Top 10 Bacterial Species in the Beyond Bacteria Cohort

The Beyond Bacteria cohort currently consists of four individuals. The microbiome compositions of these four individuals varied greatly at the species level. While in a few cases a given species was found among the top ten species in more than one individual, in most cases the overlap was minimal. We describe in more detail below the ten most abundant species across the entire cohort, followed by a short discussion of your own sample.

One of the protocols used for the Beyond Bacteria samples is called whole-genome shotgun (WGS) sequencing. This protocol randomly shears all of the DNA present in a sample into small fragments (hence the name "shotgun"). These small fragments of DNA are then read out on a sequencing instrument such as the Illumina MiSeq. The result is a vast collection of small sequences from all over the genomes of everything in your sample. These sequencing fragments can then be compared against existing reference databases to assess taxonomy and gene function. As WGS sequences everything, we're able to get a much higher level of specificity on the organisms that are represented in a sample. In contrast, the 16S rDNA protocol used for the standard American Gut sample focuses only on a small region of a single gene which greatly limits its power to differentiate strains or species.

You can find the specific top taxa per Beyond Bacteria sample here, and heatmap comparing each Beyond Bacteria sample by species here.

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1. *Lactobacillus gasseri*

The name *Lactobacillus gasseri* likely brings to mind thoughts of probiotics, as *Lactobacilli* strains are often used in probiotic mixtures. *L. gasseri* is no exception; it, too, has been studied for its probiotic potential in a number of contexts. *L. gasseri*, first isolated from the human intestine, has been demonstrated to establish in the GI tract when given as a probiotic (ref, ref). This ability is particularly advantageous, as probiotics typically have difficulties establishing in the GI tract.

The potentially beneficial effects of *L. gasseri* are numerous. It binds cholesterol (ref), prevents dextran sulfate-induced ulcerative colitis in rats (ref), and produces a bacteriocin (ref, ref), a bacterial toxin that could potentially be used as a weapon against closely related intestinal pathogens.

A 2010 study (ref) demonstrated that probiotic treatment with *L. gasseri* of individuals with obese tendencies was followed by reduced abdominal adiposity, body weight, BMI, and waist and hip measurements, indicating that *L. gasseri* could be used as a probiotic in some to prevent obesity in at-risk individuals. On the other end of the spectrum, a 2001 study (ref) demonstrated that *L. gasseri* treatment of individuals with *Helicobacter pylori* suppressed *H. pylori* and reduced gastric inflammation. These studies suggest that the probiotic potential of *L. gasseri* could be quite large, though more studies are needed to fully characterize its probiotic potential and how different individuals respond to treatment with this probiotic strain.

2. *Methanobrevibacter smithii*

Methanobrevibacter smithii (*M. smithii*) is an archaeon, not a bacterium, and has been observed as the predominant archaeon in the human gut. It is a methanogen, meaning that it produces methane (one of the gases in flatulence) as a metabolic byproduct in low-oxygen conditions; additionally, it removes excess hydrogen from the gut (including the hydrogen in methane) and thus allows for an increase in energy extraction from nutrients (ref). *M. smithii* has been observed in human feces for decades (ref, ref). Interest in *M. smithii* and other methane producers is rooted in the study of methane producers in human feces. Initial estimates determined that only about one-third of adults harbor methane producers in the gut, and that the amounts of methane produced varies by individual (ref, ref, ref).

Because *M. smithii* consumes hydrogen in the gut, this places the microbe in the unique position to potentially increase human gut health. Accumulation of hydrogen decreases the efficiency of microbial fermentation, which is involved in polysaccharide digestion (a process human cells cannot perform); therefore, M. smithii can aid in microbial fermentation (and polysaccharide digestion) by removing the fermentation-inhibiting hydrogen. Additionally, it also removes fermentation end-products (ref).

Interestingly, a 2011 study published in the International Journal of Obesity revealed that obesity-associated gut microbiota were depleted in M. smithii, while a 2009 PLoS One study noted that levels of *M. smithii* were increased in anorexic patients compared to normal-weight controls (ref). These results appear to be related to *M. smithii*'s use of nutrients in the human gut; however, the results are still preliminary and more work is needed to confirm or refute *M. smithii*'s exact role as a member of the gut microbiome. Regardless, one thing is clear: *M. smithii* is not an insignificant stand-by member of the gut microbiome and likely plays an important role in relation to nutrition and energy harvest.

