(1) Submission ID#1539900

The Neisseria gonorrhoeae transcriptional regulatory protein MpeR is strongly associated with iron and oxidative stress response genes.

Author(s)

Ashwini Sunkavalli, M.S.

Graduate student

Tufts University

Caroline Genco, n/a

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

Tufts University

Ryan McClure, PhD

Scientist

Pacific Northwest National Laboratory

Background

The obligate human pathogen Neisseria gonorrhoeae adapts to the host's oxidative and non-oxidative immune defenses through tight gene expression control, among other strategies.

Aim/Methods

1. Using the mutual information algorithm Context Likelihood of Relatedness (CLR) and a collection of in vivo and in vitro RNA-Seq data, we constructed a gene co-expression network that provides a systemic understanding of complex transcriptional regulatory interactions in N. gonorrhoeae. Furthermore, applying the hill climbing structure learning algorithm to the expression profiles of genes from each module of the above network, we identified causal interactions between transcriptional regulators and their putative target genes. 2. Next, we examined the growth kinetics and H_2O_2 sensitivity of N. gonorrhoeae wild-type strain F62 (WT) and its isogenic mutant strain (ΔmpeR) under iron-replete and -deplete conditions. We subsequently examined the transcriptional response of WT and ΔmpeR strains to, iron-replete -deplete, and H_2O_2 under iron-replete conditions.

Results

1. Network analysis suggests transcriptional regulator MpeR is strongly associated with iron and oxidative stress-response genes. 2. This analysis showed that the WT strain survived better than the ΔmpeR strain under both iron-replete and -deplete conditions. Whereas ΔmpeR strain was more resistant to H_2O_2 treatment compared to the WT strain under iron-replete condition only, with no significant differences between the H_2O_2 sensitivity of both the strains under iron-deplete condition. Comparative analysis of WT and ΔmpeR strains' transcriptional responses to iron-replete and -deplete conditions demonstrated MpeR to regulate the expression of genes involved in metabolic pathways, protein synthesis, and stress responses in an iron-dependent manner. This transcriptional study suggests that MpeR responds to H_2O_2 stress by regulating chaperone, prophage, and amino acid transport and metabolism genes' expression.

Conclusions

Current studies are aimed at determining the mechanistic details of the role of MpeR in the coordination of oxidative stress responses and antimicrobial resistance, and survival in epithelial cells. These studies will enhance the understanding of N. gonorrhoeae adaptation mechanisms and will thereby aid in the development of novel antimicrobial strategies.

Uploaded File(s)

Supplemental Document Upload

USVGLHTT-1539900-1-ANY.docx