

(1) Submission ID#1539870

Metatranscriptomic Analysis Identifies Sex Specific Coordinated Processes Between the Host Environment and *Neisseria gonorrhoeae* During Mucosal Infection

Author(s)

Ryan McClure, PhD

Scientist

Pacific Northwest National Laboratory

Ana Paula Lourenco Aran, PhD

Post doc

Department of Immunology, Tufts University School of Medicine, Boston, USA

Xiaohong Su, MD, PhD

professor

Sexually Transmitted Disease Clinic, Institute of Dermatology, Chinese Academy of Medical Sciences and Peking Union Medical College, Nanjing, China

Paola Massari, n/a

Research Associate Professor

Department of Immunology, Tufts University School of Medicine

Caroline Genco, n/a

Provost and Senior Vice President ad interim, Arthur E. Spiller, M.D. Professor of Immunology

Tufts University

Background

Neisseria gonorrhoeae is the causative agent of the sexually transmitted infection gonorrhea, a high morbidity disease worldwide. While males are typically symptomatic, females are often asymptomatic and untreated infection can lead to reproductive tract complications. Like other human pathogens, *N. gonorrhoeae* adapts to the mucosal environments encountered during infection including the host immune response as well as the functional response of the resident microbiome by altering gene expression patterns. Our studies have demonstrated that the gonococcus expresses a transcriptomic response during infection that is distinct in men and women, likely due to the contrasting environments of the male and female genital tract. A better understanding of gonococcal infection must therefore include an integrated view of the gonococcus, the host, and the resident microbiome in the context of the specific aspects of the male and female genital tract

Aim/Methods

To gain this comprehensive view, we have established a unique cohort of matched pairs of men and women at the National Center for STD Control (NCSTD) in Nanjing, China. This cohort represents 25 men with gonococcal urethritis and their matched female partners. Using metatranscriptomic analysis of urethral and

cervicovaginal lavage samples we identified sex specific transcriptomic responses of the human host, the resident microbiome, and the gonococcus during infection.

Results

We show that the host transcriptomes of men and women during infection are distinct. We also determined that the transcriptional response of the resident microbiome differs both as a function of sex and infection. As the host, microbiome and gonococcus have significant interactions during infection, we took advantage of our metatranscriptomic dataset to infer the first networks that integrate all three components into a single model. These networks revealed a suite of coordinated responses between *N. gonorrhoeae* gene expression and 1) Human genes expressed during infection in men and/or women, and 2) Microbiome genes expressed during infection in men and/or women.

Conclusions

Collectively, our studies identify key sex specific processes coordinated between the host environment and *N. gonorrhoeae* during infection. Future approaches to treat gonorrhea will be able to take advantage of our findings to better design both treatment strategies and potential gonococcal vaccines.