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Co-evolution in context: The importance of studying gut microbiomes in wild animals

Abstract

Because the gut microbiota contributes to host nutrition, health and behavior, and gut microbial community composition differs according to host phylogeny, co-evolution is believed to have been an important mechanism in the formation of the host-gut microbe relationship. However, current research is not ideal for examining this theme. Most studies of the gut microbiota are performed in controlled settings, but gut microbial community composition is strongly influenced by environmental factors. To truly explore the co-evolution of host and microbe, it is necessary to have data describing host-microbe dynamics in natural environments with variation in factors such as climate, food availability, disease prevalence, and host behavior. In this review, I use current knowledge of host-gut microbe dynamics to explore the potential interactions between host and microbe in natural habitats. These interactions include the influence of host habitat on gut microbial community composition as well as the impacts of the gut microbiota on host fitness in a given habitat. Based on what we currently know, the potential connections between host habitat, the gut microbiota, and host fitness are great. Studies of wild animals will be an essential next step to test these connections and to advance our understanding of host-gut microbe co-evolution.

Keywords

Gut microbiota • host-microbe • co-evolution • habitat • ecology • fitness

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Introduction

As sequencing technology makes data generation faster, cheaper, and more comprehensive, studies of gut microbial communities are multiplying at an astonishing rate. As a result, our understanding of the host-gut microbe relationship is constantly improving. Studies to date have demonstrated that the gut microbiota contributes to host nutrition, health and behavioral patterns by providing energy and nutrients, improving immune function, and influencing the production of neuroactive molecules [1-12]. Changes in the composition of the gut microbial community are known to lead to changes in its function, which can alter host nutrition, health and behavior [6,13-23]. Environmental factors such as diet or social contact are largely responsible for determining the composition of the gut microbial community [24-31], but host genotype also affects the abundances of some microbial genera [28,32,33].

Because host-gut microbe relationships are influenced to some extent by host genotype, and gut microbial community composition differs according to host phylogeny [34-36], discussions of the co-evolution of host and gut microbiota are common in the current literature [7,34-37]. Some researchers argue that since microbes are found in animals as simple as earthworms, the co-evolution of animals and bacteria has been occurring for more than 800 million years [38,39]. Additionally, the increased complexity and stability of gut microbial communities in vertebrates as well as the presence of fewer physical barriers to bacteria has been used to suggest that the adaptive immune system evolved in vertebrates to recognize gut bacteria and improve host-gut microbe interactions [40]. Nevertheless, while it seems likely that co-evolution is an important mechanism for understanding host-gut microbe relationships, current research is not ideal for examining the co-evolution of host and microbe.

Most studies of the gut microbiota are performed in controlled laboratory settings or are focused solely on human populations [9,16,25,41-49]. Therefore, despite an understanding that environmental factors greatly influence the host-gut microbe relationship [25,27-29,31], the effects of natural environmental variation in factors such as food availability on the host-gut microbe relationship have generally not been explored. Because the host-gut microbe mutualism evolved in a natural environment with complex patterns of climate, food availability, disease prevalence, and host behavior, a comprehensive examination of host-gut microbe dynamics must consider these factors. Specifically, we must establish the ways in which a host's habitat influences the selective environment the host imposes upon its gut microbiota, and in turn, how the gut microbiota influences the host's response to its own selective environment in a

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particular habitat. Studies of laboratory animals are only useful for addressing the topic of host-microbe co-evolution if the microbial communities in laboratory animals are representative of those in wild animals [50]. Since captive animals tend to exhibit distinct gut microbial communities compared to their wild counterparts [51-58], studies of wild animals are a critical next step for examining the co-evolution of host and gut microbe. As reduced sequencing costs make extensive sampling of large populations more feasible, we must begin to complement studies of humans and laboratory animal models with studies of other animals in diverse environments.

In this review, I highlight some of the current major themes in host-gut microbe research and discuss their relevance to understanding host-gut microbe dynamics in wild animals. I begin using our current knowledge of microbial ecology to explore how host habitat might influence the composition of the gut microbial community both in terms of exposure to microbes and in terms of food availability and host diet. I then use results from human and laboratory studies to consider the potential impacts of the gut microbiota on host fitness in a particular habitat via contributions to host nutrition, immune function and health, and nervous system function and behavior. Although I include data from a variety of metazoans, it is important to note that host-microbe interactions in vertebrates are likely to differ from those in invertebrates. Nevertheless, based on what we currently know, the potential for interactions among host habitat, the gut microbiota, and host fitness, is great, and few datasets currently describe these relationships. Therefore, while studies of human populations and laboratory animal models will continue to be important for determining cause-and-effect, studies of wild animals are essential for advancing our understanding of host-gut microbe co-evolution.

1. The influence of host habitat on microbial metacommunity dynamics

Microbial colonization of the gastrointestinal tract occurs primarily through horizontal transfer via host contact with the environment. Infants begin to acquire microbes *in utero*, in the birth canal, and from breast milk [24,59-61], and colonization continues via social contact with conspecifics and incidental contact with environmental microbes [24]. As a result, the development of an individual's gut microbial community depends to some extent on the pool of available microbes in its environment and the amount of contact it has with other individuals.

In ecology, metacommunity dynamics are often used to describe the mechanisms by which a pool of species comes to occupy a given environment or habitat. In this framework, the neutral processes of colonization, extinction, and drift result in the differentiation of communities across space [62]. Suitable habitats or environments are considered patches separated by uninhabitable space, and the size and distance of patches from one another influence the rate of transfer of taxa between patches. Patches that are closer to the source patch from which a particular taxon originates, as well as patches that are larger in size, will be colonized by that taxon more frequently based on the higher probability of individuals migrating. These dynamics result in similar communities in patches that are nearer to each other and/or larger in size. Because taxa also go extinct randomly in each patch, patches that are farther apart or smaller in size will lose species and will not be recolonized. The unique combination of colonization and extinction in each patch leads to distinct communities in these distant and/or smaller patches, a process referred to as "ecological drift."

When these metacommunity dynamics are applied to microbial communities, both host habitats and the hosts themselves can be considered patches among which microbial taxa are transferred [30,62,63]. In the first case, metacommunity dynamics predict that individuals in habitats that are farther apart from each other should exhibit more distinct communities of gut microbes [63]. Migration of microbial taxa (via host migration) becomes less frequent as distance between host habitats increases due to host dispersal limitation, and random extinctions lead to genetic drift without frequent colonization from neighboring habitats. As a result, members of the same host species that occupy different habitats are exposed to distinct microbial pools and are colonized by distinct gut microbial communities. Populations of a host species that become geographically isolated from the main population due to processes such as habitat fragmentation should also develop distinct gut microbial communities with lower taxonomic and/or functional diversity, which reflect the local microbial taxa pool.

Although these processes have not been studied in detail, evidence exists to suggest they occur [64,65]. Lankau et al. [64] detected geographical patterns in Galapagos iguana gut microbial community composition that suggest an influence of metacommunity dynamics over historical timescales. The gut microbiota of iguanas on islands farther apart from each other were most distinct, suggesting either drift in microbial communities on more geographically isolated islands or more frequent cross-colonization by microbes on geographically proximate islands as a result of iguana migration. Likewise, a study by Fallani et al. [65] demonstrated that the human infant gut microbiome differs in response to geography independently of diet. These patterns were suggested to be an influence of differences in regional microbial species pools that may have resulted from metacommunity dynamics. Additional research is necessary to determine if the patterns observed in both studies occur in other host species and whether geographical differences are truly the result of variation in the available microbial taxa in each habitat, but it seems that metacommunity dynamics may play a role.

Metacommunity dynamics can also be applied to gut microbial communities by considering individuals of a host species within a habitat to be patches. In this case, microbial communities are expected to be more similar among individuals that spend the most time in close proximity [30,62]. As a result, the social behavior of the host species impacts patterns in gut microbial community composition across individuals (Figure 1). Host species that live in more cohesive social groups with high

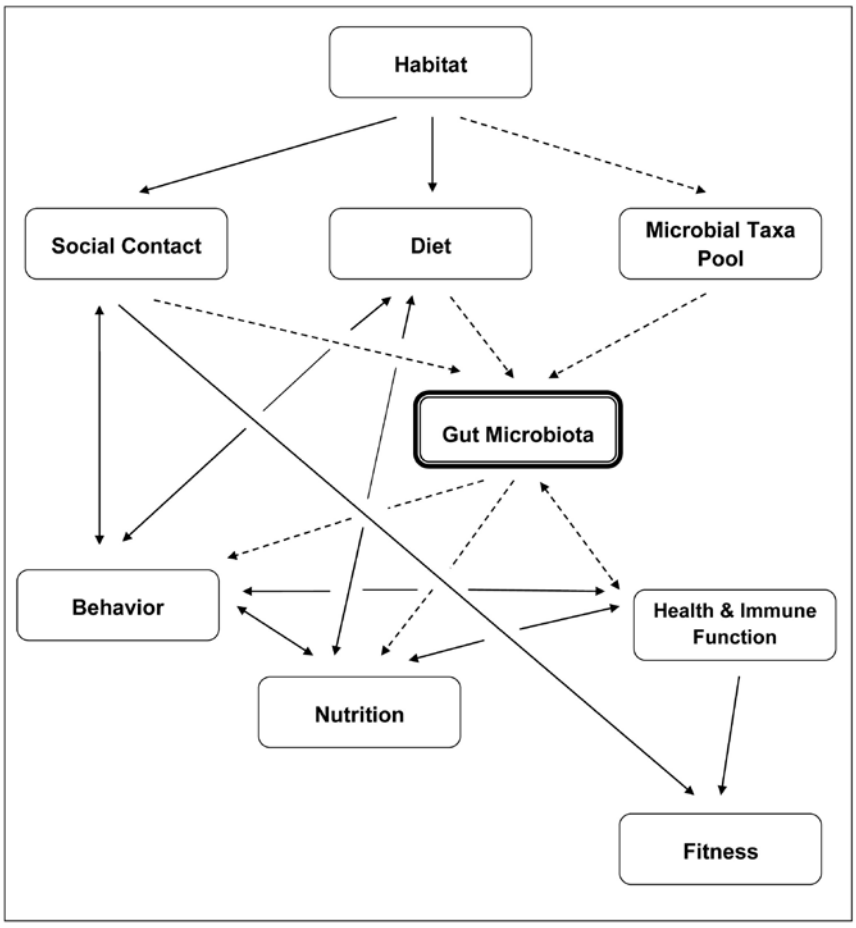

Figure 1. *Basic model of factors influencing host fitness, including predicted interactions between host and gut microbiota. Relationships and factors represented by dashed lines indicate areas that are not well studied in wild animal populations.*

frequencies of social interaction and contact are likely to have fewer inter-individual differences in gut microbial community composition than host species that spend more time solitary and less time engaged in social behavior. Although additional data are necessary to test this prediction thoroughly, data from black howler monkeys (*Alouatta pigra*) and chimpanzees provide support for it [53,66]. Howler monkeys live in highly cohesive social groups and show an inter-individual Bray-Curtis similarity index of 0.51 within social groups [53,67], while chimpanzees live in less cohesive social groups and show an index of approximately 0.20 [66,68,69].

Because social interactions within species vary in response to habitat [70-74], we would also expect different patterns in gut microbial community composition among individuals of a given species in distinct habitats. For example, a study of chacma baboons (*Papio ursinus*) showed that more grooming occurs when temperatures are higher [74]. It follows that inter-individual differences in gut microbial community composition should be smaller among baboons in warmer habitats compared to baboons in cooler habitats. Similarly, juvenile gelada baboons *(Theropithecus gelada*) spend less time playing in habitats with reduced resource availability [71]. Such a trend is likely to lead to increased inter-individual differences in juvenile gut microbiomes in these habitats. Finally, habitat differences such as forest fragmentation can alter host population densities [75-79]. In habitats with increased population densities individuals are likely to come into contact with one another more often and should therefore exhibit fewer inter-individual differences in gut microbial community composition. The opposite should occur in habitats with decreased population densities.

To date, no study measures differences in host social interactions or population densities across habitats in conjunction with analyses of the gut microbiota. However, it is likely that a relationship between individual host contact and gut microbial community composition exists. Studies of parasites and disease in wild animals frequently take these factors into account when examining patterns of transmission [80-83], and processes that are relevant for pathogenic microbes are likely to be relevant for commensal microbes as well.

Because established gut microbial communities have been shown to resist colonization by certain types of microbes [e.g. 84-87], a framework that does not include competition between

organisms is not sufficient for describing patterns in gut microbial community composition. However, despite an emphasis on neutral processes, metacommunity dynamics are important for understanding the co-evolution of host and gut microbe. Metacommunity dynamics suggest that not every microbial taxa detected in a particular host is an adaptive member of the gut microbial community. Some members of the community may be present by chance. Similarly, distinct microbial taxa that perform similar functions may occupy the same host species in different habitats as a result of chance exposure. Currently, the concept of a "core microbiome"—those microbes that are consistently associated with a certain host species across time and space—takes these neutral processes into consideration [88-92]. Even so, without a detailed exploration of the variation in gut microbial communities among individuals of the same host species occupying distinct habitats, our understanding of what constitutes the "core microbiome" and what is simply there by chance is incomplete. Human studies provide an excellent starting point, but future studies must encompass hosts from a variety of taxa and environments.

