AMERICAN SOCIETY FOR MICROBIOLOGY | Applied and Environmental Microbiology

Effect of Dietary Oxalate on the Gut Microbiota of the Mammalian Herbivore *Neotoma albigula*

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Diet is one of the primary drivers that sculpts the form and function of the mammalian gut microbiota. However, the enormous taxonomic and metabolic diversity held within the gut microbiota makes it difficult to isolate specific diet-microbe interactions. The objective of the current study was to elucidate interactions between the gut microbiota of the mammalian herbivore *Neotoma albigula* and dietary oxalate, a plant secondary compound (PSC) degraded exclusively by the gut microbiota. We quantified oxalate degradation in *N. albigula* fed increasing amounts of oxalate over time and tracked the response of the fecal microbiota using high-throughput sequencing. The amount of oxalate degraded *in vivo* was linearly correlated with the amount of oxalate consumed. The addition of dietary oxalate was found to impact microbial species diversity by increasing the representation of certain taxa, some of which are known to be capable of degrading oxalate (e.g., *Oxalobacter* spp.). Furthermore, the relative abundances of 117 operational taxonomic units (OTU) exhibited a significant correlation with oxalate consumption. The results of this study indicate that dietary oxalate induces complex interactions within the gut microbiota that include an increase in the relative abundance of a community of bacteria that may contribute either directly or indirectly to oxalate degradation in mammalian herbivores.

Mammals live in a complex and largely symbiotic relationship with their gut microbiota. This microbiota harbors 150 times more genes than the host and exhibits complex interactions with the host's diet (1–3). In mammalian herbivores, diverse intestinal bacteria ferment a diet high in recalcitrant cellulose and in turn synthesize nutrients from the diet in a form more amenable to absorption by the host (4). Furthermore, mammalian herbivores harbor greater microbial diversity in their gut than either omnivores or carnivores (1). Despite the progress of research into the interactions between the mammalian gut microbiota and diet, the isolation of specific diet-microbe interactions in such a complex system has proven to be difficult (5, 6).

In addition to having a role in fermentation, microbes play an important role in the biotransformation of dietary toxins in mammalian herbivores (4, 7–10). For some toxins, such as oxalate or 3,4-dihydroxypyridine (DHP), a single species of bacteria is capable of biotransforming the toxin, and this function can be transferred to other mammals through microbial transplants (7, 8, 11, 12). For other toxins, such as creosote resin, whole microbial community transplantation into other mammals can increase tolerance (10).

Oxalate, a widely produced and ingested plant secondary compound (PSC), serves as an excellent model to study diet-microbe interactions (13). It is the simplest organic acid and is toxic to mammals (14–16). Oxalate can bind to free calcium ions in the blood and aggregate in the kidneys to form kidney stones (17). In fact, oxalate is a constituent in 80% of kidney stones in humans (17). Oxalate is not metabolized by mammalian enzymes but rather is biotransformed into formate and CO_2 by gut microbes (7, 18–21). While some oxalate-degrading bacteria, such as *Oxalobacter formigenes*, biotransform oxalate for use as a carbon and energy source, the growth of other oxalate-degrading bacteria, such as *Lactobacillus acidophilus*, is inhibited by the presence of oxalate, even though these bacteria biotransform the compound when present (7, 22). Additionally, the by-products of microbial oxalate degradation, formate and CO_2, may be used by a number of bacteria in the process of acetogenesis or methanogenesis, potentially benefitting other gut bacteria not directly involved in the oxalate degradation function (23). While there is no direct evidence for either acetogenesis or methanogenesis, several known acetogenic taxa, such as *Clostridium*, *Streptococcus*, and *Ruminococcus*, are prevalent in the *N. albigula* gut (24–26). These attributes constitute a unique system to isolate the interactions between dietary toxins and gut microbes, along with their contribution to the overall metabolism of the host.

The wild mammalian herbivore *Neotoma albigula* (white-throated woodrat) is an ideal species to study the effects of dietary oxalate. Some populations of *N. albigula* consume a diet composed of nearly 100% *Opuntia* species cactus, which contains a high oxalate content (1.5%, dry weight) (26). *Neotoma albigula* can degrade >90% of dietary oxalate when fed artificial diets of up to 9% oxalate (dry weight). This high level of oxalate degradation has been hypothesized to be the result of microbial metabolism (27, 28). Furthermore, *N. albigula* harbors a diversity of known and potentially oxalate-degrading bacteria distributed across the gastrointestinal tract, including *Oxalobacter*, *Lactobacillus*, *Clostridium*, and *Enterococcus*, among others (26). Thus, *N. albigula* regularly consumes large amounts of oxalate and harbors a diversity of bacteria that exhibit complex interactions with oxalate, making it an ideal species to elucidate oxalate-microbiota interactions.

