The Gut Microbiome of Dogs and Cats, and the Influence of Diet

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KEYWORDS

• Healthy dog • Healthy cat • Protein • Fiber • Raw diet • Dysbiosis • Bile acids
• Short-chain fatty acids

KEY POINTS

- The gut microbiome is a functional organ, and dietary substrates are converted by different intestinal bacteria to metabolically active compounds that influence the host.
- Butyrate, for example, can be produced from either fiber or protein, suggesting that both increased fiber and increased protein in the diet may bring similar benefits and have the largest impact on the intestinal microbiome and metabolome composition.
- Although fiber and protein content appear to be main influencers of microbiome composition in both dogs and cats, the ideal fiber and protein intake to promote a healthy microbiome needs to be determined.
- Diet-induced changes in the microbiome of healthy dogs are less marked compared with microbiome changes associated with disease.

BACKGROUND

The gut microbiome is composed of bacteria, archaea, viruses, and eukaryotic organisms that reside in the gastrointestinal (GI) tract. The bacterial component is the largest and provides essential digestive functions, such as fermentation of fibers. The gut microbiome also contributes to host metabolism, protects against pathogens, and educates the immune system. Expanding knowledge of microbiome functions has revealed several remote connections leading to the coinage of terms such as the gut-brain axis, gut-skin axis, and others.

Many diseases, systemic or localized, are associated with dysbiosis. Gut dysbiosis is defined as changes in the composition of the gut microbiome that impact its function.[1] The increase in abundance of facultative anaerobic bacteria of the family Enterobacteriaceae is a hallmark of dysbiosis,[2] seen also in dogs.[3] The composition of the gut microbiota also has significant effects on immune function, and regulating the local

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production of antibodies,[4] and the differentiation of intestinal helper T (Th) cell precursors. Intestinal inflammation also can be triggered by gut dysbiosis in different diseases through bile acid dysmetabolism,[5–7] or through the decreased production of anti-inflammatory molecules, such as short-chain fatty acids (SCFAs)[8–10] and indoles.[11,12] Although outside of the scope of this review, recent work has associated dysbiosis with obesity,[13,14] metabolic diseases,[15,16] cancer,[17] neurologic disfunctions,[18,19] and many others, both in dogs and in humans. However, caution should be taken when interpreting those findings, as a causation effect is yet to be proven, and the dysbiosis may be a symptom of the disease process rather than its cause.

The gut microbiome is responsive to nutrients. Changes in bacterial taxa often require large changes in dietary macronutrients; but alterations in bacterial-derived metabolites and, therefore, microbiota function may already occur due to the addition of micronutrients, and this is an emerging area of current microbiome research. Some bacterial species ferment different types of fiber and carbohydrates, and others are strongly proteolytic. Therefore, changes in the diet that affect the availability of such substrates in the gut will result in alterations of the microbiome and metabolome. Due to its resilience, dietary-induced changes in microbiome composition are maintained only by long-term maintenance of a specific diet. A good example is a study[20] in which healthy dogs were fed diets containing only purified amino acids and easily digestible starch for 32 weeks. At the end of the trial, dogs returned to the control diet, and microbiome composition quickly returned to baseline.[20]

Microbiome changes are individualized,[21] as the microbiome is an intrinsically redundant ecosystem, in which many unrelated species occupy the same niche.[22] This has a significant evolutionary advantage, because if only a single species performed an essential function, any aggression to the microbiome (such as antibiotic treatment) affecting that species would deprive the host of that function. Therefore, multiple species are necessary for microbiome resilience, and higher species richness is considered an indicator of a healthy microbiome.[22]

The GI tract regions are colonized with different bacterial populations. The composition varies according to luminal conditions, with a predominance of oxygen-tolerating bacteria in the small, and an abundance of strict anaerobes in the large intestine.[23,24] Because sampling from the proximal intestine is difficult, most clinical studies focus on fecal microbiota, and the abundance of most relevant bacterial species for gut health in dogs can be reliably measured in feces.[3] When analyzing the microbiome along the GI tract of cats, samples clustered by individual cat rather than by site of collection, indicating that fecal samples are also representative of the cat microbiome.[24]

