Cell Host & Microbe
Review

Microbiota and Host Nutrition across Plant and Animal Kingdoms

Stéphane Hacquard,[1,12] Ruben Garrido-Oter,[1,2,3,12] Antonio González,[4,12] Stijn Spaepen,[1,12] Gail Ackermann,[4] Sarah Lebeis,[5] Alice C. McHardy,[2,3,6,*] Jeffrey L. Dangl,[7,8,*] Rob Knight,[4,9,*] Ruth Ley,[10,11,*] and Paul Schulze-Lefert[1,3,*]
[1]Department of Plant Microbe Interactions, Max Planck Institute for Plant Breeding Research, 50829 Cologne, Germany
[2]Department of Algorithmic Bioinformatics, Heinrich Heine University Duesseldorf, 40225 Duesseldorf, Germany
[3]Cluster of Excellence on Plant Sciences (CEPLAS), Max Planck Institute for Plant Breeding Research, 50829 Cologne, Germany
[4]Department of Pediatrics, University of California San Diego, La Jolla, CA 92093, USA
[5]Department of Microbiology, University of Tennessee, Knoxville, TN 37996-0845, USA
[6]Computational Biology of Infection Research, Helmholtz Center for Infection Research, 38124 Braunschweig, Germany
[7]Howard Hughes Medical Institute and Department of Biology, University of North Carolina at Chapel Hill, Chapel Hill, NC 27599, USA
[8]Curriculum in Genetics and Molecular Biology, University of North Carolina at Chapel Hill, Chapel Hill, NC 27599, USA
[9]Department of Computer Sciences and Engineering, University of California San Diego, La Jolla, CA 92093, USA
[10]Department of Molecular Biology and Genetics, Cornell University, Ithaca, NY 14853, USA
[11]Department of Microbiology, Cornell University, Ithaca, NY 14853, USA
[12]Co-first author
*Correspondence: alice.mchardy@helmholtz-hzi.de (A.C.M.), dangl@email.unc.edu (J.L.D.), robknight@ucsd.edu (R.K.), rel222@cornell.edu (R.L.), schlef@mpipz.mpg.de (P.S.-L.)
http://dx.doi.org/10.1016/j.chom.2015.04.009

Plants and animals each have evolved specialized organs dedicated to nutrient acquisition, and these harbor specific bacterial communities that extend the host's metabolic repertoire. Similar forces driving microbial community establishment in the gut and plant roots include diet/soil-type, host genotype, and immune system as well as microbe-microbe interactions. Here we show that there is no overlap of abundant bacterial taxa between the microbiotas of the mammalian gut and plant roots, whereas taxa overlap does exist between fish gut and plant root communities. A comparison of root and gut microbiota composition in multiple host species belonging to the same evolutionary lineage reveals host phylogenetic signals in both eukaryotic kingdoms. The reasons underlying striking differences in microbiota composition in independently evolved, yet functionally related, organs in plants and animals remain unclear but might include differences in start inoculum and niche-specific factors such as oxygen levels, temperature, pH, and organic carbon availability.

Physiological Functions of the Vertebrate Gut and Plant Roots

The vertebrate gut and plant roots evolved independently in animal and plant kingdoms but serve a similar primary physiological function in nutrient uptake (Figure 1). One major difference between plant and animal nutritional modes is their distinct energy production strategy. Plants are autotrophs, producing their own energy through photosynthesis (carbohydrate photo-assimilates), while animals rely entirely on the energy originally captured by other living organisms (heterotrophs). Long-distance transport mechanisms ensure the distribution of carbohydrate photo-assimilates from chloroplasts in leaves to all other body parts, including roots. Nutrient acquisition by roots to support plant growth is therefore almost exclusively limited to uptake of mineral ions and water from soil. In contrast, the mammalian gut has evolved to facilitate the uptake of simple sugars, amino acids, lipids, and vitamins in addition to ions. It is typically compartmentalized into sections with low microbial biomass in which the products of host enzymatic activity are absorbed (i.e., the human small intestine, SI) and a section for the uptake of microbe-derived fermentation products (human large intestine or hindgut, LI).

A significant fraction of the soil nutritive complement and of the dietary intake remains unavailable for plants and animals, respectively, and this defines their dietary constraints. Critical nutrients for plant growth and productivity in soil are nitrogen and phosphorus. However, plant roots can absorb only inorganic nitrogen and orthophosphate (Pi), although phosphorus is abundant in soil both in inorganic and organic pools. Pi can be assimilated via low-Pi-inducible (high-affinity) and constitutive Pi uptake systems (low-affinity) (Lambers et al., 2008; López-Arredondo et al., 2014). Plant species adapted to neutral or higher soil pH, and more aerobic soils have a preference for nitrate and deploy two nitrate uptake and transport systems that act in coordination. By contrast, plants adapted to low pH (reducing soil) as found in forests or the arctic tundra appear to assimilate ammonium or amino acids (Maathuis, 2009). Similarly, a fraction of normal human dietary intake remains undigested and therefore non-bioavailable (fiber). These non-digestible components include plant cell wall constituents such as cellulose, hemicellulose, xylan, and pectin, and certain polysaccharides such as β-glucan, inulin, and oligosaccharides that contain bonds that cannot be cleaved by mammalian hydrolytic enzymes (Tungland and Meyer, 2002).

Plant roots and animal guts are colonized by diverse microbial classes, including bacteria and archaea, fungi, oomycetes, as well as viruses (Table 1). These communities can be regarded as the host's extended genome, providing a huge range of potential functional capacities (Berendsen et al., 2012; Gill et al., 2006; Qin et al., 2010; Turner et al., 2013). Here we focus on

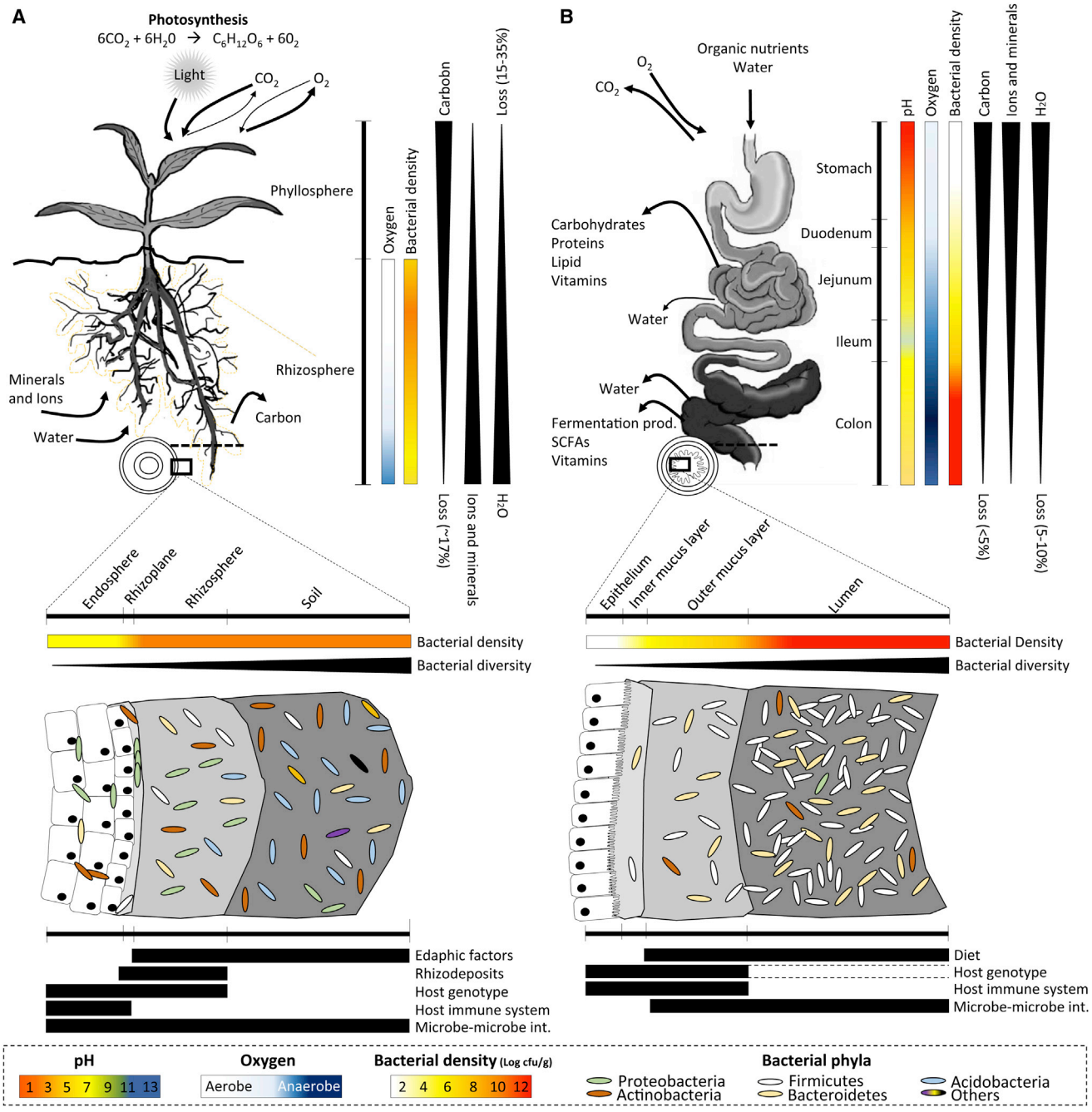


Figure 1. Physiological Functions of the Plant Roots and Human Gut in Nutrient Uptake, Spatial Aspects of Microbiota Composition, and Factors Driving Community Establishment

(A and B) Spatial compartmentalization of the plant root microbiota (A) and the human gut microbiota (B). Upper panels: the major nutrient fluxes are indicated, as well as pH and oxygen gradients in relation with the bacterial density. Lower panels: compartmentalization of the microbiota along the lumen-epithelium continuum in the gut or along the soil-endosphere continuum in the root. For each compartment, the bacterial density, the bacterial diversity, and the major represented phyla are represented for both the gut and the root organs. The main factors driving community establishment in these distinct compartments are depicted with black bars. The gut drawing is adapted from Tsabouri et al. (2014) with permission from the publisher.

bacterial microbiotas because these were shown to form reproducible taxonomic assemblies in animal and plant individuals with well-defined functions.

In plant roots, the microbiota mobilizes and provides nutrients by increasing nutrient bioavailability from soil (Bulgarelli et al., 2013). Non-nutritional functions include increased host tolerance to biotic stresses, e.g., against soil-borne pathogens (Mendes et al., 2011), and likely abiotic stresses. In addition, the root microbiota can also affect plant fitness by impacting flowering plasticity (Panke-Buisse et al., 2015; Wagner et al., 2014).

Table 1. Percentage of Shotgun Metagenome Reads Assigned to Each Kingdom of Life across Metagenome Studies

	Cucumber[a]	Wheat[a]	Soybean[b]	Wheat[c]	Oat[c]	Pea[c]	Barley[d]	Gut[e]
Bacteria	99.36	99.45	96	88.5	77.3	73.7	94.04	99.1
Archaea	0.02	0.02	<1	<0.5	<0.5	<0.5	0.054	
Eukaryotes	0.54	0.48	3	3.3	16.6	20.7	5.90	<0.1

[a]Ofek-Lalzar et al. (2014) (metagenomics of rhizoplane samples).
[b]Mendes et al. (2014) (metagenomics of rhizosphere samples).
[c]Turner et al. (2013) (metatranscriptomics of rhizosphere samples).
[d]Bulgarelli et al. (2015) (metagenomics of rhizosphere samples).
[e]Qin et al. (2010) (metagenomics of gut samples).

Similarly, the gut microbiota has a major role in host nutrition. It contributes nutrients and energy to the host via fermentation of indigestible polysaccharides into short-chain fatty acids (SCFAs) in the colon (Martins dos Santos et al., 2010; Tremaroli and Bäckhed, 2012). The human LI has incomplete peristalsis and a longer retention time, allowing fermentative microbiota to break down complex glycan bonds and liberate additional energy from the diet (Stevens and Hume, 1998). Additionally, gut microbiota provide essential vitamins to the host and modulate the absorptive capacity of the intestinal epithelium. An additional common feature of the gut and root microbiota is their protective role by competitive exclusion against invasion by opportunistic pathogens (Kamada et al., 2013).

Homeostatic balance between both microbe-microbe and host-microbe interactions is critical for a healthy host-microbiota relationship. Alteration of this balance via perturbation of the gut or the plant microbiota composition (microbial dysbiosis) may represent an important mechanism of disease (Martins dos Santos et al., 2010; Kemen, 2014; Sekirov et al., 2010). In plants, a healthy status is the norm, and soil-resident microbes contribute to plant health. This is illustrated by a higher disease severity following pathogen inoculation when plants are grown in pasteurized compared to non-pasteurized soils (Weller et al., 2002). In addition, so-called disease-suppressive soils protect plants against particular soil-borne pathogens. For example, specific bacterial genera belonging to gamma-Proteobacteria were associated with a high level of soil disease suppressiveness. The underlying mechanisms comprise competition between soil-borne microbes for plant-derived nutrients and antimicrobial compound production (Berendsen et al., 2012; Mendes et al., 2011). In the gut, commensal microbes can also suppress pathogen invasion through secretion of antimicrobial compounds, alteration of local pH, or stimulation of host immunity (Kamada et al., 2013).