Received 21 January 2016 **Accepted** 18 February 2016

Accepted manuscript posted online 19 February 2016

Citation Miller AW, Oakeson KF, Dale C, Dearing MD. 2016. Effect of dietary oxalate on the gut microbiota of the mammalian herbivore *Neotoma albigula*. Appl Environ Microbiol 82:2669–2675. doi:10.1128/AEM.00216-16.

Editor: J. Björkroth, University of Helsinki

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Supplemental material for this article may be found at http://dx.doi.org/10.1128/AEM.00216-16.

TABLE 1 Design of the diet trial[a]

Diet	Duration (days)
No oxalate	5
0.5% oxalate	3
1% oxalate	3
1.5% oxalate	3
3% oxalate	3
No oxalate	5

[a] The oxalate percentage was determined by the mass.

The purpose of the current study was to identify the ecological and functional interactions between dietary oxalate and the gut microbiota of *N. albigula*. This study has two primary objectives. The first is to quantify the effect of increasing oxalate consumption on oxalate degradation *in vivo*. The second is to determine if the gut microbiota of *N. albigula* exhibits a community-level response to oxalate consumption. Given the previously identified differential responses of oxalate-degrading bacteria to the presence of oxalate, we predicted that oxalate would stimulate the growth of some microbial taxa and inhibit the growth of others, while having a neutral effect on the remaining community. Our data support the hypothesis that a specialized microbial network of bacteria is responsible for oxalate degradation in *N. albigula*.

MATERIALS AND METHODS

Location, collection, and diet of animals. Six white-throated woodrats (*N. albigula*), were collected with Sherman live traps from Castle Valley, Utah (38.63°N, 109.41°W), in October 2012. The woodrats were immediately transported to the University of Utah Department of Biology Animal Facility and housed in individual cages (48 by 27 by 20 cm) under a 12/12-h light/dark cycle at 28°C and 20% humidity. The animals were maintained in captivity and fed high-fiber rabbit chow with 0.2% oxalate (Teklad formula 2031; Harlan, Denver, CO, USA) for 6 months prior to experimentation. All methods were approved by the Institutional Animal Care and Use Committee (IACUC) under protocol 12-12010.

To examine the interactions between dietary oxalate and gut microbes, animals were placed in a diet trial where oxalate was gradually increased over time (Table 1). The 5-day time periods for the 0.05% oxalate diet were chosen to ensure that any effect of oxalate on the microbiota was removed, while a 3-day period for each of the oxalate diet periods was chosen based on the study of Belenguer et al. (29), in which 3 days on oxalate was long enough to elicit a microbial response. Metabolic cages were used to separate urine and feces and allow for the quantification of food and water intake, which were given *ad libitum*. In metabolic cages, *N. albigula* had access to direct coprophagy (consumption of feces from the anus) but not indirect coprophagy (caching of feces to consume later). To minimize the oxalate concentration of the rabbit chow without reducing food intake, a 3:1 ratio of powdered purified rat chow (Harlan, Denver, CO, USA) to powdered rabbit chow (Harlan) was used in the study. This diet contained an oxalate concentration of 0.05%, which is herein referred to as "no oxalate" (see Table S1 in the supplemental material). The oxalate diets were prepared by mixing sodium oxalate (Fisher Scientific, Pittsburgh, PA, USA) into the powdered chow on a dry weight basis. At the end of the diet trial, all animals were returned to the no-oxalate diet to ensure that any effect on the microbiota was the result of oxalate and not some other factor. Urine and feces were collected daily in sterile 50-ml Falcon tubes for oxalate assays and microbial inventories. Additionally, we collected data on body mass, food and water intake, and fecal and urinary output daily. Using the food intake and fecal output data, we estimated the dry matter digestibility (DMD) as 1 − (dry fecal output/food consumed). These data were evaluated with a repeated-measures analysis of variance (ANOVA).

