Method Development Involving Modeling Bacterial Metabolite Regulation of Vaginal Epithelial Cell Signaling in Bacterial Vaginosis

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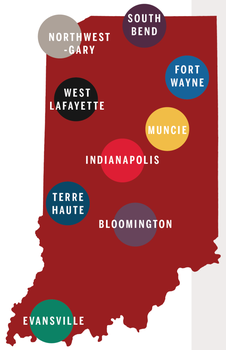
SCHOLARLY CONCENTRATIONS



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Background and Methods

Bacterial Vaginosis has a high recurrence rate despite therapy with metronidazole. Current literature suggest disruption of vaginal microbiome composition ("microbiome group") may contribute to the regulation of pro-inflammatory pathways.

Objective: To explore efficacy of ssGSEA2.0, a package within R, to characterize the relationship between vaginal metabolites, host or microbiome-derived, and transcriptomic responses in epithelial cells stratified by vaginal microbiome composition

Methods: Transcript levels and metabolite concentrations precollected from 23 East African women were processed and stratified by lactobacillus dominant microbiome groups using packages in R. Relationships between KEGG pathway enrichment scores from transcriptomic data and metabolite levels were analyzed and visualized using Heatmap3 and Cytoscape.

Figures

- Figure 1. Bacterial composition among lactobacillus dominant (LD) microbiome groups and the nonlactobacillus dominant (nLD) microbiome groups
- Figure 2. Correlation heatmap of LD patients vs nLD patients. Red indicates positive correlation and blue indicates negative correlation. Values correlate transcriptomic-inferred KEGG pathway enrichment scores with metabolite concentrations
- Figure 3. Networks for LD and nLD were created using significant correlation values (R > l0.5l, p < 0.05) to characterize relationships between individual metabolites and pathway enrichment scores. Imidazole-related metabolites were studied and displayed in the figure. A Venn diagram

Results

- Heatmaps and Networks shows differences in metabolite-regulated gene regulation
- Difference in the quantity and composition of pathways after filtering for strong correlations (R > |0.5|) and significance (p< 0.05).
- Lactobacillus dominant microbiomes showed fewer strongly associated metabolite-KEGG pathway relationships, including pro-inflammatory imidazole related pathways.

Discussion

- Differences in the heatmap and the network pathways suggests a functional rewiring of metabolite-pathway relationships among lactobacillus and nonlactobacillus dominant groups
- Results from this study showed that ssGSEA2.0 was **efficacious** in characterizing enrichment scores for this subset.
- Analysis shows that ssGSEA is plausible for any microbiome transcriptomic data set with any gene set database.
- Currently used to analyze and characterize transcriptomic data from intestinal biopsies from patients with inflammatory bowel disease (IBD) to understand the protective effects of estrogen on the pathogenesis of IBD.

FIGURE 1. VAGINAL MICROBIOME COMPOSITION

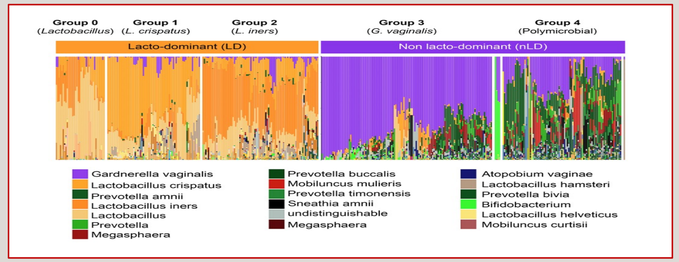

FIGURE 2. LD AND nLD HEATMAPS

FIGURE 3. IMIDAZOLE RELATED NETWORKS