RESEARCH ARTICLE

MICROBIOMES

Gut microbiome heritability is nearly universal but environmentally contingent

Laura Grieneisen[1]*, Mauna Dasari[2], Trevor J. Gould[1], Johannes R. Björk[2], Jean-Christophe Grenier[3,4], Vania Yotova[3], David Jansen[2], Neil Gottel[5], Jacob B. Gordon[6], Niki H. Learn[7], Laurence R. Gesquiere[6], Tim L. Wango[8,9], Raphael S. Mututua[8], J. Kinyua Warutere[8], Long'ida Siodi[8], Jack A. Gilbert[5], Luis B. Barreiro[3,10], Susan C. Alberts[6,11,12], Jenny Tung[6,11,12,13]†*, Elizabeth A. Archie[2]†*, Ran Blekhman[1,14]†*

Relatives have more similar gut microbiomes than nonrelatives, but the degree to which this similarity results from shared genotypes versus shared environments has been controversial. Here, we leveraged 16,234 gut microbiome profiles, collected over 14 years from 585 wild baboons, to reveal that host genetic effects on the gut microbiome are nearly universal. Controlling for diet, age, and socioecological variation, 97% of microbiome phenotypes were significantly heritable, including several reported as heritable in humans. Heritability was typically low (mean = 0.068) but was systematically greater in the dry season, with low diet diversity, and in older hosts. We show that longitudinal profiles and large sample sizes are crucial to quantifying microbiome heritability, and indicate scope for selection on microbiome characteristics as a host phenotype.

An important goal of microbiome research is to determine the heritability of gut microbiome traits (*1*–*8*). Linking microbiome variation to host genetic variation can reveal which aspects of the microbiome are capable of responding to selection on the host, suggest which microbiome traits are under host control, and connect microbial abundance to host pathways and disease states (*1*, *7*). However, current research suggests that heritable gut microbiome taxa are uncommon. In humans, only 3 to 13% of gut microbes have nonzero heritability, and one study estimated that overall microbiome heritability may be as low as 0.019 (*1*, *2*, *4*, *6*, *7*). Furthermore, the few heritable microbiome phenotypes in humans, such as the abundance of the family Christensenellaceae, exhibit widely varying heritability estimates across studies [narrow-sense heritability (h^2) = 0.31 to 0.64 (*1*, *2*, *4*, *6*, *7*, *9*)].

There are challenges in accurately estimating h^2, the proportion of phenotypic variance explained by additive genetic variance, for the human microbiome. First, relatives, especially twins and other first-degree relatives, which are the basis for most microbiome heritability studies, often share diets, behaviors, and built environments, which can cause heritability to be overestimated (*10*). Controlling for gene-environment correlations requires fine-grained, individual-based environmental and behavioral data, which have not been available in previous studies (*1*, *2*, *4*–*6*). Second, all current estimates of microbiome heritability in humans rely on cross-sectional microbiome sampling even though microbial abundances are dynamic and difficult to accurately phenotype from one-time measures (*1*, *2*, *4*, *6*, *7*, *11*). Further, h^2 can change over a host's lifetime because of shifting environmental conditions and host attributes [e.g., h^2 for body mass index decreases with age, as dietary and behavioral effects increase relative to the effects of genotype: (*12*, *13*)]. To date, no studies of gut microbiome heritability have fully accounted for this temporal variability or its dependence on the environment.

Estimating microbiome heritability in a natural primate population

To overcome these challenges, we estimated h^2 for gut microbiome traits in 585 wild baboons (*Papio cynocephalus*, the yellow baboon, with some admixture from anubis baboons, *Papio anubis*; Fig. 1A). To do so, we used 16,234 16*S* rRNA gene sequencing–based microbiome profiles from fecal samples collected longitudinally over 14 years. These samples were collected from the Amboseli baboon population (Fig. 1B), which has been the subject of individual-based research since 1971 (*14*). Each study subject had on average 28 samples collected across 4.5 years (range = 1 to 177 samples per baboon; median days between samples = 28; Fig. 1A).

Baboons lead shorter lives than humans, so these time series often span a substantial fraction of the baboon life span [female life expectancy at birth is 10 years; females and males achieve sexual maturity at 4.5 and 5.7 years respectively; (*15*)]. Each microbiome sample is accompanied by detailed information on the pedigree relationships of its donor (fig. S1), as well as fine-grained data on environmental conditions, social behavior, demography, and group-level diet composition at the time of sampling (Fig. 1C and tables S1 and S2). These complementary data allowed us to achieve precise estimates of heritability and quantify the impact of shifting environmental and social conditions on heritability. They also break apart gene-environment correlations: Baboon social groups contain a wide range of maternal relatives, paternal relatives, and nonrelatives (median within-group relatedness in a given year = 0.055, SD = 0.11), yet all group members travel in a coordinated fashion across the landscape and feed on the same seasonally available foods (*14*). Additionally, groups exhibit substantial home range overlap [Fig. 1B; (*16*)]. Here, we studied 10 social groups that varied in size from 17 to 118 members (mean = 58).

Each 16*S* gut microbiome profile was generated from a fecal sample collected from an individually recognized baboon and processed as described previously (*17*) (figs. S2 to S4 and table S3). Similar to other primates [Fig. 1D; (*18*–*21*)], the most common gut microbial phyla were Firmicutes, Bacteroidetes, and Actinobacteria (Fig. 1E). Both the abundances of these phyla and the composition of baboon diets showed cyclic fluctuations (Fig. 1, C and E), which reflect Amboseli's wet-dry seasonal dynamics (*14*).