METHODS FOR MICROBIAL ANALYSIS

Microbiological culture is useful for the subset of bacteria that are culturable, but molecular methods have largely replaced culture due to their ability to capture nonculturable bacteria.[25] Molecular methods, such as 16S ribosomal RNA (rRNA) gene sequencing and DNA shotgun sequencing, aim to measure the diversity of species present in the sample. That is accomplished by either amplifying and sequencing a fragment of a conserved region of the 16S rRNA gene, or by sequencing all available DNA in the sample (shotgun sequencing). Shotgun sequencing has the advantage of going beyond bacterial identification by also sequencing functional genes; however, it requires larger amounts of DNA from the sample, and is more expensive. Quantitative polymerase chain reaction (qPCR) is a quick, affordable, and reproducible method to quantify specific taxa that have been identified as clinically relevant.

Most studies focus on 16S rRNA gene sequencing, which generates phylogenetical data, and methods for sequencing and data analysis are in constant evolution.[26] Indeed, this is one disadvantage of these methods: different sequencing and/or data analysis methods may generate differences in the results, which prevents the development of reference intervals. When reviewing the literature, a wide variation in percentages of specific bacterial taxa can be seen, making comparisons between studies difficult.

Another limitation of most microbiome studies is that investigators typically compare the effects of environmental factors (eg, diet, storage, antibiotic treatment, breed influences, geography) with a control group or with its own baseline within the study, and often with a small sample size. Therefore, when changes (eg, due to diets) are observed, it is difficult to extrapolate the magnitude of these changes, and how they compare against a normal microbiota in a large reference population. Because of its high reproducibility, qPCR allows the development of reference intervals for specific taxa. One example is the canine fecal dysbiosis index (DI), a qPCR-based assay that quantifies 7 bacterial taxa, which are then combined into one single number.[27] Reference intervals for this assay have been established based on 120 healthy dogs from different countries and fed different commercial diets (https://tx.ag/DysbiosisGI). The DI can be used as a marker for normal microbiota, and is useful to track changes in microbiota over time in response to therapy in dogs.[26,28] The reference intervals for the 7 bacteria allow for comparison of effect sizes between studies, and whether changes in the microbiota fall within or outside the normal range (**Fig. 1**).

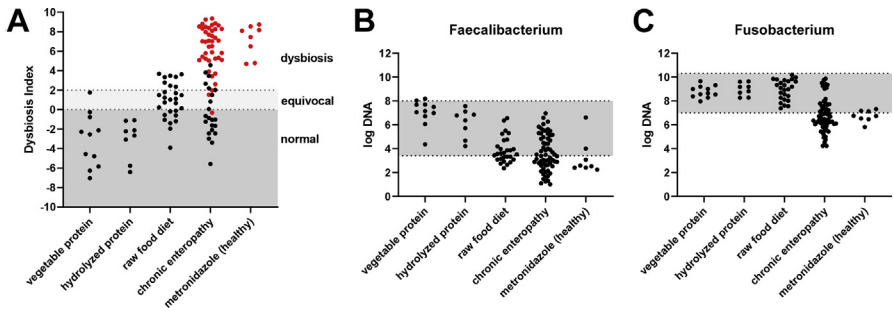

Fig. 1. The canine qPCR-based fecal DI (*A*) and key bacterial taxa *Faecalibacterium* (*B*) and *Fusobacterium* (*C*), both butyrate producers through different pathways (from carbohydrate and protein/amino acids, respectively), for different diet types, in comparison with chronic enteropathy[8] and metronidazole administration.[36] The gray areas indicate reference intervals, which allow comparison across studies and to a large reference population. Dots in red indicate dogs that also had a low abundance of *C hiranonis*, a beneficial bacterium that converts primary to secondary bile acids in the canine intestine. Dogs with chronic enteropathy and healthy dogs receiving metronidazole have a dysbiosis that is, associated with decreased *Faecalibacterium, Fusobacterium,* and *C hiranonis.* Lack of the latter results in abnormal bile acid metabolism. In contrast, dogs fed a raw food diet,[54] high in protein and fat, and low in fiber, have an increased fecal DI mostly driven due to low *Faecalibacterium* and increased *E coli* (not shown). The vegetable protein[44] and hydrolyzed protein diet[36] fed for 60 and 42 days, respectively, have similar macronutrient composition to commercial adult dog diets, despite the uniqueness of some ingredients. Accordingly, the fecal DI, and abundances of *Faecalibacterium* and *Fusobacterium* remained within normal reference intervals.

