acidophilus (M82434)</td>
</tr>
<tr>
<td>169w28(97-99%, 5clones)</td>
<td>Lactobacillus acidophilus (M82434)</td>
</tr>
</tbody>
</table>

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1. Both $^{15}$N ammonium chloride and $^{14}$C poly-glucose (a substrate resistant to mammalian digestive enzymes but fermentable by the intestinal microbiota) were given to the pigs.
2. Lysine and threonine are amino acids that are easily labeled from ammonia.
3. The similarity to the existing database sequences of 16S rRNA genes and the total number of clones are shown in parentheses.
4. The intestinal microbiota, in order to be utilized by host, must be produced in regions of the intestine where amino acid absorption occurs or proximate to these segments, or recycled by reverse peristalsis or coprophagy.
given an unlabeled diet. The \([15N]\) lysine enrichment in the plasma of the pigs given the labeled diet was three quarters that measured in intact pigs given the labeled diet, whereas that of pigs receiving labeled digesta per cecum was only one quarter that of the intact pigs 30. These results indicated small intestine was an important metabolic site for the utilization of amino acids and protein synthesized by intestinal microbiota.

Supplementation with probiotics can influence the serum amino acid levels. Wang indicated that supplementation with \emph{Bacillus subtilis} increased dramatically the serum concentration of serine, glutamic acid, alanine, cysteine, arginine, \(\text{NH}_3\), and total amino acids, however, decreased significantly the serum methionine level. The possible reason is supplementation with \emph{Bacillus subtilis} increased the \(\text{NH}_3\) or \(\text{NH}_4^+\) concentration in intestine and serum and further promoted the synthesis of some amino acids 9. Eklou Lawson found that after 2.5 g ammonia injection into the colonic lumen in pig, among AA, L-glutamine and L-arginine are significantly increased in the portal blood plasma, which can provide an indirect proof for the effects of \emph{Bacillus subtilis} on the serum amino acids 40. Very little is known about the influence of supplementation with probiotics in the diet on serum amino acid levels. More studies are needed to further clarify this issue, and to provide valuable references for the use of probiotics in animals.

There is a cooperation relation between host and intestinal microbiota. Intestinal microbiota provides many products (for example amino acid) for host by synthesis or fermentation. However, intestinal microbiota synthesizes amino acids not only for host but themselves. The source of nitrogen utilized by intestinal microbiota for \emph{de novo} amino acid synthesis, it includes diet, the tissue of gut itself (especially the mucosal enterocytes) and microbial cells 37, 38. Thus, there exists a competition relation between host and intestinal microbiota. From small intestine to large intestine, there is geometric expansion for the number of microorganisms. It means more amino acids are used for the growth of microorganisms, which may be one reason why supplementation with antibiotics in diet can promote the growth and improve the feed utilization ratio in animals.

\textbf{Intestinal microbiota influences host energy metabolism:} The intestinal microbiota is now considered as a key organ involved in host energy homeostasis. The recent researches indicate the modulation of intestinal microbiota affects host metabolism and has an impact on host energy harvest from the diet and energy storage 39. The biological functions controlled by intestinal microbiota are related to the effectiveness of energy harvest, by the bacteria, of the energy ingested but not digested by the host. Some researches found that the intestinal microbiota of obese subjects changed according to the loss of body weight occurring after a hypocaloric diet and the number of bacteroidetes bacteria depended on the weight loss whereas the firmicutes bacteria group remained unchanged 16, 40. Gordon and colleagues proposed that the intestinal microbiota from obese subjects is able to increase the energy harvested from diet, which provides extra energy for host. These experiments suggested that an environmental factor such as intestinal microbiota regulates the energy storage.

Intestinal microbiota can provide nutrition proteins, amino acids, enzymes, volatile fatty acids, vitamins and so on for host 26, 41. In pig, up to 30% of energy for maintenance could be retained by microbial degradation, particularly in the large intestine 42. In all, intestinal and host have a complex cell communication system. Intestinal microbiota has very important impact on C and N cycling of host.

\textbf{Intestinal Microbiota and Host Immunity}

\textbf{Influence of intestinal microbiota on development of immune system:} The development of host mucosal immune system takes place over a period of several weeks. However, the development largely depends on the intestinal microbiota 43. Comparison to conventional animals, germ-free animals have an undeveloped mucosal immune system and the secondary lymphoid organs such as spleen, lymph nodes and Peyer’s patch are poorly developed 44. In germ-free piglets aged 39 and 59 days, ileal and jejunal Peyer’s patch were significantly shorter than in age-matched control animals 45. With germ-free piglets of 45 days of age, the cell yield and subset patterns were comparable with those in five-day old normal animals 46. The number of intra-epithelial T lymphocytes also shows an increase that is significantly related with age and exposure to microbial antigen 43, 47.