Oxalate assays. Oxalate in the urine was quantified by following a modified protocol described by Ingale et al. (30). Urine samples were collected daily from each animal for the assays and pooled for each treatment period. Urine samples were acidified with 3 M HNO_3 to a pH of <3 to solubilize any oxalate crystals. The acidified urine was centrifuged to remove precipitates, and the supernatant was reserved. The pH of the supernatant was brought up to 7 with NaOH. Approximately 0.1 g of $CaCl_2$ was added and mixed to precipitate oxalate. The samples were then centrifuged and decanted. A volume of distilled water matching the total urinary volume was added to the calcium oxalate precipitate. The samples were then titrated as described below.

For fecal oxalate assays, feces for each animal were collected daily, dried at 45°C overnight, and pooled by animal at the end of each treatment period. The oxalate assays were conducted by following a modified protocol from Justice (28). Approximately 0.4 g of dried feces was ground and added to 5 ml of 6 N H_2SO_4 for 15 min to solubilize the oxalate. After 15 min, 25 ml of distilled water was added, and the entire solution was filtered through grade 4 Whatman filter paper. The filtrate was brought up to a pH of 7 with NaOH, and 0.1 g of $CaCl_2$ was added to precipitate the oxalate. The samples were centrifuged and decanted. After centrifugation, a volume of distilled water equal to that recovered after filtration was added, and the samples were titrated.

The urine and fecal extracts containing calcium oxalate were titrated in 5-ml aliquots with 0.01 M $KMnO_4$ in triplicate. The aliquots were first acidified with 1 ml of 6 N H_2SO_4 and heated to 70 to 90°C. The $KMnO_4$ was then added until a pink color persisted for 30 s, and the volume of $KMnO_4$ was recorded. These volumes were then compared to a standard curve. Standard curves were made by addition of 0 mM, 5 mM, 10 mM, 15 mM, or 20 mM sodium oxalate to the urine or feces of the woodrats consuming 0.05% oxalate. After extraction and titration, the volume of $KMnO_4$ required to titrate the samples with no oxalate added was subtracted from the volume of all samples to account for endogenous oxalate production. With these methods, we are able to recover 102.69% ± 12.94% of the oxalate from urine and 97.47% ± 6.78% of the oxalate from feces. Both titration curves were linear, with r^2 values of >0.9.

To estimate how much dietary oxalate was being degraded, we quantified the difference between the oxalate consumed and the total oxalate excreted. This estimate is conservative, given that some endogenously produced oxalate excreted in the urine and feces is not accounted for with this method. However, our estimates of total oxalate excretion on the no-oxalate diet indicate that the endogenous contribution is typically small ($<10\%$ of the oxalate consumed with a 0.5% oxalate diet). Furthermore, given that endogenous oxalate production is determined by the consumption of certain dietary precursors, it should not change under the diet regime used in this study and is unlikely to impact the conclusions drawn (15).

Microbial inventories. We collected fresh feces for the microbial inventories on the last day of each diet treatment, which were frozen at −80°C until DNA extraction. DNA was extracted from 180 to 220 g of feces using the QIAamp DNA stool minikit (Qiagen, Germantown, MD, USA). DNA extractions were also performed on oxalate, food, and the reagents of the extraction kit to identify potential sources of contamination. Microbial inventories from a total of 36 fecal samples were generated by amplifying the V4 region of the 16S rRNA gene with the primers 515F and 806R (31). The primers contained a 12-base barcode sequence, which allowed for multiplexing of samples within a single-lane sequencing run on an Illumina MiSeq, with paired-end sequencing of 150 bp each, as previously described (32).

Sequences were analyzed using QIIME (33). Standard quality control was conducted, and sequences were demultiplexed using the default parameters in QIIME. A *de novo* picking strategy was used to classify the operational taxonomic units (OTU) with UCLUST (34) with a minimum sequence identity of 97%. This strategy resulted in an OTU table and phylogenetic tree, which were used in downstream analyses. Sequences identified as chloroplasts or mitochondria or those that had fewer than 10

TABLE 2 Metrics associated with woodrats that were not significantly affected by oxalate[a]

Metric	Mean value ± SE (g)	*F*	*P*
Body mass	171.08 ± 12.83	0.06	1.00
Food intake	18.71 ± 0.06	1.66	0.18
Fecal output	1.907 ± 0.088	3.16	0.27
DMD	0.758 ± 0.012	0.88	0.49
Water intake	12.71 ± 2.25	0.74	0.57
Urine output	5.88 ± 0.96	0.39	0.82

[a] Means were compared over the course of the experiment with a repeated-measures ANOVA (df = 5, 30). Shown is the global mean for each metric.

representations across the data set were removed. Additionally, samples of microbial communities with fewer than 3,000 sequence reads total were removed from further data analysis. For the comparative analyses, the samples were rarified to the same sampling depth of 27,378 reads, which was the highest number that included all samples remaining after quality control.