CORE MICROBIOTA

Key bacterial species are consistently present in fecal samples of healthy dogs, indicating the presence of a core fecal bacterial community. Table 1 shows some of the most relevant bacterial taxa in fecal samples of dogs. The fecal microbiome of healthy dogs is co-dominated by 3 phyla: Firmicutes, Bacteroidetes, and Fusobacterium.[29,30] Within this core bacterial community, many major taxa belong to phylum Firmicutes, including Clostridia and Bacilli,[31,32] many of which are SCFA producers, such as *Faecalibacterium*. Bacteroidetes is another abundant phylum in fecal samples from dogs, including *Prevotella* and *Bacteroides*, which are highly variable in abundance between dogs.[3]

The genus *Fusobacterium* is typically associated with health in dogs. This is in contrast to people, in which *Fusobacterium nucleatum* is a pathogen associated with colorectal cancer.[33] In the GI tract of dogs, other *Fusobacterium* species, such as *Fusobacterium mortiferum* and *Fusobacterium perfoetens,* are typically observed,[34] and these seem to play a different role.[3] Fusobacteria are severely impacted by antibiotic treatment[35] and GI diseases,[26] and their recovery is slower than other phyla.[36] Therefore, in dogs Fusobacteria may be a therapeutic target for specific food ingredients that can increase their abundance.

Proteobacteria and Actinobacteria are also commonly identified and are typically colonizers of the small intestine, and in physiologic conditions will present in smaller numbers in fecal samples. For example, members of the family Enterobacteriaceae (eg, *Escherichia coli*) are facultative anaerobes, which allows them to take advantage of the oxygen available in the small intestine. Although part of the normal microbiome in small numbers, an increase of Enterobacteriaceae in fecal samples is a hallmark of dysbiosis[3] and is associated with many diseases, both within and outside of the GI tract.[8,37,38]

The literature on the fecal microbiome of healthy cats is less extensive. The fecal microbiome of cats is dominated in most studies by Firmicutes,[24,39–43] followed by smaller percentages of Proteobacteria, Actinobacteria, Bacteroidetes, and

Table 1
Relevant bacterial taxa in the fecal microbiome of dogs, organized according to the Greengenes database taxonomy[95]

Phylum	Class	Family	Genus/Species
Actinobacteria	Coriobacteriia	Coriobacteriaceae	*Collinsella*
Bacteroidetes	Bacteroidetes	Prevotellaceae	*Prevotella*
		Bacteroidaceae	*Bacteroides*
Firmicutes	Clostridia	Clostridiaceae	*Clostridium*
		Ruminococcaceae	*Faecalibacterium prausnitzii*
		Peptostreptococcaceae	*Peptostreptococcus*
		Lachnospiraceae	*Blautia*
		Veillonellaceae	*Megamonas*
	Bacilli	Streptococcaceae	*Streptococcus*
		Lactobacillaceae	*Lactobacillus*
		Turicibacteraceae	*Turicibacter*
Fusobacteria	Fusobacteriia	Fusobacteriaceae	*Fusobacterium*
Proteobacteria	Betaproteobacteria	Alcaligenaceae	*Sutterella*
	Gammaproteobacteria	Enterobacteriaceae	*E. coli*

Fusobacteria. One study compared the fecal microbiome of dogs and cats fed species-appropriate commercial diets, and found that cats had a larger number of species than dogs,[41] hinting at a higher diversity; however, more studies are needed to confirm that finding.

Although changes in microbiome composition can be important, they do not reflect changes in microbiome function. Recent studies are going beyond describing "Who is there?" and investigate the more pressing question of "What are they doing?" The study of bacterial metabolites through fecal metabolomics has revealed some major pathways regulated by bacteria, such as SCFA production, bile acid deconjugation and dehydroxylation, production of neurotransmitters such as serotonin and gamma-aminobutyric acid (GABA), and anti-inflammatory compounds such as indoles. Diet can influence bacterial metabolites, which can remotely affect organs such as the brain, skin, or muscle.