2. The influence of host habitat on diet and microbial community composition

In addition to neutral processes associated with exposure to gut microbes, the composition of an individual's gut microbial community is determined via selective processes. Because different microbes utilize different substrates, the substrates available to the gut microbial community, as well as competition between microbes, dictate which microbes will flourish and which will not [2,13,15,17,20,25,85,86,93,94]. Therefore, host diet creates strong selective pressure in the gut that shapes the structure of the gut microbial community [16,25,27] (Figure 1).

Studies of captive animals have demonstrated the relationship between diet and gut microbial community composition experimentally [43,95-100]. For example, changing the diet of 340 mice from a low-fat diet rich in plant polysaccharides to a high-fat, high-sugar diet, results in a dramatic increase in the abundance of several classes of bacteria in the Firmicutes phylum over the course of one day [25]. Additionally, in a study of over 700 mosquitoes, a blood diet reduced community diversity and favored enteric bacteria that cope with oxidative and nitrosative stress produced by blood breakdown [101]. In wild land snails, a sugar-cane diet reduced Firmicutes abundances by 50% and increased Bacteroidetes abundances [102], and cockroaches fed dog chow have been shown to possess more lactic acid bacteria (9.6×10^8 vs 1.0×10^5 – 1.0×10^7) compared to cockroaches fed cereal leaves, milled corn cobs, or All Bran flakes [103].

Studies of human populations have also revealed a strong influence of diet on the gut microbial community. Human gut microbial communities have been shown to express at least two stable "enterotypes," the *Bacteroides* enterotype and the *Prevotella* enterotype, which are associated with the long-term intake of either animal protein and saturated fat or plant-based resources [27,29]. Likewise, a study of children in Burkina Faso (N = 14) and Europe (N = 15) demonstrated a connection between diet and the gut microbiota with children in Burkina Faso exhibiting more *Prevotella*, associated with cellulose breakdown, more *Xylanibacter*, associated with xylan breakdown and fewer Enterobacteriaceae such as *Shigella* and *Escherichia* than children in Europe [104]. Another study detected more genes related to amino acid breakdown, vitamin synthesis, xenobiotic breakdown and bile salt metabolism in the gut microbiota of adults from the U.S. compared to Amerindians and Malawians [105]. The gut microbiota from Malawians and Amerindians included more genes for starch breakdown [105]. These differences appeared to be the result of a diet dominated by meat and fat in the U.S. versus a diet dominated by corn in Malawi and Amazon Venezuela [105].

Diet is believed to be a key factor in understanding the evolution of many animals, including humans [106-116]. However, because of its influence on the gut microbiota, diet is also likely to be a key factor in understanding the co-evolution of animals and their gut microbes [21,34,35,117]. Although most animal species are adapted to exploit certain diets [e.g., primates, 110,112,118], shifts in diet are a regular occurrence for wild animals and are closely associated with their habitats. Changes in abiotic factors such as climate across habitats and seasons, as well as anthropogenic disturbance, lead to spatial and temporal variation in food availability [119-127], and as food availability changes, many animals respond by altering their diet [119,124,128-131]. For example, mantled howler monkeys (*A. palliata*) on Barro Colorado Island, Panama spend 46% of feeding time consuming fruits during months when fruit availability is high but spend 85% of feeding time consuming leaves during months when fruit availability is low [119]. We would therefore expect howler monkeys, and other wild animals that undergo diet shifts, to exhibit distinct gut microbial communities across habitats and seasons.

Some studies of wild animals provide evidence that these patterns may be occurring. A study of 40 bees at different sites in Arizona and Maryland showed that gut microbial community composition differed between sites as well as among colonies within sites [132], and in Louisiana the stomach microbiome of six oysters was shown to differ according to site [133]. Additionally, the degree of similarity in gut microbial community composition between land and marine iguanas in the Galapagos has been attributed to the degree of habitat and diet overlap [64]. Land and marine iguanas on smaller islands, where dietary overlap is more likely, exhibit more similar gut microbial communities. A study of Hokkaido native horses also reveals changes in gut microbial community composition across seasons [134]. However, despite suggesting an influence of diet on the wild animal gut microbiota across space and time, none of these studies actually measures diet. A single study of wild black howler monkeys directly correlates differences in gut microbial community composition across four habitats with differences in diet composition (Spearman's $\rho = 0.82$; [53]), and a related study demonstrates that changes in the relative abundances of individual bacterial

genera such as *Acetivibrio* and *Butyricicoccus* are correlated with shifts in diet composition across time [135].

Based on what we know from studies of laboratory animals and humans as well as the patterns that have been observed in wild animals, data describing the relationship between host habitat, diet, and the gut microbial community are crucial for our understanding of host-gut microbe relationships. Microbes that are always associated with a particular host species, regardless of diet, can be considered part of the core microbiome, and differences in the core microbiome across species can provide us with insight regarding which microbes might facilitate a host species' ability to exploit certain food items. This information will improve our understanding of the evolution of host feeding ecology and life history processes. As the diets of mammals diverged over the course of evolution, concurrent genomic changes that affected characteristics such as gastrointestinal morphology were necessary to process new foods [115,136]. However, because bacteria have a short generation time, the gut microbial community can evolve and adapt to new diets more quickly than the host gastrointestinal tract [34,115,137]. Therefore, mammalian evolution may have depended heavily on the gut microbiota.

Similarly, determining which microbes vary in abundance with host diet will provide important information regarding host plasticity and the response of mammals to variable environments. If a subset of gut microbes can change in abundance in response to short-term changes in host diet across months or long-term changes in diet incurred by habitat alteration, it may allow hosts to adapt digestively in order to fulfill nutritional demands while maintaining activity patterns and life history processes despite changes in the types and amounts of food items available. An understanding of these dynamics has the potential to transform the study of mammalian behavioral ecology and physiology and will greatly inform our understanding of host-gut microbe co-evolution.

3.The influence of gut microbial community composition on host nutrition

For decades we have known that the gut microbiota is crucial to metazoan host nutrition. To begin with, short chain fatty acids (SCFAs) produced by the microbial breakdown of fiber in the gut can supply hosts with up to 70% of their daily energy needs [2]. They also reduce the pH of the intestinal lumen to facilitate nutrient absorption and prevent the accumulation of toxic metabolic by-products [4,12]. Germfree rats have reduced intestinal levels of SCFAs [138]. They excrete twice as many calories in urine and feces as conventional rats fed the same diet [139] and must compensate for the lack of energy-rich SCFAs by increasing their food intake [139]. Mice with a conventional microbiota have 42% more body fat than germfree mice despite eating 29% less food [140], and colonization of germfree rodents with a healthy gut microbiota results in a 57% increase in body fat [140]. As a result, germfree mice exhibit less ketogenesis during fasting [141]. They use glucose instead of ketones to maintain heart function and do not increase heart size in response to exercise [141]. These differences can have strong impacts on host health.

Interactions between microbes in the gut can also affect SCFA production [16,142,143]. For example, fermentation of dietary fructans increases when gnotobiotic mice are colonized with both *Bacteroides thetaiotaomicron* and *Methanobrevibacter smithii* [143]. *M. smithii* uses formate for methanogenesis, and *B. thetaiotaomicron* produces more acetate and formate in its presence [143]. These interactions promote more efficient fermentation and energy production in the gut, and co-colonized mice exhibit increased adiposity compared with mice colonized with only *B. thetaiotaomicron* [143]. Changes in gut microbial community composition can alter the interactions between microbes and ultimately affect energy production and host nutrition. Studies of humans have demonstrated that distinct gut microbial communities produce different amounts of SCFAs [14,104,144,145]. For example, children in Burkina Faso possess a distinct gut microbiome compared to children in Europe and produce more SCFAs such as butyrate [104]. Similarly, treatment of seven short bowel patients with *Lactobacillus* and *Bifidobacterium* led to double the concentration of SCFAs in fecal material [144], and six patients gained weight as a result [144].

In addition to producing SCFAs, the gut microbiota affects host nutrition by regulating xenobiotic metabolism [146] and producing vitamins [11]. For example, the health benefits of soya—such as improvements in vasomotor symptoms, osteoporosis, prostate cancer and cardiovascular disease—have been attributed to (*S*)-equol produced by gut bacteria [147]. It has also been suggested that the production of folic acid by the gut microbiota benefits women and female nonhuman primates during reproduction [135,148]. Differences in the relative abundances of bacterial taxa in the gut therefore may influence host nutrition by affecting the production of these compounds. A study of seven individuals from a Chinese family provided evidence for this process by demonstrating that relative abundances of *Bacteroides*, *Clostridium*, and *Bifidobacteria* were correlated with the concentrations of urinary metabolites, and variation in the relative abundance of *Faecalibacterium prausnitzii* was associated with changes in eight urinary metabolites [149]. Germfree rats have also been shown to become anemic when fed a low-iron diet and exhibit increased fecal iron content compared to rats with a healthy microbiota [150].

Based on what we know from studies of humans and laboratory animals, we would expect differences in gut microbial community composition across habitats and seasons to affect energy and vitamin production in wild animals. However, virtually no studies examine these relationships [135,151]. A new generation of investigations is necessary to better understand the contributions of the gut microbiota to wild host nutrition and fitness (Figure 1). Assuming wild animal gut microbial community composition is linked to nutrition, random differences in gut microbial community composition that result from host exposure to local microbial taxa pools could have important fitness

consequences via their impacts on host nutrition. An individual in a given habitat might receive more energy or vitamins to use for reproduction based solely on the chance development of a more nutritionally beneficial gut microbiota.

Additionally, differences in gut microbial community composition in response to diet across habitats and seasons might be expected to improve host nutrition by improving digestive efficiency. If diet selects for those microbes that most efficiently break down a substrate, and the same microbes that process the host diet most efficiently also provide the host with the most energy and nutrients, diet-induced shifts in gut microbial community composition are likely to be adaptive to the host. In this scenario, differences in the gut microbiota might allow hosts to endure shifts in diet across space and time without negative nutritional consequences. For example, as the nutritional content of host diet decreased or the nutritional demands of host reproduction and growth increased, the energy and nutrients produced by an adaptive gut microbiota could compensate. This process would make reductions in host activity levels and birth and growth rates less common during periods of reduced food availability or in habitats with fewer food resources. In contrast, if changes in the gut microbiota are not always adaptive to host nutrition, as has been suggested by preliminary data in howler monkeys [53], studies must determine what factors dictate whether changes are beneficial or not and pinpoint the potential detrimental effects of the gut microbiota on the host.

By understanding how changes in gut microbial community composition influence host nutrition, we can improve our understanding of wild animals' responses to variability in food availability. Although shifts in behavior such as reducing day range may help animals meet nutritional demands during times of limited food availability, the gut microbiota may also play a role. Similarly, the ability of the gut microbiota to adapt to novel diets may in part explain the ability of a particular host species to colonize new habitats and/or persist in degraded habitats. These processes are critical to understanding host fitness and evolution and therefore must be considered in discussions of host-gut microbe co-evolution.

4. The influence of gut microbial community composition on host health

Although the gut microbial community has a strong influence on host health through nutrition, other aspects of host health are closely related to gut microbial community composition and function. To begin with, a healthy gut microbial community excludes pathogenic microbes from the gastrointestinal system [30,86,152] and attenuates inflammation [153]. For example, the production of acetate by *Bifidobacterium longum* appears to improve rodents' ability to survive infection by a lethal *E. coli* strain [154]. Mice that are not colonized by *B. longum* show more inflammation of colonocytes, higher levels of toxic *E. coli* protein in blood, and higher mortality rates compared to mice that are colonized [154]. Germfree mice are also more susceptible to infection by *Shigella flexneri*, *Bacillus anthracis*, and *Leishmania* [155]. Piglets raised in natural environments with a high diversity of microbes are more resistant to invasion by pathogenic gut microbes than those raised in more sterile environments [156], and bees with a normal gut microbiota exhibit parasite abundances (*Crithidia bombi*) an order of magnitude lower than those without [157]. Probiotics have also been shown to reduce the effects of pathogenic bacteria in fish [158-162].

In addition to protecting the host from pathogenic microbes, the gut microbiota contributes to the development of the host intestinal mucosal and systemic immune systems [1,4,5,12]. The development of gut-associated lymphoid tissue (GALT), which is used by the intestinal mucosa for defense, is dependent on the gut microbial community [5,12,163]. Germfree mice possess fewer Peyer's patches, mesenteric lymph nodes, and cellular lamina propria in the small intestine as well as fewer intraepithelial lymphocytes compared to mice with healthy microbiota [164-170]. Epithelial cells in the gut also exhibit fewer Toll-like receptors (TLRs) and class II major histocompatibility complex molecules [171,172], which are involved in pathogen detection. Conventionalization of germfree mice leads to induction of MHC II molecules and glycolipids on small intestinal epithelial cells and improves immune function [173], and the gut microbiota has been shown to incite TLRs and improve host resistance to intestinal damage [174]. Almost 50% of genes regulated in response to microbial colonization are related to immune response [175].

