Deciphering the Endometrial Host-Microbiome Interactions Associated with Reproductive Health

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Background
16S rRNA sequencing-based results linked an endometrial microbiota with a higher abundance of *Lactobacillus* spp. to live birth following in vitro fertilization (IVF); however, the presence of pathogenic bacteria associated with poorer reproductive outcomes, including no pregnancy, biochemical pregnancy, or clinical miscarriage (PMID: 34980280).
To understand how bacteria impact endometrial function, we paired shotgun metagenomics (WMS) and metatranscriptomics (MTX) to study the interactions between bacterial taxa and host gene functions during implantation.
Methods
WMS and MTX analyses were conducted on paired endometrial fluid samples and biopsies obtained from seventy-six infertile female patients undergoing IVF. Twenty-six achieved a live birth, while fifty had no pregnancy. WMS was performed using the Illumina DNA prep system and sequencing on the NovaSeq platform. Illumina Stranded total RNA with RiboZero was employed for MTX. DIABLO models from the mixOmics R package were used to perform an integrative analysis of transcriptomics and microbiome data to unravel the relationship between the host and bacteria.
Results
In patients with no pregnancy, genes related to humoral and cell-mediated (*IL1B, IL27, OSM*) and innate (*CEACAM3, LILRA3, MEFV*) immunity, post-transcriptional regulation (*MIR223, MIR4420*), and G protein-coupled receptor (GPCR) signaling (*CCRL2, FFAR2, GPR84*) interacted with commensal bacteria, showing negative correlations with *Lactobacillus* (including *L. crispatus*) and positive correlations with *Streptomyces*. Immunoglobulins involved in defense response to other organisms and phagocytosis (e.g., *IGHG1, IGHV3-15, IGHV4-39*) displayed a unique negative correlation with endometrial pathogens such as *Gardnerella vaginalis and Atopobium vaginae*.
Conclusions
Lactobacillus spp. possess a favorable association with the expression of immune-related genes and GPCR signaling in the endometrium, while pathogenic bacteria negatively correlate with immune defense- and phagocytosis-associated genes. These findings shed light on the impact of different endometrial microbial profiles in endometrial cells during embryo implantation.
Conflict of interest
DP-V is employed by Igenomix R&D. YY, and JY are employed by Ferring.