Compartmentalization of the Gut and Root Microbiota

Relevant biotic and abiotic gradients exist in both the gut and root, leading to microbial compartmentalization (Figure 1). Along the soil-root continuum, four compartments can be distinguished: soil, rhizosphere, rhizoplane, and endosphere (Figure 1A). Bacterial diversity in soil is high, with estimates suggesting that >2,000 species populate 0.5 g of soil (Schloss and Handelsman, 2006). The rhizosphere corresponds to the zone of soil directly influenced by root exudation, while the root compartment can be separated in two distinct niches, rhizoplane and endosphere. The rhizoplane harbors a suite of microbes that tightly adhere to the root surface, while the endosphere is composed of microbes inhabiting the interior of roots. Microbial density is high in the rhizosphere, and species richness gradually decreases along the soil-endosphere continuum (Bulgarelli et al., 2012, 2015; Edwards et al., 2015; Lundberg et al., 2012) (Figure 1A). Therefore, the bacterial community shifts from a dense and diverse soil-borne community to a host-adapted community with reduced diversity.

A spatial heterogeneity of microbial density exists along the digestive track (Stearns et al., 2011). Densities are lowest in the stomach and duodenum (proximal SI) (10^1–10^3 bacteria per gram of content) and increase along the length of the SI with a higher density in the distal ileum (10^4–10^7 bacteria per gram). Cell densities in the LI can reach 10^{12}–10^{13} bacteria per gram of content, representing the highest density recorded so far in any environment and exceeding the density detected in the rhizosphere by 2–3 orders of magnitude. Although the density is high, the diversity is relatively low (Stearns et al., 2011; Walter and Ley, 2011). Using low-error 16S rRNA gene sequencing (LEA-seq) of the human fecal gut microbiota (low depth coverage), the number of bacterial species is estimated at 101 ± 27, which is in alignment with estimates of culture-based techniques (Faith et al., 2013; Mitsuoka, 1992). Compartmentalization exists also from the inside to the outside of the intestinal tube, defined by the intestinal lumen, mucus, and epithelial surface. Similar to the compartmentalization in the root, a decrease in bacterial density is observed from the lumen to the epithelial surface (Swidsinski et al., 2005, Van den Abbeele et al., 2011; Zhang et al., 2014) (Figure 1B). In the LI, the mucus is subdivided into an inner firmly adherent layer largely devoid of bacteria and an outer layer that is looser and non-adherent and allows some microbial colonization (Johansson et al., 2008).

Community Structure of the Vertebrate Gut and Plant Root Microbiota

Where Do They Come from?

A relevant difference for experimentation on the plant root and vertebrate gut microbiota is the ease with which the start inoculum of the root microbiota can be defined. This is due to a predominant horizontal acquisition of root endophytes from the surrounding soil biome, although in some plant species there is evidence for additional vertical transmission of seed-borne endophytes (Barret et al., 2014). These endophytes mainly belong to Proteobacteria and can colonize seeds via different colonization routes, including flowers, fruits as well as roots, leaves, and stems (Truyens et al., 2015). Even though vertical

transmission in mammals is not as explicit as in plants (none are transferred with the germline), vertical transmission nevertheless occurs. The transmission from parent to offspring results from the birth process itself, from milk, and from the close contact that comes from parental care (Unger et al., 2015). In humans, vaginal birth inoculates the newborn with a set of strains that can be matched to the mother, whereas caesarean section results in colonization with skin microbes originating from various caregivers (Dominguez-Bello et al., 2010). Breast milk is also an important source of microbiota and antibodies that shape the gut microbiome (Newburg and Morelli, 2015), and introduction of solid foods brings rapid shifts in the bacterial community composition toward an adult-like microbiome (Koenig et al., 2011). Vertical transmission from mother to infant gut microbiota is sometimes behaviorally increased in mammals by feeding mother's fecal matter to their infants. In koalas, for instance, this transmission is believed to participate in the digestion of eucalyptus (Osawa et al., 1993). Additionally, group living is known to aid the transmission of commensal microbes between members of family groups (humans), troupes (primates), and most likely herds as well. Co-habitation in humans leads to sharing of microbiota, which is enhanced when dogs also co-habit in the same house (Song et al., 2013). Ironically, hygiene measures aimed at reducing pathogen transmission may have had broad negative impacts on the transmission of commensals and may underlie the loss of diversity observed in the West (Blaser and Falkow, 2009).

Who Are They?

Despite the vast prokaryotic biodiversity found in the biosphere (currently >80 bacterial phyla are described), the host-associated microbiota is dominated numerically by a few phyla. The rhizosphere and the root endophytic compartment of unrelated plant species is often enriched for bacteria belonging to three main phyla (Proteobacteria, Actinobacteria, and Bacteroidetes). In contrast, abundant soil bacteria belonging to the phylum Acidobacteria are excluded from the endophytic compartment (Bulgarelli et al., 2013). Compared with the surrounding soil, microbiota members belonging to the phylum Proteobacteria are consistently enriched in the rhizosphere/endosphere compartments of monocotyledonous and dicotyledonous plants, including perennial and annual plants (Bulgarelli et al., 2012, 2015; Edwards et al., 2015; Lundberg et al., 2012; Ofek-Lalzar et al., 2014; Peiffer et al., 2013; Schlaeppi et al., 2014; Shakya et al., 2013; Zarraonaindia et al., 2015). This likely reflects niche adaptation (nutrient availability, oxygen levels) and the ability to efficiently invade and persist inside or outside the roots of divergent plant species. Firmicutes and Bacteroidetes are by far the two most-abundant phyla detected in adult human and mouse feces. Other phyla represented include the Actinobacteria, Verrucomicrobia, and a number of less-abundant phyla such as the Proteobacteria, Fusobacteria, and Cyanobacteria (Eckburg et al., 2005). Similar to the rhizosphere compartment, the mucus layer of the gut represents a particular niche favoring the proliferation of specialized inhabitants. It has been estimated that at least 1% of the gut microbiota can degrade mucins as a source for carbon and nitrogen (Hoskins and Boulding, 1981). Select types of bacteria can also attach to mucins, such as *Bifidobacterium bifidum*, which has the ability to stimulate mucin production via butyrate-induced expression of *MUC2*, while others can degrade the nine-carbon sugar sialic acid found in host glycoconjugates (Almagro-Moreno and Boyd, 2009; Gaudier et al., 2004; Leitch et al., 2007).

Are There Structural Similarities across Diverse Host-Associated Microbial Communities?

Striking physiological (dis-)similarities exist between organs dedicated to nutrient acquisition in hosts belonging to different taxonomic lineages. However, the extent to which microbial communities living in association with phylogenetically divergent hosts overlap with each other is largely unknown. In an attempt to unravel host-specific and conserved signatures in the microbiota, we retrieved and re-analyzed the raw sequencing data contributed by 14 previous large-scale 16S rRNA gene survey studies (Table S1). These comprise >3,200 samples from more than 40 different host species, including human, other mammals, and fish gut, as well from the root and rhizosphere of the flowering plant *Arabidopsis thaliana* and relative species, maize, rice, barley, and grapevine. In addition, we included samples from several species of cnidarian hydra, a freshwater basal animal featuring a gut forming a hollow cavity within the body with one opening, the mouth.

To analyze the data, we followed the QIIME (Caporaso et al., 2010) closed-reference protocol and used SortMeRNA (Kopylova et al., 2012) to cluster the sequences into operational taxonomic units (OTUs) at 97% sequence similarity (see Supplemental Experimental Procedures). Analyses of beta-diversity using principal coordinate analysis (PCoA) revealed a clear clustering of samples according to their respective host species (Figure 2A; Supplemental Experimental Procedures). Although all samples are derived from organs with a dedicated function in nutrient uptake, we found striking qualitative differences between their associated microbial communities. This disparity can be explained by the increased abundance of members of the Bacteroidetes phylum in the mammalian stool samples (particularly those belonging to the orders Bacteroidales and Clostridiales) and the enrichment of members of the families Pseudomonadaceae, Streptomycetaceae, and Comamonadaceae in the rhizosphere and plant root compartments (Figure 3). Intriguingly, the bacterial communities in the fish gut are more closely related to those in the root and rhizosphere samples than to the mammalian gut, partially due to an increased abundance in Proteobacteria (45.08% and 54.44% in root-associated samples and fish gut, respectively, compared with 4.20% in the case of the human gut; Figure 4). In addition, the microbial communities from infant gut (from Koenig et al., 2011) are more closely related to those of plant roots (and therefore soil microbiota) than those associated to adults (Figure S1). Together, this suggests that shared environmental and physiological features, rather than phylogenetic relatedness of the hosts, are decisive for community establishment.

Analysis of alpha-diversity (Figures 2B and 3B) shows that the bacterial richness is low in the gut of aquatic organisms and higher in the root and in the rhizosphere of different plant species, consistent with the bacterial diversity detected in their respective surrounding environments (aquatic versus soil environments; Curtis et al., 2002). For all plant species surveyed, the bacterial diversity is lower in the endosphere compartment (root) compared to the rhizosphere compartment (Figures 2B), in concordance with previous studies (Bulgarelli et al., 2012;

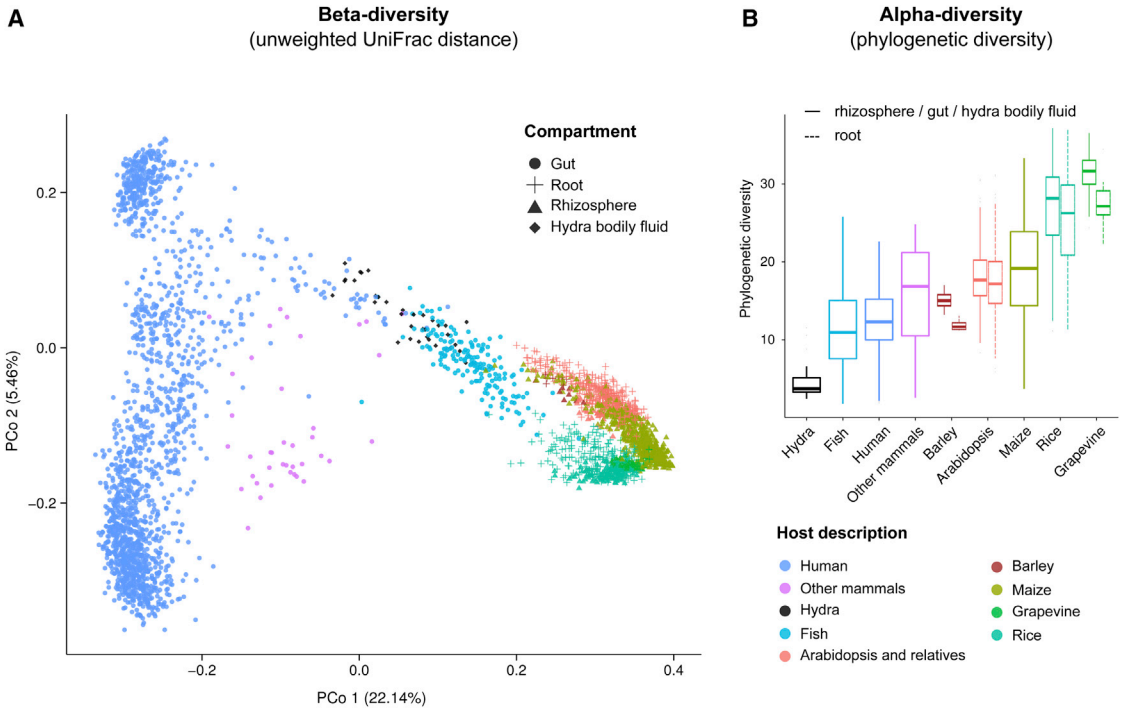


Figure 2. Alpha- and Beta-Diversity Analyses

(A) Principal coordinate analysis (PCoA) of pairwise unweighted UniFrac distances between samples. The color and shape of each point represent the host and compartment, respectively.

(B) Comparison of alpha-diversity between hosts based on the whole tree phylogenetic diversity index (PD), sorted by ascending order of complexity. See Table S1 for more information about the individual host species included in each study.

Edwards et al., 2015; Lundberg et al., 2012). The extent of this gradient in diversity, as well as the differentiation between the two compartments, appears to be dependent on the plant species, indicating a strong host-dependent effect on community establishment.

A phylogenetic comparison of the abundant community members across hosts (OTUs, with a relative abundance higher than 0.1% on average) reveals clear qualitative structural differences between mammalian gut and plant root and rhizosphere samples (Figure 5). These distinct sets of bacterial communities show virtually no overlap even at high taxonomic levels. Samples obtained from human and mammalian guts are dominated by OTUs belonging to the orders Bacteroidales and Clostridiales (34.55% and 51.26% relative abundances, respectively), while these are almost completely absent in the root and rhizosphere samples (0.70% and 0.80%, respectively). This striking difference in community composition in independently evolved, yet functionally related, gut and root organs might be explained by adaptations to specific host and environmental needs, including niche-specific factors such as oxygen levels, pH, and organic carbon availability. Our findings also make a direct transfer and persistence of microbiota members from numerous root-derived dietary plant products in the human gut unlikely.