Using these microbiome profiles, we estimated the h^2 of 1034 gut microbiome phenotypes. These included seven community phenotypes, or measures of microbiome community composition [amplicon sequence variant (ASV) richness, ASV Shannon's H index, and the first five principal coordinates (PCs) of a Bray-Curtis dissimilarity matrix], and 283 single-taxon phenotypes representing the relative abundance of individual microbiome taxa, from ASVs through phyla, found in >50% of samples [figs. S5 and S6; (*1*–*6*, *17*, *22*)]. We also estimated h^2 for 744 presence/absence phenotypes, which reflect

[1]Department of Genetics, Cell Biology, and Development, University of Minnesota, Minneapolis, MN 55455, USA. [2]Department of Biological Sciences, University of Notre Dame, Notre Dame, IN 46556, USA. [3]Department of Genetics, CHU Sainte Justine Research Center, Montréal, Quebec H3T 1C5, Canada. [4]Research Center, Montreal Heart Institute, Montréal, Quebec H1T 1C8, Canada. [5]Marine Biology Research Division, Scripps Institution of Oceanography, University of California, San Diego, La Jolla, CA 92093. [6]Department of Biology, Duke University, Durham, NC 27708, USA. [7]Department of Ecology and Evolutionary Biology, Princeton University, Princeton, NJ 08544, USA. [8]Amboseli Baboon Research Project, Amboseli National Park, Kenya. [9]The Department of Veterinary Anatomy and Animal Physiology, University of Nairobi, Kenya. [10]Section of Genetic Medicine, Department of Medicine, University of Chicago, Chicago, IL 60637, USA. [11]Department of Evolutionary Anthropology, Duke University, Durham, NC 27708, USA. [12]Duke Population Research Institute, Duke University, Durham, NC 27708, USA. [13]Canadian Institute for Advanced Research, Toronto, Ontario M5G 1M1, Canada. [14]Department of Ecology, Evolution, and Behavior, University of Minnesota, Minneapolis, MN 55455, USA.
*Corresponding author. Email: lgrienei@umn.edu (L.G.); blekhman@umn.edu (R.B.); earchie@nd.edu (E.A.A.); jenny.tung@duke.edu (J.T.)
†These authors contributed equally to this work.

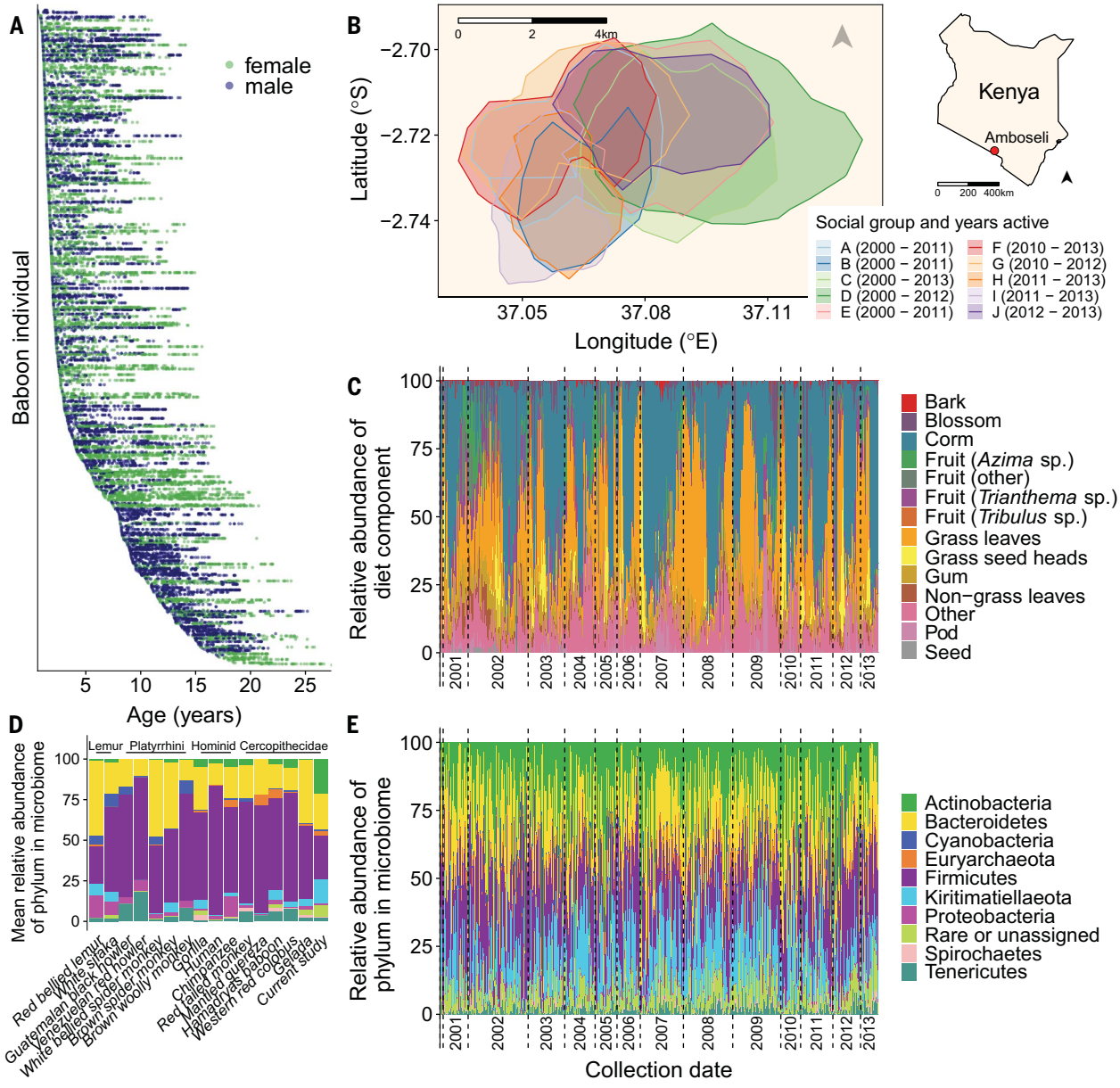

Fig. 1. Time-series data used to estimate microbiome heritability. (**A**) Dataset consisting of 16,234 microbiome samples collected from 585 individually recognized baboons. Each point represents a sample; the *y*-axis is ordered by baboon age at first sample collection. (**B**) Map of the 90% kernel density estimate (KDE) home ranges and active dates for the 10 baboon social groups sampled over the study period based on 71,645 GPS points collected during group monitoring. (**C**) For each microbiome sample, we had data on the diet consumed by members of the corresponding social group in the 30 days before sample collection. Each vertical bar represents one sample, ordered by collection date. Colors represent diet components (see table S1). (**D**) The relative abundances of microbial phyla in the current study are similar to prior primate studies (*18*–*21*). (**E**) Relative abundance of microbial phyla in all 16,234 samples ordered by collection date. "Rare" taxa: <0.5% mean relative abundance per sample. In (C) and (E), the *x*-axis starts at the year 2000. The same legend applies for (D) and (E).

whether a taxon is present or absent in a sample, respectively (limited to taxa found in 10 to 90% of samples).