We calculated the α-diversity metrics species richness (Margalef's richness index), evenness (equitability), and Shannon index. The community membership and structure were determined using unweighted and weighted UniFrac analyses, respectively, to compare levels of microbial community similarity across individuals and diet treatments. The unweighted UniFrac analysis compares the members of a community, whereas the weighted analysis also takes into consideration relative abundances (35). Comparisons were made with analysis of similarity (ANOSIM) after 999 permutations. Additionally, a repeated-measures Pearson correlation analysis between the relative abundance of an OTU and oxalate consumption was conducted for all samples and OTU. The open-source software QIIME was used for diversity, ANOSIM, and correlation metrics, with a false discovery rate (FDR) correction for the Pearson correlation. Significance was set at a *P* value of <0.05 for all analyses.

RESULTS

Oxalate degradation. Body mass, food intake, DMD, water intake, and urine output did not differ significantly among the treatments (Table 2). The oxalate intake increased significantly with increasing dietary oxalate concentrations ($P < 0.001$), and the amount of oxalate degraded correlated significantly with oxalate consumption (Fig. 1). When the excretion of endogenous oxalate is taken into consideration (i.e., by subtracting the amount excreted on the no-oxalate diet), the oxalate degradation exceeded 90% of that consumed regardless of the concentration in the diet. Furthermore, 94 to 99% of the excreted dietary oxalate was found in the feces, indicating that little oxalate was absorbed into the blood.

Response of gut microbiota. High-throughput sequencing yielded a total of 2,208,347 high-quality sequences of 150 overlapping base pairs. The data set from one animal was removed because two of the microbial inventories contained <3,000 sequence reads. Furthermore, a total of 38,723 OTU were removed from the data set, having fewer than 10 sequence reads total. The remaining inventories contained an average of 69,010 ± 5,353 sequences per sample. A rarefaction analysis concluded that the diversity at 27,378 is a good estimate of the true diversity (see Fig. S1 in the supplemental material). With a cutoff of 27.378, an additional 15 OTU were removed from the data set. When DNA was extracted from oxalate or food and used as the template for PCR with universal 16S rRNA primers, no amplification products were detected following gel electrophoresis. Similarly, the DNA extraction reagents used in the study yielded no PCR amplification of 16S rRNA, indicating that there was no detectable contamination. Across all fecal samples, sequences were assigned to 6,232 OTU. Of these OTU, 97.6% were assigned to 14 bacterial phyla with 25.3% assigned to 88 genera. The fecal microbiota showed a composition typical of woodrats and other mammals that was dominated by *Bacteroidetes*, particularly the family S24-7 that comprised between 49.8 to 67.2% of the microbiota (26). There were no significant differences in community membership or community structure across treatments, based on the ANOSIM ($P = 0.496$ and 0.691, respectively) (Fig. 2). Species richness and the Shannon index increased significantly with dietary oxalate concentration; however, levels of evenness did not differ significantly (Fig. 3). Species richness correlated significantly with oxalate consumption (Fig. 4). However, a repeated-measures ANOVA followed by a *post hoc* Tukey analysis revealed that only species richness with a 3% oxalate diet was significantly different from that with the no-oxalate diet (Fig. 3A). This shift in α-diversity prompted us to further investigate the microbial involvement in oxalate biotransformation.

Of the 6,232 identified OTU, a total of 116 OTU exhibited a significant positive correlation ($P < 0.05$ after an FDR correction) with oxalate consumption, while 1 OTU exhibited a negative correlation (Table 3). Those OTU exhibiting a positive correlation included known oxalate-degrading bacteria: *Oxalobacter*, another *Oxalobacteraceae* sp., *Clostridiales*, and *Lachnospiraceae*, among others. The taxonomic clade with the greatest number of OTU that exhibited a positive correlation was the S24-7 family.

A subset of identified OTU were shared across all animals and treatments. A total of 103 OTU were present in all six animals on the no-oxalate diet, and 282 OTU were shared by animals on the 3% oxalate diet, including all of those present in all animals on the no-oxalate diet (see Table S2 in the supplemental material).