The gut microbiota also supports intestinal immune homeostasis by influencing immune function during and after development. In the gut, T-regs cells, which suppress unwanted immune reactions, and Th-17 cells, which stimulate the epithelium to produce anti-microbial proteins, are partially regulated by the gut microbial community [175-182]. Vitamin A deficiency, which leads to reduced Firmicutes and Proteobacteria in the gut, is associated with fewer Th-17 cells [96]. Similarly, immunoglobulin A (IgA), which is secreted into the lumen of the gut as secretory IgA (sIgA), is used by the mammalian innate immune system to tag potential pathogenic invaders and prevent them from entering the body. There are one to two orders of magnitude fewer IgA-producing cells in germfree animals and none in neonates [183-185]. However, colonizing germfree mice with segmented filamentous bacteria leads to a 24-63% increase in IgA production in the small intestine [186], suggesting that exposure to gut microbes is critical for normal development of the immune system.

Host systemic immune function is also closely associated with the gut microbiota. Germfree mice possess reduced numbers of helper T cells in the spleen, fewer and smaller germinal centers within the spleen, and reduced systemic antibody levels [42,187-189], but colonization with *Bacteroides fragilis* eliminates many of these differences [188]. Additionally, mice treated with antibiotics and then infected with an influenza virus have reduced immunoglobulin and T cell responses [190], indicating reduced immune function. In fish, a variety of studies have demonstrated that the gut microbiota enhances

the immune response to a variety of infections [160,191-193]. This phenomenon is likely due to interactions that mirror those between the gut microbiota and the innate immune system in mammals. For humans, the Hygiene Hypothesis suggests that sanitation and antibiotic use have reduced exposure to microorganisms in some environments and consequently have led to suppressed development of the immune system, resulting in increased rates of allergies, autoimmunity, and other immune inflammatory conditions [4,194-196]. This effect has been observed in germfree mice that have an accumulation of natural killer T cells in the colon and lungs and increased sensitivity to colitis and asthma [197].

Finally, the gut microbiota has been shown to have both positive and negative effects on host health via the production of metabolic compounds. For example, germfree mice do not possess antioxidant metabolites such as indole-3-propionic acid in their blood plasma, and metabolites such as serotonin are observed in higher quantities in conventional mice [198]. Similarly, differences in gut microbial community composition have been associated with increased toxic hydrogen sulfide production in the gut of captive howler monkeys [53], and in mice and humans, many gastrointestinal diseases are also associated with shifts in the gut microbial community [47,48,199-201]. Additionally, it has been shown that gut microbes can incite nematode parasite eggs to hatch via interactions between the eggs and the bacterial cell surface [202].

Studies in germfree individuals represent a phenotypic extreme unlikely to be observed in wild populations, and much remains to be learned regarding the conventional interactions of the host immune system and the gut microbiota. Nevertheless, together, the studies cited suggest that differences in gut microbial community composition and diversity may allow wild animals to better fight parasites and infections in some habitats and during some seasons. Such variation in host susceptibility to disease and parasite infection across habitats and seasons has been reported for some animals [203-207]. For example, Mexican black howler monkeys have more parasites in forest fragments compared to continuous forests [204], contrary to the theory that increased species diversity in continuous forests should result in increased prevalence and abundance of parasites [208]. These patterns may be the result of reduced gut microbial diversity or changes in the composition of the gut microbial community. However, no study directly measuring wild animal health or immune function has considered the effects of the gut microbiota composition. Only differences in the abundances of microbial sulfate-reduction genes (such as *dsrA*) that may be associated with potential health risks in howler monkeys provide preliminary evidence that the gut microbiota may be important to host health across habitats and seasons [53].

Regardless of whether they result from neutral metacommunity dynamics or the selective influence of diet, if differences in gut microbial community composition impact host health, they will likely influence host fitness since increased rates of disease and/or mortality will lead to decreased birth rates. Therefore, investigations of host-gut microbe co-evolution must take into account the effects of gut microbial community composition on host immune function and metabolite production across habitats and seasons. Additionally, because the host immune system monitors and regulates the gut microbial community independently of environmental factors [5,37,165], studies of host-gut microbe dynamics must also consider the feedback between host and microbe and how it affects host health. While laboratory studies provide important data regarding cause-and-effect for health risks associated with the gut microbiota, only studies of wild animals will allow us to understand how the gut microbe-host health relationship evolved.

5. The influence of gut microbial community composition on host behavior

In addition to nutrition and health, the gut microbiota is also thought to affect host behavior by altering gene expression and impacting the neuronal circuits involved in motor control and anxiety [1]. Measures of plasma adrenocorticotropic hormone (ACTH) and corticosterone responses indicate that germfree mice are more susceptible to stress when physically restrained than specific pathogen-free mice [8]. Compared to conventional mice, germfree mice have also been reported to exhibit more locomotor activity, exploratory behavior, and reduced anxiety behavior in light-dark boxes and elevated mazes [209,210]. These differences have been linked to variation in neurotransmitters, signaling pathways, and the expression of genes related to emotional behavior [209,210] and may have important fitness consequences since reduced anxiety can make mice more vulnerable to predators.

Probiotic treatment has also been shown to affect host mood and behavior. In one study, the administration of *Lactobacillus* and *Bifidobacterium* reduced stress, anxiety-, and depressive-like responses in both rats and humans [211]. The same supplements also altered gut microbial community composition and reduced anxiety scores in 35 people with chronic fatigue disorder who were treated for eight weeks [212]. In mice, *Lactobacillus rhamnosus* has been shown to alter gamma-aminobutyric acid (GABA) receptor mRNA levels in the brain and reduce corticosterone and anxiety- and depression-related behaviors in maze and forced swim tests [213,214] while *Bifidobacteria* probiotics reduced immobility during forced swim tests in maternally-separated mice [215]. These probiotics have similar effects on host anxiety and depression assays during infection. 39 mice infected with the *Trichuris muris* parasite showed increased anxiety-like behavior [216], but *B. longum* supplements provided over ten days reduced these behaviors and normalized brain-derived neurotropic factor [216]. Similarly, increased anxiety-like behaviors in mice given a dextran sodium sulfate toxin to induce colitis can be reversed with *B. longum* supplements [217].

The gut microbiota is believed to have these impacts on host mood and behavior via a variety of mechanisms [218,219]. Although it has been suggested that gut microbes can alter gene

expression and signaling pathways [209,210,220,221], changes in gut microbial composition that induce changes in SCFA or metabolite production may also influence host behavior. For example, in a study of 36 mice, anxiety and aggression increased in response to lactic acid and VFA production on a fermentable diet [222]. In contrast, conventionalization of germfree mice leads to 2.8 fold increase in plasma serotonin levels [198]. Additionally, because inflammation can induce fatigue and depression in hosts [223], the gut microbiota may influence host behavior through its interaction with the immune system. The anti-inflammatory effects of the gut microbiota [5,153,170,224] may reduce host susceptibility to disease-associated emotional symptoms.

The effects of the gut microbiota on the development and health of the host brain are also likely to impact host behavior. Both pre- and post-natal brain development depends heavily on an individual's nutrient intake [225]. Because some microbial genera produce important nutrients such as folic acid [148,226], the composition of the maternal gut microbiota is likely to impact prenatal brain development during pregnancy by influencing the availability of these nutrients *in utero*. A study of obesity and pregnancy provides evidence for this mechanism by reporting an association between infant birth weight and the maternal abundances of certain microbial genera such as *Lactobacillus* and *Escherichia* [148]. Furthermore, low birth weight and pre-term infants tend to exhibit reduced growth in terms of weight, length and head circumference, and infants with reduced gestational periods have an increased potential for delayed cognitive development [227]. It is therefore possible that the maternal gut microbiota has strong effects on infant brain development, cognition, and behavior. Similarly, the gut microbiota is likely to impact postnatal brain development via the production of key nutrients and other contributions to overall nutrition, but the relationship between the gut microbiota, postnatal brain development, and cognition is not well studied. Finally, the gut microbial community may affect host brain health in adults. In a study of 35 mice, probiotic treatment with *Bacteroides* and *Lactobacillus* reduced cell death in the brain after a heart attack [228]. Improved brain health is likely to positively affect host nervous function and behavior.

Similar to studies of the immune system, germfree studies of behavior represent extreme phenotypes, and much remains to be learned about host behavior and the gut microbiota even in controlled settings. However, based on what we know from existing studies about the effect of the gut microbial community on host behavior, it is possible that individuals of the same species occupying distinct habitats exhibit different behaviors as a result of either random or diet-induced differences in the gut microbial community. Likewise, seasonal variation in host behavior could be associated with changes in the gut microbial community to some extent. While patterns in animal behavior across seasons and habitats are widely studied, variation in behavior is normally attributed to factors such as food availability or social interactions [229-234]. Nothing is known regarding the potential influence of the gut microbiota on host behavior in the wild.

Understanding the interaction between the gut microbial community and host behavior is important for understanding host-gut microbe co-evolution in the context of host ecology and evolution. For example, if a particular gut microbial community increases host symptoms of anxiety or depression, it may ultimately influence host activity levels and social interactions. Although a relationship to the gut microbiota was not established, a study of human children has shown that undernourishment can lead to reduced sociality [235]. In the wild, animals that are less active may forage less and experience reduced nutrition, while animals that are isolated or do not interact with group members may lose some of the benefits of group living such as access to feeding sites or protection from predation [236-240]. In both scenarios, we would expect host fitness to be reduced. Gut microbial community composition may also directly influence host fitness by influencing mating patterns. A study of *Drosophila* demonstrated that individuals raised on molasses and starch preferred to mate only with each other in 29 of 38 matings as a result of their gut microbiota. Although the mechanism behind this behavior could not be determined, the effect could be eliminated with antibiotic treatment and influenced using infection with a mixture of bacteria or pure *Lactobacillus* culture [10].

Studies of animal personalities should also begin to consider the effects of the gut microbiota. Personality is typically described using qualities such as "boldness" and "reactivity" [241-244]. Since different gut microbes result in different amounts of exploratory, aggressive, and anxiety-like behavior in hosts [209,213,222], it is likely that a link between the gut microbiota and host personality exists. If individuals of the same species in different habitats tend to exhibit distinct personalities, gut microbial community composition may play a role in determining host personality in addition to factors such as social interactions and predation [245-247]. In fact, a link between host personality and metabolism has been suggested [248]. Because host personality affects host fitness through processes such as feeding, mating and predation [249-252], an understanding of the plasticity of personality and its potential relationship to the gut microbial community is important to understanding host fitness and evolution.

Finally, while host mood and behavior are affected by the gut microbiota, they in turn may also influence it. Changes in patterns of host diet and inter-individual contact incited by the gut microbiota may ultimately feedback to affect gut microbial community composition. Likewise, in addition to being affected by gut microbes, stress has been shown to affect the abundances of some microbial genera. For example, a study of captive rhesus macaques (*Macaca mulatta*) indicated that six-to-nine-month-old infants separated from their mothers showed increases in plasma cortisol and a significant reduction in fecal lactobacilli starting the third day after separation [253]. The same effect of has also been documented in mice [214], and rats and chicks exposed to stress from heat and crowding possess distinct gut microbiota compared to individuals not exposed to these stressors [254]. Therefore, studies of host-gut microbe co-

evolution must take into account that feedback loops likely exist between host behavior and the gut microbiota.

6. Discussion

Because current studies of the gut microbial community focus on laboratory animals and humans [9,16,25,41-49], our current understanding of the co-evolutionary relationship between host and gut microbe is limited. While we know that host genotype influences the composition of the gut microbial community to some extent [28,32,33], studies overwhelmingly indicate that environmental factors such as exposure to local microbial taxa pools and host diet exert the strongest influence on gut microbial community composition [24-30,64]. However, until recently virtually no studies examined the relationship between gut microbial community composition and environmental factors in natural habitats where variation in host exposure to microbes and in food availability and diet are common [53,55]. Additionally, while studies of laboratory animals and humans indicate that the gut microbiota has important impacts on host nutrition, health, and behavior, we do not fully understand the consequences of these impacts for host fitness. Birth and death rates associated with different gut microbial communities have not been measured in any study, and in natural habitats the effects of differences in the gut microbial community on host nutrition, health, and behavior have barely been explored [53,135].

To begin to clarify the mechanisms involved in the co-evolution of host and gut microbe, we must be able to pinpoint the effects of the host (and its habitat) on the composition and fitness of the gut microbial community as well as the effects of the gut microbial community on the fitness of the host. For example, resource availability in a given habitat determines host diet, which influences the gut microbiota. However, the beneficial effects of the gut microbiota on host metabolism may allow animals to exploit wider variety of food resources than possible based on physiology alone [34,255,256], allow animals to persist in habitats with limited resource ability, or reduce the impact of resource availability on reproduction. Figure 1 illustrates these potential host-gut microbe interactions in relation to other factors that are known to affect host fitness in wild animal populations. Although studies of host-gut microbe relationships in controlled environments allow us to predict how the gut microbiota is affected by host ecology and evolution, as well as how it might affect it, additional studies are necessary to test these interactions. Because the host-gut microbe relationship evolved in natural habitats, these studies must be performed, at least in part, in natural habitats. While studies of the human gut microbiota are beginning to target more diverse populations and habitats with this aim [257], studies of other animals must follow suit.

Discussions of co-evolution also require a comparison of phylogenetic patterns in host and microbe, and several studies use patterns in gut microbial community composition associated with host phylogeny to argue for the importance of co-evolution [26,34,132,258,259]. Although these studies offer an important starting point, representation from a wider variety of species is necessary. Furthermore, many of these studies utilize samples from captive populations [9,25,34,41-43], but captive animals have consistently been shown to possess a distinct gut microbiota compared to their wild counterparts [51-58]. Therefore, phylogenetic studies must begin to sample wild animals more widely to more accurately depict the phylogenetic relationship between host and microbe.