We estimated h^2 separately for each phenotype using the animal model implemented in ASReml-R v3 [tables S4 and S5; (*23*)]. This mixed-effects model estimates each individual's additive genetic value as a random effect based on the expected covariance in additive genetic effects between relatives in a pedigree (*24*–*26*). It also partitions phenotypic variance across additive genetic variance and other random effects, after conditioning on fixed effects. Following the typical approach in human genetics and plant and animal breeding, we estimated total phenotypic variance (the denominator of h^2) after correcting for fixed effects (*12*, *24*, *27*). This allowed us to exclude the effects of environmentally variable traits such as diet and rainfall, technical effects, and demographic variables such as sex and age (figs. S7 and S8).

Genetic effects on the gut microbiome are nearly universal

We found that 97% of single-taxon and community phenotypes were significantly heritable, including all seven community phenotypes and 93% (273/283) of single-taxon phenotypes [likelihood ratio test; false discovery rate (FDR) threshold = 0.1; Fig. 2, A and B; figs. S9 and S10; and table S6]. Heritability was not limited to prevalent taxa because 95% of the 744 presence/absence phenotypes were also

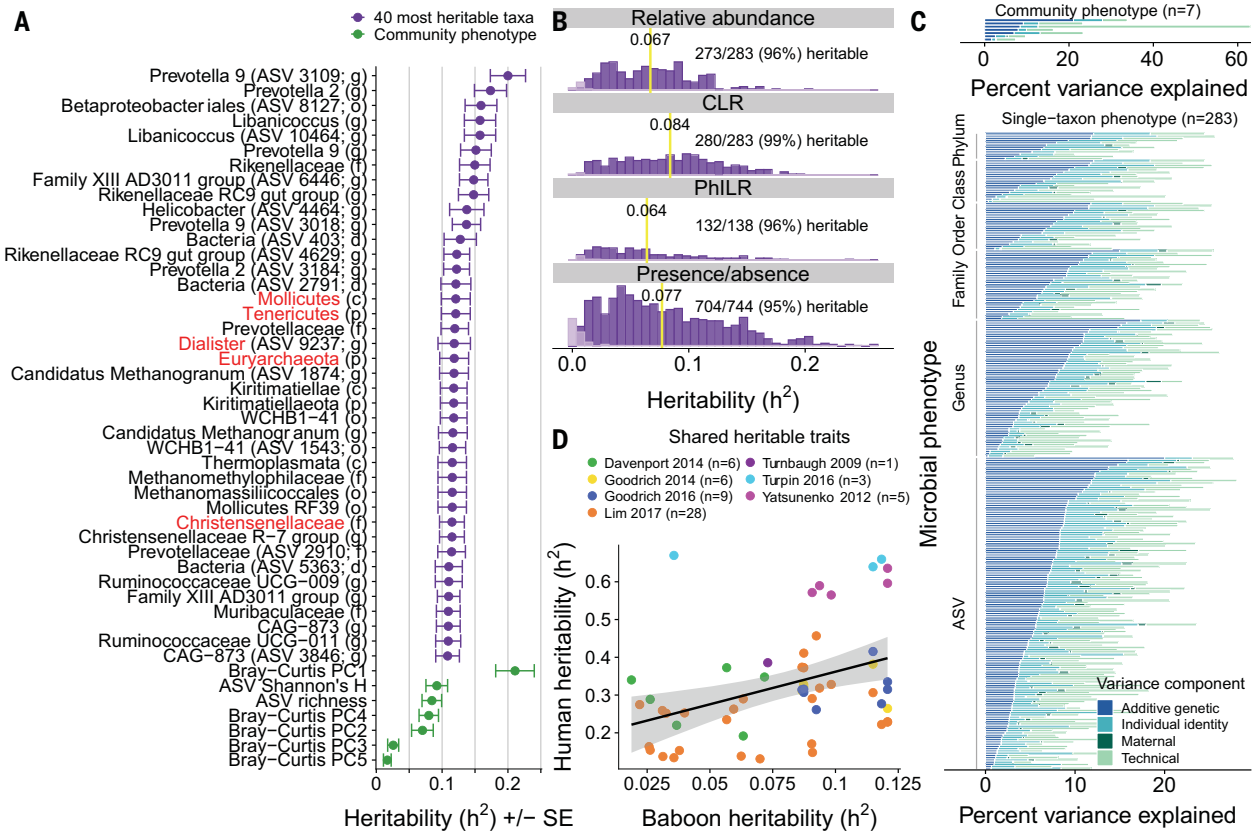

Fig. 2. Most microbiome phenotypes are heritable. (**A**) Heritability estimates for the 40 most heritable single-taxon phenotypes and all seven community phenotypes. Red text indicates taxa that are also heritable in humans (*1*, *2*, *4*–*6*). (**B**) Heritability estimates were robust across data transformations. Dark purple bars show significantly heritable phenotypes; thin yellow bars indicate mean heritability. (**C**) Additive genetic variance explained significantly more variance in microbiome phenotypes than host identity or maternal effects. The *y*-axis is ordered by taxonomic level and h^2, as given in table S7. (**D**) For the 32 microbial taxa heritable in our study (*x*-axis) and at least one human study [*y*-axis; (*1*, *2*, *4*–*6*, *32*, *33*)], h^2 was correlated between baboons and humans (Pearson's R = 0.52, P = 0.002).

significantly heritable, some of which were found in only 10% of samples (Fig. 2B; fig. S9, A to C; and table S7). However, more prevalent taxa tended to have higher h^2 (Pearson's R = 0.28, $P = 2.3 \times 10^{-15}$; fig. S9D). The proportion of significantly heritable single-taxon phenotypes was robust across phylogenetically and compositionally aware data transformations [phylogenetic isometric log-ratio (PhILR) transformation = 96% heritable; centered log-ratio (CLR) transformation = 99% heritable; FDR threshold = 0.1; Fig. 2B and tables S8 and S9]. Heritability estimates were correlated between single-taxon phenotypes and CLR-transformed single-taxon phenotypes (Pearson's R = 0.82, $P = 2.3 \times 10^{-69}$), and between single-taxon phenotypes and presence/absence phenotypes (Pearson's R = 0.68, $P = 3.2 \times 10^{-29}$; fig. S9, E and F).

