clusters. Subsequent work has shown that the range of variability in the gut microbiota of children and of non-Western populations greatly exceeds the variability captured in the populations used to define the original enterotypes; in addition, even in Western populations, the variability follows more of a continuum dominated by a gradient in the abundance of the genera *Bacteroides* and *Prevotella*. Another consideration in enterotype analysis is whether location on a map defined by healthy human variation is relevant to predisposition to disease or whether instead rare species with particular functions are more important discriminants.

**Functional Redundancy** *Functional redundancy* arises when functions are performed by many bacterial taxa. Thus interpersonal differences in microbial bacterial diversity (i.e., which bacteria are present) are not necessarily accompanied by comparable degrees of difference in functional diversity (i.e., what these bacteria can do). Characterization of a microbiome by shotgun sequencing is important because, unlike SSU rRNA analyses, shotgun sequencing provides a direct readout of the genes (and, via comparative genomics, their functions) in a given community. One fundamental question is the degree to which variations in the species occupying a given body habitat correlate with variations in a community's functional capabilities. For example, the *neutral theory of community assembly* developed by macroecologists suggests that species are added to the community without respect to function, automatically endowing the community with functional redundancy. If applicable to the microbial world, neutral community assembly would predict a high level of variation in the types of microbial lineages that occupy a given body habitat in different individuals, although the broad functions encoded in the microbiomes of these communities could be quite similar.

Shotgun sequencing of the fecal microbiome has revealed that different microbial communities converge on the same functional state: in other words, there is a group of microbial genes represented in the guts of unrelated as well as related individuals. The same principle holds true at other body sites (Fig. 86e-2). The "core" gut microbiome is enriched in functions related to microbial survival (e.g., translation; metabolism of nucleotides, carbohydrates, and amino acids) and in functions that benefit the host (nutrient and energy partitioning from the diet to microbes *and* host). The latter functions encompass the food webs mentioned above, in which products of one type of microbe become the substrates for other microbes. These webs, which can be incredibly elaborate, change as microbes adjust their patterns of gene expression and metabolism in response to alterations in nutrient availability. Thus the sum of all the activities of the members of a microbial community can be viewed as an emergent rather than a fixed property.

It is important to note that pairwise comparisons have shown that family members have functionally more similar gut microbiomes than do unrelated individuals. Thus, intrafamilial transmission of a gut microbiome within a given generation and across multiple generations could shape the biologic features of humans belonging to a kinship and modulate/mediate risks for a variety of diseases.

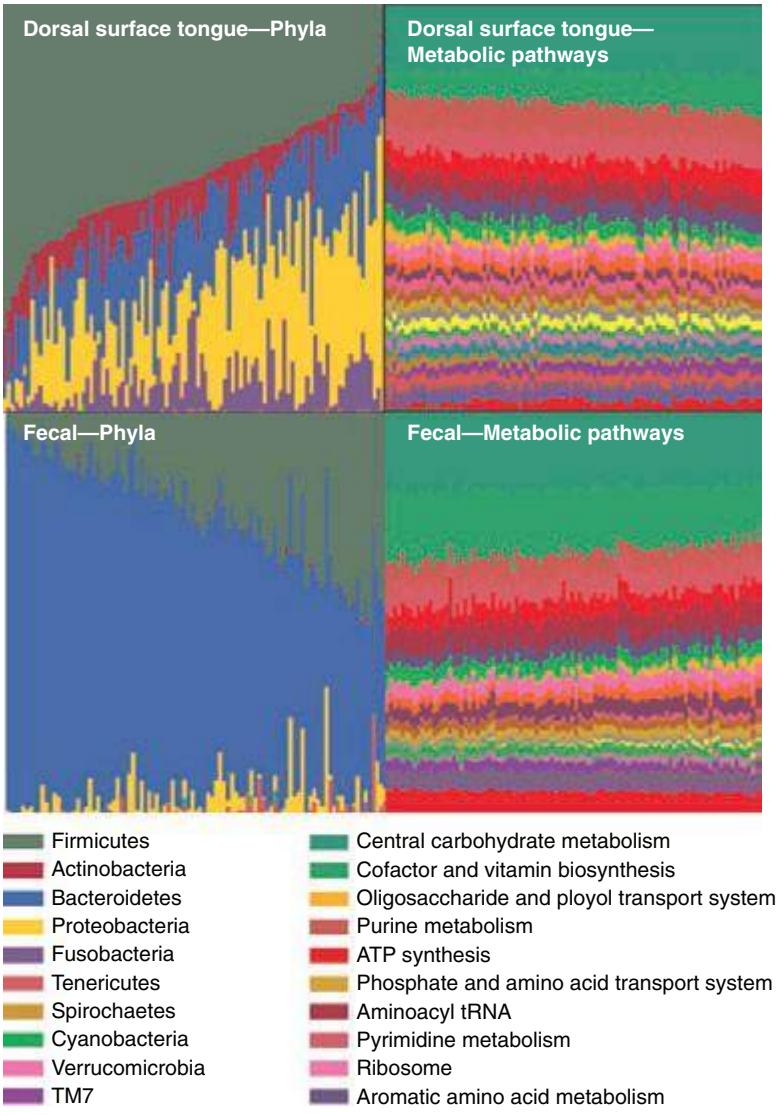


**FIGURE 86e-2 Interpersonal variation in organismal representation in body habitat–associated communities is more extensive than interpersonal variation in gene functional features.** Bacterial taxonomy and metabolic function are compared in 107 oral microbiota and microbiome samples (top) and in 139 fecal microbiota and microbiome samples (bottom). Samples represent an arbitrarily chosen subset from 242 healthy young adults living in the United States, with equal numbers of men and women. The same DNA extracts from the same samples were used for both taxonomic and functional classifications; each sample was analyzed by bacterial 16S rRNA amplicon sequencing (mean, 5400 sequences per sample) and by shotgun sequencing of community DNA (mean, 2.9 billion bases per sample). Taxonomic groups vary dramatically in their representation among different samples, with different characteristic bacterial phyla in the oral versus the fecal microbiota; e.g., members of the Actinobacteria and Fusobacteria are far more common in the mouth than in the gut, while members of Bacteroidetes are far more common in fecal samples. In contrast, metabolic pathways are far more consistently represented in different samples, even when the species that contribute to these pathways are completely different. These results suggest a high degree of functional redundancy in microbial ecosystems—similar to that observed in macroecosystems, in which many fundamentally different lineages of organisms can play the same ecologic roles (e.g., pollinator or top predator). *(Adapted from Human Microbiome Project Consortium: Nature 486:207, 2012; and CA Lozupone et al: Nature 489:220, 2012.)*

**Stability** Like other ecosystems, human body habitat–associated microbial communities vary over time, and an understanding of this variation is essential for a functional understanding of our microbiota. Few high-resolution time series of individual healthy adults have been published to date, but one available daily time series suggests that individuals tend to resemble themselves microbially day to day over a span of 6–15 months, retaining their separate identities during cohabitation. The development of low-error amplicon sequencing methods has provided a much more reliable way for defining stability at the strain level than was available in the past. Application of these methods to the guts of healthy individuals sampled over time has disclosed that a healthy adult gut harbors a persistent collection of ~100 bacterial species and several hundred strains. The stability of the bacterial components follows a *power law*: bacterial strains acquired early in life can persist in the gut for decades, although