EFFECTS OF DIETS ON MICROBIOTA IN DOGS

Most microbiome studies in dogs have evaluated effects of extruded diets, which represent up to 95% of the dog food market. Extruded diets typically include a high carbohydrate load, but high-protein low-carbohydrate alternatives are available. Also increasingly popular are raw diets, frozen or freeze-dried, which are typically meat based and include low carbohydrate percentages. A small but increasing percentage of owners feed homemade diets, either raw or cooked.

Studies have shown that gut microbiome profiles in different species reflect their diet composition, especially when large macronutrient differences such as carnivore versus herbivore diets are considered.[44–46] In omnivore species, including humans, the short-term consumption of diets composed entirely of animal or plant products is enough to alter the microbial community structure and overwhelm interindividual differences in microbial gene expression.[46] In humans, the consumption of an animal-based diet increased the dietary intake of fat and protein, and decreased fiber intake to nearly zero. Such changes led to an increase in the abundance of bile-tolerant microorganisms and decreases the levels of Firmicutes, which includes species known to metabolize dietary plant polysaccharides.

For the canine gut microbiome, the ingredients seem to be less important than the overall macronutrient content. One study found that an extruded diet prepared exclusively with plant sources of protein did not significantly alter the microbiome of dogs when compared with a traditional (mixed animal and plant) extruded diet with similar macronutrient content.[44]

Major shifts in macronutrient composition were tested in a study in healthy dogs, which included 4 dry prescription diets formulated for weight loss, for renal disease, to be low-fat, or anallergenic.[47] The weight loss diet had the most drastic changes in macronutrients (higher protein and fiber) and resulted in the largest shift in microbiome composition. Increased protein content was associated with increased Fusobacteria. The abundance of SCFA producers *Bacteroides*, *Prevotella*, and *Faecalibacterium* was significantly increased in dogs fed the weight loss diet, and *Faecalibacterium* was increased in the low-fat diet. The weight-loss (28.1% fiber) and low-fat (8.6% fiber) diets both included soluble and insoluble fiber (beet pulp, fructooligosaccharide [FOS], and psyllium), and the increase in those genera is likely related to increased fiber content and different fiber types.

Different fibers have been studied for their prebiotic properties, and induce specific changes in the microbiome (**Table 2**). Most fibers act by enriching fiber-fermenting SCFA-producing Firmicutes.[29,48–52] Inulin-type fructans can increase SCFA,[48]

Table 2
Main effects of different types of fiber in the fecal microbiome and metabolome of dogs

Fiber Type	Main Findings	Method	References
Beet pulp	↓ Erysipelotrichi and Fusobacteria ↑ Firmicutes and Clostridia	16S rRNA seq.	Middelbos et al,[29] 2010
Inulin-type fructans	↑ Firmicutes, Erysipelotrichaceae, and Turicibacteraceae	16S rRNA seq.	Alexander et al,[50] 2018
Inulin	↓ Enterobacteriaceae ↑ *Megamonas* and *Lactobacillus*	16S rRNA seq.	Beloshapka et al,[52] 2013
Potato fiber	↓ *Prevotella* and *Fusobacterium* ↑ *Faecalibacterium, Lachnospira*, fecal acetate, propionate and butyrate	16S rRNA seq.	Panasevich et al,[48] 2013; Panasevich et al,[49] 2015
Soybean husk	↓ *Clostridium* cluster XI ↑ Total lactobacilli, *Faecalibacterium*, *Bacteroides-Prevotella-Porphyromonas*, and *Clostridium* cluster XIVa	qPCR	Myint et al,[51] 2017
Yeast cell wall	↑ *Bifidobacterium*	16S rRNA seq.	Beloshapka et al,[52] 2013

Abbreviations: qPCR, quantitative polymerase chain reaction; rRNA seq., ribosomal RNA sequencing.
↑ Up arrows indicate increased abundance
↓ Down arrows indicate decreased abundance

including acetate, butyrate and propionate, total fecal bile acids,[50] and decrease Enterobacteriaceae.[50,52]