Do They Fluctuate over Time?

Despite the fact that infancy or the seedling stage for plants are critical windows for microbiota assembly, very little is known about the earliest steps driving host colonization by pioneer bacteria. Assembly of the infant gut microbiome begins at birth (early reports described it as chaotic), and diversity levels slowly increase until ~2–3 years of age (Koenig et al., 2011; Palmer et al., 2007; Yatsunenko et al., 2012). Sampling from birth to 2.5 years of age revealed the following: (i) community richness increased gradually over time, (ii) the use of antibiotics, changes in diet, and infections led to jumps from one stable consortium of species to another, and (iii) members of the Bacteroidetes phylum were co-dominant with members of the Firmicutes phylum after the introduction of solid foods (Koenig et al., 2011). The adult-like microbiota is characterized by a greater stability (David et al., 2014a; Spor et al., 2011). About 60% of the bacterial strains in the intestine are detected over a 5-year time frame, and Bacteroidetes and Actinobacteria were identified as the most stable phyla (Faith et al., 2013). In contrast to the chaotic microbial succession described for the infant gut, the structure of the root microbiota during the plant life cycle appears rather stable. Despite a higher variability observed during the seedling stage (Chaparro et al., 2014), microbiota acquisition from soil appears to occur relatively rapidly, initiating within 24 hr after sowing and approaching a steady state within 2 weeks (Edwards et al., 2015). Once established, there is little evidence for dramatic changes even late in the life cycle of annual *A. thaliana* plants, when organic carbon and nitrogen are spatially re-allocated during the transition from vegetative to reproductive growth for seed formation (Lundberg et al., 2012). This surprising stability might be explained by the sessile nature of plants, together with a rather stable soil-borne inoculum source, which prevents extreme fluctuations in input communities throughout

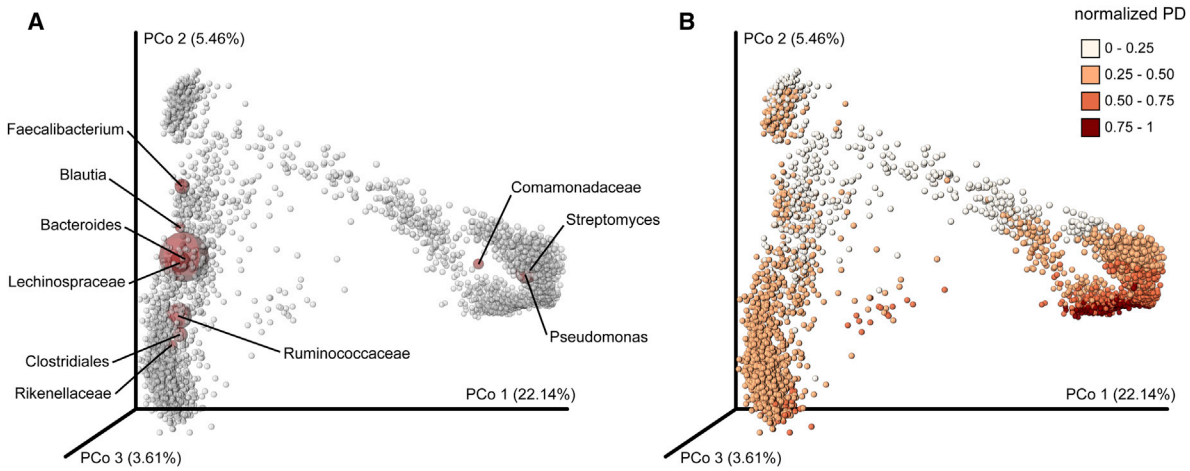


Figure 3. 3D PCoA Plots

(A) Biplots depicting the taxa with the largest contribution to the ordination space (order Clostridiales; families Ruminococcaceae, Rikenellaceae, Lechinospraceae, Comamonadaceae; genera Streptomyces, Pseudomonas, Bacteroides, Blautia, Faecalibacterium).

(B) PCoA plot showing the alpha-diversity variation as measured by the PD index across all samples included in the study.

a rapid annual plant's life cycle. Whether this also applies to longer-lived perennials and to repeated croppings of the same species at the same location remains to be further substantiated (Donn et al., 2015).

Major Factors Driving Community Establishment and Composition

Inter-individual differences in the gut and the plant microbiota are likely to be dictated by many modulating factors, including environmental parameters but also diet/soil-type, microbe-microbe interactions, host genotype, and host immune system (Figure 1).

Environmental Factors

pH. Bacterial community composition is strongly correlated with differences in soil pH, with soils at near-neutral pH showing the highest microbial diversity (Fierer and Jackson, 2006). Roots can acidify the rhizosphere up to two pH units compared to the surrounding soil through release of protons, bicarbonate, organic acids, and CO_2 (Hinsinger et al., 2003). Along the digestive tract, the increase in bacterial titer can be attributed to several factors, such as pH and bile acids. The pH is very low in the stomach (pH 1.5–5), restricting bacterial growth, increases in the SI (duodenum pH 5–7, jejunum 7–9, ileum 7–8) and drops in the colon (pH 5–7) (Walter and Ley, 2011) (Figure 1B). Many types of bacteria, in both the gut and the soil, are sensitive to pH, and this is thought to structure communities to a large degree (Duncan et al., 2009), although it is difficult to disentangle the exact contribution of pH on the overall community structure due to likely interaction with many other factors.

Oxygen. Although both gut and root systems are dedicated for nutrient uptake, O_2 levels are controlled in opposing directions. In the vertebrate gut, luminal microbes generally face anaerobic conditions favoring fermentative metabolism, while in soil and along the root (micro-)aerobic conditions are found (Figure 1). This might be a major factor explaining structural and functional differences between the microbiota of the vertebrate gut and plant roots (Figure 5). The gut microbiota of healthy individuals is dominated by anaerobic bacteria, which outnumber aerobic and facultative anaerobic bacteria by a factor of 100–1,000:1 (Quigley and Quera, 2006), while the root microbiota is enriched for Proteobacteria, a phylum dominated by aerobic species. Consistent with this, genes encoding high-affinity oxidases that use O_2 as a terminal electron acceptor are overrepresented in gut metagenomes, whereas those encoding low-affinity oxidases are enriched in soil metagenomes (Morris and Schmidt, 2013). It is arguably in the host's interest to limit respiration, because (i) limiting respiration will control bacterial growth and (ii) promoting fermentation will result in SCFA availability. Nonetheless, there is a biologically relevant gradient of oxygen levels in both the soil and the gut that is likely to influence microbial community structure at the micro-levels. Despite the fact that plant roots generally face (micro-)aerobic conditions, soil O_2 levels can also fluctuate as a function of soil wetting/drying (Noll et al., 2005), with anoxic niches in the center of soil aggregates. Similarly, a higher O_2 concentration is found at the surface of the epithelium compared with the lumen. Some facultative aerobes can grow along this oxygen gradient by respiring O_2 close to the epithelium using flavins and thiols as electron shuttles to respire at "long distance" (Khan et al., 2012).

Temperature. While thermal stability exists in the gut of mammals (endotherm), higher temperature fluctuation is observed for plants or ectothermic animals that rely on the external temperature to regulate their internal body temperature. It has been reported that the bacterial community in soil is modulated by temperature (Bárcen as-Moreno et al., 2009), although plant microbiota functions must remain stable under a wide range of temperatures.

Nutritional Drivers

For both plant roots and vertebrate guts, diet (for plants, soil type defines the diet) is a major driver for microbial community structure (Bulgarelli et al., 2012; Cotillard et al., 2013; Carmody et al., 2015; David et al., 2014b; Edwards et al., 2015; Ley et al., 2008a; Lundberg et al., 2012; Muegge et al., 2011; Schlaeppi et al., 2014; Peiffer et al., 2013; Turnbaugh et al., 2009).

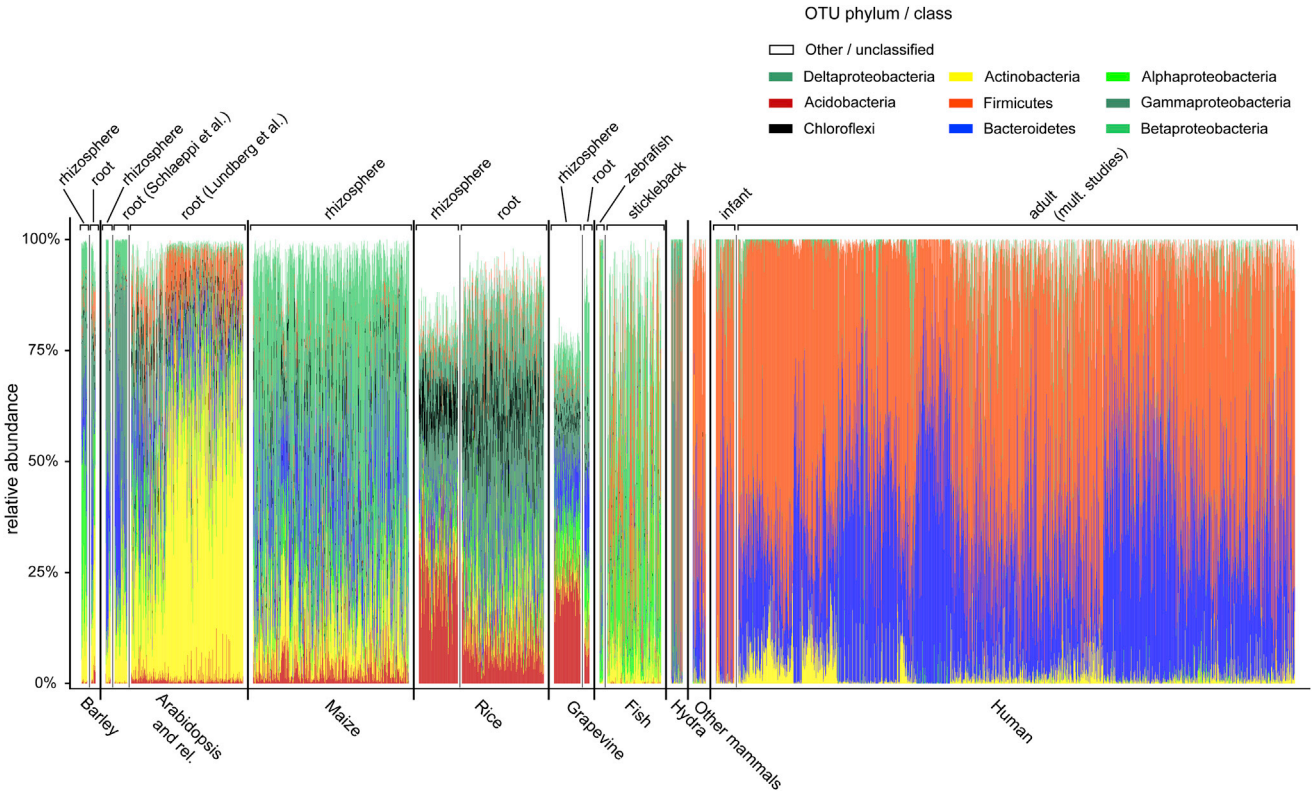


Figure 4. Cumulative Abundance Plots
Relative abundances grouped at the phylum or class taxonomic level for each sample included in the meta-analysis. The bar plots have been arranged along the x axis separating different host groups as well as different species and compartments.

Organic carbon is widely considered to be the most important factor limiting bacterial growth in different soils (Demoling et al., 2007). Isotope probing experiments using different plant species revealed that an average of 17% of all photosynthetically fixed carbon is transferred to the rhizosphere through root exudates (Nguyen, 2003), highlighting a considerable organic carbon deposition in soil. Low molecular weight carbon substrates such as dicarboxylic acids, exuded by roots in large quantities to acidify the rhizosphere, also enhance the availability of Pi and micronutrients such as manganese, iron, and zinc. These dicarboxylic acids are an important driver mediating soil community shifts, leading to an increase in the relative abundance of beta-Proteobacteria, gamma-Proteobacteria, and Actinobacteria (Eilers et al., 2010).