Finally, researchers are beginning to investigate the evolution of gene functions in gut bacteria to determine if and how the ability to synthesize novel compounds that maintain the host-gut microbe mutualism evolved [21,46,255,260,261]. As resources become available, these studies must be expanded to include a variety of host species outside the laboratory environment. Because the microbial genome has the potential to evolve quickly due to short generation times and horizontal gene transfer, it is possible that microbial gene functions have evolved differently in laboratory environments compared to natural environments. As a result, recent evolutionary patterns detected in microbial genes in laboratory populations must be verified via comparison to wild populations.

General guidelines for wild animal studies

For questions of co-evolution, studies of animals with minimal human contact are ideal, but sites with any wild animal population that does not have direct physical contact with areas heavily utilized by humans, receives no medical intervention from humans, and does not utilize domesticated food items should provide a representative gut microbiome sample. For questions regarding the effects of diet and social contact on the gut microbiota and of gut microbial shifts on host nutrition, health, and behavior, populations in reserves and sanctuaries with food supplements as well as populations in fragmented or anthropogenically disturbed environments can be used to provide contrasts to wild populations. However, while data from these dramatically altered habitats can be used to discuss the plasticity of the gut microbiota and potential evolutionary implications for hosts, they should not be used in direct examinations of host-microbe co-evolution. The composition of the gut microbial community as well as host nutritional status and health status are likely to be altered in ways not observed in unaltered habitats with no human intervention.

Despite their importance, studies of wild animal populations are associated with a variety of sampling challenges including access to animals and the collection and preservation of samples. However, many of these challenges can be overcome through collaboration between ecologists with established field projects and microbiologists with established microbiome analysis protocols. For example, many primatologists have long-term field sites where continuous collection of data regarding the primates and their environments occurs [e.g. 262-265]. In most of these sites, permits for non-invasive sample collection are already in place for analyses of variables such as parasite prevalence and genotype. At some sites, permits for more

invasive sampling via darting also exist. Similar situations exist for studies of other mammals, amphibians, and birds [e.g. 266-269]. Furthermore, many field projects either utilize bands or dyes for individual identification or depend on researchers' ability to visually distinguish individuals [270-272]. Therefore, by accompanying field workers or training them in sample preservation, gut microbiome researchers should be able to obtain samples from identified host individuals fairly easily. These types of collaborations should also result in a wealth of contextual ecological data collected simultaneously with microbial data, which will broaden our ability to address important themes in host-microbe dynamics.

Fecal samples are generally the easiest type of sample to obtain from wild animals and the easiest to transport. As a result, researchers should rely upon fecal samples for gut microbial analyses when possible. Because fecal samples will normally come into contact with the ground or other parts of the environment regardless of whether an animal is being followed or handled, sample contamination is likely to occur. Care should be taken to collect samples with sterile equipment and to avoid obvious contamination by only taking parts of the sample that have not come into direct contact with the environment. Accidental observer-subject microbe transmission is also a possibility, especially with terrestrial host species. To avoid this, personal protective equipment should be worn at all times if animals are being handled, and researchers should avoid depositing refuse in study areas. If result-altering environmental or observer contamination is suspected despite these precautions, some tools are available to help identify and remove artifact sequences during and after analysis [273].

While immediate freezing tends to be the sample preservation method of choice for microbiome studies [274-276], liquid nitrogen and/or freezers are not always available at field sites. In these cases, the use of RNAlater or ethanol is more feasible and reliable. Additionally, even if freezers are available, not all commercial shippers allow the use of dry ice so the risk of samples thawing or going through freeze-thaw cycles during transport must be considered [277]. Preservatives that minimize these risks and have limited effects on sample quality are ideal. Both RNAlater and ethanol have been deemed acceptable for sample preservation in these scenarios, but it is ideal for samples to be frozen and for nucleic acids to be extracted as soon as possible in both cases [275,278-282]. Experiments should be used to determine the impact of preservation method on sample quality and microbiome results if any doubts exist.

Finally, it is important to remember that fieldwork has its own limitations. In addition to the issues of sample collection and preservation outlined above, researchers have limited practical control over the study and potential confounding factors. For example, although I focus on the impact of host habitat on the gut microbiota in this review, there are a variety of other factors that can shape the composition of the gut microbial community. Birth mode and parental care differ across species and are likely to affect the development of the gut microbiota in offspring. Specifically, we would expect parents and offspring to exhibit more similar gut microbial communities in animals that give birth to live offspring and provide parental care than in animals that lay eggs or do not provide parental care since live birth and parental care implicate more parent-offspring contact. The amount of parental care and the transition time from a modified diet such as milk to an adult diet should also influence the trajectory and speed of gut microbial development in offspring. Additionally, in humans and primates, reproductive status and age/sex class have been associated with differences in gut microbial community composition both among individuals and within individuals over time [66,135,283]. For animals that breed on a seasonal basis, temporal changes in the gut microbiota associated with reproductive status may occur in a predictable pattern and must be isolated from seasonal changes associated with diet. Similarly, if animals undergo seasonal bouts of stress due to mating or food availability [284-287], they are likely to exhibit temporal changes in gut microbial community composition that must be separated from diet. By carefully designing studies and/or sampling a variety of populations across seasons, researchers should obtain sufficient data to separate and identify the effects these factors. However, the type of control afforded by a laboratory setting can never be achieved.

Conclusion

Based on what we currently know regarding the host-gut microbe relationship, both studies of gut microbial communities and studies of their hosts are lacking. Many studies of the gut microbiota fail to present data from wild populations, and many studies of wild animal ecology and evolution ignore the importance of the gut microbiota to host nutrition, health, and behavior. As a result, collaborations between researchers studying the gut microbiota and researchers studying the ecology and evolution of wild animals are critical for the advancement of both fields. Ultimately, understanding of the co-evolution of host and gut microbe depends on the co-evolution of research techniques. A true examination of co-evolutionary relationships between host and microbe requires increased interdisciplinary interactions that address both the fitness of the gut microbial community and the fitness of the host.

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References

[1] Forsythe P., Sudo N., Dinan T., Taylor V.H., Bienenstock J. Mood and gut feelings. Brain Behav Immun 2010; 24: 9-16

[2] Flint H.J., Bayer E.A. Plant cell wall breakdown by anaerobic microorganisms from the mammalian digestive tract. Ann NY Acad Sci 2008: 280-288

[3] Flint H.J., Duncan S.H., Louis P., Impact of intestinal microbial communities upon health., In: Rosenberg E, Gophna U. (Eds.), Beneficial Microorganisms in Multicellular Life Forms Springer, Berlin, 2011 243-252.

[4] Sekirov I., Russel S.I., Antunes C.M., Finlay B.B. Gut microbiota in health and disease. Physiol Rev 2010; 90: 859-904

[5] Hooper L.V., Littman D.R., Macpherson A.J. Interactions between the microbiota and the immune system. Science 2012; 336: 1268-1273

[6] Hooper L.V., Midtvedt T., Gordon J.I. How host-microbial interactions shape the nutrient environment of the mammalian intestine. Annu Rev Nutr 2002; 22: 283-307

[7] Dethlefsen L., McFall-Ngai M., Relman D.A. An ecological and evolutionary perspective on human-microbe mutualism and disease. Nature 2007; 449: 811-818

[8] Sudo N. Stress and gut microbiota: does postnatal microbial colonization programs the hypothalamic-pituitary-adrenal system for stress response? Int Cong Ser 2006; 1287: 350-354

[9] Sudo N., Chida Y., Aiba Y., Sonoda J., Oyama N., Yu X.N., et al. Postnatal microbial colonization programs the hypothalamic-pituitary-adrenal system for stress response in mice. J Physiol 2004; 558: 263-275

[10] Sharon G., Segal D., Ringo J.M., Hefetz A., Zilber-Rosenberg I., Rosenberg E. Commensal bacteria play a role in mating preference of Drosophila melanogaster. Proc Natl Acad Sci USA 2010; 107: 20051

[11] Hill M.J. Intestinal flora and endogenous vitamin synthesis. Eur J Cancer Prev 1997; 6: S43-S45

[12] Neish A.S. Microbes in gastrointestinal health and disease. Gastroenterol 2009; 136: 65-80

[13] Brinkworth G.D., Noakes M., Clifton P.M., Bird A.R. Comparative effects of very low-carbohydrate, high-fat and high-carbohydrate, low-fat weight-loss diets on bowel habit and faecal short-chain fatty acids on bacterial populations. Br J Nutr 2009; 101: 1493-1502

[14] Donohoe D.R., Garge N., Zhang X., Sun W., O'Connell T.M., Bunger M.K., et al. The microbiome and butyrate regulate energy metabolism and autophagy in the mammalian colon. Cell Metab 2011; 13: 517-526

[15] Duncan S.H., Belenguer A., Holtrop G., Johnstone A.M., Flint H.J., Lobley G.E. Reduced dietary intake of carbohydrates by obese subjects results in decreased concentrations of buyrate and butyrate-producing bacteria in feces. Appl Environ Microbiol 2007; 73: 1073-1078

[16] Duncan S.H., Scott K.P., Ramsay A.G., al. e. Effects of alternative dietary substrates on competition between human colonic bacteria in an anaerobic fermentor system. Appl Environ Microbiol 2003; 69: 1136-1142

[17] Macfarlane G.T., Cummings J.H., Allison C. Protein degradation by human intestinal bacteria. Microbiology 1986; 132: 1647-1656

[18] Macfarlane S., Macfarlane G.T. Regulation of short-chain fatty acid production. Proc Nutr Soc 2003; 65: 67-72

[19] Fraser M.D., Theobald V.J., Davies D.R., Moorby J.M. Impact of diet selected by cattle and sheep grazing heathland communities on nutrient supply and faecal micro-flora activity. Agric Ecosyst Environ 2009; 129: 367-377

[20] Flint H.J., Scott K.P., Duncan S.H., Louis P., Forano E. Microbial degradation of complex carbohydrates in the gut. Gut Microbes 2012; 3: 289-306

[21] Nicholson J.K., Holmes E., Kinross J., Burcelin R., Gibson G., Jia W., et al. Host-gut microbiota metabolic interactions. Science 2012; 336: 1262-1267

[22] Secor S.M. Regulation of digestive performance: a proposed adaptive response. Comp Biochem Physiol 2001; 128: 565-577

[23] Turnbaugh P.J., Ley R.E., Mahowald M.A., Magrini V., Mardis E.R., Gordon J.I. An obesity-associated gut microbiome with increased capacity for energy harvest. Nature 2006; 444: 1027-1031

[24] Mackie R.I., Sghir A., Gaskins H.R. Developmental microbial ecology of the neonatal gastrointestinal tract. Am J Clin Nutr 1999; 69: 1035S-1045S

[25] Turnbaugh P.J., Ridaura V.K., Faith J.J., Rey F.E., Knight R., Gordon H.A. The effect of diet on the human gut microbiome: A metagenomic analysis in humanized gnotobiotic mice. Sci Transl Med 2009; 1: 6ra14

[26] Muegge B.D., Kuczynski J., Knights D., Clemente J.C., Gonzalez A., Fontana L., et al. Diet drives convergence in gut microbiome functions across mammalian phylogeny and within humans. Science 2011; 332: 970-974

[27] Wu G.D., Chen J., Hoffmann C., Bittinger K., Chen Y.Y., Keilbaugh S.A., et al. Linking long-term dietary patterns with gut microbial enterotypes. Science 2011; 334: 105-108

[28] Benson A.K., Kelly S.A., Legge R., Ma F., Low S.J., Kim J., et al. Individuality in gut microbiota composition is a complex polygenic trait shaped by multiple environmental and host genetic factors Proc Natl Acad Sci USA 2010; 107: 18933-18938

[29] Arumugam M., Raes J., Pelletier E., Le Paslier D., Yamada T., Mende D.R., et al. Enterotypes of the human gut microbiome. Nature 2011; 473: 174-180

[30] Costello E.K., Stagaman K., Dethlefsen L., Bohannan B.J., Relman D.A. An application of ecological theory toward an understanding of the human microbiome. Science 2012; 336: 1255-1262

[31] Friswell M.K., Gika H., Stratford I.J., Theodoridis G., Telfer B., Wilson I.D., et al. Site and strain-specific variation in gut

microbiota profiles and metabolism in experimental mice. PLoS One 2010; 5: e8584

[32] Buhnik-Rosenblau K., Danin-Poleg Y., Kashi Y., Host genetics and gut microbiota., In: Rosenberg E, Gophna U. (Eds.), Beneficial Microorganisms in Multicellular Life Forms Springer, Berlin, 2011 281-295.

