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NEWS AND VIEWS

Perspective

Microbiome maturation during a unique developmental window

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Shortly after birth, mammals are colonized by a multitude of microbes derived from the mother and the environment. Studies in model organisms have demonstrated that the structure and composition of the gut microbiome of offspring steadily mature with increasing diversity during nursing and weaning (Sommer & Bäckhed, 2013). This period of microbiome assembly is critical for young mammals because the gut microbes they acquire will help train their immune system (Lathrop et al., 2011) with potential long-lasting effects on their health (Cox et al., 2014). In an article in this issue of *Molecular Ecology*, Stoffel et al. (2020) investigated the gut microbiota of northern elephant seals (*Mirounga angustirostris*) during a key developmental window. A month after giving birth, elephant seal mothers stop nursing their pups and return to the sea. As a consequence, their pups go from a diet of milk rich in fat to abruptly enter a post weaning fasting period which lasts for about two months while they remain with the colony. This particular life-history trait therefore offered the authors a unique and exciting opportunity to evaluate intrinsic factors contributing to gut microbiota development in a wild marine mammal.

KEYWORDS

fasting, genetic relatedness, microbiota, sexual dimorphism, weaning

Intrinsic factors potentially contributing to the microbiome (e.g., age, sex, genetics) are more easily studied in model organisms and domestic animals where scientists can control for a large amount of external variation from the environment. Wild animals may differ in diet and habitat use, not only among individuals, but single individuals may also exhibit differences on a temporal and spatial scale. While the one month long nursing period of elephant seal pups may present variation in terms of maternal factors, the post weaning period minimizes extrinsic factors such as diet and habitat due to fasting and remaining within the colony (Figure 1). Stoffel et al. (2020) used this rare opportunity to study natural gut microbiome development in 40 elephant seal pups during three time points, T1: directly after weaning, T2: 15 days later, and T3: 30 days later.

Similar to other gut microbiome studies (Palmer, Bik, DiGiulio, Relman, & Brown, 2007), Stoffel et al. (2020) found that host individuals explained a major part of the total microbiome variation between samples (40%–44%, depending on model). This interindividual variation was largely followed by age, as determined by the three sampling time points (T1–T3; Figure 2a). On a higher taxonomic level, the dominant phyla Bacteroidetes, Firmicutes, and Proteobacteria remained stable during the post weaning fasting period, whereas Fusobacteria decreased in relative abundance. At finer taxonomic scales, however, a more dynamic pattern emerged. Core ASVs (defined as ASVs that were present in at least 95% of samples) at T1 came primarily from the genera *Fusobacterium* and *Bacteroides*. Whereas an ASV from the genus *Ezakiella* was the most dominant one at T2 and T3, *Bacteroides*, which started out as the second most abundant genus, decreased in relative abundance over time. Microbial alpha diversity, measured with the Shannon index, appeared stable during the three time points. Previous studies on gut microbiota during fasting generally report an increase in microbial diversity; however, this will depend largely on host species (Kohl, Amaya, Passement, Dearing, & McCue, 2014).

When it comes to sex differences in vertebrate gut microbiomes, these are sometimes present, but often small (Campbell et al., 2012; Tung et al., 2015). A particular fascinating aspect with northern elephant seals, however, is that they represent one of the most sexually dimorphic mammals, with males weighing several times more than the females. Interestingly, Stoffel et al. (2020) found that this discrepancy between the sexes was prominent in the gut microbiota even during the post weaning period when male and female offspring do not yet show differences in morphology or size. In addition, the effect of sex on the microbial community seemed to increase from T1 to the two later time points. These findings certainly raise the question how male and female elephant seal pups differ that enable these microbial patterns to establish already at two months of age. It has been previously reported that notorious “milk thieves” (weaned pups that suckle from unwary nursing females other than their mother) are predominantly male. Reiter, Stinson, and Le Boeuf (1978) observed that 26 out of 30 milk thieves were male, and males attempted to steal milk more frequently, were more persistent, and more successful, compared to their female counterparts. Related to this, Reiter et al. (1978) also reported that all pups designated as “superweaners” (exceptionally large animals) were all males and that males more frequently engaged in aggressive social behaviour. These early sex differences in size and behaviour suggest that the extreme sexual dimorphism seen in adults starts at a very young age, which corroborates the differences in gut microbiota found by Stoffel et al. (2020).