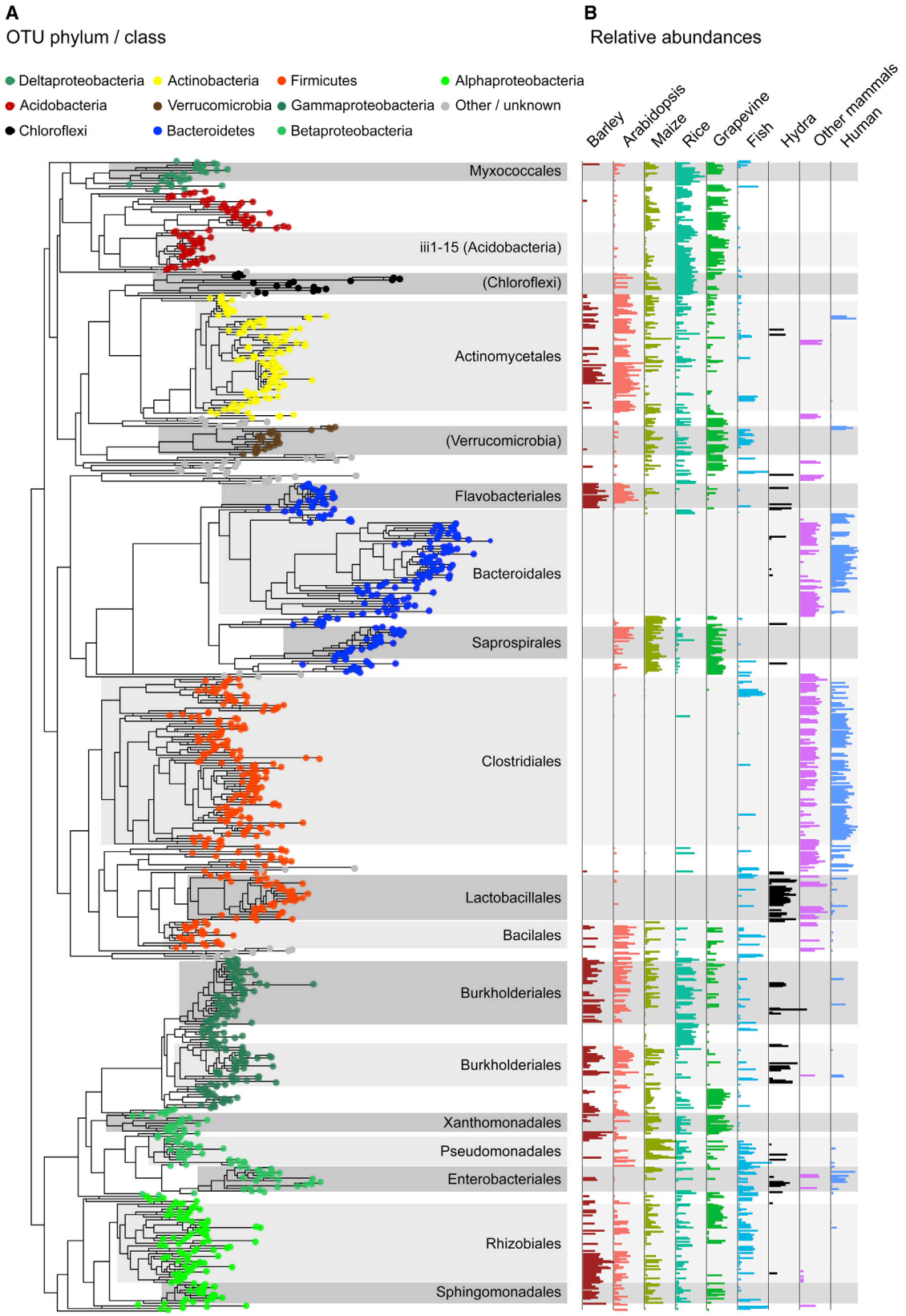
The evolution of the mammalian gut microbiota has been greatly influenced by host diet. Mammals, their gut microbiota, and their diet types are part of a dynamic tripartite coevolution (Ley et al., 2008b). The majority (80%) of extant mammals are herbivorous, which stands in contrast to the early mammals that were most likely carnivorous based on their tooth morphology. The rise in herbivory could only have been accomplished with the necessary changes in gut microbes, since mammalian genomes lack the necessary genes encoding plant cell wall degrading enzymes. Comparisons of microbiomes between host species highlight the specific adaptations of the microbiota to the host diet, such as an increased abundance of genes encoding the necessary enzymes and their respective pathways (Eilam et al., 2014), as exemplified in a comparison between the termite hindgut and the bovine rumen metagenome (Brulc et al., 2009). The latter is enriched for genes encoding glycoside hydrolases, cellulosome enzymes, and nitrogen-related uptake proteins. In contrast, the termite hindgut microbiome showed an enrichment for genes involved in the degradation of the cellulose backbone and nitrogen fixation. This clearly reflects the differences in diet of the hosts (forages and legumes versus nitrogen-poor wood).

Microbe-Microbe Interactions

The role of microbe-microbe interactions is also critical for shaping microbiota structure in both plant and animal systems (Bulgarelli et al., 2015; Fraune et al., 2014; Hacquard and Schadt, 2015; Trosvik et al., 2010). The combination of synergistic, beneficial, and antagonistic interactions among microbiota members colonizing the gut and plants is likely to have a major impact on overall community structure. Therefore, individual members of a community may contribute to the overall stability of the system, and consequently, each community member must be viewed as a potential internal driver of microbial community assemblage. Microbial co-occurrence and co-exclusion patterns are now emerging as important concepts for understanding the rules guiding microbial community assembly (Cardinale et al., 2015; Faust et al., 2012; Zhang et al., 2014)

Host Genotype

Intra-species plant genetic diversity explains less variation in community structure than soil type and root fraction (soil,



(legend on next page)

rhizosphere, and endosphere). Surveys of the bacterial community structure of 27 maize inbred lines, 6 cultivated rice varieties, 3 barley accessions, and several *A. thaliana* accessions each point to a small (~5%–6% of variation) but significant role of the host genotype on community composition (Bulgarelli et al., 2012, 2015; Edwards et al., 2015; Lundberg et al., 2012; Peiffer et al., 2013; Schlaeppi et al., 2014). This suggests a link between host diversification and microbial community establishment (see below).

In humans, family members are often observed to have more similar microbiotas than unrelated individuals (Tims et al., 2013; Turnbaugh et al., 2009; Yatsunenko et al., 2012). Familial similarities are usually attributed to shared environmental influences, such as dietary preference, a powerful shaper of microbiome composition (Cotillard et al., 2013; David et al., 2014b; Wu et al., 2011). However, host genetics also play a small but statistically significant role in shaping the composition and structure of the gut microbiome. Studies comparing microbiota between human subjects differing at specific genetic loci have shown gene-microbiota interactions (Khachatryan et al., 2008; Rehman et al., 2011). A more general approach to this question has linked genetic loci with abundances of gut bacteria in mice (Benson et al., 2010; McKnite et al., 2012), although diet effects outweigh the host genotype effects (Parks et al., 2013). In humans, earlier twin studies failed to reveal significant genotype effects on microbiome diversity (Turnbaugh et al., 2009; Yatsunenko et al., 2012). However, a recent report by Goodrich et al. (2014) comparing monozygotic (MZ) with dizygotic (DZ) twin pairs identified specific taxa as heritable (i.e., the variability in the relative abundances of these taxa across the population was partially driven by host genotype variation). These taxa include health-associated Faecalibacterium and Bifidobacterium and lean phenotype-mediating Christensenella (Goodrich et al., 2014).

Host Immune Systems and Microbiota Homeostasis

Plants and animals each engage structurally related pattern recognition receptors (PRRs) for recognition of evolutionarily conserved non-self microbial structures (i.e., lipopolysaccharides [LPS], lipopeptides, flagellin, chitin) at the cell surface, and activation of these is typically sufficient to halt microbial proliferation. However, successful plant and animal pathogens have evolved mechanisms to dampen or escape PRR-mediated host responses to foster virulence. In response, members of the NLR (nucleotide-binding domain leucine-rich repeat containing) family of intracellular immune receptors in plants and animals are activated by the action of pathogen virulence factors or by direct binding of the virulence factors themselves (Boller and Felix, 2009; Jones and Dangl, 2006; Maekawa et al., 2011). Active animal PRRs and NLR inflammasomes each can instruct the mammalian adaptive immune system and cause spatially dispersed response in plants, as detailed below.

Detection of microbial patterns via PRRs constitutes the first layer of immunity in plants and animals and triggers a variety of output responses. In animals, these include instruction and either activation or suppression of the adaptive immune system via cytokine signaling and cell migration to and from infection sites and lymphoid organs. Because there are no circulating cells in plants, PRR- and NLR-dependent signaling can lead to differential local and systemic signals that result in adequate defense outputs at and directly surrounding the site of infection and a poised defense in distal organs. Analogous to cytokines, plants deploy a handful of defense phytohormones that have variable domains of signaling and instruct cells neighboring an infection site, and even systemically to distal organs, to be ready to respond to infection (Pieterse et al., 2012).

The lack of circulating immunocytes also demands that each plant cell in an organ be capable of recognizing all pathogens adapted to that organ. This drives a complicated requirement for coordination of normal cellular functions, mediated by growth-regulating hormones, and immune output mediated by the defense phytohormones. This coordination is manifested as trade-offs between growth and immunity (Belkhadir and Jaillais, 2015). Thus, systemic acquired resistance in above-ground organs is triggered by biotrophic pathogens and mediated by salicylic acid (SA), while induced systemic resistance, also active in leaves, is triggered in roots by rhizobacteria and is mediated by jasmonic acid (JA) and ethylene (Spoel and Dong, 2008; van Loon et al., 1998).

Because plant defense phytohormones are key signaling molecules between microbial perception and immune system outputs, their production and perception are common pathways targeted by both potential pathogens and beneficial microbes. Hence, there is evidence that during the early stages of colonization both arbuscular mycorrhizal (AM) and Rhizobium species locally suppress SA signaling (García-Garrido and Ocampo, 2002; Stacey et al., 2006), suggesting that defense phytohormones normally act to inhibit microbial survival in the root. Indeed, culture-dependent studies in *A. thaliana* have demonstrated a significantly lower load of culturable bacteria in rhizospheres of plants with either defective JA signaling or, conversely, constitutive SA production (Doornbos et al., 2011). Beyond defense phytohormones, other immune outputs have also been implicated by recent studies. In particular, metagenomic studies in rice uncovered genes present in root endophytic bacteria, notably detoxification of reactive oxygen species (Sessitsch et al., 2012).

The overall structure of the *Arabidopsis* root microbiota remains largely robust to host mutations leading to hypo- or hyper-immunity. However, sets of mutants with altered defense phytohormone biosynthesis and/or perception had specifically altered root microbiome taxonomic compositions compared to wild-type. These alterations were congruent with the known effects of the mutants on immune system outputs in leaves. Experiments using both wild soil and its natural community or synthetic soil microcosms in the presence of a synthetic bacterial community demonstrated that SA and/or SA-dependent processes are major contributors to root microbiome

Figure 5. Phylogenetic Analysis of OTU Abundances

(A) Phylogeny inferred from the representative sequences of all OTUs that had at least 0.1% relative abundance on average for all samples of a host species (1,133 in total). The color of each leaf depicts the taxonomic classification of its corresponding OTU.

(B) Average relative abundances of abundant OTUs across all samples of each host (log-transformed). Note that in the case of plant hosts, abundances are averaged across all root compartments.

composition (S.L., unpublished data). Together, these studies represent some of the insights into mechanisms used by the plant immune system to shape its microbiota.

In the animal gut, a first line of defense consists of the secretion of antimicrobial peptides that are produced deep within the crevices of the epithelial layer, in the crypts between the villi. While some antimicrobial agents are continuously secreted, others are secreted in response to bacterial triggering of specific PRRs (Toll-like receptors, TLRs) on the epithelial cell surfaces. The mucus layer is crucial to prevent systematic activation of these immune responses. When the inner mucus layer is removed chemically (i.e., with dextran sodium sulfate [DSS]) or through gene mutation (*MUC2* mutants), bacteria come into contact with epithelial cells and cause an inflammatory response (Johansson et al., 2010; Van der Sluis et al., 2006). In contrast to plants, the adaptive immune system also plays a role for sequestering symbiotic bacteria in the lumen through the secretion of immunoglobin A (IgA) that target epitopes of intestinal bacteria. Like the antimicrobial activity of the innate immune system, the adaptive immune system can be regulated in parts by TLR signaling (Iwasaki and Medzhitov, 2010). Together, the adaptive and innate immune systems have mechanisms for detecting surface-associated bacteria and work together to reduce inflammation. Because the adaptive immune system is (largely) unique to vertebrates, and based on the observation that vertebrates, notably mammals, harbor microbial communities with much greater complexity than do invertebrates, McFall-Ngai et al. (2013) have proposed that the adaptive immune system itself is important in the shaping and maintenance of high microbial diversity.

Co-diversification of Host-Microbe Communities

By comparing the bacterial communities associated with maize genotypes or other grasses, a significant correlation between rhizobacterial communities and the host phylogenetic distance has been detected, suggesting that the host's evolutionary history can be a good predictor of root microbiota structure (Bouffaud et al., 2014). A comparison of inter-species host phylogeny and microbiota diversification in four Brassicaceae plant species, including *A. thaliana*, which diverged ~35 Ma revealed only quantitative differences. This diversification cannot be explained solely by the phylogenetic distance of these hosts but likely includes plant species-specific ecological adaptations (Schlaeppi et al., 2014). However, qualitative differences can be observed when comparing more distantly related plant species such as *A. thaliana* and barley (dicotyledonous versus monocotyledonous plants), which diverged ~150 Ma (Bulgarelli et al., 2015). Marked differences in microbiota composition were also reported for *Hydra vulgaris* and *Hydra oligactis*, cnidarian animal groups that diverged approximately 100 Ma and have been cultivated under identical laboratory conditions for decades (Franzenburg et al., 2013).

