**Metabolic Analysis of the *Gardnerella* Pangenome *in silico***

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**Abstract Text:**

Bacterial vaginosis (BV) is one of the most common vaginal conditions in reproductive-age women with vaginal complaints (Schwiertz et al., 2006). *Gardnerella* is the primary pathogenic bacterial genus present in the polymicrobial infection known as bacterial vaginosis (BV). Despite BV's high prevalence and associated chronic and acute women's health impacts, the *Gardnerella* pangenome is largely uncharacterized at both the genetic and functional metabolic levels. Here we used *in silico* analysis via genome scale metabolic models to characterize 110 *Gardnerella* strains, representative of the known *Gardnerella* pangenome. Metabolic capacity varied widely across the pangenome, with 38.2% of reactions considered core reactions, compared to 49.6% of reactions identified as unique. Amino acid metabolism was disproportionately represented by unique metabolism (58.4%) compared to core metabolism (33.5%). Conversely, glycan metabolism was found to be enriched in core metabolism (55.6%) compared to unique metabolism (33.3%). We identified 57 essential genes across the pangenome via *in silico* gene essentiality screens within two simulated vaginal metabolic environments. Four genes – *gpsA, fas, suhB, psd* – were identified as conserved essential genes.

*psd* specifically has been found to play a role in bacterial membrane biogenesis and has been identified as a potential antimicrobial target (Voelker, 1997). *psd* activity in *Plasmodium falciparum* has been successfully inhibited using 4-quinolinamine compounds (Choi et al., 2016). Conserved essential genes could serve as novel targets for drug development. Additionally, flux balance analysis of all model reaction flux values, as well as transport flux values specifically, showed limited clustering based on sample isolation source, with the exception of lab strain isolates. These findings highlight the need for research using patient sample strains in order to accurately characterize *Gardnerella* present during infection. These data represent the first metabolic modeling of the *Gardnerella* pangenome and illustrate strain specific vaginal metabolic-interactions across the pangenome.