[33] Zoetendal E.G., Akkermans A.D.L., Akkermans-va Vliet W.M., de Visser J.A.G.M., De Vos W.M. The host genotype affects the bacterial community in the human gastrointestinal tract. Microb Ecol Health Dis 2001; 13: 129-134

[34] Ley R.E., Hamady M., Lozupone C., Turnbaugh P.J., Ramey R.R., Bircher J.S., et al. Evolution of mammals and their gut microbes. Science 2008; 320: 1647-1651

[35] Ley R.E., Lozupone C., Hamady M., Knight R., Gordon H.A. Worlds within worlds: Evolution of the vertebrate gut microbiota. Nature 2008; 6: 776-788

[36] Yeoman C.J., Chia N., Yildirim S., Berg Miller M.E., Kent A., Stumpf R.M., et al. Towards an evolutionary model of animal-associated microbiomes. Entropy 2011; 13: 570-594

[37] Kau A.L., Abern P.P., Griffin N.W., Goodman A.L., Gordon J.I. Human nutrition, the gut microbiome and the immune system. Nature 2011; 474: 327-336

[38] Savage D.C. Microbial ecology of the gastrointestinal tract. Annu Rev Microbiol 1977; 31: 107-133

[39] Schramm A., Davidson S.K., Dodsworth J.A., Drake H.L., Stahl D.A., Dubilier N. Acidovorax-like symbionts in the nephridia of earthworms. Environ Microbiol 2003; 5: 804-809

[40] McFall-Ngai M. Adaptive immunity: Care for the community. Nature 2007; 445: 153

[41] Backhed F., Manchester J.K., Semenkovich C.F., Gordon J.I. Mechanisms underlying the resistance to diet-induced obesity in germ-free mice. Proc Natl Acad Sci USA 2007; 104: 979-984

[42] Bauer H., Horowitz R.E., Levenson S.M., Popper H. The response of the lymphatic tissue to the microbial flora. Studies on germfree mice. Am J Pathol 1963; 42: 471-483

[43] Faith J.J., McNulty N.P., Rey F.E., Gordon J.I. Predicting a human gut microbiota's response to diet in gnotobiotic mice. Science 2011; 333: 101-104

[44] Armougom F., Henry M., Vialettes B., Raccah D., Raoult D. Monitoring bacterial community of human gut microbiota reveals an increase in Lactobacillus in obese patients and Methanogens in aneroxic patients. PLoS One 2009; 4: e7125

[45] Costello E.K., Lauber C.L., Hamady M., Fierer N., Gordon J.I., Knight R. Bacterial community variation in human body habitats across space and time. Science 2009; 326: 1694-1697

[46] Kurokawa K., Itoh T., Kuwahara T., Oshima K., Toh H., Toyoda A., et al. Comparative metagenomics revealed commonly enriched gene sets in human gut microbiomes. DNA Research 2007; 14: 169-181

[47] Larsen N., Vogensen F.K., van den Berg F.W.J., Nielsen D.S., Andreasen A.S., Pedersen B.K., et al. Gut microbiota in human adults with type 2 diabetes differs from non-diabetic adults. PLoS One 2010; 5: e9085

[48] Ley R.E. Obesity and the human microbiome. Curr Opin Gastroenterol 2010; 26: 5-11

[49] Mariat D., Firmesse O., Levenez F., Guimaraes V.D., Sokol H., Dore J., et al. The Firmicutes/Bacteroidetes ratio of the human microbiota changes with age. BMC Microbiol 2009; 9: 123-129

[50] Roeselers G., Mittge E.K., Stephens W.Z., Parichy D.M., Cavanaugh C.M., Guillemin K., et al. Evidence for a core gut microbiota in the zebrafish. ISME J 2011; 5: 1595-1608

[51] Xenoulis P.G., Gray P.L., Brightsmith D., Palculict B., Hoppes S., Steinger J.M., et al. Molecular characterization of the cloacal microbiota of wild and captive parrots. Vet Microbiol 2010; 146: 320-325

[52] Nelson T.M., Rogers T.L., Carlini A.R., Brown M.V. Diet and phylogeny shape the gut microbiota of Antarctic seals: A comparison of wild and captive animals. Environ Microbiol 2012; 15: 1132-1145

[53] Amato K.R., Yeoman C.J., Kent A., Carbonero F., Righini N., Estrada A.E., et al. Habitat degradation impacts primate gastrointestinal microbiomes. 2013; 7: 1344-1353

[54] Nakamura N., Amato K.R., Garber P.A., Estrada A.E., Mackie R.I., Gaskins H.R. Analysis of the hydrogenotrophic microbiota of wild and captive black howler monkeys (Alouatta pigra) in Palenque National Park, Mexico. Am J Primatol 2011; 73: 909-919

[55] Schwab C., Cristescu B., Boyce M.S., Stenhouse G.B., Ganzle M. Bacterial populations and metabolites in the feces of free roaming and captive grizzly bears. Can J Microbiol 2009; 55: 1335-1346

[56] Zhu L., Wu Q., Dai J., Zhang S., Fuwen W. Evidence of cellulose metabolism by the giant panda gut microbiome. Proc Natl Acad Sci USA 2011; 108: 17714-17719

[57] Uenishi G., Fujita S., Ohashi G., Kato A., Yamauchi S., Matsuzawa T., et al. Molecular analyses of the intestinal microbiota of chimpanzees in the wild and in captivity. Am J Primatol 2007: 367-376

[58] Dhanasiri A.K.S., Brunvold L., Brinchmann M.F., Korsnes K., Bergh O., Kiron V. Changes in the intestinal microbiota of wild Atlantic cod Gadus morhua L. upon captive rearing. Microbial Ecology 2011; 61: 20-30

[59] Donnet-Hughes A., Perez P.F., Dore J., Leclerc M., Levenez F., Benyacoub J., et al. Potential role of the intestinal microbiota of the mother in neonatal immune education. Proc Nutr Soc 2010; 69: 407-415

[60] Mshvildadze M., Neu J., Shuster J., Theriaque D., Li N., Mai V. Intestinal microbial ecology in premature infants assessed using non-culture based techniques. J Pediatr 2010; 156: 20-25

[61] Jimenez E., Marin M.L., Martin R., Odriozola J.M., Olivares M., Xaus J., et al. Is meconium from healthy newborns actually sterile? Res Microbiol 2008; 159: 187-193

[62] Hubbell S.P., The Unified Neutral Theory of Biodiversity and Biogeography. Princeton University Press, Princeton, New Jersey, 2001:

[63] Freeland W.J. Primate social groups as biological islands. Ecology 1979; 60: 719-728

[64] Lankau E.W., Hong P.Y., Mackie R.I. Ecological drift and local exposures drive enteric bacterial community differences within species of Galapagos iguanas. Mol Ecol 2012; 21: 1779-1788
[65] Fallani M., Young D., Scott J., Norin, E., Amarri S., Adam, R., et al. Intestinal microbiota of 6-week-old infants across Europe: Geographic influence beyond delivery mode, breast-feeding and antibiotics. J Pediatr Gastr Nutr 2010; 51: 77-84
[66] Degnan P.H., Pusey A.E., Lonsdorf E.V., Goodall J., Wroblewski E.E., Wilson M.L., et al. Factors associated with the diversification of the gut microbial communities within chimpanzees from Gombe National Park. Proc Natl Acad Sci USA 2012; 109: 13034-13039
[67] Pavelka M.S., Mechanisms of cohesion in black howler monkeys., In: Susmann RW, Cloninger CR, editors, Origins of altruism and cooperation Springer, New York, 2011 167-178.
[68] Chapman C.A., Chapman L.J., Wrangham R.W. Ecological constraints on group size - An analysis of spider monkey and chimpanzee subgroups. Behav Ecol Sociobiol 1995; 36: 59-70
[69] Bates L.A., Byrne R.W. Sex differences in the movement patterns of free-ranging chimpanzees (Pan troglodytes schweinfurthii): Foraging and border checking. Behav Ecol Sociobiol 2009; 64: 247-255
[70] Sommer V., Mendoza-Granados D. Play as an indicator of habitat quality: A field study of Langur monkeys (Presbytis entellus). Ethology 1995; 99: 177-192
[71] Barrett L., Dunbar R.I.M., Dunbar P. Environmental influences on play behaviour in immature gelada baboons. Anim Behav 1992; 44: 11-115
[72] Banks S.C., Piggott M.P., Stow A.J., Taylor A.C. Sex and sociality in a disconnected world: A review of the impacts of habitat fragmentation on animal social interactions. Can J Zool 2007; 85: 1065-1079
[73] Hart B.L., Hart L.A., Mooring M.S., Olubayo R. Biological basis of grooming behavior in antelope: The body-size, vigilance and habitat principles. Anim Behav 1992; 44: 615-631
[74] Hill R.A. Thermal constraints on activity scheduling and habitat choice in baboons. Am J Phys Anthr 2006; 129: 242-249
[75] Bowers M.A., Matter S.F. Landscape ecology of mammals: Relationships between density and patch size. J Mammal 1997; 78: 999-1013
[76] Cristobal-Azkarate J., Arroyo-Rodriguez V. Diet and activity pattern of howler monkeys (Alouatta palliata) in Los Tuxtlas, Mexico: Effects of habitat fragmentation and implications for conservation. Am J Primatol 2007; 69: 1013-1029
[77] Glessner K.D.G., Britt A. Population density and home range size of Indri indri in a protected low altitude rain forest. Int J Primatol 2005; 26: 855-872
[78] Chiarello A.G., Melo F.R. Primate population densities and sizes in Atlantic forest remnants of northern Espirito Santo, Brazil. Int J Primatol 2001; 22: 379-396
[79] Fahrig L. Effects of habitat fragmentation on biodiversity. Annu Rev Ecol Evol Syst 2003; 34: 487-515
[80] Altizer S., Nunn C.L., Thrall P.H., Gittleman J.L., Antonovis J., Cunningham A.A., et al. Social organization and parasite risk in mammals: integrating theory and empirical studies. Annu Rev Ecol Evol Syst 2003: 517-547
[81] Johnson M.B., Lafferty K.D., van Oosterhout C., Cable J. Parasite transmission in social interacting hosts: Monogenean epidemics in guppies. PLoS One 2011; 6: e22634
[82] Ryder J.J., Miller M.R., White A., Knell R.J., Boots M. Host-parasite population dynamics under combined frequency- and density-dependent transmission. Oikos 2007; 116: 2017-2026
[83] Arneberg P., Skorping A., Grenfell B., Read A.F. Host densities as determinants of abundance in parasite communities. Proc Royal Soc B 1998; 265: 1283-1289
[84] McNulty N.P., Yatsunenko T., Hsaio A., Faith J.J., Muegge B.D., Goodman A.L., et al. The impact of a consortium of fermented milk strains on the gut microbiome of gnotobiotic mice and monozygotic twins. Sci Transl Med 2011; 3: 1-14
[85] Fons M., Gomez A., Karjalainen T. Mechanisms of colonisation resistance of the digestive tract. Part 2: Bacteria/bacteria interactions. Microb Ecol Health Dis 2000; 12: 240-246
[86] Servin A.L. Antagonistic activities of lactobacilli and bifidobacteria against microbial pathogens. FEMS Microbiol Rev 2004; 28: 405-440
[87] Kennedy M.J., Volz P.A. Ecology of Candida albicans gut colonization: Inhibition of Candida adhesion, colonization, and dissemination from the gastrointestinal tract by bacterial antagonism. Infect Immun 1985; 49: 654-663
[88] Turnbaugh P.J., Gordon H.A. The core gut microbiome, energy balance and obesity. J Physiol 2009; 587: 4153-4158
[89] Turnbaugh P.J., Hamady M., Yatsunenko T., Cantarel B.L., Duncan A., Ley R.E., et al. A core gut microbiome in obese and lean twins. Nature 2009; 457: 480-484
[90] Turnbaugh P.J., Ley R.E., Hamady M., Fraser-Liggett C.M., Knight R., Gordon J.I. The Human Microbiome Project. Nature 2007; 449: 804-810
[91] Hamady M., Knight R. Microbial community profiling for human microbiome projects: Tools, techniques and challenges. Genome Res 2009; 19: 1141-1152
[92] Shade A., Handelsman J. Beyond the Venn diagram: The hunt for a core microbiome. Environ Microbiol 2011; 14: 4-12
[93] Degnan B.A., Transport and metabolism of carbohydrates by anaerobic gut bacteria. University of Cambridge, 1992
[94] Flint H.J., Bayer E.A., Rincon M.T., Lamed R., White B.A. Polysaccharide utilization by gut bacteria: potential for new insights from genomic analysis. Nature 2008; 6: 121-131
[95] Kohl K.D., Dearing M.D. Experience matters: Prior exposure to plant toxins enhances diversity of gut microbes in herbivores. Ecol Lett 2012; 15: 1008-1015
[96] Cha H.R., Chang S.Y., Chang J.H., Kim J.O., Yang J.Y., Kim C.H., et al. Downregulation of Th17 cells in the small intestine

by disruption of gut flora in the absence of retinoic acid. J Immunol 2010; 184: 6799-6806

[97] Broderick N.A., Raffa K.F., Goodman R.M., Handelsman J. Census of the bacterial community of the gypsy moth larval midgut by using culturing and culture-independent methods. Appl Environ Microbiol 2004; 70: 293-300

[98] Ringo E., Sperstad S., Myklebust R., Refstie S., Krogdahl A. Characterisation of the microbiota associated with intestine of Atlantic cod (Gadus morhua L.): The effect of fish meal, standard soybean meal and a bioprocessed soybean meal. Aquaculture 2006; 261: 829-841

[99] Hildebrandt M.A., Hoffman C., Sherrill-Mix S.A., Keilbaugh S.A., Hamady M., Chen Y.Y., et al. High-fat diet determines the composition of the murine gut microbiome independently of obesity. Gastroenterol 2009; 137: 1716-1724