In mammals, similarities in microbial community composition between members of the same species raise the question of whether the bacterial communities track mammalian phylogeny. This would be expected if the bacteria are passed vertically from parent to offspring, which some mammal species encourage behaviorally. Patterns of relatedness of the bacterial communities were compared to the mammalian phylogeny (Ley et al., 2008a). For subsets of the mammalian phylogeny, the trees matched at a rate that is greater than expected by chance. For instance, this pattern was observed in the case of bears, which are an animal group candidate for mother-offspring transmission due to prolonged contact between the cub and the mother, implying that an ancestral microbial population diversified at the same time that bears speciated. A comparison of the microbial communities associated to great ape species, including *Homo sapiens*, also revealed that the host species phylogeny was congruent to the pattern of relatedness of their gut microbial communities, which diverged in a manner consistent with vertical inheritance (Ochman et al., 2010). However, a comparative analysis of the gut microbiota of humans with the ape species indicates an accelerated change in the microbiota composition of humans that cannot be explained by evolutionary distance (Moeller et al., 2014). A recent study of one isolated Amazonian tribe revealed the highly diverse gut microbiota, in both composition and functions, including a broad range of antibiotic resistance genes, suggesting that the Western lifestyle has dramatically reduced bacterial diversity (Clemente et al., 2015).

Taken together, these data indicate generally that a correlation between microbiota and host phylogeny can be explained by co-diversification from common ancestors. Nonetheless, the hugely different generation times of bacteria compared to their associated eukaryotic hosts together with the high density of microbes in the gut or surrounding the root system suggest that the evolution of host-microbe communities is mainly determined by other selective forces, including microbe-microbe and host-microbe-environment interactions.

Metagenome Analysis-Inferred Functions of the Gut and the Plant Microbiota

The gut microbiota is dominated by a few bacterial phyla, but more variation is observed when focusing on lower taxonomic levels. The relative abundance of individual species can vary over a 10-fold range among individual humans (Spor et al., 2011). In contrast, at the level of gene functions, less variability is observed among individuals, pointing to functional redundancy within the bacterial microbiota and the existence of a conserved functional core (Huttenhower et al., 2012; Turnbaugh et al., 2009).

Given the critical function in nutrient acquisition, it is not surprising that gene functions found in the gut microbial community are influenced by both long- and short-term changes in diet (David et al., 2014b; Muegge et al., 2011; Suez et al., 2014; Wu et al., 2011). Pathways found over all human body parts ("core" pathways) include translational machinery, nucleotide charging, ATP synthesis, and glycolysis (Huttenhower et al., 2012). The functional categories found specifically enriched in the gut microbiota are related to metabolism categories (genes involved in starch, sucrose, and monosaccharide metabolism, including many glycoside hydrolase families). More specifically, functions related to fermentation of complex sugars and glycans to SCFAs, methanogenesis, synthesis of essential amino acids and vitamins, and hydrolysis of phenolic glycosidic conjugates are enriched (Gill et al., 2006; Huttenhower et al., 2012; Qin et al., 2010; Turnbaugh et al., 2009). Some of these functions, such as fermentation and carbohydrate metabolism and vitamin biosynthesis, are also highly expressed in the gut microbiome,

as assessed by metatranscriptome analysis (Turnbaugh et al., 2010).

For plant studies, experimental design is more standardized across individuals, which often allows for direct or indirect tests of functional enrichment (Bulgarelli et al., 2015; Mendes et al., 2014; Ofek-Lalzar et al., 2014), in contrast to the human gut microbiome. Shared functional categories found across at least two plant rhizosphere studies relate to iron transport and metabolism, nitrogen metabolism, transport and secretion systems, as well as chemotaxis and motility (Mendes et al., 2014; Ofek-Lalzar et al., 2014; Sessitsch et al., 2012). Similar functions were also found in a metaproteogenomics study of the rice rhizosphere, although in addition, a major role for one-carbon compound recycling could be identified (Knief et al., 2012). However, considerable differences were found in these studies, and additionally no specific function can be assigned for a large proportion of annotated genes in metagenomic studies (42%–86% in the gut; 59% in the plant rhizosphere) (Gill et al., 2006; Huttenhower et al., 2012; Ofek-Lalzar et al., 2014; Qin et al., 2010). A striking commonality between the gut and root metagenome studies is the significant enrichment/high abundance of phage-related functions (Bulgarelli et al., 2015; Qin et al., 2010), but the exact role of these functions is not known.

To gain further insight into the evolutionary forces acting on genes in relation to their functional roles, natural selection was assessed using dN/dS ratios for gene families in the barley rhizosphere and human gut microbiomes (Bulgarelli et al., 2015; Schloissnig et al., 2013). Positive selection is a hallmark of protein families implicated in molecular arms races between two competing organisms. In the rhizosphere, proteins involved in host-pathogen interactions showed significant signs of positive selection, such as the type III secretion system and its associated effectors, phage elements, and microbial CRISPR proteins (Bulgarelli et al., 2015). Similarly, CRISPR-related families, as well as transposases and families related to antibiotic resistance, showed signatures of positive selection in the human gut microbiome (Schloissnig et al., 2013).

Concluding Remarks and Perspectives

To complement large-scale community profile and metagenome studies, reference collections of several hundred isolates from different human body sites and their corresponding genome sequences have been generated (Goodman et al., 2011). For plant-associated microbial communities, similar projects aiming to maximize phylogenetic diversity of cultured bacteria through cross-referencing with culture-independent community profiling experiments are about to be concluded (P.S.-L. and J.L.D., unpublished data). In the future, these genome collections may allow determination of multi-locus reference gene collections for the identification of individual strains within a community, as an alternative to lower-resolution 16S rRNA-based taxon identification, as well as comparative analyses of thousands of genomes for association-based analyses, to link genes and genetic variants to particular phenotypes. The construction of defined (synthetic) communities and their assessment under controlled environments with germ-free eukaryotic hosts allows studies of community resilience and responses to perturbation at the level of individual members and simplifies testing of specific hypotheses relating to individual attributes of other community members and the host (Faith et al., 2014; Guttman et al., 2014). Controlled experimental systems will reduce the noise inherent to any natural environmental sample and will drive the next phase of plant and gut microbiota research in which scientific conclusions are based on causation rather than correlations.

For a detailed description of the meta-analysis, see Supplemental Experimental Procedures. The OTU count matrices and taxonomic information as well as the scripts used to analyze the data and generate the figures of this study are available at http://www.mpipz.mpg.de/R_scripts.

SUPPLEMENTAL INFORMATION

Supplemental Information includes Supplemental Experimental Procedures, one figure, and one table and can be found with this article online at http://dx.doi.org/10.1016/j.chom.2015.04.009.

AUTHOR CONTRIBUTIONS

S.H., R.G.-O., S.S., and P.S.-L. designed research. R.G.-O., A.G., and R.K. designed and R.G.-O., A.G., and G.A. performed the computational analysis. S.H., R.G.-O., S.S., S.L., A.C.M., J.L.D., R.K., R.L., and P.S.-L. wrote the paper.

ACKNOWLEDGMENTS

Work in the different research groups was supported by the Max Planck Society (to P.S.-L.), a European Research Council advanced grant (ROOTMICROBIOTA to P.S.-L.), the "Cluster of Excellence on Plant Sciences" program (funded by the Deutsche Forschungsgemeinschaft to P.S.-L. and A.C.M.), NSF Microbial Systems Biology (grant IOS-0958245 to J.L.D.), NSF INSPIRE (grant IOS-1343020 to J.L.D.), and DOE Feedstocks (grant SC0010423 to J.L.D). S.S. was supported by a postdoctoral grant from the Research Foundation – Flanders (FWO-Vlaanderen). J.L.D. is an Investigator of the Howard Hughes Medical Institute, supported by the HHMI and the Gordon and Betty Moore Foundation (GBMF3030).

REFERENCES

Almagro-Moreno, S., and Boyd, E.F. (2009). Sialic acid catabolism confers a competitive advantage to pathogenic vibrio cholerae in the mouse intestine. Infect. Immun. *77*, 3807–3816.

Bárcen as-Moreno, G., Gómez-Brandón, M., Rousk, J., and Bååth, E. (2009). Adaptation of soil microbial communities to temperature: comparison of fungi and bacteria in a laboratory experiment. Glob. Change Biol. *15*, 2950–2957.

Barret, M., Briand, M., Bonneau, S., Préveaux, A., Valière, S., Bouchez, O., Hunault, G., Simoneau, P., and Jacques, M.-A. (2014). Emergence shapes the structure of the seed-microbiota. Appl. Environ. Microbiol. Published online December 12, 2014. http://dx.doi.org/10.1128/AEM.03722-14.

Belkhadir, Y., and Jaillais, Y. (2015). The molecular circuitry of brassinosteroid signaling. New Phytol. *206*, 522–540.

Benson, A.K., Kelly, S.A., Legge, R., Ma, F., Low, S.J., Kim, J., Zhang, M., Oh, P.L., Nehrenberg, D., Hua, K., et al. (2010). Individuality in gut microbiota composition is a complex polygenic trait shaped by multiple environmental and host genetic factors. Proc. Natl. Acad. Sci. USA *107*, 18933–18938.

Berendsen, R.L., Pieterse, C.M.J., and Bakker, P.A.H.M. (2012). The rhizosphere microbiome and plant health. Trends Plant Sci. *17*, 478–486.

Blaser, M.J., and Falkow, S. (2009). What are the consequences of the disappearing human microbiota? Nat. Rev. Microbiol. *7*, 887–894.

Boller, T., and Felix, G. (2009). A renaissance of elicitors: perception of microbe-associated molecular patterns and danger signals by pattern-recognition receptors. Annu. Rev. Plant Biol. *60*, 379–406.

Bouffaud, M.-L., Poirier, M.-A., Muller, D., and Moënne-Loccoz, Y. (2014). Root microbiome relates to plant host evolution in maize and other Poaceae. Environ. Microbiol. *16*, 2804–2814.

Brulc, J.M., Antonopoulos, D.A., Miller, M.E.B., Wilson, M.K., Yannarell, A.C., Dinsdale, E.A., Edwards, R.E., Frank, E.D., Emerson, J.B., Wacklin, P., et al. (2009). Gene-centric metagenomics of the fiber-adherent bovine rumen microbiome reveals forage specific glycoside hydrolases. Proc. Natl. Acad. Sci. USA *106*, 1948–1953.

Bulgarelli, D., Rott, M., Schlaeppi, K., Ver Loren van Themaat, E., Ahmadinejad, N., Assenza, F., Rauf, P., Huettel, B., Reinhardt, R., Schmelzer, E., et al. (2012). Revealing structure and assembly cues for Arabidopsis root-inhabiting bacterial microbiota. Nature *488*, 91–95.

Bulgarelli, D., Schlaeppi, K., Spaepen, S., Ver Loren van Themaat, E., and Schulze-Lefert, P. (2013). Structure and functions of the bacterial microbiota of plants. Annu. Rev. Plant Biol. *64*, 807–838.

Bulgarelli, D., Garrido-Oter, R., Münch, P.C., Weiman, A., Dröge, J., Pan, Y., McHardy, A.C., and Schulze-Lefert, P. (2015). Structure and function of the bacterial root microbiota in wild and domesticated barley. Cell Host Microbe *17*, 392–403.

Caporaso, J.G., Kuczynski, J., Stombaugh, J., Bittinger, K., Bushman, F.D., Costello, E.K., Fierer, N., Peña, A.G., Goodrich, J.K., Gordon, J.I., et al. (2010). QIIME allows analysis of high-throughput community sequencing data. Nat. Methods *7*, 335–336.

Cardinale, M., Grube, M., Erlacher, A., Quehenberger, J., and Berg, G. (2015). Bacterial networks and co-occurrence relationships in the lettuce root microbiota. Environ. Microbiol. *17*, 239–252.

Carmody, R.N., Gerber, G.K., Luevano, J.M., Jr., Gatti, D.M., Somes, L., Svenson, K.L., and Turnbaugh, P.J. (2015). Diet dominates host genotype in shaping the murine gut microbiota. Cell Host Microbe *17*, 72–84.

Chaparro, J.M., Badri, D.V., and Vivanco, J.M. (2014). Rhizosphere microbiome assemblage is affected by plant development. ISME J. *8*, 790–803.

Clemente, J.C., Pehrsson, E.C., Blaser, M.J., Sandhu, K., Gao, Z., Wang, B., Magris, M., Hidalgo, G., Contreras, M., Noya-Alarcón, Ó., et al. (2015). The microbiome of uncontacted Amerindians. Sci. Adv. *1*, e1500183.

Cotillard, A., Kennedy, S.P., Kong, L.C., Prifti, E., Pons, N., Le Chatelier, E., Almeida, M., Quinquis, B., Levenez, F., Galleron, N., et al.; ANR MicroObes consortium (2013). Dietary intervention impact on gut microbial gene richness. Nature *500*, 585–588.

Curtis, T.P., Sloan, W.T., and Scannell, J.W. (2002). Estimating prokaryotic diversity and its limits. Proc. Natl. Acad. Sci. USA *99*, 10494–10499.