The most heritable phenotype among the single-taxon and community phenotypes was the first PC of a principal coordinates analysis of Bray-Curtis dissimilarities, which captures a global summary of variation in the baboon gut microbiome [h^2 = 0.21; $P = 5.7 \times 10^{-15}$; Fig. 2A; Bray-Curtis PC1 explained 19% of the variance in microbiome composition overall (*17*)]. More closely related ASVs tended to have similar h^2 (Moran's I = 0.0996, P = 0.001; and Pagel's lambda = 0.73, P = 0.001), especially ASVs belonging to the families Prevotellaceae, Lachnospiraceae, and Ruminococcaceae (local Moran's I, $P < 0.05$; fig. S11), suggesting a phylogenetic signal in microbe heritability.

Although h^2 for single-taxon and community phenotypes tended to be low to modest (mean h^2 among the 280 significant phenotypes = 0.068; range = 0.008 to 0.21; Fig. 2C), heritability values for presence/absence traits were significantly higher (paired t test $P = 2.2 \times 10^{-27}$; mean h^2 = 0.077, maximum h^2 = 0.26; Fig. 2B and fig. S9, A, B, C, and F), as were heritability estimates from compositionally aware abundance transformations (paired t test $P = 2.7 \times 10^{-27}$; mean h^2 = 0.084, maximum h^2 = 0.20; Fig. 2B and fig. S9E). Overall, these values are similar to the heritability of social behavioral traits in nonhuman primates (fig. S12 and table S10) and traits with strong social components in humans (*28*, *29*) but exceed most available estimates for fitness in animal populations (*30*).

Across traits, host genotype explained more variance than host identity (paired t test $P = 2.4 \times 10^{-27}$) or maternal effects (paired t test $P = 5.5 \times 10^{-86}$). These results suggest that host genotype is more important in creating familial similarity in baboon microbiome composition than matrilines, even though matrilines form the core kinship units in baboon societies (Fig. 2C and fig. S9, B and C). Further, we found no evidence that microbial transmission between relatives or assortative mating inflates h^2. Parent pairs did not have more similar microbiome composition than non-parent female-male pairs, as would be expected under assortative mating by microbiome composition (Mantel test r = 0.004, P = 0.22; fig. S7B). In addition, accounting for grooming-based social interaction networks (in the subset of models where such networks could be robustly estimated; n = 500) decreased h^2 by only 0.0051 on average and did not significantly improve any models (fig. S7C and table S11). The weak effects of social networks on microbiome similarity were likely due to the longitudinal nature of this dataset. In our population, social effects on microbiome composition are strongest between samples collected in the same month, and samples from social partners separated by long time periods are not especially similar (*18*, *31*).

Humans and baboons share heritable taxa

We next investigated whether similar gut microbiome taxa are influenced by host genotype across baboons and humans, which would suggest that trait heritability in the microbiome is conserved. Heritability estimates were correlated for the 32 microbiome taxa found to be heritable in both our study and in at least one of seven human datasets from five studies [n = 3511 aggregate sample size in total; (*1*, *2*, *4*–*6*, *17*, *32*, *33*)] despite substantial methodological variation in data collection and methods for h^2 estimation (Pearson's R = 0.52, P = 0.002; results are consistent using a linear mixed model that controls for study: b = 0.91, P = 0.014; Fig. 2D and table S12). Shared, heritable taxa include the family Christensenellaceae, one of the most consistently heritable phenotypes in humans [baboon: single-taxon h^2 = 0.12; presence/absence h^2 = 0.20; humans: 0.31 to 0.64; Fig. 2A and fig. S9A; (*1*, *2*, *4*, *6*, *7*, *9*, *34*)]. In contrast to a previous study in humans, heritable taxa did not co-occur more frequently than expected within hosts (*1*). However, more heritable taxa did exhibit higher connectivity in taxon co-occurrence networks (Pearson's R = 0.58, P = 0.006; fig. S13).

Year, season, and host age modify heritability estimates

To understand why microbiome h^2 estimates often vary across studies (*1*, *2*, *4*–*6*), we then investigated social and environmental factors that systematically influence trait heritability. Here, we focused on a refined set of 100 collapsed phenotypes, including the seven community phenotypes and 93 single-taxon phenotypes in which we collapsed phylogenetically nested taxa to the lowest taxonomic level [as described previously (*1*, *2*, *6*); fig. S14 and table S13]. We found that host traits and environmental conditions had substantial effects on h^2. Across years, h^2 calculated for a single year can differ by up to 0.24 compared with h^2 calculated using all years (n = 15 most heritable collapsed phenotypes, evaluated in years with at least 150 individuals and 1000 samples; table S11 and Fig. 3A). For example, although h^2 for the *Christensenellaceae* R-7 group (the collapsed phenotype for Christensenellaceae) was 0.12 across all years, its