[100] Williams C.L., Willard S., Kouba A., Sparks D., Holmes W., Falcone J., et al. Dietary shifts affect the gastrointestinal microflora of the giant panda (Ailuropoda melanoleuca). J Anim Physiol Anim Nutr 2012:

[101] Wang Y., Gilbreath T.M., III, Kukutla P., Yan G., Xu J. Dynamic gut microbiome across life history of the malaria mosquito Anopheles gambiae in Kenya. PLoS One 2011; 6: e24767

[102] Cardoso A.M., Cavalcante J.V., Vieira R.P., Lima J.L., Grieco M.A.B., Clementino M.M., et al. Gut bacterial communities in the giant land snail Achatina fulica and their modification by sugarcane-based diet. PLoS One 2012; 7: e33440

[103] Kane M.D., Breznak J.A. Effect of host diet on production of organic acids and methane by cockroach gut bacteria. Appl Environ Microbiol 1991; 57: 2628-2634

[104] De Filippo C., Cavalieri D., Di Paola M., Ramazzotti M., Poullet J.B., Massart S., et al. Impact of diet in shaping gut microbiota revealed by a comparative study in children from Europe and rural Africa. Proc Natl Acad Sci USA 2010; 107: 14691-14696

[105] Yatsunenko T., Rey F.E., Manary M.J., Trehan I., Dominguez-Bello M.G., Contreras M., et al. Human gut microbiome viewed across age and geography. Nature 2012:

[106] Marshall A.J., Boyko C.M., Feilen K.L., Boyko R.H., Leighton M. Defining fallback foods and assessing their importance in primate ecology and evolution. Am J Phys Anthr 2009; 140: 603-614

[107] Hoffman R.R. Evolutionary steps of ecophysiological adaptation and diversification of ruminants: A comparative view of their digestive system. Oecologia 1989; 78: 443-457

[108] Darwin C., On the Origin of Species by Means of Natural Selection, or the Preservation of Favoured Races in the Struggle for Life. John Murray, London, 1859

[109] Santos J.C., Coloma L.A., Cannatella D.C. Multiple recurring origins of aposematism and diet specialization in poison frogs. Pro Natl Acad Sci USA 2003; 100: 12792-12797

[110] Lambert J.E., Primate nutritional ecology: Feeding biology and diet at ecological and evolutionary scales, In: Campbell C, Fuentes A, MacKinnon KC, Panger M, Bearder SK, (Eds.), Primates in Perspective, Second edition ed Oxford University Press, New York, 2011: 512-522.

[111] Leonard W.R., Robertson M.L. Evolutionary perspectives on human nutrition: The influence of brain and body-size on diet and metabolism. Am J Hum Biol 1994; 6: 77-88

[112] Norconk M.A., Wright B.W., Conklin-Brittain N.L., Vinyard C.J., Mechanical and nutritional properties of food as factors in platyrrhine dietary adaptations, In: Garber PA, Bicca-Marques JC, Estrada AE, Heymann EW, Strier KB. (Eds.), South American Primates, Developments in Primatology: Progress and Prospects Springer, New York, 2009: 279-319.

[113] Ragir S. Diet and food preparation: Rethinking early hominid behavior. Evol Anthr 2000; 9: 153-155

[114] Kaplan H., Hill K., Lancaster J., Hurtado A.M. A theory of human life history evolution: Diet, intelligence, and longevity. Evol Anthr 2000; 9: 156-185

[115] Cordain L., Eaton S.B., Sebastian A., Mann N., Lindeberg S., Watkins B.A., et al. Origins and evolution of the Western diet: Health implications for the 21st century. Am J Clin Nutr 2005; 81: 341-354

[116] Fleagle J.G., Primate Adaptation and Evolution. Academic Press, San Diego, 2013:

[117] Vrieze A., Holleman F., Zoetendal E.G., de Vos W.M., Hoekstra J.B.L., Nieuwdorp M. The environment within: how gut microbiota may influence metabolism and body composition. Diabetol 2010; 53: 606-613

[118] Chivers D.J., Hladik C.M. Morphology of the gastrointestinal tract in primates: Comparisons with other mammals in relation to diet. J Morphol 1980; 166: 337-386

[119] Milton K., The foraging strategy of howler monkeys. Columbia University Press, New York, 1980

[120] Chapman C.A., Chapman L.J., Rode K.D., Hauck E.M., McDowell L.R. Variation in the nutritional value of primate foods: Among trees, time periods, and areas. Int J Primatol 2003; 24: 317-333

[121] Gates J. Habitat alteration, hunting and the conservation of folivorous primates in African forests. Aust J Ecol 2006; 21: 1-9

[122] Gonzalez V., Zunino G.E., Kowalewski M.M., Bravo S.P. Densidad de monos aulladores (Alouatta caraya) y composición y estructura de la selva de inundación en una isla del Río Paraná medio. Revista Mus Argentino de Ciencias Naturales 2002; 4: 7-12

[123] Boinski S. Sex-differences in the foraging behavior of squirrel monkeys in a seasonal habitat. Behav Ecol Sociobiol 1988; 23: 177-186

[124] van Schaik C.P., Terborgh J.W., Wright S.J. The phenology of tropical forests: Adaptive significance and consequences for primary consumers. Annu Rev Ecol Syst 1993; 24: 353-377

[125] Albon S.D., Langvatn R. Plant phenology and the benefits of migration in a temperate ungulate. Oikos 1992; 65: 502-513

[126] Cleland E.E., Chuine I., Menzel A., Mooney H.A., Schwartz M.D. Shifting plant phenology in response to global change. Trends Ecol Evol 2007; 22: 357-365

[127] Poulin B., Lefebvre G., McNeil R. Tropical avian phenology in relation to abundance and exploitation of food resources. Ecology 1992; 73: 2295-2309

[128] Galetti M. Diet of the scaly-headed parrot (Pionus maximiliani) in a semideciduous forest in southeastern Brazil. Biotropica 1993; 25: 419-425
[129] Andelt W.F., Kie J.G., Knowlton F.F., Cardwell K. Variation in coyote diets associated with season and successional changes in vegetation. J Wildl Manage 1987; 51: 273-277
[130] Cantu-Salazar L., Hidalgo-Mihart M.G., Lopez-Gonzalez C.A., Gonzalez-Romero A. Diet and food resource use by the pygmy skunk (Spilogale pygmaea) in the tropical dry forest of Chamela, Mexico. J Zool 2005; 267: 283-289
[131] Cerling T.E., Viehl K. Seasonal diet changes of the forest hog (Hylochoerus meinertzhageni Thomas) based on the carbon isotopic composition of hair. Afr J Ecol 2004; 42: 88-92
[132] Moran N.A., Hansen A.K., Powell J.E., Sabree Z.L. Distinctive gut microbiota of honey bees assessed using deep sampling from individual worker bees. PLoS One 2012; 7: e36393
[133] King G.M., Judd C., Kuske C.R., Smith C. Analysis of stomach and gut microbiomes of the eastern oyster (Crassostrea virginica) from coastal Louisiana, USA. PLoS One 2012; 7: e51475
[134] Kobayashi Y., Koike S., Miyaji M., Hata H., Tanaka K. Hingut microbes, fermentation and their seasonal variations in Hokkaido native horses compared to light horses. Ecological Research 2006; 21: 285-291
[135] Amato K.R., Black howler monkey (Alouatta pigra) nutrition: Integrating the study of behavior, feeding ecology, and the gut microbial community. University of Illinois, Urbana, 2013
[136] Chivers D.J., Hladik C.M., Diet and gut morphology in primates., Food acquisition and processing in primates, Springer, U.S.A., 1984: 213-230.
[137] Hume I.D., Warner A.C.I., Evolution of microbial digestion in mammals., Digestive physiology and metabolism in ruminants Springer, Netherlands, 1980 665-684.
[138] Hoverstad T., Midtvedt T. Short-chain fatty acids in germ free mice and rats. J Nutr 1986; 116: 1772-1776
[139] Wostmann B.S., Larkin C., Moriarty A., Bruckner-Kardoss E. Dietary intake, energy metabolism, and excretory losses of adult male germfree Wistar rats. Lab Anim Sci 1983; 33: 46-50
[140] Backhed F., Ding H., Wang T., Hooper L.V., Koh G.Y., Nagy A., et al. The gut microbiota as an environmental factor that regulates fat storage. Proc Natl Acad Sci USA 2004; 101: 15718-15723
[141] Crawford P.A., Crowley J.R., Sambandam N., Muegge B.D., Costello E.K., Hamady M., et al. Regulation of myocardial ketone body metabolism by the gut microbiota during nutrient deprivation. Proc Natl Acad Sci 2009; 106: 11276-11281
[142] Flint H.J., Duncan S.H., Scott K.P., Louis P. Interactions adn competition within the microbial community of the human colon: Links between diet and health. Environ Microbiol 2007; 9: 1101-1111
[143] Samuel B.S., Gordon J.I. A humanized gnotobiotic mouse model of host-Archael-bacterial mutualism. Proc Natl Acad Sci USA 2006; 103: 10011-10016
[144] Kanamori Y., Sugiyama M., Hashizume K., Yuki N., Morotomi M., Tanaka R. Experience of long-term synbiotic therapy in seven short bowel patients with refractory enterocolitis. Journal of Pediatric Surgery 2004; 39: 1686-1692
[145] Pryde S.E., Duncan S.H., Hold G.H., Stewart C.S., Flint H.J. The microbiology of butyrate formation in the human colon. FEMS Microbiol Lett 2002; 217: 133-139
[146] Bjorkholm B., Bok C.M., Lundin A., Rafter J., Hibberd M.L., Pettersson S. Intestinal microbiota regulate xenobiotic metabolism in the liver. PLoS One 2009; 4: e6958
[147] Jackson R.L., Greiwe J.S., Schwen R.J. Emerging evidence of the health benefits of S-equol, an estrogen receptor beta agonist. Nutr Rev 2011; 69: 432-448
[148] Santacruz A., Collado M.C., Garcia-Valdes L., Segura M.T., Martin-Lagos J.A., Anjos T., et al. Gut microbiota composition is associated with body weight, weight gain and biochemical parameters in pregnant women. Br J Nutr 2010; 104: 83-92
[149] Li M., Wang B., Zhang M., Rantalainen M., Wang S., Zhou H., et al. Symbiotic gut microbes modulate human metabolic phenotypes. Proc Natl Acad Sci USA 2008; 105: 2117-2122
[150] Reddy B.S., Pleasants J.R., Wostmann B.S. Effect of intestinal microflora on iron and zinc metabolism, and on activities of metalloenzymes in rats. J Nutr 1972; 102: 101-107
[151] Milton K., Van Soest P., Robertson J. Digestive efficiencies of wild howler monkeys. Physiol Zoo 1980; 53: 402-409
[152] Rosenfeld J.S. Functional redundancy in ecology and conservation. Oikos 2002; 98: 156
[153] Kelly D., Campbell J.I., King T.P., Grant G., Jansson E.A., Coutts A.G.P., et al. Commensal anaerobic gut bacteria attenuate inflammation by regulating nuclear-cytoplasmic shutting of PPAR-γ and RelA. Nat Immun 2003; 5: 104-112
[154] Fukuda S., Toh H., Hase K., Oshima K., Nakanishi Y., Yoshimura K., et al. Bifidobacteria can protect from enteropathogenic infection through production of acetate. Nature 2011; 469: 543-549
[155] Smith K., McCoy K.D., Macpherson A.J. Use of axenic animals in studying the adaptation of mammals to their commensal intestinal microbiota. Seminars in immunology 2007; 19: 59-69
[156] Mulder I.E., Schmidt B., Stokes C.R., Lewis M., Bailey M., Aminov R.I., et al. Environmentally-acquired bacteria influence microbial diversity and natural innate immune responses at gut surfaces. BMC Biol 2009; 7: 79
[157] Koch H., Schmid-Hempel P. Socially transmitted gut microbiota protect bumble bees against an intestinal parasite. Proc Natl Acad Sci USA 2001; 108: 19288-19292
[158] Panigrahi A., Kiron V., Kobayashi T., Puangkaew J., Satoh S., Sugita H. Immune responses in rainbow trout Oncorhynchus mykiss induced by a potential probiotic bacteria Lactobacillus rhamnosus JCM 1136. Vet Immunol Immunop 2004; 102: 379-388
[159] Balc'azar J.L., Vendrell D., de Blas I., Ruiz-Zarzuela I., Giron'es O., Muzquiz J.L. Immune modulation by probiotic strains: Quantification of phagocytosis of Aeromonas

salmonicida by leukocytes isolated from gut of rainbow trout(Oncorhynchus mykiss) using a radiolabelling assay. Comp Immunol Microbiol 2006; 29: 335-343

[160] Balc'azar J.L., de Blas I., Ruiz-Zarzuela I., Vendrell D., Calvo A.C., M'arquez I., et al. Changes in intestinal microbiota and humoral immune response following probiotic administration in brown trout (Salmo trutta). . Br J Nutr 2007; 97: 522-527

[161] Irianto A., Austin B. Use of probiotics to control furunculosis in rainbow trout Oncorhynchus mykiss (Walbaum). Journal of Fish Disease 2002; 25: 333-342