A few studies[53–55] have evaluated the impact of meat-based raw diets on the gut microbiome of healthy dogs. Meat-based raw diets are typically very different in macronutrient content compared with control diets, with higher protein and lower carbohydrate and fiber. Dogs fed raw diets showed overall decreases in Firmicutes[54] and Bacteroidetes,[53] as shown in **Table 3**. Most decreased bacteria are associated with SCFA production from dietary carbohydrate,[56] indicating a decrease in carbohydrate fermentation due to decreased intake. Proteobacteria, Fusobacteria, and protein-associated genera increased in abundance.[53,54] One study with 6 dogs fed a raw diet for more than 1 year found increased microbiome diversity,[55] and an increased abundance of *Clostridium perfringens* and *Fusobacterium varium*, both known to produce butyrate from protein,[56] suggesting an adaptation to the diet.

Although Clostridiaceae can be associated with GI disease, it has been suggested that their increase when protein-rich diets are fed to dogs may not be detrimental to their health,[53] but are rather associated with protein digestion. In addition, Clostridiaceae were also found to positively correlate with protein digestibility and firmer fecal scores, and negatively correlate with fecal protein content (ie, more Clostridiaceae results in less undigested protein in feces) and less fecal output.[53]

Clostridium hiranonis is a bacterial species associated with normal bile acid (BA) metabolism,[6,57] and was found to increase in 2 studies with higher protein diets.[55,57] *C hiranonis* is often decreased in dogs with gastrointestinal disease, and after treatment with antibiotics (see **Fig. 1**). A study[54] reported normal BA metabolism in healthy dogs fed bones and raw foods (BARF) diets, with no significant difference from kibble-fed controls (see **Fig. 1**). BA metabolism is an important pathway not only for lipid

Table 3
Summary of findings from studies that evaluated the effect of high-protein diets on the fecal microbiome of dogs

Diet	Main Findings	Time on diet, n	Reference
Bones and raw foods (BARF)	↓ *Bifidobacterium* and *Faecalibacterium*; ↑ Fusobacteria, *Escherichia coli*, *Streptococcus*, and *Clostridium*	4 wk to 9 y, n = 27	Schmidt et al,[54] 2018
Red meat	↓ *Faecalibacterium*, *Peptostreptococcus*, *Bacteroides,* and *Prevotella* ↑ *Fusobacterium*, *Lactobacillus*, and *Clostridium*	9 wk, n = 7	Bermingham et al,[53] 2017
Raw diet	↑ Richness, evenness, *Clostridium perfringens, Clostridium hiranonis*, *Dorea*, and *Fusobacterium varium*	At least 1 y, n = 6	Kim et al,[55] 2017
Kibble with boiled beef	↓ *Faecalibacterium prausnitzii* ↑ *Clostridium hiranonis, Dorea, Slackia,* and unidentified Clostridiaceae	1 wk per combination, n = 11	Herstad et al,[57] 2017

digestion, but also for regulation of intestinal inflammation, and is commonly altered in chronic gastrointestinal diseases.[6,7]

Bifidobacterium, *Lactobacillus*, and *Faecalibacterium* are considered beneficial in omnivores, and the effect of diet on their abundances is often investigated.[58] Their benefit is due to their role in carbohydrate fermentation resulting in butyrate. The role of butyrate, an SCFA, in intestinal health is undisputed, as butyrate is the preferred energy source for colonocytes.[59]

However, butyrate can be found in fecal samples of all mammals regardless of their food sources. Therefore, in mammals that consume little to no carbohydrates, alternative pathways for butyrate production must be present. In a study comparing high-fat with high-starch diets in dogs, acetate, butyrate, and propionate levels were not different between dogs fed either diet, indicating that the production of SCFA in dogs is not exclusively dependent on carbohydrate content.[60] Supporting that hypothesis, another study[57] found that the addition of minced meat to a dry food diet actually led to a small increase in fecal butyrate and isovalerate.