The colonization of germ-free animals with known bacteria provides a valuable model for studying the effects of microbial exposure on the host immune system 48. Some colonization studies indicated that segmented filamentous bacteria appeared in high numbers shortly after weaning in a wide range of species, e.g. mice and pig 48. These bacteria show a preference for attachment to epithelia covering the lymphoid tissue of the Peyer’s nodes, and are thought to play an important role in the stimulation of host mucosal immune system 50, 51. Such studies confirm the importance of microbial exposure for the proper development of mucosal immunity and of the intestinal epithelia.

\textbf{Host-intestinal microbiota interaction at the gut epithelium:} Paneth cell is the specialized epithelium situated at the base of the small intestinal crypt that produces most of the antimicrobial peptides in the small intestine 52. Microbial colonization in GF animal initiates the expression of a complex antimicrobial transcriptionsal program by MyD88-dependent TLR activation. However, Paneth cell–MyD88 signaling also plays a role in limiting intestinal barrier penetration by commensal and pathogenic bacteria. Thus, MyD88 signaling in Paneth cells contributes to host–microbial homeostasis by regulating the production of antimicrobial peptides that can limit the number of bacteria at the mucosal surface. At the same time, commensal induced antimicrobial peptides also have important roles in host immune modulation at steady state.

Intestinal microbiota plays a role in maintaining the integrity of the intestinal epithelium. The rate of proliferation of intestinal epithelial cells is lower in germ-free than in conventional animal 53, 54, which suggests that intestinal microbiota can induce the proliferation of intestinal epithelial cells. Commensal flora recognition by Tool-like Receptors (TLRs) is a necessary step for the proliferation of intestinal epithelial cells and for protection against intestine injury and associated mortality 55. Colonization of germ-free animal with \emph{Bacteroides thetaiotaomicron} can activate a lot of genes’ expression involved in intestinal functions, including fortification of the intestinal epithelial barrier 56. Moreover, TLR-2 signaling can enhance tight junctions in the intestinal epithelium 57, 58. In addition, the recognition of peptidoglycan from Gram-negative bacteria by nucleotide
oligomerization domain (NOD) 1 expression in epithelial cells induces genesis of isolated lymphoid follicles \(^6^7\). Therefore, the recognition of commensal bacteria by epithelial TLRs and NODs plays a crucial role not only in recognition and induction of inflammation against pathogens, but in host–microbial symbiosis.

**Obesity and diabetes:** Obesity in humans is a major public health crisis worldwide and is a leading risk factor for insulin resistance, type II diabetes, atherosclerosis, stroke, hypertension, and some types of cancer (including colon and breast cancers). Unfortunately, clinicians have few tools to fight the obesity epidemic, because current anti-obesity drugs are not highly effective and are fraught with side effects. Recent work has shown that there is a close relation between intestinal microbiota, nutrition utilization and energy storage by host organism. The host–bacterial mutualism is associated with altered energy extraction from the diet and may produce differences in energy intake and body composition in obese and lean subjects. The obese microbiome has an increased capacity to harvest energy from the diet. Furthermore, this trait is transmissible: colonization of germ-free mice with an obese microbiota results in a significantly greater increase in total body fat than colonization with a lean microbiota. The manifestation of inverse relationship was confirmed in two dominant bacterial divisions, i.e. reduction of the genera of Bacteroides and a proportional increase of the Firmicutes in gut of genetically obese mice \(^1^9\). Similarly, the relative proportion of Bacteroides to Firmicutes was decreased in obese people as compared with lean people, and this proportion increases with body-mass loss on low-caloric diet \(^1^6,^6^0\). These results identify the intestinal microbiota as an additional contributing factor to the pathophysiology of obesity.

Type 2 diabetes is a metabolic disease that is caused by obesity-linked insulin resistance. Diabetes is characterized by a state of chronic low-grade inflammation with abnormal expression and production of multiple inflammatory mediators such as tumor necrosis factor and interleukins \(^6^1\). Recent studies have shown that intestinal microbiota is an important impact factor for diabetes. For example, the abundance of *Bifidobacterium* significantly and positively correlated with improved glucose-tolerance and low-grade inflammation in probiotic treated-mice \(^6^1,^6^2\). Moreover, the development of diabetes type 1 in rats was related to higher amounts of *Bacteroides* spp. \(^6^3\). It is suggested that the intestinal microbiota increased monosaccharide uptake from host gut and instructed host to increase hepatic production of triglycerides associated with the development of insulin resistance \(^6^4\).

The intestinal microbiota is a massive and complex community, essential to host for health and well-being. The intestinal microbiota is associated with many diseases such as obesity, diabetes, pancreatitis, colitis, atopic disorder and so on. An improved understanding of the complex relationship between host immune system and indigenous intestinal microbiota will help to establish strategies to promote host health and control relative diseases.