[162] Pirarat N., Kobayashi T., Katagiri T., Maita M., Endo M. Protective effects and mechanisms of a probiotic bacterium Lactobacillus rhamnosus against experimental Edwardsiella tarda infection in tilapia (Oreochromis niloticus). Vet Immunol Immunop 2006; 113: 339-347

[163] Bauer E., Williams B.A., Smidt H., Verstegen M.W., Mosenthin R. Influence of the gastrointestinal microbiota on development of the immune system in young animals. Curr Issues Intest Microbiol 2006; 7: 35-51

[164] Falk P.G., Hooper L.V., Midtvedt T., Gordon H.A. Creating and maintaining the gastrointestinal ecosystem: What we know and need to know from gnotobiology. Microbiol Mol Biol Rev 1998; 62: 1157-1170

[165] Macpherson A.J., Harris N.L. Interactions between commensal intestinal bacteria and the immune system. Nat Rev Immunol 2004; 4: 478-485

[166] Pollard M., Sharon N. Responses of Peyer's patches in germ-free mice to antigenic stimulation. Infect Immun 1970; 2: 96-100

[167] Glaister J.R. Factors affecting the lymphoid cells in the small intestinal epithelium of the mouse. Int Arch Allergy Appl Immunol 1973; 45: 719-730

[168] Umesaki Y., Setoyama H., Matsumoto S., Okada Y. Expansion of alpha beta T-cell receptor-bearing intestinal intrepithelial lymphocytes after microbial colonization in germ-free mice and its independence from thymus. Immunology 1993; 79: 32-37

[169] Imaoka A., Matsumoto S., Setoyama H., Okada Y., Umesaki Y. Proliferative recruitment of intestinal intraepithelial lymphocytes after microbial colonization of germ-free mice. Eur J Immunol 1996; 26: 945-948

[170] Round J.L., Mazmanian S.K. The gut microbiota shapes intestinal immune responses during health and disease. Nat Rev Immunol 2009; 9: 313-323

[171] Lundin A., Bok C.M., Aronsson L., Bjorkholm B., Gustafsson J.A., Pott S., et al. Gut flora, Toll-like receptors and nuclear receptors: A tripartite communication that tunes innate immunity in large intestine. Cell Microbiol 2008; 10: 1093-1103

[172] Matsumoto S., Setoyama H., Umesaki Y. Differential induction of major histocompatability complex molecules on mouse intestine by bacterial colonization. Gastroenterol 1992; 103: 1777-1782

[173] Umesaki Y., Okada Y., Matsumoto S., Imaoka A., Setoyama H. Segmented filamentous bacteria are indigenous intestinal bacteria that activate intraepithelial lymphocytes and induce MHC class II molecules and fucosyl asialo GM1 glycolipids on the small intestinal epithelial cells in the ex germ-free mouse. Microbiol Immunol 1995; 39: 555-562

[174] Rakoff-Nahoum S., Paglino S., Eslami-Varzaneh F., Edberg S., Medzhitoz R. Recognition of commensal microflora by Toll-like receptors is required for intestinal homeostasis. Cell 2004; 118: 229-241

[175] Gaboriau-Routhiau V., Rakotobe S., Lecuyer E., Mulder I.E., Lan A., Bridonneau C., et al. The key role of segmented filamentous bacteria in the coordinated maturation of gut helper T cell responses. Immunity 2009; 31: 677-689

[176] Round J.L., Mazmanian S.K. Inducible Fox p3+ regulatory T-cell development by a commensal bacterium of the intestinal microbiota. Proc Natl Acad Sci USA 2010; 107: 12204-12209

[177] Neiss J.H., Leithauser F., Adler G., Reimann J. Commensal gut flora drives the expansion of proinflammatory CD4 T cells in the colonic lamina propria under normal and inflammatory conditions. J Immunol 2008; 180: 559-568

[178] Hall J.A., Bouladoux N., Sun C.M., Wohlfert E.A., Blank R.B., Zhu Q., et al. Commensal DNA limits regulatory T cell conversion and is a natural adjuvant of intestinal immune responses. Immunity 2008; 29: 637-649

[179] O'Mahony C., Scully P., O'Mahony D., Murphy S., O'Brien F., Lyons A., et al. Commensal-induced regulatory T cells mediate protection against pathogen-stimulated NF-KB activation. PLoS Pathogens 2008; 4: e1000112

[180] Ivanov I.I., Atarashi K., Manel N., Brodie E.L., Shima T., Karaoz U., et al. Induction of intestinal Th17 cells by segmented filamentous bacteria. Cell 2009; 139: 485-498

[181] Atarashi K., Nishimura A., Shima T., Umesaki Y., Yamamoto M., Onoue M., et al. ATP drives lamina propria T(H)17 cell differentiation. Nature 2008; 455: 808-812

[182] Wen L., Ley R.E., Volchkov P.Y., Stranges P.B., Avanesyan L., Stonebraker A.C., et al. Innate immunity and intestinal microbiota in the development of Type 1 diabetes. Nature 2008; 455: 1109-1113

[183] Macpherson A.J., McCoy K.D., Johansen F.E., Brandtzaeg P. The immune geography of IgA induction and function. Nat Rev 2008; 1: 11-22

[184] Benveniste J., Lespinats G., Salomon J.C. Serum and secretory IgA in axenic and holoxenic mice. J Immunol 1971; 108: 1656-1662

[185] Benveniste J., Lespinats G., Adam C., Salomon J.C. Immunoglobulins in intact, immunized, and contaminated axenic mice: Study of serum IgA. J Immunol 1971; 107: 1647-1655

[186] Talham G.L., Jiang H.Q., Bos N.A., Cebra J.J. Segmented filamentous bacteria are potent stimuli of a physiologically normal state of the murine gut mucosal immune system. Infect Immun 1999; 67: 1992-2000

[187] Noverr M.C., Huffnagle G.B. Does the microbiota regulate immune responses outside the gut? Trends Microbiol 2004; 12: 562-568

[188] Mazmanian S.K., Liu C.H., Tzianabos A.O., Kasper D.L. An immunomodulatory molecule of symbiotic bacteria directs maturation of the host immune system. Cell 2005; 122: 107-118

[189] Hansen C.H.F., Nielsen D.S., Kverka M., Zakostelska Z., Klimesova K., Hudcovic T., et al. Patterns of early gut colonization shape future immune responses of the host. PLoS One 2012; 7: e34043

[190] Ichinohe T., Pang I.K., Kumamoto Y., Peaper D.R., Ho J.H., Murray T.S., et al. Microbiota regulates immune defense against respiratory tract influenza A virus infection. Proc Natl Acad Sci USA 2011; 108: 5354-5359

[191] Kim D.H., Austin B. Innate immune responses in rainbow trout (Oncorhynchus mykiss, Walbaum) induced by probiotics. Fish Shellfish Immunol 2006; 21: 513-524

[192] Balc'azar J.L., de Blas I., Ruiz-Zarzuela I., Vendrell D., Giron'es O., Muzquiz J.L. Enhancement of the immune response and protection induced by probiotic lactic acid bacteria against furunculosis in rainbow trout (Oncorhynchus mykiss). FEMS Immunol Med Microbiol 2007; 51: 185-193

[193] Nikoskelainen S., Ouwehand A.C., Bylund G., Salminen S., Lilius E.M. Immune enhancement in rainbow trout (Oncorhynchus mykiss) by potential probiotic bacteria (Lactobacillus rhamnosus). Fish Shellfish Immunol 2003; 15: 443-452

[194] Strachan D.P. Hay fever, hygiene, and household size. BMJ 1989; 299: 1259-1260

[195] Okada H., Kuhn C., Feillet H., Bach J.-F. The 'hygiene hypothesis' for autoimmune and allergic diseases: An update. Clin Exp Immunol 2010; 160: 1-9

[196] von Mutius E., Vercelli D. Farm living: Effects on childhood asthma and allergy. Nat Rev Immunol 2010; 10: 861-868

[197] Olszak T., An D., Zeissig S., Vera M.P., Richter J.E., Franke A., et al. Microbial exposure during early life has persistent effects on natural killer T cell function. Science 2012; 336: 489-493

[198] Wikoff W.R., Anfora A.T., Liu J., Schultz P.G., Lesley S.A., Peters E.C., et al. Metabolomics analysis reveals large effects of gut microflora on mammalian blood metabolites. Proc Natl Acad Sci USA 2009; 106: 3698-3703

[199] Devkota S., Wang Y., Musch M.W., Leone V., Fehlner-Peach H., Nadimpalli A., et al. Dietary-fat-induced taurocholic acid promotes pathobiont expansion and colitis in Il10-/- mice. Nature 2012; 487: 104-108

[200] Kassinen A., Krogius-Kurikka L., Makivuokko H., Rinttila T., Paulin L., Corander J., et al. The fecal microbiota of irritable bowel syndrome patients differs significantly from that of healthy subjects. Gastroenterol 2007; 133: 24-33

[201] Ley R.E., Turnbaugh P.J., Klein S., Gordon J.I. Human gut microbes associated with obesity. Nature 2006; 444: 1022-1023

[202] Hayes K.S., Bancroft M., Goldrick M., I. P., Roberts I.S., Grencis R.K. Exploitation of the intestinal microflora by the parasitic nematode Trichuris muris. Science 2010; 328: 1391-1394

[203] Martinez-Mota R., Valdespino C., Sanchez-Ramos M.A., Serio-Silva J.C. Effects of forest fragmention on the physiological stress of black howler monkeys. Anim Cons 2007; 10: 374-379

[204] Trejo-Macias G., Estrada A.E., Mosqueda Cabrera M.A. Survey of helminth parasites in populations of Alouatta palliata mexicana and A. pigra in continuous and in fragmented habitat in Southern Mexico. Int J Primatol 2007; 28: 931-945

[205] Gillespie T.R., Chapman C.A. Forest fragmentation, the decline of an endangered primate ,and changes in host-parasite interactions relative to an unfragmented forest. Am J Primatol 2008: 222-230

[206] Mulvey M., Aho J.M., Lydeard C., Leberg P.L., Smith M.H. Comparative population genetic structure of a parasite (Fascioloides magna) and its definitive host. Evolution 1991; 45: 1628-1640

[207] Carey C. Hypothesis concerning the disappearance of boreal toads from the mountains of Colorado. Conserv Biol 1993; 7: 355-362

[208] Hudson P.J., Dobson A.P., Lafferty K.D. Is a healthy ecosystem one that is rich in parasites? Trends Ecol Evol 2006; 21: 382-385

[209] Heijtz R.D., Wang S., Anuar F., Qian Y., Bjorkholm B., Samuelsson A., et al. Normal gut microbiota modulates brain development and behavior. Proc Natl Acad Sci USA 2011; 108: 3047-3052

[210] Neufeld K.M., Kang N., Bienenstock J., Foster J.A. Reduced anxiety-like behavior and central neurochemical change in germ-free mice. Neurogastroenterology and Motility 2011; 23: 255-264

[211] Messaoudi M., Lalonde R., Violle N., Javelot H., Desor D., Nejdi A., et al. Assessment of psychotropic-like properties of a probiotic fomulation (Lactobacillus helveticus R0052 and Bifidobacterium longum R0175) in rats and human subjects. Br J Nutr 2010; 105: 755-764

[212] Rao A.V., Bested A.C., Beaulne T.M., Katzman M.A., Iorio C., Berardi J.M., et al. A randomized, double-blind, placebo-controlled pilot study of a probiotic in emotional symptoms of chronic fatigue syndrome. Gut Pathogens 2009; 1: 6

[213] Bravo J.A., Forsythe P., Chew M.V., Escaravage E., Savignac H.M., Dinan T.G., et al. Ingestion of Lactobacillus strain regulates emotional behavior and central GABA receptor expression in a mouse via the vagus nerve. Proc Natl Acad Sci USA 2011; 108: 16050-16055

[214] Gareau M.G., Jury J., MacQueen G., Sherman P.M., Perdue M.H. Probiotic treatment of rat pups normalises corticosterone release and ameliorates colonic dysfunction induced by maternal separation. Gut 2007; 56: 1522-1528

[215] Desbonnet L., Garrett L., Clarke G., Kiely B., Cryan J.F., Dinan T. Effects of the probiotic Bifidobacterium infantis in the maternal separation model of depression. Neuroscience 2010; 170: 1179-1188

[216] Bercik P., Verdu E.F., Foster J.A., Macri J., Potter M., Huang X., et al. Chronic gastrointestinal inflammation induces anxiety-like behavior and alters central nervous

sytem biochemistry in mice. Gastroenterol 2010; 139: 2102-2112

[217] Bercik P., Park A.J., Sinclair D., Khoshdel A., Lu J., Huang X., et al. The anxiolytic effect of Bifidobacterium longum NCC3001 involves vagal pathways for gut-brain communication. Neurogastroenterology and Motility 2011; 23: 1132-1139

[218] Foster J.A., McVey Neufeld K.A. Gut-brain axis: How the microbiome influences anxiety and depression. Cell 2013; 36: 305-312

[219] Saulnier D.M., Ringel Y., Heyman M.B., Foster J.A., Bercik P., Shulman R.J., et al. The intestinal microbiome, probiotics and prebiotics in neurogastroenterology. Landes Bioscience 2012; 4: 17-27

[220] McVey Neufeld K.A., Mao Y.K., Bienenstock J., Foster J.A., Kunze W. The microbiome is essential for normal gut intrinsic primary afferent neuron excitability in the mouse. Neurogastroent Motil 2013; 25: 183-188