A recent study has highlighted that in carnivores, Clostridiaceae, and in particular *C perfringens*, are associated with the butyrate kinase butyrate-synthesis pathway, which allows the production of butyrate from protein.[56] Another bacterium known to produce butyrate from protein sources is *F varium*,[61] which was more abundant in a group of dogs fed meat-based raw diets for more than 1 year, suggesting an adaptation of the microbiome to the long-term diet.[55] In addition, members of the Fusobacteriaceae family have been found to be more abundant in other carnivore species (cats,[62,63] wolves,[64,65] other carnivora[56,66]), and dogs fed high-protein raw diets.[53,54,67]

Those findings bring into question whether bacteria that specialize in carbohydrate fermentation bring the same benefits described in omnivores to the carnivore GI tract.[53] It is possible that in carnivores the butyrate production may be at least partially accomplished by other bacterial species such as members of the Clostridiaceae and Fusobacteriaceae families, which could be the reason for their increase in dogs fed raw diets.

Another bacteria-derived metabolite that can be affected by diet is GABA, a neurotransmitter, and its precursor gamma-hydroxybutyric acid (GHB).[54] BARF diets have also been found to increase fecal levels of GABA and GHB.[54] Ketogenic diets in mice have also led to microbiome-mediated increases in GABA,[68] and it is possible that the high fat and low carbohydrate content of BARF diets trigger similar changes. Both GABA and GHB are quickly absorbed from the GI tract when administered orally,[69,70] and fermented foods rich in GABA-producing bacteria (*Lactobacillus* and *Bifidobacterium*) are available in Japan for the treatment of hypertension.[71,72] The BARF diet also resulted in increased abundance of lactic acid bacteria such as Lactobacillales and *Steptococcus*,[54] which both of which can produce GABA.[73] The connection between the gut and the brain has been studied in many diseases, in dogs and other species, and ketogenic diets have been shown to be beneficial for dogs with neurologic diseases.[74,75] Recent studies[76,77] have shown that ketogenic diets impact microbiome composition, which may be one of the mechanisms by which they reduce seizure frequency.

EFFECTS OF DIETS ON MICROBIOTA IN CATS

High-protein/low-carbohydrate diets (HPLC), both extruded and raw, have been studied in cats compared with traditional moderate protein extruded diets. In cats, canned diets are an additional higher protein alternative, which is commonly fed alone or in combination with extruded diets. The use of moist foods in cats is supported by research indicating that their consumption leads to increased water intake,[78,79] decreased voluntary energy intake,[79] and decreased urine specific gravity,[79] which may be beneficial for certain health conditions.

Studies[80–82] have evaluated the microbiome of kittens weaned onto HPLC extruded diets compared with kittens weaned onto medium protein/medium carbohydrate (MP/MC) diets. There was some agreement between the studies, and their main findings are summarized in **Table 4**. Interestingly, species diversity was increased by HPLC,[82] and 5 genera that increased in HPLC-fed kittens[81] are known butyrate producers: *Clostridium* and *Eubacterium* may produce butyrate either from carbohydrate through the *but* pathway, or from protein through the *buk* pathway, whereas *Faecalibacterium*, *Ruminococcus,* and *Blautia* are producers through the *but* pathway.[56] Differences between kittens fed either diet affected 194 metabolic pathways, including pathways related to amino acid biosynthesis and metabolism, indicating that the protein:carbohydrate ratio has a significant effect on microbiome function.[82] However, the impact of such metabolite differences on overall health is still unknown.

The literature evaluating raw meat–based diets on the gut microbiome is less extensive in cats. Feeding raw 1-day-old to 3-day-old chicks,[83] or raw beef[84] to adult cats resulted in increases in genera known to be SCFA-producers[84,85] (see **Table 4**). Although the butyrate concentration was not increased in cats fed raw beef, the butyrate molar ratio was higher, indicating a shift in the proportions of different SCFAs. However, when plant fiber (2% as fed, inulin and cellulose) was added to raw beef, the microbiome became more similar to that of cats fed the control extruded diet, and fecal acetate:propionate:butyrate ratio was almost identical to that of controls.[84]