David, L.A., Materna, A.C., Friedman, J., Campos-Baptista, M.I., Blackburn, M.C., Perrotta, A., Erdman, S.E., and Alm, E.J. (2014a). Host lifestyle affects human microbiota on daily timescales. Genome Biol. *15*, R89.

David, L.A., Maurice, C.F., Carmody, R.N., Gootenberg, D.B., Button, J.E., Wolfe, B.E., Ling, A.V., Devlin, A.S., Varma, Y., Fischbach, M.A., et al. (2014b). Diet rapidly and reproducibly alters the human gut microbiome. Nature *505*, 559–563.

Demoling, F., Figueroa, D., and Bååth, E. (2007). Comparison of factors limiting bacterial growth in different soils. Soil Biol. Biochem. *39*, 2485–2495.

Dominguez-Bello, M.G., Costello, E.K., Contreras, M., Magris, M., Hidalgo, G., Fierer, N., and Knight, R. (2010). Delivery mode shapes the acquisition and structure of the initial microbiota across multiple body habitats in newborns. Proc. Natl. Acad. Sci. USA *107*, 11971–11975.

Donn, S., Kirkegaard, J.A., Perera, G., Richardson, A.E., and Watt, M. (2015). Evolution of bacterial communities in the wheat crop rhizosphere. Environ. Microbiol. *17*, 610–621.

Doornbos, R.F., Geraats, B.P.J., Kuramae, E.E., Van Loon, L.C., and Bakker, P.A.H.M. (2011). Effects of jasmonic acid, ethylene, and salicylic acid signaling on the rhizosphere bacterial community of *Arabidopsis thaliana*. Mol. Plant Microbe Interact. *24*, 395–407.

Duncan, S.H., Louis, P., Thomson, J.M., and Flint, H.J. (2009). The role of pH in determining the species composition of the human colonic microbiota. Environ. Microbiol. *11*, 2112–2122.

Eckburg, P.B., Bik, E.M., Bernstein, C.N., Purdom, E., Dethlefsen, L., Sargent, M., Gill, S.R., Nelson, K.E., and Relman, D.A. (2005). Diversity of the human intestinal microbial flora. Science *308*, 1635–1638.

Edwards, J., Johnson, C., Santos-Medellín, C., Lurie, E., Podishetty, N.K., Bhatnagar, S., Eisen, J.A., and Sundaresan, V. (2015). Structure, variation, and assembly of the root-associated microbiomes of rice. Proc. Natl. Acad. Sci. USA *112*, E911–E920.

Eilam, O., Zarecki, R., Oberhardt, M., Ursell, L.K., Kupiec, M., Knight, R., Gophna, U., and Ruppin, E. (2014). Glycan degradation (GlyDeR) analysis predicts mammalian gut microbiota abundance and host diet-specific adaptations. MBio *5*, e01526–e14.

Eilers, K.G., Lauber, C.L., Knight, R., and Fierer, N. (2010). Shifts in bacterial community structure associated with inputs of low molecular weight carbon compounds to soil. Soil Biol. Biochem. *42*, 896–903.

Faith, J.J., Guruge, J.L., Charbonneau, M., Subramanian, S., Seedorf, H., Goodman, A.L., Clemente, J.C., Knight, R., Heath, A.C., Leibel, R.L., et al. (2013). The long-term stability of the human gut microbiota. Science *341*, 1237439.

Faith, J.J., Ahern, P.P., Ridaura, V.K., Cheng, J., and Gordon, J.I. (2014). Identifying gut microbe-host phenotype relationships using combinatorial communities in gnotobiotic mice. Sci. Transl. Med. *6*, 20ra11.

Faust, K., Sathirapongsasuti, J.F., Izard, J., Segata, N., Gevers, D., Raes, J., and Huttenhower, C. (2012). Microbial co-occurrence relationships in the human microbiome. PLoS Comput. Biol. *8*, e1002606.

Fierer, N., and Jackson, R.B. (2006). The diversity and biogeography of soil bacterial communities. Proc. Natl. Acad. Sci. USA *103*, 626–631.

Franzenburg, S., Walter, J., Künzel, S., Wang, J., Baines, J.F., Bosch, T.C., and Fraune, S. (2013). Distinct antimicrobial peptide expression determines host species-specific bacterial associations. Proc. Natl. Acad. Sci. USA *110*, E3730–E3738.

Fraune, S., Anton-Erxleben, F., Augustin, R., Franzenburg, S., Knop, M., Schröder, K., Willoweit-Ohl, D., and Bosch, T.C. (2014). Bacteria-bacteria interactions within the microbiota of the ancestral metazoan Hydra contribute to fungal resistance. ISME J. http://dx.doi.org/10.1038/ismej.2014.239.

García-Garrido, J.M., and Ocampo, J.A. (2002). Regulation of the plant defence response in arbuscular mycorrhizal symbiosis. J. Exp. Bot. *53*, 1377–1386.

Gaudier, E., Jarry, A., Blottière, H.M., de Coppet, P., Buisine, M.P., Aubert, J.P., Laboisse, C., Cherbut, C., and Hoebler, C. (2004). Butyrate specifically modulates MUC gene expression in intestinal epithelial goblet cells deprived of glucose. Am. J. Physiol. Gastrointest. Liver Physiol. *287*, G1168–G1174.

Gill, S.R., Pop, M., Deboy, R.T., Eckburg, P.B., Turnbaugh, P.J., Samuel, B.S., Gordon, J.I., Relman, D.A., Fraser-Liggett, C.M., and Nelson, K.E. (2006). Metagenomic analysis of the human distal gut microbiome. Science *312*, 1355–1359.

Goodman, A.L., Kallstrom, G., Faith, J.J., Reyes, A., Moore, A., Dantas, G., and Gordon, J.I. (2011). Extensive personal human gut microbiota culture collections characterized and manipulated in gnotobiotic mice. Proc. Natl. Acad. Sci. USA *108*, 6252–6257.

Goodrich, J.K., Waters, J.L., Poole, A.C., Sutter, J.L., Koren, O., Blekhman, R., Beaumont, M., Van Treuren, W., Knight, R., Bell, J.T., et al. (2014). Human genetics shape the gut microbiome. Cell *159*, 789–799.

Guttman, D.S., McHardy, A.C., and Schulze-Lefert, P. (2014). Microbial genome-enabled insights into plant-microorganism interactions. Nat. Rev. Genet. *15*, 797–813.

Hacquard, S., and Schadt, C.W. (2015). Towards a holistic understanding of the beneficial interactions across the *Populus* microbiome. New Phytol. *205*, 1424–1430.

Hinsinger, P., Plassard, C., Tang, C., and Jaillard, B. (2003). Origins of root-mediated pH changes in the rhizosphere and their responses to environmental constraints: A review. Plant Soil *248*, 43–59.

Hoskins, L.C., and Boulding, E.T. (1981). Mucin degradation in human colon ecosystems. Evidence for the existence and role of bacterial subpopulations producing glycosidases as extracellular enzymes. J. Clin. Invest. *67*, 163–172.

Huttenhower, C., Gevers, D., Knight, R., Abubucker, S., Badger, J.H., Chinwalla, A.T., Creasy, H.H., Earl, A.M., FitzGerald, M.G., Fulton, R.S., et al.; Human Microbiome Project Consortium (2012). Structure, function and diversity of the healthy human microbiome. Nature *486*, 207–214.

Iwasaki, A., and Medzhitov, R. (2010). Regulation of adaptive immunity by the innate immune system. Science *327*, 291–295.

Johansson, M.E.V., Phillipson, M., Petersson, J., Velcich, A., Holm, L., and Hansson, G.C. (2008). The inner of the two Muc2 mucin-dependent mucus layers in colon is devoid of bacteria. Proc. Natl. Acad. Sci. USA *105*, 15064–15069.

Johansson, M.E.V., Gustafsson, J.K., Sjöberg, K.E., Petersson, J., Holm, L., Sjövall, H., and Hansson, G.C. (2010). Bacteria penetrate the inner mucus layer before inflammation in the dextran sulfate colitis model. PLoS ONE *5*, e12238.

Jones, J.D.G., and Dangl, J.L. (2006). The plant immune system. Nature *444*, 323–329.

Kamada, N., Chen, G.Y., Inohara, N., and Núñez, G. (2013). Control of pathogens and pathobionts by the gut microbiota. Nat. Immunol. *14*, 685–690.

Kemen, E. (2014). Microbe-microbe interactions determine oomycete and fungal host colonization. Curr. Opin. Plant Biol. *20*, 75–81.

Khachatryan, Z.A., Ktsoyan, Z.A., Manukyan, G.P., Kelly, D., Ghazaryan, K.A., and Aminov, R.I. (2008). Predominant role of host genetics in controlling the composition of gut microbiota. PLoS ONE *3*, e3064.

Khan, M.T., Duncan, S.H., Stams, A.J.M., van Dijl, J.M., Flint, H.J., and Harmsen, H.J.M. (2012). The gut anaerobe *Faecalibacterium prausnitzii* uses an extracellular electron shuttle to grow at oxic-anoxic interphases. ISME J. *6*, 1578–1585.

Knief, C., Delmotte, N., Chaffron, S., Stark, M., Innerebner, G., Wassmann, R., von Mering, C., and Vorholt, J.A. (2012). Metaproteogenomic analysis of microbial communities in the phyllosphere and rhizosphere of rice. ISME J. *6*, 1378–1390.

Koenig, J.E., Spor, A., Scalfone, N., Fricker, A.D., Stombaugh, J., Knight, R., Angenent, L.T., and Ley, R.E. (2011). Succession of microbial consortia in the developing infant gut microbiome. Proc. Natl. Acad. Sci. USA *108* (1), 4578–4585.

Kopylova, E., Noé, L., and Touzet, H. (2012). SortMeRNA: fast and accurate filtering of ribosomal RNAs in metatranscriptomic data. Bioinformatics *28*, 3211–3217.

Lambers, H., Raven, J.A., Shaver, G.R., and Smith, S.E. (2008). Plant nutrient-acquisition strategies change with soil age. Trends Ecol. Evol. *23*, 95–103.

Leitch, E.C.M., Walker, A.W., Duncan, S.H., Holtrop, G., and Flint, H.J. (2007). Selective colonization of insoluble substrates by human faecal bacteria. Environ. Microbiol. *9*, 667–679.

Ley, R.E., Hamady, M., Lozupone, C., Turnbaugh, P.J., Ramey, R.R., Bircher, J.S., Schlegel, M.L., Tucker, T.A., Schrenzel, M.D., Knight, R., and Gordon, J.I. (2008a). Evolution of mammals and their gut microbes. Science *320*, 1647–1651.

Ley, R.E., Lozupone, C.A., Hamady, M., Knight, R., and Gordon, J.I. (2008b). Worlds within worlds: evolution of the vertebrate gut microbiota. Nat. Rev. Microbiol. *6*, 776–788.

López-Arredondo, D.L., Leyva-González, M.A., González-Morales, S.I., López-Bucio, J., and Herrera-Estrella, L. (2014). Phosphate nutrition: improving low-phosphate tolerance in crops. Annu. Rev. Plant Biol. *65*, 95–123.

Lundberg, D.S., Lebeis, S.L., Paredes, S.H., Yourstone, S., Gehring, J., Malfatti, S., Tremblay, J., Engelbrektson, A., Kunin, V., del Rio, T.G., et al. (2012). Defining the core *Arabidopsis thaliana* root microbiome. Nature *488*, 86–90.

Maathuis, F.J.M. (2009). Physiological functions of mineral macronutrients. Curr. Opin. Plant Biol. *12*, 250–258.

Maekawa, T., Kufer, T.A., and Schulze-Lefert, P. (2011). NLR functions in plant and animal immune systems: so far and yet so close. Nat. Immunol. *12*, 817–826.

Martins dos Santos, V., Müller, M., and de Vos, W.M. (2010). Systems biology of the gut: the interplay of food, microbiota and host at the mucosal interface. Curr. Opin. Biotechnol. *21*, 539–550.

McFall-Ngai, M., Hadfield, M.G., Bosch, T.C.G., Carey, H.V., Domazet-Lošo, T., Douglas, A.E., Dubilier, N., Eberl, G., Fukami, T., Gilbert, S.F., et al. (2013). Animals in a bacterial world, a new imperative for the life sciences. Proc. Natl. Acad. Sci. USA *110*, 3229–3236.

McKnite, A.M., Perez-Munoz, M.E., Lu, L., Williams, E.G., Brewer, S., Andreux, P.A., Bastiaansen, J.W.M., Wang, X., Kachman, S.D., Auwerx, J., et al. (2012). Murine gut microbiota is defined by host genetics and modulates variation of metabolic traits. PLoS ONE *7*, e39191.

Mendes, R., Kruijt, M., de Bruijn, I., Dekkers, E., van der Voort, M., Schneider, J.H., Piceno, Y.M., DeSantis, T.Z., Andersen, G.L., Bakker, P.A.H.M., and Raaijmakers, J.M. (2011). Deciphering the rhizosphere microbiome for disease-suppressive bacteria. Science *332*, 1097–1100.

Mendes, L.W., Kuramae, E.E., Navarrete, A.A., van Veen, J.A., and Tsai, S.M. (2014). Taxonomical and functional microbial community selection in soybean rhizosphere. ISME J. *8*, 1577–1587.

