Looking For Therapeutic Targets in Bacterial Vaginosis

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The human body hosts complex communities of microbes that differ at each body site. These microbes can impact human physiology and health through production of metabolites that directly affect human cells or microbial community composition. The human vagina hosts a limited number of Lactobacillus species, but in the dysbiotic condition bacterial vaginosis (BV), the bacterial community shifts to complex communities of diverse anaerobes.

BV is a highly prevalent condition in the United States, where it affects up to 29% of women and has been associated with numerous adverse outcomes including preterm birth, pelvic inflammatory disease, and elevated risks for sexually transmitted infections including HIV. It is unclear how BV-associated bacteria mediate these increased health risks, and there have been few studies linking vaginal bacterial communities to detailed metabolite profiles.

Identification of the metabolites present in the vagina of women affected by this condition may elucidate how different bacterial populations thrive, and this knowledge could be used for disrupting metabolic pathways present in deleterious bacteria. Dr. Srinivasan and coworkers from Dr. David Fredriks' Laboratory (Vaccine and Infectious Disease Division) at Fred Hutch pursued a metabolomics-based approach wherein gas or liquid chromatography was coupled with mass spectrometry to measure hundreds of low molecular weight metabolites in vaginal fluid and to link these metabolites to particular bacteria detected by PCR.

"The novelty of our study," explained Dr. Srinivasan, "is the breadth and depth of the approach, and the linking of important metabolites with concentrations of bacteria and clinical findings in women. BV is associated with strong metabolic signatures affecting multiple pathways including amino acid, carbohydrate and lipid metabolism, with significant differences in concentrations of 62% of metabolites detected in women with BV." The study indeed demonstrated a different pattern of metabolites in women with BV. Such metabolites correlated with the presence of BV-associated bacteria and were associated with characteristics distinctive of BV, such as an elevated pH, amine odor, vaginal discharge and presence of clue cells, which are vaginal epithelial cells covered by bacteria. Furthermore, antibiotic treatment resulted in the increase of metabolites prevalent in women not diagnosed with BV.

Women with BV have metabolic profiles marked by much lower concentrations of amino acids and dipeptides, concomitant with higher levels of amino acid catabolites and polyamines, suggesting that BV-associated bacteria may use amino acids as carbon sources. In contrast, lactobacilli are known to metabolize sugars such as glycogen derived from the host and do not appear to rely on amino acids as their primary carbon source which are more elevated in women not diagnosed with BV.

"This study has advanced our understanding of the functional status of bacterial communities in BV. Insights from this work may provide opportunities for developing novel approaches for treatment or prevention of BV," commented Dr. Srinivasan. Given the absence of a vaccine and a durable therapy for BV, these results give hope that the solution to this condition is getting closer.

Srinivasan S, Morgan MT, Fiedler TL, Djukovic D, Hoffman NG, Raftery D, Marrazzo JM, Fredricks DN. 2015. Metabolic signatures of bacterial vaginosis. *MBio* 6(2): e00204-15.

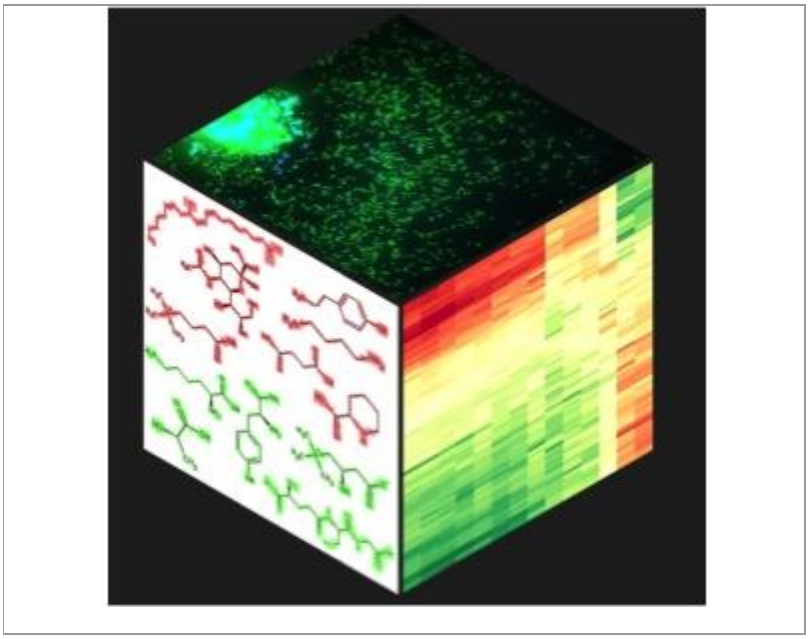

Image courtesy of Sue Bartlett

Bacteria, metabolites and their associations in the human vagina. Bacteria in vaginal fluid from a woman with bacterial vaginosis (BV) are detected by fluorescence in situ hybridization in the top panel. A selection of metabolites in vaginal fluid (left) and a heat map of associations between metabolites and vaginal bacteria (right) are presented in the lower panels.