DISCUSSION

The current study sought to address two important gaps in gut microbiota research. First, there is a need to understand the fac-

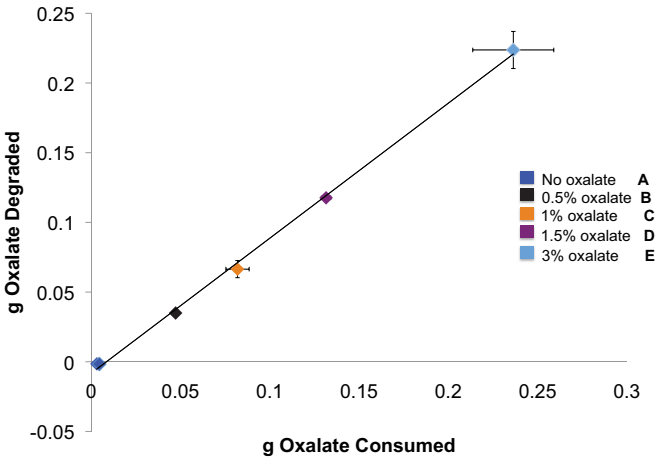

FIG 1 The amount of oxalate consumed is correlated with the amount of oxalate degraded (estimated from the differential between oxalate consumed and the total oxalate excreted in the urine and feces). The data were analyzed with a repeated-measures Pearson correlation ($r = 0.99845$, $P < 0.001$). The oxalate consumed also increased significantly with increasing oxalate consumption as determined by a repeated-measures ANOVA with a *post hoc* Holm-corrected Tukey analysis (the statistical groups are shown by bold letters).

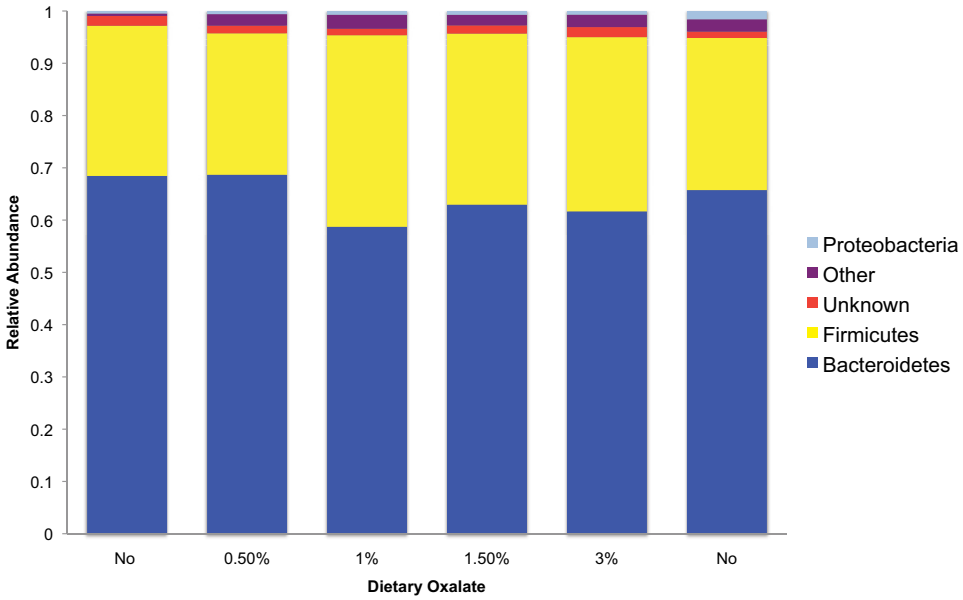

FIG 2 Relative abundances of the major phyla present within the gut at different dietary oxalate concentrations over time. The "Other" category contains several phyla with minor contributions to the microbiota. The columns are ordered relative to the time series of the experiment. Neither community membership nor structure changed with oxalate treatment ($P = 0.496$ or 0.691, respectively).

tors that contribute to changes in the form and function of the mammalian gut microbiota, both to aid in the development of personalized therapies and to advance ecological theories (5, 6). However, studying these factors is confounded by the complexity inherent within the gut microbiota, with its immense and variable diversity and considerable microbe-microbe and microbe-host interactions (2, 6, 36). Second, there is a need to understand how oxalate affects the mammalian gut microbiota as a whole. Previous research has focused on the role of individual taxa in oxalate degradation (7, 20, 29, 37, 38). However, several oxalate-degrading taxa have now been identified from the mammalian gut, and other taxa may be affected by oxalate in obscure ways (20, 26, 39, 40). To address the gaps, we combined controlled laboratory diet trials, physiological assays, and microbial ecology to examine the taxonomic and functional response of the whole gut microbiota in a mammalian herbivore, *N. albigula*, which naturally consumes large amounts of oxalate in its diet, a simple compound that is metabolized exclusively by the gut microbiota (18, 26).

