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Functional analysis of Neisseria gonorrhoeae infection in the genital microbiome

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Background

An obligate human pathogen, Neisseria gonorrhoeae (Ngo) typically infects the endocervix or male urethral tract. One of the primary determinants in this infection involves the interaction between Ngo and the native flora of the genital tract, which can either lead to heightened or lowered susceptibility and severity of infection. This is most apparent in the vaginal microbiome, where different patterns of populations, defined as community state types (CSTs), can interact differently with Ngo. CST I and V, dominated by Lactobacillus crispatus and Lactobacillus jensenii respectively, are protective against N. gonorrhoeae and other STI infection. These CSTs are associated with asymptomatic infection and protective effects in ex vivo models. CST IV, which is not dominated by a particular bacterium and contains many bacterial vaginosis (BV)-associated bacteria, is associated with symptomatic infection and a loss of the protective phenotype. In the male urethral microbiome, this interaction is relatively understudied.

Aim/Methods

To further characterize both genital microbiome-Ngo infection interfaces, I aim to profile microbiome changes beyond taxonomy by examining the functional changes induced by gonorrheal infection. To accomplish this, I will employ the three main tools used for assessment of the microbiome: 16S rRNA gene sequencing, shotgun metagenomics sequencing, and metatranscriptomics. 16S studies will provide a base examination of the changes in bacterial abundance, while metagenomics will capture the full range of genes that exists in a microbiome. Metatranscriptomics provides the most accurate picture of function, sequencing the mRNA expressed by Neisseria gonorrhoeae and the microbiome during infection.

Results

Currently, I have finished compiling a metatranscriptomics analysis pipeline, which has been tested on a stool sample dataset for the purpose of optimizing differential expression techniques. This analysis pipeline is ready to be applied to a metatranscriptomics dataset containing male urethral infection samples, which are in the final stages of pre-processing. Additionally, I have begun sequencing metagenomics and 16S samples

collected from a mouse model of Ngo infection.

Conclusions

Both datasets should yield results shortly, with initial examination of the male urethral samples confirming Ngo transcripts comprising a majority of detected expressed genes.