

Detailed Phylogenetic Analysis Reveals Microbial Basis of Clinical Criteria

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Bacterial vaginosis (BV) affects approximately 29% of reproductive age women in the United States, and is associated with increased risks for pelvic inflammatory disease, preterm birth, and HIV acquisition. Despite this high prevalence, the microbiota associated with BV is not well characterized and many bacterial species found in the vagina are currently uncultivated. Given that different bacterial species can have different interactions with the host and therefore varying clinical significance, it is important to first identify bacteria to the species level to better understand their contributions to the biology of BV. Previously, few studies have described the complexity and diversity of microbial communities using both deep sequencing methods and species-level taxonomic classification, as done here. This study was led by the Vaccine and Infectious Disease Division's Dr. Sujatha Srinivasan, working with Dr. David Fredricks, collaborators in Computational Biology at the FHCRC, and collaborators at the University of Washington.

In this study, vaginal samples from 220 women with and without BV were subjected to broad range 16S rRNA gene PCR with high throughput pyrosequencing. The millions of resulting reads per sample were then passed through the researchers' "taxonomic classification pipeline," which utilized a phylogenetic tree containing a broad representation of vaginal bacteria for optimal classification. The combination of deep sequencing coupled with species-level classification also revealed several yet-unnamed bacteria. Women with BV have complex vaginal bacterial communities compared to women without BV, and no single bacterial species is universally present in all BV cases. Some women with BV had bacterial communities dominated by *Leptotrichia* or *Sneathia* species, others with *Prevotella* species, and others with an uncultivated bacterium designated BVAB-1. It may be that these subtypes of BV could potentially have varying effects on the different risks associated with BV. Women without BV had communities dominated by either *Lactobacillus crispatus* or *L. iners* (see figure).

Different bacterial species appear to impact varying elements of the four BV clinical criteria, which may explain the discrepancies in definitive BV diagnosis. Through this extensive analysis, new insights into the complex relationships between bacterial communities have also been revealed, as co-occurrence of bacterial taxa was evaluated statistically. In some subgroups of BV-associated

bacteria, there were strong positive correlations in species occurrence, possibly indicating metabolic dependencies. In other cases, bacteria were negatively correlated with each other, suggesting competition among species or mutual growth inhibition. Importantly, the researchers' development of bioinformatics tools that facilitate species-level microbial classification may be adapted to other regions of the human body or to ecosystems, for use in classifying high-throughput sequence reads of large numbers of microbial species.

[Srinivasan S, Hoffman NG, Morgan MT, Matsen FA, Fiedler TL, Hall RW, Ross FJ, McCoy CO, Bumgarner R, Marrazzo JM, Fredricks DN. 2012. Bacterial communities in women with bacterial vaginosis: high resolution phylogenetic analyses reveal relationships of microbiota to clinical criteria. *PLoS One*. 7\(6\): e37818](#)

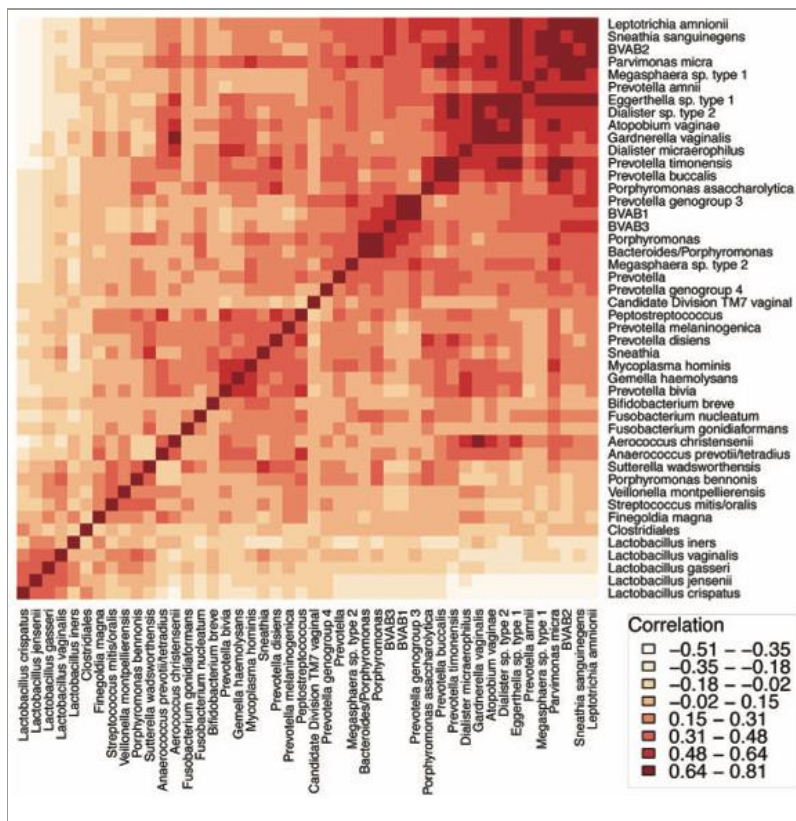


Image courtesy of authors

Co-occurrence analysis of bacterial taxa. Hierarchically clustered Pearson coefficients between abundant bacterial taxa, with correlation values ranging from -0.51 (light) to 0.81 (dark). Several sub-groups of bacteria associated with BV show strong positive associations.