Mitsuoka, T. (1992). Intestinal flora and aging. Nutr. Rev. *50*, 438–446.

Moeller, A.H., Li, Y., Mpoudi Ngole, E., Ahuka-Mundeke, S., Lonsdorf, E.V., Pusey, A.E., Peeters, M., Hahn, B.H., and Ochman, H. (2014). Rapid changes in the gut microbiome during human evolution. Proc. Natl. Acad. Sci. USA *111*, 16431–16435.

Morris, R.L., and Schmidt, T.M. (2013). Shallow breathing: bacterial life at low O(2). Nat. Rev. Microbiol. *11*, 205–212.

Muegge, B.D., Kuczynski, J., Knights, D., Clemente, J.C., González, A., Fontana, L., Henrissat, B., Knight, R., and Gordon, J.I. (2011). Diet drives convergence in gut microbiome functions across mammalian phylogeny and within humans. Science *332*, 970–974.

Newburg, D.S., and Morelli, L. (2015). Human milk and infant intestinal mucosal glycans guide succession of the neonatal intestinal microbiota. Pediatr. Res. *77*, 115–120.

Nguyen, C. (2003). Rhizodeposition of organic C by plants: mechanisms and controls. Agronomie *23*, 375–396.

Noll, M., Matthies, D., Frenzel, P., Derakshani, M., and Liesack, W. (2005). Succession of bacterial community structure and diversity in a paddy soil oxygen gradient. Environ. Microbiol. *7*, 382–395.

Ochman, H., Worobey, M., Kuo, C.H., Ndjango, J.-B.N., Peeters, M., Hahn, B.H., and Hugenholtz, P. (2010). Evolutionary relationships of wild hominids recapitulated by gut microbial communities. PLoS Biol. *8*, e1000546.

Ofek-Lalzar, M., Sela, N., Goldman-Voronov, M., Green, S.J., Hadar, Y., and Minz, D. (2014). Niche and host-associated functional signatures of the root surface microbiome. Nat. Commun. *5*, 4950.

Osawa, R., Blanshard, W.H., and Ocallaghan, P.G. (1993). Microbiological studies of the intestinal microflora of the koala, Phascolarctos Cinereus 0.2. Pap, a special maternal feces consumed by juvenile koalas. Aust. J. Zool. *41*, 611–620.

Palmer, C., Bik, E.M., DiGiulio, D.B., Relman, D.A., and Brown, P.O. (2007). Development of the human infant intestinal microbiota. PLoS Biol. *5*, e177.

Panke-Buisse, K., Poole, A.C., Goodrich, J.K., Ley, R.E., and Kao-Kniffin, J. (2015). Selection on soil microbiomes reveals reproducible impacts on plant function. ISME J. *9*, 980–989.

Parks, B.W., Nam, E., Org, E., Kostem, E., Norheim, F., Hui, S.T., Pan, C., Civelek, M., Rau, C.D., Bennett, B.J., et al. (2013). Genetic control of obesity and gut microbiota composition in response to high-fat, high-sucrose diet in mice. Cell Metab. *17*, 141–152.

Peiffer, J.A., Spor, A., Koren, O., Jin, Z., Tringe, S.G., Dangl, J.L., Buckler, E.S., and Ley, R.E. (2013). Diversity and heritability of the maize rhizosphere microbiome under field conditions. Proc. Natl. Acad. Sci. USA *110*, 6548–6553.

Pieterse, C.M.J., Van der Does, D., Zamioudis, C., Leon-Reyes, A., and Van Wees, S.C.M. (2012). Hormonal modulation of plant immunity. Annu. Rev. Cell Dev. Biol. *28*, 489–521.

Qin, J., Li, R., Raes, J., Arumugam, M., Burgdorf, K.S., Manichanh, C., Nielsen, T., Pons, N., Levenez, F., Yamada, T., et al.; MetaHIT Consortium (2010). A human gut microbial gene catalogue established by metagenomic sequencing. Nature *464*, 59–65.

Quigley, E.M.M., and Quera, R. (2006). Small intestinal bacterial overgrowth: roles of antibiotics, prebiotics, and probiotics. Gastroenterology *130* (1), S78–S90.

Rehman, A., Sina, C., Gavrilova, O., Häsler, R., Ott, S., Baines, J.F., Schreiber, S., and Rosenstiel, P. (2011). Nod2 is essential for temporal development of intestinal microbial communities. Gut *60*, 1354–1362.

Schlaeppi, K., Dombrowski, N., Oter, R.G., Ver Loren van Themaat, E., and Schulze-Lefert, P. (2014). Quantitative divergence of the bacterial root microbiota in *Arabidopsis thaliana* relatives. Proc. Natl. Acad. Sci. USA *111*, 585–592.

Schloissnig, S., Arumugam, M., Sunagawa, S., Mitreva, M., Tap, J., Zhu, A., Waller, A., Mende, D.R., Kultima, J.R., Martin, J., et al. (2013). Genomic variation landscape of the human gut microbiome. Nature *493*, 45–50.

Schloss, P.D., and Handelsman, J. (2006). Toward a census of bacteria in soil. PLoS Comput. Biol. *2*, e92.

Sekirov, I., Russell, S.L., Antunes, L.C.M., and Finlay, B.B. (2010). Gut microbiota in health and disease. Physiol. Rev. *90*, 859–904.

Sessitsch, A., Hardoim, P., Döring, J., Weilharter, A., Krause, A., Woyke, T., Mitter, B., Hauberg-Lotte, L., Friedrich, F., Rahalkar, M., et al. (2012). Functional characteristics of an endophyte community colonizing rice roots as revealed by metagenomic analysis. Mol. Plant Microbe Interact. *25*, 28–36.

Shakya, M., Gottel, N., Castro, H., Yang, Z.K., Gunter, L., Labbé, J., Muchero, W., Bonito, G., Vilgalys, R., Tuskan, G., et al. (2013). A multifactor analysis of fungal and bacterial community structure in the root microbiome of mature *Populus deltoides* trees. PLoS ONE *8*, e76382.

Song, S.J., Lauber, C., Costello, E.K., Lozupone, C.A., Humphrey, G., Berg-Lyons, D., Caporaso, J.G., Knights, D., Clemente, J.C., Nakielny, S., et al. (2013). Cohabiting family members share microbiota with one another and with their dogs. eLife *2*, e00458.

Spoel, S.H., and Dong, X. (2008). Making sense of hormone crosstalk during plant immune responses. Cell Host Microbe *3*, 348–351.

Spor, A., Koren, O., and Ley, R. (2011). Unravelling the effects of the environment and host genotype on the gut microbiome. Nat. Rev. Microbiol. *9*, 279–290.

Stacey, G., McAlvin, C.B., Kim, S.-Y., Olivares, J., and Soto, M.J. (2006). Effects of endogenous salicylic acid on nodulation in the model legumes Lotus japonicus and Medicago truncatula. Plant Physiol. *141*, 1473–1481.

Stearns, J.C., Lynch, M.D.J., Senadheera, D.B., Tenenbaum, H.C., Goldberg, M.B., Cvitkovitch, D.G., Croitoru, K., Moreno-Hagelsieb, G., and Neufeld, J.D. (2011). Bacterial biogeography of the human digestive tract. Sci Rep *1*, 170.

Stevens, C.E., and Hume, I.D. (1998). Contributions of microbes in vertebrate gastrointestinal tract to production and conservation of nutrients. Physiol. Rev. *78*, 393–427.

Suez, J., Korem, T., Zeevi, D., Zilberman-Schapira, G., Thaiss, C.A., Maza, O., Israeli, D., Zmora, N., Gilad, S., Weinberger, A., et al. (2014). Artificial sweeteners induce glucose intolerance by altering the gut microbiota. Nature *514*, 181–186.

Swidsinski, A., Weber, J., Loening-Baucke, V., Hale, L.P., and Lochs, H. (2005). Spatial organization and composition of the mucosal flora in patients with inflammatory bowel disease. J. Clin. Microbiol. *43*, 3380–3389.

Tims, S., Derom, C., Jonkers, D.M., Vlietinck, R., Saris, W.H., Kleerebezem, M., de Vos, W.M., and Zoetendal, E.G. (2013). Microbiota conservation and BMI signatures in adult monozygotic twins. ISME J. *7*, 707–717.

Tremaroli, V., and Bäckhed, F. (2012). Functional interactions between the gut microbiota and host metabolism. Nature *489*, 242–249.

Trosvik, P., Stenseth, N.C., and Rudi, K. (2010). Convergent temporal dynamics of the human infant gut microbiota. ISME J. *4*, 151–158.

Truyens, S., Weyens, N., Cuypers, A., and Vangronsveld, J. (2015). Bacterial seed endophytes: genera, vertical transmission and interaction with plants. Environ. Microbiol. Rep. *7*, 40–50.

Tsabouri, S., Priftis, K.N., Chaliasos, N., and Siamopoulou, A. (2014). Modulation of gut microbiota downregulates the development of food allergy in infancy. Allergol. Immunopathol. (Madr.) *42*, 69–77.

Tungland, B.C., and Meyer, D. (2002). Nondigestible oligo- and polysaccharides (dietary fiber): their physiology and role in human health and food. Compr. Rev. Food Sci. F. *1*, 90–109.

Turnbaugh, P.J., Hamady, M., Yatsunenko, T., Cantarel, B.L., Duncan, A., Ley, R.E., Sogin, M.L., Jones, W.J., Roe, B.A., Affourtit, J.P., et al. (2009). A core gut microbiome in obese and lean twins. Nature *457*, 480–484.

Turnbaugh, P.J., Quince, C., Faith, J.J., McHardy, A.C., Yatsunenko, T., Niazi, F., Affourtit, J., Egholm, M., Henrissat, B., Knight, R., and Gordon, J.I. (2010). Organismal, genetic, and transcriptional variation in the deeply sequenced gut microbiomes of identical twins. Proc. Natl. Acad. Sci. USA *107*, 7503–7508.

Turner, T.R., James, E.K., and Poole, P.S. (2013). The plant microbiome. Genome Biol. *14*, 209.

Unger, S., Stintzi, A., Shah, P., Mack, D., and O'Connor, D.L. (2015). Gut microbiota of the very-low-birth-weight infant. Pediatr. Res. *77*, 205–213.

Van den Abbeele, P., Van de Wiele, T., Verstraete, W., and Possemiers, S. (2011). The host selects mucosal and luminal associations of coevolved gut microorganisms: a novel concept. FEMS Microbiol. Rev. *35*, 681–704.

Van der Sluis, M., De Koning, B.A.E., De Bruijn, A.C.J.M., Velcich, A., Meijerink, J.P.P., Van Goudoever, J.B., Büller, H.A., Dekker, J., Van Seuningen, I., Renes, I.B., and Einerhand, A.W. (2006). Muc2-deficient mice spontaneously develop colitis, indicating that MUC2 is critical for colonic protection. Gastroenterology *131*, 117–129.

van Loon, L.C., Bakker, P.A.H.M., and Pieterse, C.M.J. (1998). Systemic resistance induced by rhizosphere bacteria. Annu. Rev. Phytopathol. *36*, 453–483.

Wagner, M.R., Lundberg, D.S., Coleman-Derr, D., Tringe, S.G., Dangl, J.L., and Mitchell-Olds, T. (2014). Natural soil microbes alter flowering phenology and the intensity of selection on flowering time in a wild Arabidopsis relative. Ecol. Lett. *17*, 717–726.

Walter, J., and Ley, R. (2011). The human gut microbiome: ecology and recent evolutionary changes. Annu. Rev. Microbiol. *65*, 411–429.

Weller, D.M., Raaijmakers, J.M., Gardener, B.B., and Thomashow, L.S. (2002). Microbial populations responsible for specific soil suppressiveness to plant pathogens. Annu. Rev. Phytopathol. *40*, 309–348.

Wu, G.D., Chen, J., Hoffmann, C., Bittinger, K., Chen, Y.-Y., Keilbaugh, S.A., Bewtra, M., Knights, D., Walters, W.A., Knight, R., et al. (2011). Linking long-term dietary patterns with gut microbial enterotypes. Science *334*, 105–108.

Yatsunenko, T., Rey, F.E., Manary, M.J., Trehan, I., Dominguez-Bello, M.G., Contreras, M., Magris, M., Hidalgo, G., Baldassano, R.N., Anokhin, A.P., et al. (2012). Human gut microbiome viewed across age and geography. Nature *486*, 222–227.

Zarraonaindia, I., Owens, S.M., Weisenhorn, P., West, K., Hampton-Marcell, J., Lax, S., Bokulich, N.A., Mills, D.A., Martin, G., Taghavi, S., et al. (2015). The soil microbiome influences grapevine-associated microbiota. MBio *6*, e02527–e14.

Zhang, Z., Geng, J., Tang, X., Fan, H., Xu, J., Wen, X., Ma, Z.S., and Shi, P. (2014). Spatial heterogeneity and co-occurrence patterns of human mucosal-associated intestinal microbiota. ISME J. *8*, 881–893.