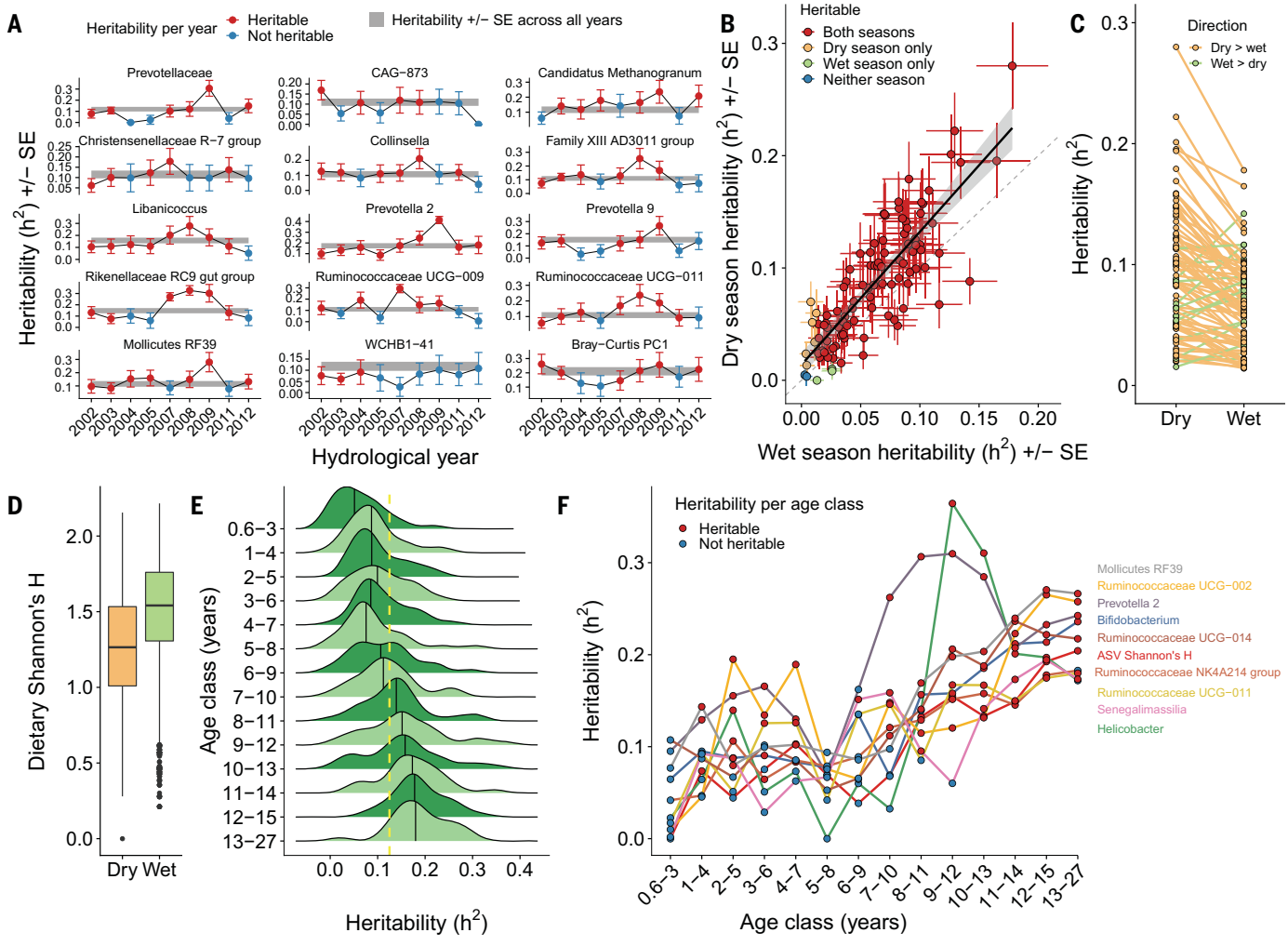

Fig. 3. Heritability estimates are affected by year, season, and host age. (**A**) Heritability estimates varied across years. Panels show h^2 for the 15 most heritable collapsed phenotypes in years with sufficient sample size (>150 baboons and >1000 total samples). (**B**) Heritability estimates for all 100 collapsed phenotypes were highly correlated between seasons (black line; R = 0.83, P = 4.7 × 10^{-27}). Dashed line indicates $x = y$. (**C**) Heritability estimates for collapsed phenotypes were higher in the dry season than in the wet season (n = 89 taxa heritable in both seasons; paired t test P = 4.4 × 10^{-12}). (**D**) Dietary diversity was higher in the wet season (paired t test P = 4.2 × 10^{-5}). (**E**) Heritability increased with age for 29/100 collapsed phenotypes. Each density plot represents the observed h^2 for these 29 collapsed phenotypes across 3-year sliding age classes. The dashed yellow line indicates mean h^2 across all age classes. (**F**) Heritability estimates per age window for the 10 collapsed phenotypes with the steepest increase in h^2 with host age.

annual h^2 estimates ranged from 0.06 (in 2002) to 0.18 (in 2007).

Within years, we also observed systematic effects of wet/dry seasonal dynamics on microbiome heritability. On the basis of the 89 collapsed phenotypes that were heritable in both dry and wet season samples (estimated separately; red points in Fig. 3B), we found that h^2 was, on average, 48% higher in the dry season than in the wet season (paired t test $P = 4.4 \times 10^{-12}$; Fig. 3C) even though h^2 estimates were strongly correlated between seasons (Pearson's $R = 0.81$, $P = 3.5 \times 10^{-22}$; Fig. 3B). These seasonal differences in h^2 may be explained by seasonal changes in phenotypic variance (V_p): Weather in Amboseli is highly variable during the 7-month wet season, with periods of intense rain followed by several weeks with little or no rain, compared with the near invariant dry season. In support of this, V_p for microbiome phenotypes was higher in wet versus dry seasons (paired t test $P = 4.2 \times 10^{-5}$; fig. S15A). Baboons also consume a greater diversity and evenness of food types in the wet season compared with the dry season (linear mixed model; $b = 0.15$, $P = 5.9 \times 10^{-114}$; Fig. 3D). Although diet composition and rainfall per se are included in our models, individuals who eat diverse diets may also experience season-dependent environmental variation that our model does not capture. To test this hypothesis, we stratified the data by dietary diversity and found that heritability estimates were higher in the low–diet-diversity dataset (paired t test $P = 1.0 \times 10^{-11}$; fig. S15, B and C; 72% of samples in the high–diet-diversity dataset were collected in the wet season).

Host characteristics such as age can also modify trait heritability (*13*, *35*). Indeed, we found that for many of the microbiome phenotypes, h^2 increased with host age. When we stratified the 100 collapsed phenotypes into overlapping 3-year age classes of similar sample size (table S14), we found that h^2 changed significantly with age for 32% of phenotypes, and 91% of these phenotypes (29 of 32) resulted in higher h^2 in older animals (linear models $P < 0.05$; Fig. 3E), with a total increase in h^2 of up to 0.24 (Fig. 3F). This observation is driven by both increasing genetic contributions to gut microbiome variation with host age (i.e., increased V_A; linear mixed model, $b = 1.7 \times 10^{-5}$, $P = 0.0085$) and decreasing contributions from residual environmental variance (i.e., decreased V_R; linear mixed model, $b = -2.9 \times 10^{-5}$, $P = 1.5 \times 10^{-4}$). Older baboons ate less diverse diets than younger baboons regardless of season (linear mixed model; effect of age on diet diversity in the wet season: $b = -1.6 \times 10^{-2}$, $P = 1.6 \times 10^{-24}$; effect of age on diet diversity in the dry season: $b = -1.2 \times 10^{-2}$, $P = 2.0 \times 10^{-11}$; fig. S16, A and B). In addition, females exhibited reduced social partner diversity with age (linear mixed model; $b = -0.35$, $P = 1.4 \times 10^{-19}$; fig. S16, C and D). Moreover, microbiome diversity (Shannon's H) also decreased slightly with age (linear mixed model; $b = -0.0063$, $P = 0.024$; fig. S16E) and its h^2 exhibited the sixth strongest increase with age (linear model; $b = 0.013$, $P = 2.5 \times 10^{-5}$; Fig. 3F). A possible explanation for this pattern is behavioral canalization that is not fully captured by the diet composition effects in our models, whereby older baboons increase in behavioral conservatism with age.