The microbiota of *N. albigula* is exceptional in its capacity to degrade oxalate. The animals exhibited no adverse effects associated with oxalate intake (Table 1), and the microbiota was capable of degrading >90% of dietary oxalate regardless of the amount of oxalate consumed, showing a strong microbial response to oxalate consumption. Studies conducted on other mammals indicate that the level of dietary oxalate degradation in *N. albigula* is unique (27, 28). The Norway rat (*Rattus norvegicus*) becomes hyperoxaluric on a 1.5% oxalate diet (41; unpublished data), whereas another study demonstrated that *N. albigula* can tolerate 9% oxalate with no detrimental effect (27). One potential morphological characteristic that may facilitate oxalate degradation in *N. albigula* is the presence of a foregut that houses a microbiota with a high potential for oxalate degradation (10, 26). In metabolic cages, *N. albigula* animals have access to direct coprophagy (consumption of feces from the anus), which may help to inoculate the foregut with oxalate-degrading bacteria. Given the results of the current and previous studies, the gut microbiota of *N. albigula* appears to have a considerable capacity for oxalate degradation, indicative of a rapid microbial response to oxalate consumption.

Our work shows that dietary oxalate affects both the diversity of the microbial community as a whole in *N. albigula* and the relative abundances of specific OTU. The correlation between oxalate consumption and species richness (Fig. 3A) suggests that OTU that were present below detectable limits in animals on a no-oxalate diet increased in relative abundance with higher oxalate consumption to detectable levels. Such a correlation between the consumption of (natural) dietary toxins and gut microbiota diversity has been observed in other woodrat studies and is likely indicative of a dynamic, community-wide adaptation to dietary change (42). Although there was a strong individual signature to the gut microbiota in the current study, some OTUs both were broadly distributed among animals in general and exhibited a significant correlation with oxalate consumption (Table 3; see also Table S2 in the supplemental material). The subset of microbes that increased with oxalate consumption may represent a core community of microbes essential for the function of oxalate degradation, or an "oxalate microbiome."

A core gut microbiota has previously been associated with diverse mammalian host phenotypes (43–45). In the current study, we have identified a core set of bacteria that are commonly distributed across individuals and are responsive to oxalate, suggesting that this microbial network may be important in reducing oxalate absorption in *N. albigula*. Some of the bacteria in this group, such as *Oxalobacter*, may engage in oxalate degradation directly. Others, such as *Oscillospira* and *Clostridiales*, may benefit indirectly from oxalate degradation possibly via acetogenesis and facilitate the continued presence of those bacteria that degrade oxalate.