Cell Host & Microbe, Volume *17*

Supplemental Information

Microbiota and Host Nutrition across Plant and Animal Kingdoms

Stéphane Hacquard, Ruben Garrido-Oter, Antonio González, Stijn Spaepen, Gail Ackermann, Sarah Lebeis, Alice C. McHardy, Jeffrey L. Dangl, Rob Knight, Ruth Ley, Paul Schulze-Lefert

Supplemental Information

Supplemental Experimental Procedures

To analyze sequence data we followed the QIIME (**Caporaso et al., 2010**) close reference protocol against the 97% similarity 13_8 release of the GreenGenes database (**McDonald et al., 2012**) using Qiita (http://qiita.microbio.me). In short, we retrieved the raw sequence files, demultiplexed samples and performed a quality filtering using default parameters using the script *split_libraries.py* and subsampled at an even depth of 500 reads. Subsequently, all sequences were clustered into OTUs at 97% sequence similarity against the GreenGenes database using SortMeRNA (**Kopylova et al., 2012**). All sequences that failed to match the reference were discarded. Analyses of alpha and beta diversity were conducted using a combination of QIIME and custom R scripts. Principal Coordinate Analyses were generated based on the unweighted UniFrac distance (**Lozupone and Knight, 2005**) and visualized in Emperor (**Vázquez-Baeza et al., 2013**). A list of all the datasets included in this study can be found in Table S1.

The OTU count matrices and taxonomic information, as well as the scripts used to analyze the data and generate the figures of this study are available at http://www.mpipz.mpg.de/R_scripts.

Table S1

Studies included in the meta-analysis

study	host	number of samples	technology	journal
Wu *et al.*, 2011	Human	96	454	Science
David *et al.*, 2014	Human	820	illumina/GAIIx	Genome Biol.
Koenig *et al.*, 2010	Human	61	454	PNAS
Muegge *et al.*, 2011	Other mammals	39	454	Science
Peiffer *et al.*, 2013	Maize	464	454	PNAS
Roeselers *et al.*, 2011	Zebrafish	25	454	ISME
Bolnick *et al.*, 2014	Stickleback	192	illumina MiSeq	Mol. Ecol.
Edwards *et al.*, 2015	Rice	402	illumina MiSeq	PNAS
Franzenburg *et al.*, 2013	Hydra	45	454	PNAS
Schlaeppi *et al.*, 2014	*A. thaliana* and rel.	77	454	PNAS
Bulgarelli *et al.*, 2015	Barley	42	454	CHOM
Lundberg *et al.*, 2012	*A. thaliana*	1,248	454	Nature
Goodrich *et al.*, 2014	Human	1,082	illumina MiSeq	Cell
Zarraonaindia *et al.*, 2015	Grapevine	751	illumina MiSeq	MBio

Table S1. Studies included in the meta-analysis. The group 'Arabidopsis and relatives' contains root and rhizosphere samples from *A. thaliana*, *A. alpina*, *A. haleri* and *Cardamine hirsuta*. The host species included in Muegge *et al.,* referred in the main text as 'wild animals' include the following assortment of mammals: African elephant, Angolan black and white colobus monkey, BigHorn sheep, Black lemur, Black rhinoceros, Bush dog, Capybara, Chimpanzee, European rabbit, Gazelle, Hamadryas baboon, Horse, Lion, Marmoset, North American black bear, Okapi, Polar bear, Red kangaroo, Reticulated giraffe, Ring-tailed lemur, Rock hyrax, Short-beaked echidna, Southern three-banded armadillo, Spectacled bear, Spotted hyena, Springbok, Squirrel, Sumatran orangutan, Transcaspian Urial sheep, Visayam warty pig, Western lowland gorilla, White-faced saki, Zebra.

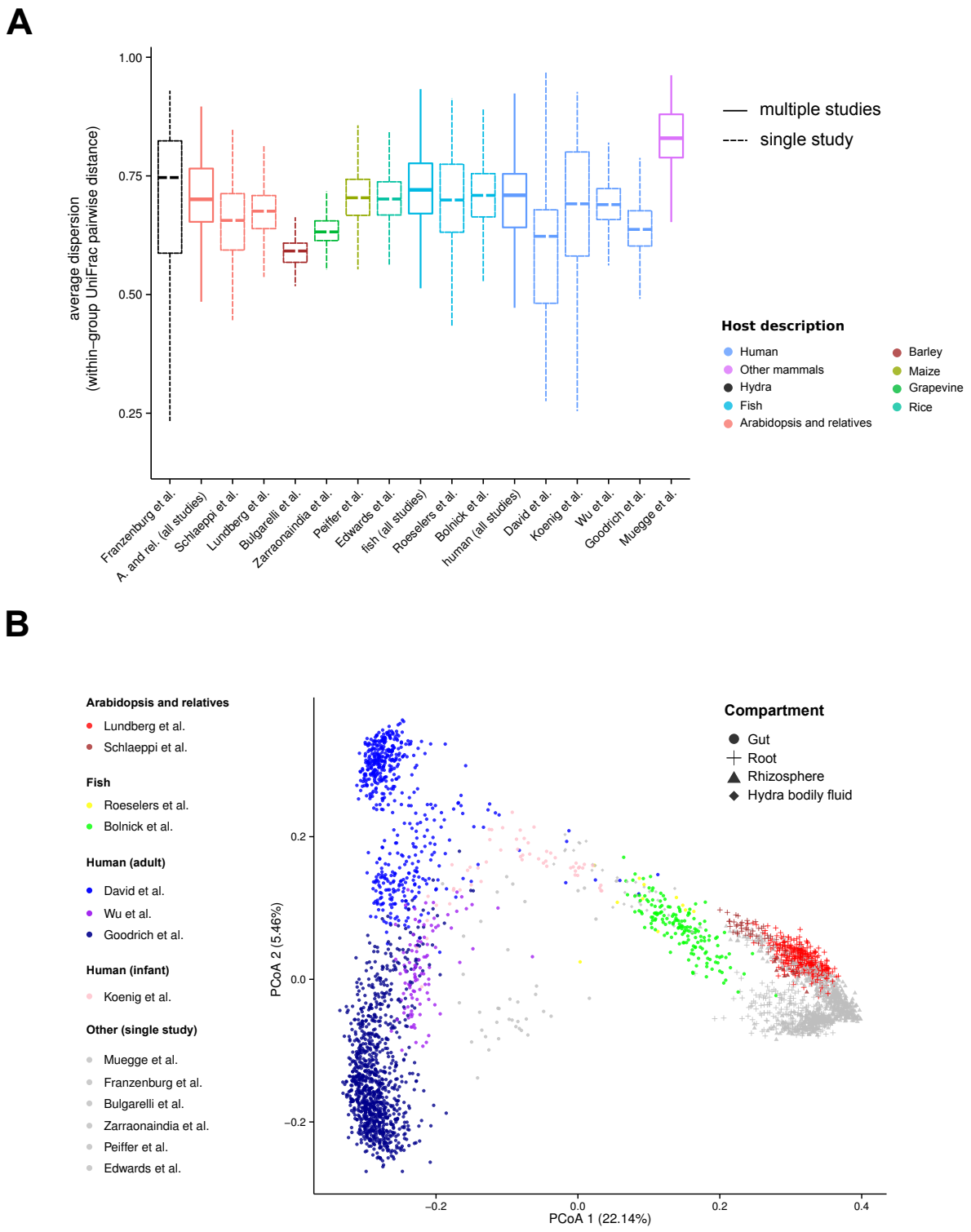


Figure S1. Analysis of diversity between studies associated to the same host species. **(A)** Analysis of dispersion per group of samples measured as average pairwise UniFrac distance. Individual studies are shown in dashed lines and groups of studies associated to the same host in solid lines. **(B)** Principal Coordinate Analysis (PCoA) of pairwise unweighted UniFrac distances between samples. Shapes correspond to the different compartments and colors depict hosts with samples from more than one study. Samples for single-study hosts are shown in gray.

References

Bolnick, D.I., Snowberg, L.K., Caporaso, J.G., Lauber, C., Knight, R., and Stutz, W.E. (2014). Major Histocompatibility Complex class IIb polymorphism influences gut microbiota composition and diversity. Mol. Ecol. *23*, 4831-4845.

Bulgarelli, D., Garrido-Oter, R., Münch, P.C., Weiman, A., Dröge, J., Pan, Y., McHardy, A.C., and Schulze-Lefert, P. (2015). Structure and function of the bacterial root microbiota in wild and domesticated barley. Cell Host Microbe *17*, 392-403.

Caporaso, J.G., Kuczynski, J., Stombaugh, J., Bittinger, K., Bushman, F.D., Costello, E.K., Fierer, N., Peña, A.G., Gordon, J.I., Huttley, G.A., et al. (2010). QIIME allows analysis of high-throughput community sequencing data. Nat. Methods 7, 335-336

David, L.A., Materna, A.C., Friedman, J., Campos-Baptista, M.I., Blackburn, M.C., Perrotta, A., Erdman, S.E., and Alm, E.J. (2014). Host lifestyle affects human microbiota on daily timescales. Genome Biol. *15*, R89.

Edwards, J., Johnson, C., Santos-Medellín, C., Lurie, E., Podishetty, N.K., Bhatnagar, S., Eisen, J.A., and Sundaresan, V. (2015). Structure, variation, and assembly of the root-associated microbiomes of rice. Proc. Natl. Acad. Sci. USA *112*, E911-920.

Franzenburg, S., Walter, J., Künzel, S., Wang, J., Baines, J.F., Bosch, T.C., and Fraune, S. (2013). Distinct antimicrobial peptide expression determines host species-specific bacterial associations. Proc. Natl. Acad. Sci. USA *110*, E3730-3738.

Goodrich, J.K., Waters, J.L., Poole, A.C., Sutter, J.L., Koren, O., Blekhman, R., Beaumont, M., Van Treuren, W., Knight, R., Bell, J.T., et al. (2014). Human genetics shape the gut microbiome. Cell *159*, 789-799.

Koenig, J.E., Spor, A., Scalfone, N., Fricker, A.D., Stombaugh, J., Knight, R., Angenent, L.T., and Ley, R.E. (2011). Succession of microbial consortia in the developing infant gut microbiome. Proc. Natl. Acad. Sci. USA *108 (Suppl 1)*, 4578-4585.

Kopylova E., Noé L., and Touzet H. (2012). SortMeRNA: fast and accurate filtering of ribosomal RNAs in metatranscriptomic data. Bioinformatics *28*, 3211-3217.

Lozupone C., and Knight R. (2005). UniFrac: a new phylogenetic method for comparing microbial communities. Appl. Environ. Microbiol. *71*, 8228-8235.

Lundberg, D.S., Lebeis, S.L., Paredes, S.H., Yourstone, S., Gehring, J., Malfatti, S., Tremblay, J., Engelbrektson, A., Kunin, V., del Rio, T.G., et al. (2012). Defining the core *Arabidopsis thaliana* root microbiome. Nature *488*, 86-90.

McDonald, D., Price, M.N., Goodrich, J., Nawrocki, E.P., DeSantis, T.Z., Probst, A., Andersen, G.L., Knight, R., and Hugenholtz, P. (2012). An improved Greengenes taxonomy with explicit ranks for ecological and evolutionary analyses of bacteria and archaea. ISME J. *6*, 610-618.

Muegge, B.D., Kuczynski, J., Knights, D., Clemente, J.C., González, A., Fontana, L., Henrissat, B., Knight, R., and Gordon, J.I. (2011). Diet drives convergence in gut microbiome functions across mammalian phylogeny and within humans. Science *332*, 970-974.

Peiffer, J.A., Spor, A., Koren, O., Jin, Z., Tringe, S.G., Dangl, J.L., Buckler, E.S., and Ley, R.E. (2013). Diversity and heritability of the maize rhizosphere microbiome under field conditions. Proc. Natl. Acad. Sci. USA *110*, 6548-6553.

Roeselers, G., Mittge, E.K., Stephens, W.Z., Parichy, D.M., Cavanaugh, C.M., Guillemin, K., and Rawls, J.F. (2011). Evidence for a core gut microbiota in the zebrafish. ISME J *5*, 1595-1608.

Schlaeppi, K., Dombrowski, N., Oter, R.G., Ver Loren van Themaat, E., and Schulze-Lefert, P. (2014). Quantitative divergence of the bacterial root microbiota in *Arabidopsis thaliana* relatives. Proc. Natl. Acad. Sci. USA *111*, 585-592.

Vázquez-Baeza, Y., Pirrung, M., Gonzalez, A., Knight, R. (2013). EMPeror: a tool for visualizing high-throughput microbial community data. Gigascience *2*: 16.

Wu, G.D., Chen, J., Hoffmann, C., Bittinger, K., Chen, Y.Y., Keilbaugh, S.A., Bewtra, M., Knights, D., Walters, W.A., Knight, R., et al. (2011). Linking long-term dietary patterns with gut microbial enterotypes. Science *334*, 105-108.

Zarraonaindia, I., Owens, S.M., Weisenhorn, P., West, K., Hampton-Marcell, J., Lax, S., Bokulich, N.A., Mills, D.A., Martin, G., Taghavi, S., et al. (2015). The soil microbiome influences grapevine-associated microbiota. mBio *6*, e02527-14.