Longitudinal sampling affects heritability estimation

Together, our results qualitatively differ from similar research on humans: Instead of a very small number of heritable microbiome phenotypes, we found nearly universal heritability (*1*, *2*, *4*, *6*, *7*, *9*). Further, we explain systematic variation in h^2 on the basis of temporal, environmental, and individual characteristics. These findings suggest that deep, longitudinal

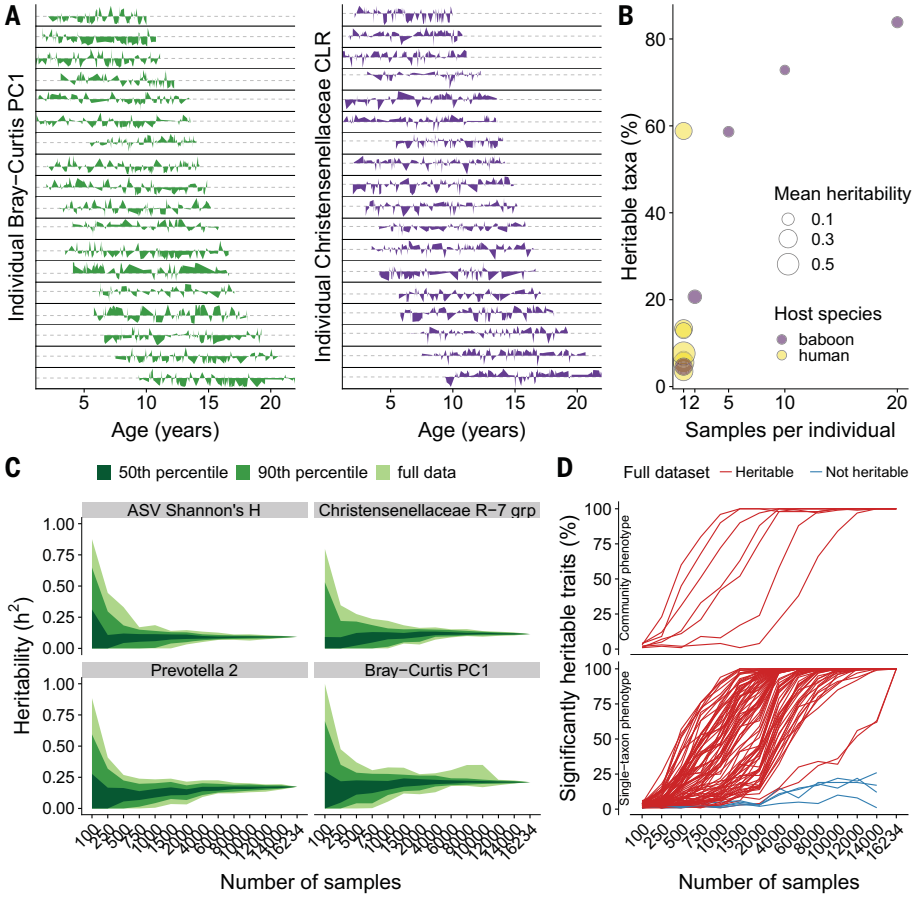

Fig. 4. Microbiome phenotypes are dynamic and sampling design affects heritability estimates. (**A**) Highly heritable microbiome phenotypes fluctuate in abundance (*y*-axis) in individual hosts over time (*x*-axis), as shown by Bray-Curtis PC1 and Christensenellaceae. Each row represents a baboon with >100 samples. (**B**) Longitudinal sampling improves the detection of heritable phenotypes. Purple circles indicate the percent of significantly heritable taxa in our dataset when subset from 1 to 20 samples per individual. Yellow circles are the percentage of significantly heritable microbiome phenotypes in seven human datasets from five studies (*1*, *2*, *4*–*6*, *32*, *33*); note that the plotted points from (*33*) and (*32*) show nearly perfect overlap. (**C**) Heritability varies widely at lower sampling depths, even for highly heritable phenotypes (*x*-axis). The range of h^2 from 100 random subsets at each sampling depth is shown on the *y*-axis. (**D**) The percentage of significantly heritable traits rises with increasing sample size. Plot shows the percentage of models (out of 100 subsamples) that were improved by adding pedigree information. Each line represents one of the 100 collapsed phenotypes.

sampling is required to accurately characterize microbiome heritability and account for potentially extensive temporal variation [Fig. 4A; note that trait heritability was not correlated with its variability across the life course (coefficient of variation in abundance): $R = -0.14$, $P = 0.15$ for $n = 357$ individuals with >10 samples; fig. S17].

In support of the importance of deep longitudinal sampling, we found that sample size and longitudinal sampling affected both our ability to detect heritable microbiome phenotypes and the heritability estimates themselves. Specifically, if we simulated cross-sectional data by randomly subsetting our collapsed phenotype dataset to one sample per individual ($n = 585$ samples, repeated 100 times), we found that <5% of phenotypes were significantly heritable, on average (mean = 4.6%; 95% confidence interval = 3.1 to 6.1%; Fig. 4B and table S12). This proportion is comparable to that described in most human studies but increases with more longitudinal samples per individual (Fig. 4B). Further, when we randomly subsetted our collapsed phenotype dataset to 1000 samples (including repeated samples for some individuals), h^2 estimates fell outside their standard error in the full dataset in an average of 74% of cases (across 100 random subsamples; Fig. 4C, fig. S18, and table S15). Increasing the subset size to 10,000 samples dropped this percentage to 11% (Fig. 4C and fig. S18) and increased the number of significantly heritable phenotypes. With 1000 samples, heritable microbiome phenotypes detected in the full dataset were significantly heritable in only 38% of 100 subsamples, on average (Fig. 4D), but at 10,000 samples, this concordance rose to 98%.

