The Vaginal Microbiota during Pregnancy: Structured Resistomes and Strain-Level Genomics

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Résumé

The vaginal microbiota (VM) is a structured microbial ecosystem that plays a key role in reproductive health and antibiotic resistance dynamics. In a metagenomic analysis of 1,957 samples from pregnant women in the InSPIRe cohort, we identified widespread carriage of acquired antibiotic resistance genes (ARGs), with macrolide and tetracycline resistance genes, including *lsa(C)*, *erm(B)*, and *tet(M)*, among the most prevalent and abundant. These ARGs displayed strong associations with specific microbial community state types (CSTs), and co-abundance networks revealed taxon-specific modularity linking *Gardnerella*, *Prevotella*, and Enterobacterales to distinct ARG and mobile element profiles. The clinical relevance of resistomes are a function of their antibiotics spectrum. To better quantify this functional resistance capacity, we developed the Phenotypic Resistance Diversity Index (PRDI), which we used to reveal a delayed but significant post-antibiotic expansion in resistance breadth. Given this structured resistome landscape, we explored the ecological and genomic basis of dominant CSTs. Focusing on *Lactobacillus crispatus*, *L. iners*, and *Gardnerella vaginalis*, we performed comparative pangenomic (Pan-GWAS) analyses across hundreds of high-quality assembled genomes from our cohort. Substantial species-specific variation in accessory gene content, including mobile elements, adhesion factors, and niche-adaptive traits, was associated with community structure and stability. These findings suggest that strain-level genomic traits shape the structure and resilience of the VM, with implications for ARG carriage, transmission, and new avenues for diagnostics and therapeutic design.

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