[221] Kunze W., Mao Y.K., Wang B., Huizinga J.D., Ma F., Forsythe P., et al. Lactobacillus reuteri enhances excitability of colonic AH neurons by inhibiting calcium-dependent potassium channel opening. J Cell Mol Med 2009; 13: 2261-2270

[222] Hanstock T.L., Clayton E.H., Li K.M., Mallet P.E. Anxiety and aggression associated with the fermentation of carbohydrates in the hindguts of rats. Physiol Behav 2004; 82: 357-368

[223] Dantzer R., O'Connor J.C., Freund G.G., Johnson R.W., Kelley K.W. From inflammation to sickness and depression: When the immune system subjugates the brain. Nat Rev Neurosci 2008; 9: 46-56

[224] Sokol H., Pigneur B., Watterlot L., Lakhdari O., Bermudez-Humaran L.G., Gratadoux J.J., et al. Faecalibacterium prausnitzii is an anti-inflammatory commensal bacterium identified by gut microbiota analysis of Crohn disease patients. Proc Natl Acad Sci USA 2008; 105: 16731-16736

[225] Benton D. The influence of dietary status on the cognitive performance of children. Mol Nutr Food Res 2010; 54: 457-470

[226] Collado M., Isolauri E., Laitinen K., Salminen S. Distinct composition of gut microbiota during pregnancy in overweight and normal-weight women. Am J Clin Nutr 2008; 88: 894-899

[227] Gutbrod T., Wolke D., Soehne B., Ohrt B., Riegel K. Effects of gestation and birth weight on the growth and development of very low birthweight small for gestational age infants: A matched group comparison. Arch Dis Child Fetal Neonatal Ed 2000; 82: F208-F214

[228] Girard S.A., Bah T.M., Kaloustian S., Lada-Moldovan L., Rondeau I., Tompkins T.A., et al. Lactobacillus helveticus and Bifidobacterium longum taken in combination reduce the apoptosis propensity in the limbic system after myocardial infarction in a rat model. Br J Nutr 2009; 102: 1420-1425

[229] Behie A.M., Pavelka M.S. The short-term effects of a hurricane on the diet and activity of black howlers (Alouatta pigra) in Monkey River, Belize. Folia Primatologia 2005; 76: 1-9

[230] Chaves O.M., Stoner K.E., Arroyo-Rodriguez V. Seasonal differences in activity patterns of Geoffroyi's spider monkeys (Ateles geoffroyi) living in continuous and fragmented forests in southern Mexico. Int J Primatol 2011; 32: 960-973

[231] Overdorff D.J., Strait S.G., Telo A. Seasonal variation in activity and diet in a small-bodied folivorous primate, Hapalemur griseus, in southeastern Madagascar. Am J Primatol 1997; 43: 211-223

[232] Ables E.D. Activity studies of red foxes in southern Wisconsin. J Wildl Manage 1969: 145-153

[233] Relyea R.A. Activity of desert mule deer during the breeding season. J Mammal 1994: 940-949

[234] Martin J., Lopez P. Social status of male Iberian rock lizards (Lacerta monticola) influences their activity patterns during the mating season. Can J Zool 2000; 78: 1105-1109

[235] Baker-Henningham H., Hamadani J.D., Huda S.N., Grantham-McGregor S.M. Undernourished children have different temperaments than better-nourished children in rural Bangladesh. J Nutr 2009; 139: 1765-1771

[236] Janson C.H. Testing the predation hypothesis for vertebrate sociality: Prospects and pitfalls. Behaviour 1998; 135: 389-410

[237] Hill R.A., Dunbar R.I.M. An evaluation of the roles of predation rate and predation risk as selective pressures on primate grouping behavior. Behaviour 1998; 135: 411-430

[238] Alexander R.D. The evolution of social behavior. Ann Rev Ecol Syst 1974; 5: 325-383

[239] Wilson E.O., Sociobiology. Harvard University Press, Cambridge, 1980

[240] Clark C., Mangel M. The evolutionary advantages of group foraging. Theor Pop Biol 1986; 30: 45-75

[241] Bergmuller R., Animal personality and behavioural syndromes., Animal Behaviour: Evolution and Mechanisms Springer, Berlin, 2010 587-621.

[242] Sih A., Bell A.M., Johnson J.C. Behavioral syndromes: An ecological and evolutionary overview. Trends Ecol Evol 2004; 19: 372-378

[243] Clark A., Ehlinger T.J. Pattern and adaptation in individual behavioral differences. Perspectives in Ethology 1987; 7: 1-47

[244] Sih A., Bell A.M., Insights for behavioral ecology from behavioral syndromes., Advances in the Study of Behavior2008 227-281.

[245] Frost A.J., Winrow-Giffen A., Ashley P.J., Sneddon L.U. Plasticity in animal personality traits: Does prior experience alter the degree of boldness? Proc Royal Soc B 2007; 274: 333-339

[246] Bell A.M., Sih A. Exposure to predation generates personality in threespined sticklebacks (Gasterosteus aculeatus). Ecol Lett 2007; 10: 828-834

[247] Bergmuller R., Taborsky M. Animal personality due to social niche specialisation. Trends Ecol Evol 2010; 25: 504-511

[248] Careau V., Thomas D., Humphries M.M., Reale D. Energy metabolism and animal personality. Oikos 2008; 117: 642-653

[249] Biro P.A., Stamps J.A. Are animal personality traits linked to life-history productivity? Trends Ecol Evol 2008; 23: 361-368
[250] Stamps J.A. Growth-mortality tradeoffs and 'personality traits' in animals. Ecol Lett 2007; 10: 355-363
[251] Dingemanse N.J., Both C., Drent P.J., Tinbergen J.M. Fitness consequences of avian personalities in a fluctuating environment. Proc Royal Soc B 2004; 271: 847-852
[252] Wilson A.D.M., Godin J.-G.J., Ward J.W. Boldness and reproductive fitness correlates in the Eastern mosquitofish, Gambusia holbrooki. Ethology 2009; 116: 96-104
[253] Bailey M., Coe C.L. Maternal separation disrupts the integrity of the intestingal micoflora in infant rhesus monkeys. Dev Psychobiol 1999; 35: 146-155
[254] Suzuki K., Harasawa R., Yoshitake Y., Mitsuoka T. Effect of crowding and heat stress on intestinal flora, body weight gain, and feed efficiency of growing rats and chicks. Nippon Juigaku Zasshi 1983; 45: 331-338
[255] Xu J., Mahowald M.A., Ley R.E., Lozupone C., Hamady M., Martens E.C., et al. Evolution of symbiotic bacteria in the distal human intestine. PLoS Biol 2007; 5: e156
[256] Mackie R.I. Mutualistic fermentative digestion in the gastrointestinal tract: Diversity and evolution. Integr Comp Biol 2002; 42: 319-326
[257] Benezra A., DeStefano J., Gordon J.I. Anthropology of microbes. Proc Natl Acad Sci USA 2012; 109: 6378-6381
[258] Ochman H., Worobey M., Kuo C.H., Ndjango J.B.N., Peeters M., Hahn B.H., et al. Evolutionary relationships of wild hominids recapitulated by gut microbial communities. PLoS Biol 2010; 8: e1000546
[259] Yildirim S., Yeoman C.J., Sipos M., Torralba M., Wilson B.A., Goldberg T.L., et al. Characterization of the fecal microbiome from non-human wild primates reveals species specific microbial communities. PLoS One 2010; 5: e13963
[260] Xu J., Gordon J.I. Honor thy symbionts. PNAS 2003; 100: 10452-10459
[261] Zaneveld J., Turnbaugh P.J., Lozupone C., Ley R.E., Hamady M., Gordon J.I., et al. Host-bacterial coevolution and the search for new drug targets. Curr Opin Chem Biol 2008; 12: 109-114
[262] Strier K.B., Boubli J.P. A history of long-term research and conservation of northern muriquis (Brachyteles hypoxanthus) at the Estacao Biologica de Caratinga/RPPN-FMA. Primate Conservation 2006; 20: 53-63
[263] Alberts S.C., Watts H.E., Altmann J. Queuing and queue-jumping: Long-term patterns of reproductive skew in male savannah baboons, Papio cynocephalus. Anim Behav 2003; 65: 821-840
[264] Pusey A.E., Pintea L., Wilson M.L., Shadrack K., Goodall J. The contribution of long-term research at Gombe National Park to chimpanzee conservation. Conserv Biol 2007; 21: 623-634
[265] Koenig A., Borries C., Social organization and male residence pattern in Phayre's leaf monkeys., In: Kappeler PM, Watts DP, (Eds.), Long-term Field Studies of Primates, Springer, Berlin Heidelberg, Heidelberg, 2012: 215-236.
[266] Skelly D.K., Werner E.E., Cortwright S.A. Long-term distributional dynamics of a Michigan amphibian assemblage. Ecology 1999; 80: 2326-2337
[267] Holmes R.T., Sherry T.W., Sturges S.W. Bird community dynamics in a temperate deciduous forest: Long-term trends at Hubbard Brook. Ecol Monogr 1986; 56: 201-220
[268] Durant S.M., Bashir S., Maddox T., Laurenson K. Relating long-term studies to conservation practice: The case of the Serengeti Cheetah Project. Conserv Biol 2007; 21: 602-611
[269] Clutton-Brock T., Sheldon B.C. Individuals and populations: The role of long-term, individual-based studies of animals in ecology and evolutionary biology. Trends Ecol Evol 2010; 25: 562-573
[270] Petit S., Waudby H.P., Walker A.T., Zanker R., Rau G. A non-mutilating method for marking small wild mammals and reptiles. Aust J Zool 2012; 60: 64-71
[271] Pagano A.M., Peacock E., McKinney M.A. Remote biopsy darting and marking of polar bears. Mar Mammal Sci 2013; doi: 10.1111/mms.12029
[272] Sikes R.S., Gannon W.L. Guidelines of the American Society of Mammologists for the use of wild mammals in research. J Mammal 2011; 92: 235-253
[273] Knights D., Kuczynski J., Charlson E.S., Zaneveld J., Mozer M.C., Collman R.G., et al. Bayesian community-wide culture-independent microbial source tracking. Nat Methods 2011; 8: 761-763
[274] Wu G.D., Lewis J.D., Hoffman C., Chen Y.Y., Knight R., Bittinger K., et al. Sampling and pyrosequencing methods for characterizing bacterial communities in the human gut using 16S sequence tags. BMC Microbiol 2010; 10: 206
[275] Vlckova K., Mrazek J., Kopecny J., Petrzelkova K.J. Evaluation of different storage methods to characterize the fecal bacterial communities of captive western lowland gorillas (Gorilla gorilla gorilla). J Microbiol Methods 2012; 91: 45-51
[276] Pakpour S., Milani A.S., Chenier M.R. A multi-criteria decision-making approach for comparing sample preservation and DNA extraction methods from swine feces. Am J Mol Biol 2012; 2: 159-169
[277] Rossmanith P., Roder B., Fruhwirth K., Vogl C. Mechanisms of degradation of DNA standards for calibration function during storage. Appl Microbiol Biotechnol 2011; 89: 407-417
[278] Gray M.A., Pratte Z.A., Kellogg C.A. Comparison of DNA preservation methods for environmental bacterial community samples. FEMS Microb Ecol 2012; 83: 468-477
[279] Deevong P., Hongoh Y., Inoue T., Trakulnaleamsai S., Kudo T., Noparatnaraporn N., et al. Effect of temporal sample preservation on the molecular study of a complex microbial community in the gut of the termite Microcerotermes sp. Microbes Environ 2006; 21: 78-85
[280] Simister R.L., Schmitt S., Taylor M.W. Evaluating methods for the preservation and extraction of DNA and RNA for

analysis of microbial communities in marine sponges. J Exp Mar Biol Ecol 2011; 397: 38-43

[281] Nechvatal J.M., Ram J.L., Basson M.D., Namprachan P., Niec S.R., Badsha K.Z., et al. Fecal collection, ambient preservation, and DNA extraction for PCR amplification of bacterial and human markers from human feces. J Microbiol Methods 2008; 72: 124-132

[282] Moreau C.S., Wray B.D., Czekanski-Moir J.E., Rubin B.E.R. DNA preservation: A test of commonly used preservatives for insects. Invertebr Syst 2013; 27: 81-86

[283] Koren O., Goodrich J.K., Cullender T.C., Spor A., Laitinen K., Backhed H.K., et al. Host remodeling of the gut microbiome and metabolic changes during pregnancy. Cell 2012; 150: 470-480

[284] Kitaysky A.S., Wingfield J.C., Piatt J.F. Dynamics of food availability, body condition and physiological stress response in breeding Black-legged Kittiwakes. Funct Ecol 2002; 13: 577-584

[285] Chapman C.A., Saj T.L., Snaith T.V. Temporal dynamics of nutrition, parasitism, and stress in colobus monkeys: implications for population regulation and conservation. Am J Physiol Anthr 2007: 240-250

[286] Kotrschal K., Hirschenhauser K., Mostl E. The relationship between social stress and dominance is sesaonal in greylag geese. Animal Behaviour 1998; 55: 171-176

[287] Romero L.M. Seasonal changes in plasma glucocorticoid concentrations in free-living vertebrates. Gen Comp Endocrinol 2002; 128: 1-24