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"Longitudinal Shotgun Metagenomic Analysis of the Vaginal Microbiome during the Onset of Bacterial Vaginosis"

Introduction: Bacterial Vaginosis (BV) is a common disorder associated with the vaginal microbiome characterized by the displacement of lactobacillus with an overgrowth of anaerobes. Symptomatic cases can be associated with Pelvic Inflammatory Disease (PID), complications with pregnancy, and greater susceptibility to sexually transmitted infections. In cases where antibiotics are needed to treat BV, recurrence commonly occurs within 3 months to a year. Despite the prevalence of BV, the specific mechanism associated with the onset is unclear. In this pilot study we utilized shotgun metagenomics to identify the discrete changes occurring in the vaginal microbiome leading up to the onset of BV with the goal of better understanding the etiology of BV.

Methods: A cohort of women with a baseline healthy vaginal microbiome (no Amsel Criteria and Nugent Score of 0 - 3) were prospectively followed for 90 days. Vaginal samples were self-collected daily to screen for incident BV (iBV). Shotgun metagenomic sequencing was carried out retrospectively following an iBV diagnosis (two consecutive days of Nugent Score $\geq$ 7). Sequencing was carried out on samples collected up to 12 days leading up to iBV as well as the day of the iBV diagnosis. Samples were sequenced using the Illumina Hiseq 4000. Sequencing data was analyzed using two methods, metagenomic assembly through the Atlas workflow 2.62a, and mapping of sequenced reads to reference databases with Biobakery 3.

Discussion: Both taxonomic and functional metagenomic data highlights the community changes that occur during the onset of iBV. Taxonomic analysis showed elevated abundance of BV associated bacteria such as *Gardnerella vaginalis*, *Prevotella bivia*, and *Atopobium vaginae* during iBV, while the relative abundance of Lactobacillus species was strikingly diminished. Functional analysis reflects the shift in dominance to BV associated anaerobes with an increased abundance of genes associated with oxidative metabolism during BV.

Conclusion: Metagenomic analysis provides a new deeper level of insight into the microbial community changes that occur leading up to the onset of iBV.

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