Similarly to raw diets, canned cat food has higher average protein and fat content, and lower carbohydrates content, compared with extruded dry foods. The microbiome of adult cats and kittens fed canned diets is more diverse[62,86] (see **Table 4**). As with other high-protein diets, many genera enriched by canned diets are associated with butyrate production, and may therefore be beneficial for intestinal health.[84]

Table 4
Summary of findings from studies that evaluated the effect of high-protein diets in the fecal microbiome of cats

Diet	Main Findings	Age	Time on Diet, n	Reference
High-protein low-carbohydrate dry food	↓ *Lactobacillus*, *Bifidobacterium*, and *Escherichia coli*	Kitten, weaning diet	8 wk, n = 7	Vester et al,[80] 2009
	↓ Actinobacteria, *Bifidobacterium*, *Dialister*, *Acidaminococcus*, *Megasphera*, and *Mitsuokella* ↑ Fusobacteria, *Clostridium*, *Faecalibacterium*, *Ruminococcus*, *Blautia*, and *Eubacterium*	Kitten, weaning diet	8 wk, n = 7	Hooda et al,[81] 2013
	↑ species diversity; Affected 194 metabolic pathways, including amino acid synthesis and metabolism	Kitten, weaning diet	8 wk, n = 6	Deusch et al,[82] 2014
to 3-day-old chicks	↑ *Peptococcus*, *Pseudobutyrivibrio*, and unidentified Lachnospiraceae	Adult	10 d, n = 5	Kerr et al,[83] 2014
Raw	↑ *Clostridium*, *Fusobacterium*, *Eubacterium*, and molar ratio of butyrate	Adult	3 wk, n = 12	Butowski et al,[84] 2019
Raw plus plant fiber	↓ *Clostridium*, *Fusobacterium*, and *Eubacterium* ↑ *Prevotella*	Adult	3 wk, n = 12	Butowski et al,[84] 2019
Canned	↓ Firmicutes, *Bacteroides*, *Lactobacillus*, and *Streptococcus* ↑ *Fusobacterium*, *Clostridium*, unidentified Peptostreptococcaceae and Prevotellaceae	Kitten, weaning diet	9 wk, n = 10	Bermingham et al,[86] 2013
	↓ *Lactobacillus*, *Megasphera*, and *Olsenella* ↑ richness, Fusobacteria, Proteobacteria, *Clostridium*, *Blautia*, *Bacteroides*, and unidentified Peptostreptococcaceae	Adult	5 wk, n = 16	Bermingham et al,[62] 2013
	↓ *Lactobacillus*, *Bifidobacterium*, and *Collinsella* ↑ *Bacteroides*, *Clostridium*, *Fusobacterium*, genes involved in vitamin biosynthesis, metabolism and transport	Kitten, weaning diet	9 wk, n = 10	Young et al,[88] 2016

Due to the strict carnivorous nature of cats, hindgut fermentation was considered unimportant.[87] However, several studies have evaluated the impact of dietary fiber on fecal microbiome composition in cats, and their results are summarized in **Table 5**. Similar to dogs, prebiotic fibers increase SCFA-producing bacterial

Table 5
Main effects of different types of fiber in the fecal microbiome and metabolome of cats

Fiber Type	Main Findings	Method	References
FOS	↑ *Bifidobacterium*	qPCR	Kanakupt et al.[89] 2011
	↑ Actinobacteria	16S rRNA seq.	Barry et al,[39] 2012
GOS	↑ *Bifidobacterium*	qPCR	Kanakupt et al,[89] 2011
FOS and GOS	↑ *Bifidobacterium,* total SCFA, butyrate and valerate	qPCR	Kanakupt et al,[89] 2011
FOS and inulin	↓ Gammaproteobacteria ↑ Veillonaceae	16S rRNA seq.	Garcia-Mazcorro et al,[42] 2017
Inulin	↓ *Faecalibacterium* and *Fusobacterium* ↑ *Bifidobacterium*	16S rRNA seq.	Young et al,[88] 2016
Cellulose	No changes	16S rRNA seq.	Barry et al,[39] 2012
Wool hydrolysate	No changes	16S rRNA seq.	Deb-Choudhury et al,[96] 2018
Pectin	↑ Firmicutes	16S rRNA seq.	Barry et al,[39] 2012
Mixed insoluble fibers	↓ isobutyric, 2-methylbutyric, and isovaleric acids ↑ *Blautia*, *Bacteroides*, *Turicibacter,* acetic and propionic acids	16S rRNA seq.	Wernimont et al,[97] 2019
Inulin and cellulose	↓ *Clostridium*, *Fusobacterium*, and *Eubacterium* ↑ *Prevotella*, *Bifidobacterium*, *Lactobacillus*, *Megamonas*, and unclassified Lachnospiraceae	16S rRNA seq.	Hooda et al,[81] 2013