3. *Roseburia intestinalis*

Like many species on this list, *Roseburia intestinalis* was first isolated from human feces. *R. intestinalis* produces butyrate via fermentation of dietary plant-derived polysaccharides such as xylan (ref, ref), a molecule that plays a very important role in intestinal health. Not only does butyrate represent an energy source for intestinal epithelial cells (ref), but it also is capable of counteracting inflammation-mediated ulcerative colitis and colorectal cancer (ref) through its ability to suppress colonic inflammation (ref).

Because of butyrate's positive effects on GI tract health, bacterial species that produce butyrate, such as *R. intestinalis*, are likely important players in maintaining intestinal health. *R. intestinalis* is not as well characterized as other members of the gut microbiome, but a recent study demonstrated that *R. intestinalis* abundances were lower in type 2 diabetes patients (ref). Additionally, a study in India indicated that *R. intestinalis* abundance was decreased in ulcerative colitis patients with more severe disease (ref). Consistent with that finding, butyrate was also significantly decreased in those patients.

4. *Roseburia inulinivorans*

Roseburia inulininovorans, a close relative of *R. intestinalis*, was also first isolated from human feces. Like *R. intestinalis*, *R. inulinivorans* also produces butyrate, but it does so by degrading the plant polysaccharides starch and inulin and the sugar fucose instead of xylan (ref). In addition to butyrate, *R. intestinalis* can also produce propionate. Like butyrate, propionate can increase host health, although its action is not focused on the gut epithelium. It is thought to decrease lipogenesis (the conversion of simple sugars to fatty acids), serum cholesterol levels, and carcinogenesis (the transformation of normal cells into cancer cells) (ref). *R. inulinivorans* is therefore a potentially important player in maintaining host health in multiple ways-both via butyrate and via propionate. However, because *R. inulinivorans* has only been recently described, no specific work describing its impact on human health or disease has been published to date.

5. *Akkermansia muciniphila*

Akkermansia muciniphila is known for its ability to degrade mucin, a protein produced by epithelial tissues and that forms gels. The ability to form gels means mucin can serve a number of functions, from lubrication to forming chemical barriers (ref). *A. muciniphila* is a common member of the human gastrointestinal tract (ref), and is even present in infants as well as adults, though its abundance decreases in elderly individuals (ref). It appears to play an important role in gut barrier integrity and favorable modulation of the mucosal immune response (ref). Interestingly, *A. muciniphila* was reported to be decreased in autism (ref), a disorder associated with a range of gastrointestinal disorders.

A number of research groups have focused on the association between *A. muciniphila* and diabetes and obesity. In both humans and in animal models, *A. muciniphila* abundance decreases as host weight increases. An elegant 2012 study demonstrated that in obese diabetic mice (type 2 diabetes, ref). *A. muciniphila* was decreased; however, treatment of these mice with *A. muciniphila* reversed high-fat diet induced metabolic disorders, including insulin resistance. Treatment was also associated with increased intestinal levels of molecules called endocannabinoids, which control inflammation and gut barrier integrity.

Although much work is yet to be done, the evidence points to an important role for *A. muciniphila* in gut barrier integrity, with likely associations between decreased levels of *A. muciniphila* and diseases such as obesity and diabetes. It is important to remember that whether this decrease in *A. muciniphila* is simply a result of the disease or whether it actually plays an active role in the disease process is unknown.

6. *Prevotella copri*

Prevotella copri is another intestinal microbe, but unlike some of the others discussed here, it doesn't have any known or presumed roles in maintaining human health. In fact, the opposite appears to be the case. *P. copri* is most famous for its alleged connection to rheumatoid arthritis, an accusation that was first presented in 2013 when a research group found that *P. copri* was strongly correlated with disease in patients with new-onset rheumatoid arthritis (ref). This group also identified unique *Prevotella* genes that also correlated with disease, and when they colonized mice with *P. copri*, the mice became more susceptible to chemical-induced colitis. Although exciting, this study is preliminary and the first to suggest a connection between *P. copri* and arthritis. More work needs to be done to determine whether *P. copri* is associated with inflammation in this autoimmune disease or not, and before we brand *P. copri* as a "bad" or "good" player in human health. This cautionary statement is especially underscored when we take into account that in the same year in which *P. copri* was suspected to be connected to rheumatoid arthritis, a second research group determined that *P. copri* related species are decreased in the gut microbiomes of autistic children (ref).