Conclusions

Nearly all gut microbiome taxa are heritable in baboons, including both prevalent and rare taxa. Although the magnitude of these heritability estimates is typically small, some traits exhibit $h^2 > 0.15$ ($n = 59/744$ presence/absence phenotypes; 6/283 single-taxon phenotypes; 1/7 community phenotypes). The universal role played by host genetic variation in our dataset contrasts with previous work in humans finding few heritable taxa (*1*, *2*, *4*, *6*, *7*). These datasets may have had limited power because all human studies to date have been cross-sectional and may have lacked data on key environmental variables that mask or modify heritability levels (*1*, *2*, *4*, *6*, *7*). Further, h^2 for traits detected in both baboons and humans are correlated (Fig. 2D), suggesting that traits with low h^2 in baboons may also be heritable but have gone undetected in humans.

Our findings do, however, agree with the observation that environmental effects on gut microbiome variation are larger than additive genetic effects (*7*). Future work will help to refine our understanding of these environmental influences, including whether they mediate and/or interact with the effects of host genotype. Additionally, as 16*S* rRNA-sequencing data have limited resolution, large-scale metagenomic data will be important for understanding whether individual microbial strains or gene content are also heritable and, perhaps more interestingly, whether microbial genotype affects host heritability. Our work argues for a qualitative change in perspective, from a microbial landscape largely unaffected by host genotype to one in which host genetics play a consistent and sometimes appreciable role. These qualities imply that microbiome traits are therefore visible to natural selection on the host genome.

REFERENCES AND NOTES

1. J. K. Goodrich *et al.*, *Cell* **159**, 789–799 (2014).
2. J. K. Goodrich *et al.*, *Cell Host Microbe* **19**, 731–743 (2016).
3. R. Blekhman *et al.*, *Genome Biol.* **16**, 191 (2015).
4. E. R. Davenport *et al.*, *PLOS ONE* **10**, e0140301 (2015).
5. M. Y. Lim *et al.*, *Gut* **66**, 1031–1038 (2017).
6. W. Turpin *et al.*, *Nat. Genet.* **48**, 1413–1417 (2016).
7. D. Rothschild *et al.*, *Nature* **555**, 210–215 (2018).
8. A. Kurilshikov *et al.*, Large-scale association analyses identify host factors influencing human gut microbiome composition. bioRxiv 173724 [Preprint]. 16 December 2020. https://doi.org/10.1101/2020.06.26.173724.
9. J. K. Goodrich, E. R. Davenport, A. G. Clark, R. E. Ley, *Annu. Rev. Genet.* **51**, 413–433 (2017).
10. S. Lax *et al.*, *Science* **345**, 1048–1052 (2014).
11. B. H. Schlomann, R. Parthasarathy, *Curr. Opin. Microbiol.* **50**, 56–63 (2019).
12. P. M. Visscher, W. G. Hill, N. R. Wray, *Nat. Rev. Genet.* **9**, 255–266 (2008).
13. T. Ge, C.-Y. Chen, B. M. Neale, M. R. Sabuncu, J. W. Smoller, *PLOS Genet.* **13**, e1006711 (2017).
14. S. C. Alberts, J. Altmann, "The Amboseli Baboon Research Project: 40 years of continuity and change," in *Long-Term Field Studies of Primates*, P. M. Kappeler, D. P. Watts, Eds. (Springer, 2012), pp. 261–287.
15. A. M. Bronikowski *et al.*, *Sci. Data* **3**, 160006 (2016).
16. A. C. Markham, V. Guttal, S. C. Alberts, J. Altmann, *Behav. Ecol. Sociobiol.* **67**, 875–884 (2013).
17. Materials and methods are available as supplementary materials.
18. J. Tung *et al.*, *eLife* **4**, e05224 (2015).
19. L. E. Grieneisen, J. Livermore, S. Alberts, J. Tung, E. A. Archie, *Integr. Comp. Biol.* **57**, 770–785 (2017).
20. K. Berer *et al.*, *Proc. Natl. Acad. Sci. U.S.A.* **114**, 10719–10724 (2017).
21. A. E. Mann *et al.*, *ISME J.* **14**, 609–622 (2020).
22. W. A. Walters *et al.*, *Proc. Natl. Acad. Sci. U.S.A.* **115**, 7368–7373 (2018).
23. A. R. Gilmour, "ASREML for testing fixed effects and estimating multiple trait variance components," in Proceedings of the Association for the Advancement of Animal Breeding and Genetics (AABG, 1997), vol. 12, pp. 386–390.
24. L. E. B. Kruuk, *Philos. Trans. R. Soc. Lond. B Biol. Sci.* **359**, 873–890 (2004).
25. A. J. Wilson *et al.*, *J. Anim. Ecol.* **79**, 13–26 (2010).
26. A. J. Wilson, *J. Evol. Biol.* **21**, 647–650 (2008).
27. L. E. B. Kruuk, J. D. Hadfield, *J. Evol. Biol.* **20**, 1890–1903 (2007).
28. N. Barban *et al.*, *Nat. Genet.* **48**, 1462–1472 (2016).
29. D. Cesarini, P. M. Visscher, *NPJ Sci. Learn.* **2**, 4 (2017).
30. A. P. Hendry, D. J. Schoen, M. E. Wolak, J. M. Reid, *Annu. Rev. Ecol. Evol. Syst.* **49**, 457–476 (2018).
31. T. Ren, L. E. Grieneisen, S. C. Alberts, E. A. Archie, M. Wu, *Environ. Microbiol.* **18**, 1312–1325 (2016).
32. T. Yatsunenko *et al.*, *Nature* **486**, 222–227 (2012).
33. P. J. Turnbaugh *et al.*, *Nature* **457**, 480–484 (2009).
34. J. L. Waters, R. E. Ley, *BMC Biol.* **17**, 83 (2019).
35. R. Plomin, I. J. Deary, *Mol. Psychiatry* **20**, 98–108 (2015).
36. A. Gonzalez *et al.*, *Nat. Methods* **15**, 796–798 (2018).
37. L. Grieneisen *et al.*, Data for: Gut microbiome heritability is nearly universal but environmentally contingent, Zenodo (2021); https://doi.org/10.5281/zenodo.4662081.