Abbreviations: FOS, fructooligosaccharides; GOS, galactooligosaccharides; qPCR, quantitative polymerase chain reaction; rRNA seq., ribosomal RNA sequencing; SCFA, short-chain fatty acid.

genera,[39,81,87] but also *Bifidobacterium*.[81,86,88] The combination of FOS and galactooligosaccharides also led to increased concentrations of total SCFA, butyrate, and valerate.[89]

DIET VERSUS DISEASE EFFECTS ON THE MICROBIOME

Although diet can change microbiome composition significantly, and result in changes both in metabolic pathways and production of metabolites, those changes are typically much smaller than those that accompany disease.[26] In sick animals, and in particular those with gastrointestinal disease (eg, chronic enteropathies), microbiome diversity is quickly reduced, and many core species, such as *C hiranonis*, *Fusobacterium* spp, and *Faecalibacterium praunitzii*, are decreased[6,8,26,28] (see **Fig. 1**). Therefore, although dietary manipulations of microbiome composition can likely play a role in fostering a healthy and resilient microbe community, they are in most cases unlikely to generate changes comparable in magnitude to those observed in disease.

Diet modification, prebiotics, and probiotics are often used, alone or together with medications, to ameliorate clinical signs of diseases including diarrhea. The changes in microbiome composition associated with diarrhea are extensive and have been reviewed elsewhere,[26] and are accompanied by functional changes in digestion and motility that modify the luminal environment, further affecting microbiome composition. Hypoallergenic diets, formulated to reduce immunogenicity and facilitate digestion, do not significantly affect the microbiome of healthy dogs,[36,44] but have been associated with improved microbiome composition in dogs with food-responsive diarrhea.[44,90] Similarly, prebiotic fibers can aid recovery of beneficial bacterial populations and restore SCFA production. Probiotics, which are beneficial bacterial species, also can be fed to aid recovery. Although their colonization is typically transient,[31,91] probiotics can still be metabolically active during their transit, and produce beneficial metabolites that help improve clinical signs.[92] Probiotics have been reported to have a protective effect on acute diarrhea outbreaks, and to have beneficial effects on mucosal homeostasis,[93] speeding disease remission[94] in dogs with chronic diarrhea.

SUMMARY

The gut microbiome is a functional organ, and is responsive to the nutrient composition of diet. However, major shifts in microbiome composition are only observed with major changes in macronutrient composition, such as high-protein or high-fiber diets. More importantly, changes in bacterial composition may affect the production of metabolites in the gut. Indeed, fiber, starch, and protein content seem to be the key modulating players, and changes in those nutrient profiles cause rapid shifts in microbiome and metabolome composition, likely due to the changes in substrate availability. Because of the redundancy of the microbial communities, key metabolites can be produced by different bacteria. Butyrate, for example, can be produced from either fiber or protein, suggesting that both increased fiber or increased protein in the diet may bring similar benefits; however, the ideal levels of fiber and protein remain to be determined. The microbiome of healthy dogs and cats is resilient and adaptable, and it is capable of quickly restoring itself to baseline composition once the animal returns to its usual diet, indicating that sustained change requires long-term administration of a specific diet. Although diet affects the microbiome and metabolome of healthy dogs, changes associated with disease are of greater magnitude. In those cases, dietary change, prebiotic fibers, and probiotic bacteria can be beneficial to help improve microbial diversity and metabolite production.

DISCLOSURE

R. Pilla and J.S. Suchodolski are employed by the Gastrointestinal Laboratory at Texas A&M University, which provides assay for intestinal function and microbiota analysis on a fee-for-service basis.

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