7. *Bifidobacterium breve*

Like *Lactobacillus gasseri*, *Bifidobacterium breve* is often used as a probiotic; however, most studies in humans have been done on infants, rather than adults. Several studies have demonstrated beneficial, anti-inflammatory properties possessed by *B. breve*. Treatment with *B. breve* combined with other probiotic species or carbohydrate molecules reduces inflammation in animal models of asthma (ref, ref), and significantly reduces the risk of developing atopic dermatitis, the development of asthma symptoms, and allergic markers in infants (ref, ref, ref).

The beneficial effects observed in the studies referenced above are likely due to the purported ability of *B. breve* to positively influence the immune system. By adding *B. breve*-produced proteins to cells in the laboratory, investigators were able to determine that *B. breve* not only accelerated Peyer's patch cell proliferation, but also enhanced antibody (B cell) production (ref). Additionally, *B. breve* induced dendritic cell maturation, activation, and survival, and inhibited the negative effects of bacterial lipopolysaccharide on these immune cells (ref). Additionally, *B. breve* significantly reduced GI tract expression of inflammatory genes in newborn rat pups (ref).

8. *Eubacterium eligens*

Although *Eubacterium* are often isolated from human feces, not much is known about these bacteria. Like many other species in this list, *E. eligens* is capable of fermenting several plant polysaccharides (ref), and the *Eubacterium* genus in general produces GI-tract health-promoting butyrate (ref, ref). However, no specific studies thoroughly analyzing the potential beneficial (or harmful) actions of *E. eligens* have been published to date. A related species, *Eubacterium aerofaciens*, has been shown to be closely associated with a low risk for colon cancer (ref), while the genus *Eubacterium* was significantly decreased in children born to obese mothers than those born to normal-weight mothers (ref), and in another study was also more abundant in normal-weight individuals compared to overweight individuals (ref). Therefore, it seems as though *Eubacterium* may have a beneficial role in human health, but the existence of so few studies illustrates the need for a focused research effort to fully characterize the role of not only *E. eligens* but other *Eubacterium* species.

9. *Eubacterium rectale*

Eubacterium rectale is a close relative to *E. eligens*, and as such, little research has been done on this member of the *Eubacterium* genus. As mentioned above, some preliminary work suggests that *Eubacterium* may play a beneficial role in human health, though much work is still needed to fully characterize the role of *Eubacterium spp.* in health and disease. As described above, studies have indicated that the genus *Eubacterium* is positively associated with a healthy weight; a 2008 study determined that *E. rectale* increased in individuals on a weight loss diet compared to those on a weight-maintenance diet (ref). Studies have also shown that *E. rectale* is decreased in patients with ulcerative colitis (ref) and additionally is not a major member of bacterial biofilms in inflammatory bowel disease (IBD) patients (ref). Interestingly, *E. rectale* was a major member of bacterial biofilms in inflammatory bowel syndrome (IBS) patients (ref).

10. *Faecalibacterium prausnitzii*

Like *Roseburia spp.*, *Faecalibacterium prausnitzii* is an important butyrate producer in the human GI tract. Numerous studies have described associations between *F. prausnitzii* and health and several disease states, solidly establishing this species as an importer player in maintaining host health.

Much work has been focused on the association between the presence or absence of *F. prausnitzii* in the gut microbiome and gut diseases, and a wealth of evidence suggests that *F. prausnitzii* promotes gut health in a number of contexts. Lower abundances of *F. prausnitzii* have been observed in IBD (ref) and infectious colitis patients (ref) as well as Crohn's disease patients (ref) and ulcerative colitis patients (ref). In several animal models of colitis, *F. prausnitzii* exerts a number of beneficial anti-inflammatory effects (ref, ref, ref). Beneficial effects have also been observed in humans, with colonization with *F. prausnitzii* associated with the maintenance of clinical remission in ulcerative colitis patients (ref). Additionally, immune cells that are induced by *F. prausnitzii*, are deficient in IBD patients (ref).

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