ACKNOWLEDGMENTS

We thank J. Altmann for her stewardship of the Amboseli Baboon Research Project (ABRP) and for collecting the fecal samples used in this manuscript (see complete ABRP acknowledgments at https://amboselibaboons.nd.edu/acknowledgements/); K. Pinc for ABRP database design; T. Voyles, A. Dumaine, Y. Zhang, M. Rao, T. Vilgalys, A. Lea, N. Snyder-Mackler, P. Durst, J. Zussman, G. Chavez, S. Mukherjee, and R. Debray for fecal sample processing; and three anonymous reviewers for their constructive comments. We also thank the Kenya Wildlife Service, the National Council for Science, Technology, and Innovation, and the National Environment Management Authority for permission to conduct research and collect biological samples in Kenya. We thank the University of Nairobi, Institute of Primate Research, National Museums of Kenya, the Amboseli-Longido pastoralist communities, the Enduimet Wildlife Management Area, Ker & Downey Safaris, Air Kenya, and Safarilink for support in Kenya. The research in this study was approved by the institutional animal care and use committees at Duke University, Princeton University, and the University of Notre Dame, and adhered to the laws and guidelines of the Kenyan government. **Funding:** This work was directly supported by NSF DEB 1840223 (E.A.A., J.A.G.), NIH R21 AG055777 (E.A.A., R.B.), NIH R01 AG053330 (E.A.A.), and NIGMS R35 GM128716 (R.B.). We also acknowledge support from the University of Minnesota Grand Challenges in Biology Postdoctoral Fellowship (to L.G.), the Duke University Population Research Institute P2C-HD065563 (pilot award to J.T.), and Notre Dame's Eck Institute for Global Health (E.A.A.) and Environmental Change Initiative (E.A.A.). Since 2000, ABRP has been supported by NSF and NIH, including IOS 1456832 (S.C.A.), IOS 1053461 (E.A.A.), DEB 1405308 (J.T.), IOS 0919200 (S.C.A.), DEB 0846286 (S.C.A.), DEB 0846532 (S.C.A.), IBN 0322781 (S.C.A.), IBN 0322613 (S.C.A.), BCS 0323553 (S.C.A.), BCS 0323596 (S.C.A.), P01AG031719 (S.C.A.), R21AG049936 (J.T., S.C.A.), R03AG045459 (J.T., S.C.A.), R01AG034513 (S.C.A.), R01HD088558 (J.T.), and P30AG024361 (S.C.A.). We also thank Princeton University, the Chicago Zoological Society, the Max Planck Institute for Demographic Research, the L.S.B. Leakey Foundation, and the National Geographic Society. **Author contributions:** L.G., R.B., E.A.A., L.B.B., J.A.G., and J.T. designed the research; S.C.A., E.A.A., J.T., R.B., L.B.B., M.D., T.J.G., V.Y., D.J., N.G., J.B.G., N.H.L., L.R.G., T.L.W., R.S.M., J.K.W., L.S., and J.A.G. produced the data; L.G., J.R.B., M.D., T.J.G., and D.J. analyzed the data; L.G., R.B., J.T., and E.A.A. wrote the manuscript with important contributions from all authors. **Competing interests:** The authors declare no competing interests. **Data and materials availability:** Our data and code are publicly available, but the original biological and DNA samples cannot be shared due to restrictions on third-party sharing for CITES-regulated samples exported from Kenya. The fecal samples and DNA extracts used in this study are subject to material transfer agreements between Duke University and the University of Notre Dame in the United States and the Kenya Wildlife Service in Kenya. These biological materials are maintained at J.T.'s laboratory at Duke University and E.A.A.'s laboratory at the University of Notre Dame and can only be shared with third parties with prior written authorization from the Kenya Wildlife Service. 16*S* rRNA gene sequences are deposited on EBI-ENA (project ERP119849) and Qiita [study 12949; (*36*)]. Analyzed data and code are available on Zenodo (*37*).

SUPPLEMENTARY MATERIALS

science.sciencemag.org/content/373/6551/181/suppl/DC1
Materials and Methods
Figs. S1 to S18
Tables S1 to S15
References (*38*–*129*)
MDAR Reproducibility Checklist

View/request a protocol for this paper from *Bio-protocol*.

18 February 2020; resubmitted 25 January 2021
Accepted 17 May 2021
10.1126/science.aba5483

Gut microbiome heritability is nearly universal but environmentally contingent

Laura Grieneisen, Mauna Dasari, Trevor J. Gould, Johannes R. Björk, Jean-Christophe Grenier, Vania Yotova, David Jansen, Neil Gottel, Jacob B. Gordon, Niki H. Learn, Laurence R. Gesquiere, Tim L. Wango, Raphael S. Mututua, J. Kinyua Warutere, Long'ida Siodi, Jack A. Gilbert, Luis B. Barreiro, Susan C. Alberts, Jenny Tung, Elizabeth A. Archie and Ran Blekhman

Science **373** (6551), 181-186.
DOI: 10.1126/science.aba5483

Baboons inform on human gut microbiota

Commensal bacteria are found throughout an organism, but it is not known whether associations between gut bacteria and their host are heritable. Grieneisen *et al.* examined changes in the microbiomes of 585 wild baboons from fecal samples collected over 14 years (see the Perspective by Cortes-Ortiz and Amato). Almost all microbiome traits tested demonstrated some level of statistically significant heritability. Most heritability values were low but varied over time correlating with the age of the host. Baboons live in an environment similar to that postulated for early humans and have a microbiome similar to that of humans. Thus, this heritability of the microbiome may reflect similar genetic determinants in humans, for which similar datasets are not available.

Science, aba5483, this issue p. 181; see also abj5287, p. 159

Science (print ISSN 0036-8075; online ISSN 1095-9203) is published by the American Association for the Advancement of Science, 1200 New York Avenue NW, Washington, DC 20005. The title *Science* is a registered trademark of AAAS.