**Probiotics supplementation:** Probiotics are defined as “viable microbial food supplements, which, when taken in the right doses, beneficially influence host health” \(^6^5\). The host benefits that have been attributed to consumption of microbial microorganisms are diverse, and have been substantiated to different degrees. Microorganisms employed as probiotics are often members of *Lactobacillus*, *Bifidobacterium* or *Bacillus*, but *Escherichia coli*, *Enterococcus faecium* and *Saccharomyces boulardii* are also used \(^6^6\).

The potential mechanism whereby probiotics influence the composition of intestinal microbiota is unknown. However, some hypotheses are suggested. Consumption of probiotic cultures may modulate intestinal microbiota or change its metabolic properties by competition for nutritional substrates. The experiment conducted by Gordon and colleagues by transcriptional microarrays showed that introducing a probiotic into mouse gut changed the way that the endogenous microbiota metabolized diet \(^6^7\). The experiments by metabolic profiling methods showed the metabolites produced by probiotics may also impact on the intestinal microbiota. When lactobacilli were supplemented to mouse diet, the composition of intestinal microbiota changed. Accompanied with microbiome modification, the concentrations of short chain fat acids in colon and the fecal levels of diverse metabolites including choline, acetate, ethanol, bile acids, and a range of putative N-acetylated metabolites markedly changed \(^6^8\). Furthermore, it is likely that such gross changes in metabolic profile also have important influences on the composition of host intestinal microbiota. In addition, probiotics can impact on the general microbiota by direct antagonism. For example, probiotic *Lactobacillus salivarius* strains inhibit the growth of *Helicobacter pylori* *in vitro* \(^6^9\). Many of probiotics can produce bacteriocins, a kind of anti-bacteria material, to directly kill pathogens and prevent host infection.

Probiotics can produce positive effects on intestinal microbiota. Administration of a mixture containing lactobacilli, bifidobacteria, enterococci, and pediococci increased numbers of *Bifidobacterium* spp., *Lactobacilli*, and Gram-positive cocci in broiler chickens \(^7^0\). Supplement of a probiotic *Enterococcus faecium* strain reduced *Enterococcus faecalis* numbers in the intestine of weanling piglets \(^7^1\). *Lactobacillus* supplement reduced Enterobacteriaceae numbers in pig intestine \(^7^2\). However, some researches indicated that administration of probiotics had negative effects upon the composition microbiota \(^7^3\). High dose supplement of probiotics can lead to the interruption of the balance of host intestinal microbiota, further introduce diseases such as irritable bowel syndrome, *Helicobacter pylori* eradication, diarrhea and Crohn’s disease. Probiotic combinations may have additive and synergistic effects, but different strains and species may also counteract each other’s positive effects. More studies need be conducted to clarify the potential mechanisms of the interaction between host and intestinal microbiota. The future target is to increase the genomic information on both probiotics and microbiota’s activities. Then the goal is to apply the knowledge of intestinal microbiota composition and aberrancies on selecting the right probiotics to maintain healthy intestinal microbiota and to promote host health.

**Conclusions**

Intestinal microbiota displays remarkable metabolic and immune versatility. They serve as an important “organ” for synthesis of a variety of molecules with enormous importance, and also regulate key metabolic pathways and processes that are vital to the growth, development, health and homeostasis of organism. These findings exemplified the power of basic research on intestinal microbiota nutrition and immunity to discover new knowledge and solve significant practical problems in animal agriculture. Diet
supplementation with one or mixture of probiotics may be beneficial for (1) maintaining gut functions; (2) promoting the development of immune system and (3) keeping host health.

Studies of intestinal microbiota have been largely based on traditional approaches (e.g. culture-dependent method, polymerase chain reaction denaturing gradient gel electrophoresis (PCR-DGGE), 16S rRNA gene sequencing, as well as terminal restriction fragment length polymorphism (T-RLFP)). These techniques have played historically significant roles in the development of this field. However, recent advances of metagenome sequencing, transcriptomics, metabolomics and proteomics have provided new insight into the complex interactions between the mammalian host and intestinal microbiota. Using these approaches it became increasingly evident that gut microbiota may shape the host metabolic and immune network activity. It would be important to capitalize on these revolutionary methods in future endeavors so as to rapidly and extensively expand our knowledge of intestinal microbiota nutrition, immunity and health in mammals and other species.

Acknowledgements

This research was jointly supported by grants from the National Natural Science Foundation of China (31001015, 31001016 and 31072042, 3090104030901041, 3092801830901040, 30928018), the Cooperative Projects of Guangdong Province and Chinese Academy of Science (2009B091300043, 2009B091300079, 2009B091300089) and Nitrogen and Phosphorus Cycling and Manipulation for Agro-ecosystems, the Knowledge Innovation Program of the Chinese Academy of Sciences KZCX2-YW-T07 and the National Basic Research Program of China (No. 2009CB118800).

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