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Neisseria gonorrhoeae Transcriptional Response During Natural Mucosal Infection in Men and Women.

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Background

Neisseria gonorrhoeae colonizes and infects the male and female genital tract, two distinct environments characterized by intrinsic tissue, cellular, molecular, and microbial community differences. Our previous studies on the global transcriptomic analysis of *N. gonorrhoeae* in samples obtained from infected male and female subjects showed an increased expression of gonococcal antimicrobial resistance genes in men compared to women. Since infected men develop symptomatic urethritis, they often seek treatment or self-medicate. In contrast, infected women rarely present overt symptoms of gonococcal cervicitis, unless infection leads to subsequent pelvic inflammatory disease. Thus, most gonococcal infections in women are undiagnosed, underreported, and untreated, increasing the risk of transmission.

Aim/Methods

In the current study, we examined the *N. gonorrhoeae* response in the context of the male and female sex-specific host environment. Using mucosal samples obtained from matched male-female subjects, we analyzed genomic and transcriptomic data of the respective *N. gonorrhoeae* infecting strains, the genital microbial community, and the host.

Results

Phylogenetic analysis based on whole genome core single nucleotide polymorphisms of the *N. gonorrhoeae* isolates demonstrated that 92% of female subjects were infected by *N. gonorrhoeae* strains genetically identical to the strain infecting their matched male partner. Analysis of the gonococcal transcriptome detected 474 genes that were differentially expressed in a sex-specific manner, with 22% being expressed at increased levels in men compared to women and 78% with decreased expression. Principal component analysis (PCA) confirmed a higher variance of gonococcal gene expression in women. PCA of the host transcriptome showed sex-specific differences in host response gene expression to gonococcal infection. Analysis of the genital microbiome using 16s amplicon sequencing revealed unique microbial communities in men and women. Proteobacteria predominated the urethral microbiome, while the vaginal microbiome was more diverse, with Firmicutes, Actinobacteria, Bacteroidetes, Tenericutes, and Proteobacteria predominant.

Conclusions

Current studies are focused on an integrated network that includes transcriptomic data from these three components under a host sex-dependent perspective.