Strategies to utilize known oxalate-degrading bacteria as pro-

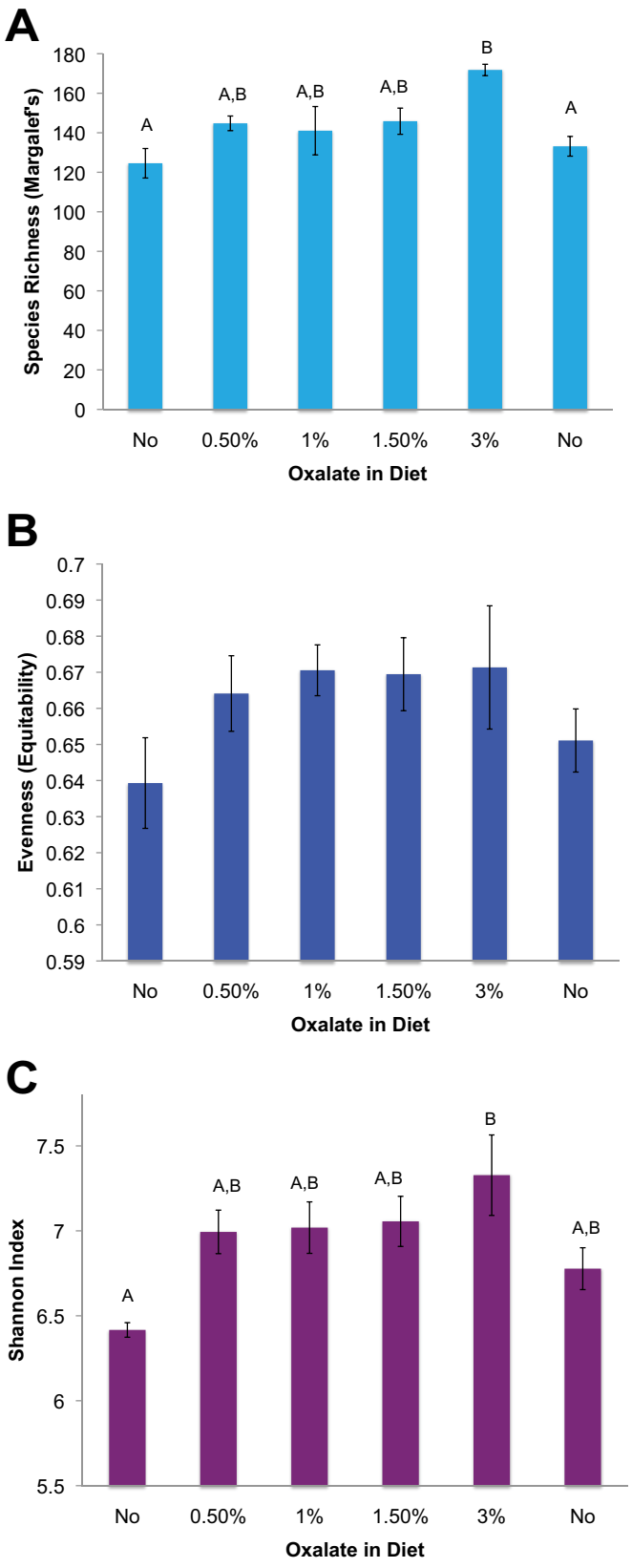

FIG 3 α-Diversity metrics between different dietary oxalate treatments. Species richness was determined with Margalef's richness index, species evenness was determined by their equitability, and the Shannon index is a combination of species richness and evenness. The statistical analyses were repeated -measures ANOVAs followed by a Holm-corrected paired *t* test. The same letters indicate statistically similar treatment groups. The order of the columns reflects the time series of the experiment. (A) Species richness as demonstrated by repeated-measures ANOVA [$F(5, 30) = 2.67$, $P = 0.044$]; (B) species evenness as demonstrated by repeated-measures ANOVA [$F(5, 30) = 1.1126$, $P = 0.38$]; (C) Shannon index as determined by repeated-measures ANOVA [$F(5, 30) = 2.9928$, $P = 0.031$].

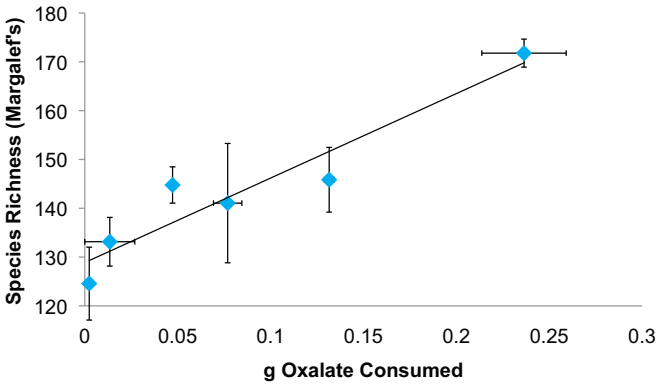

FIG 4 Species richness was correlated with oxalate consumption (repeated-measures Pearson correlation with a *P* of 0.001 and an *r* of 0.529). The symbols represent mean oxalate consumption and species richness for each treatment.

biotic therapies to reduce urinary oxalate excretion in humans and rat models typically result in only an ephemeral reduction of urinary oxalate and a transient colonization by the probiotic bacteria (11, 37, 41, 46, 47). This is in contrast to mammals that are natural hosts to oxalate-degrading bacteria, such as the animals in the current study, which maintain those populations and their associated functions across generations and respond to increasing dietary oxalate even after long periods of time without oxalate in the diet (38, 48, 49). The transient colonization of the oxalate-degrading bacteria following probiotic treatment suggests that these transplanted bacteria are unable to integrate successfully into a foreign community, implying that there are underlying mechanisms of support for these bacteria in their natural hosts.