FIGURE 1 Northern elephant seal pups during the post weaning stage. Photo credit: Martin Stoffel

Another neat aspect of this study was the inclusion of a health measurement to further try to explain microbiome variation. Health condition in wildlife is difficult to assess, and ecoimmunological measurements can encompass everything from parasite abundances to serological assays (Pedersen & Babayan, 2011). Here, the authors counted the number of white blood cell types from blood smears collected at T1 and T3, and compared these values against previously reported measures. Individuals were classified as “clinically abnormal” if they had higher or lower leucocyte counts than within the normal range. This health status could only explain a negligible part (2.5%) of the microbiome beta diversity when taking age into account, with slightly higher effects at T1 when analyzed separately from T3. Although studies in model organisms usually report large effects of health measures on microbiome composition (Sekirov, Russell, Antunes, & Finlay, 2010), the minor effect found probably reflects a coarseness in the method's ability to assign health status rather than an exact designation of health.

Finally, one of the most interesting parts of the study concerned the measure of host genetic relatedness. Few studies of wildlife have explored the relationship between microbiome similarity and host genotype, partly because studies in humans have found only minor effects of host genetics, but primarily due to the difficulties in simultaneously controlling for extrinsic factors such as habitat that are likely to mask small underlying effects. The authors found that the genetic relatedness of elephant seals (based on microsatellite

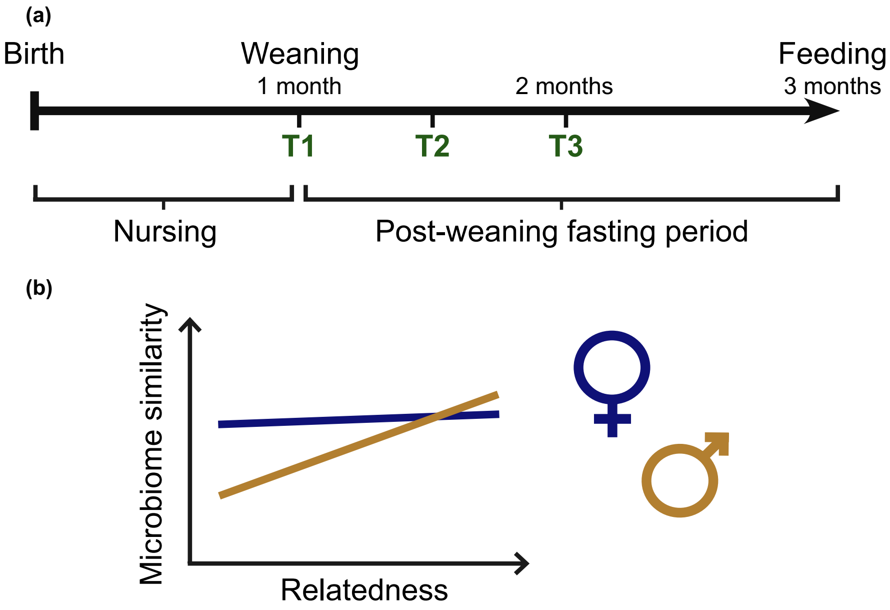

FIGURE 2 Northern elephant seal microbiome development. (a) Timeline of the approximate three month long nursing, weaning, and post weaning period. Sampling time points by Stoffel et al. (2020) during the post weaning period are designated as T1–T3. (b) Summary graph illustrating the discrepancy between the two sexes in host genetic relatedness and microbiome similarity

genotyping) positively correlates with gut microbiome similarity (Bray-Curtis distances). However, this pattern was curiously enough only present in males, as the females did not show any such relationship (Figure 2b). Future studies of adult northern elephant seals gut microbiota will be necessary in order to determine if this sex-specific genetic relatedness-effect persists into adulthood.

By including valuable measures such as health status, genetic relatedness, and age, the study by Stoffel et al. (2020) represents a major step forward in wildlife microbiome research. The authors provide important results to further our understanding of gut microbiome maturation in wild mammals, and show how sex-specific effects are present already at early ages in a species with extreme sexual dimorphism as adults.

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