The S24-7 family appears to play a critical role both in the oxalate microbiome specifically and in the gut microbiota of *N. albigula* generally. This family comprised 43% of the OTU that exhibited a significant correlation with oxalate consumption and consistently makes up >50% of the entire gut microbiota in *N. albigula* (10; this study). This family is commonly found in rats, mice, goats, and humans and has also been correlated with a high-fat diet, immunoglobin A, tapeworms, etc. Thus, the S24-7 family may generally be sensitive to dietary shifts (50–54). Given the widespread distribution of this family and correlation with a number of dietary components, S24-7 represents a significant gap in our understanding of the gut microbiota form and function.

Oxalate is a simple molecular compound with characteristics that make it amenable to elucidating specific diet-microbiota interactions within the mammalian gut. In the current study, we were able to predict the identities of a subcommunity of microbes that exhibits a strong, rapid response to oxalate ingestion. Our results suggest that a distinct oxalate-metabolizing microbiome that increases in abundance when oxalate is consumed exists. Furthermore, we have shown that the methods utilized here are effective at identifying subcommunities within the mammalian gut

TABLE 3 Microbial OTUs whose relative abundances were positively correlated with oxalate intake[a]

Lowest assigned taxonomy	Taxonomic level	No. of OTU	Relative abundance with diet of:		*r*	*P*
			0% oxalate	3% oxalate		
Oscillospira	Genus	4	1×10^{-4}	5.8×10^{-3}	0.54 ± 0.037	0.009–0.037
Oxalobacter	Genus	1	6.39×10^{-5}	5.24×10^{-4}	0.54	0.031
Clostridiales	Order	16	9.13×10^{-6}	1.03×10^{-3}	0.52 ± 0.015	0.009–0.04
Ruminococcus	Genus	5	0	3.29×10^{-4}	0.52 ± 0.015	0.031–0.038
Allobaculum	Genus	3	0	3.29×10^{-4}	0.51 ± 0.017	0.031–0.034
S24-7	Family	50	1.01×10^{-3}	1.27×10^{-2}	0.51 ± 0.007	0.009–0.041
Lactobacillus	Genus	1	0	2.44×10^{-5}	0.51	0.031
Oxalobacteraceae	Family	1	5.48×10^{-5}	6.09×10^{-4}	0.51	0.032
RF39	Order	1	0	1.22×10^{-5}	0.51	0.031
Bifidobacterium	Genus	3	9.13×10^{-6}	1.83×10^{-3}	0.50 ± 0.022	0.031–0.04
Unassigned	NA	19	4.57×10^{-5}	8.52×10^{-4}	0.49 ± 0.007	0.031–0.044
Ruminococcaceae	Family	3	2.74×10^{-5}	3.17×10^{-4}	0.48 ± 0.02	0.031–0.044
Lachnospiraceae	Family	3	3.65×10^{-5}	2.19×10^{-4}	0.48 ± 0.017	0.031–0.043
Rikenellaceae	Family	4	9.13×10^{-6}	1.87×10^{-3}	0.48 ± 0.004	0.034–0.037
Coprococcus	Genus	1	0	2.44×10^{-5}	0.48	0.034
Proteus	Genus	1	0	2.44×10^{-5}	0.46	0.04
Salinibacterium	Genus	1	2.74×10^{-5}	0	−0.46	0.039

[a] We tested 6,232 OTU. Comparisons were performed by Pearson correlation regression analysis with a false discovery rate (FDR) correction for multiple comparisons. For taxa with multiple OTU that were correlated with oxalate consumption, the average *r* values and the range of *P* values are given and the relative abundance refers to the group of OTU as a whole. NA, not applicable.

microbiota that engage in a particular function of interest and that may be useful to manipulate in a therapeutic context.

ACKNOWLEDGMENTS

We thank Kevin Kohl for help collecting animals, Jesse Nelson for help with diet trials, and Ky-Phuong Luong for comments on the manuscript. We thank Bob Weiss for feedback on the experiment.

We declare no conflicts of interest.

FUNDING INFORMATION

This work, including the efforts of Aaron W. Miller, was funded by HHS | National Institutes of Health (NIH) (1F32DK102277-01A1). This work, including the efforts of Colin Dale and M. Denise Dearing, was funded by National Science Foundation (NSF) (DEB-1342615).

The funding agencies had no role in study design, data collection and interpretation, or the decision to submit the work for publication.

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