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Alternative sulfur acquisition pathways in Neisseria gonorrhoeae

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Background

Sulfur is an essential element for all life, supporting a plethora of fundamental cellular functions. Bacterial pathogens acquire this essential element, in the form of organic or inorganic sulfur, readily available at the host-pathogen interface. Once acquired, all sulfur metabolism pathways convene at cysteine, either by processing organic sulfur compounds into cysteine or reducing inorganic sulfur for de novo cysteine biosynthesis. Among many other roles, cysteine is a crucial intermediate in making environmental sulfur available to microbial cells and is an essential precursor in the synthesis of biomolecules required for successful infection. De novo cysteine biosynthesis appears to be upregulated during N. gonorrhoeae infection of the urogenital tract in women (McClure et al., 2015), yet this pathway is poorly characterized. Due to large genomic deletions and pseudogenes, N. gonorrhoeae is incapable of inorganic sulfur acquisition via traditional routes and therefore cannot grow when sulfate is the only available sulfur source. N. gonorrhoeae can, however, grow on thiosulfate yet lacks the ability to reduce thiosulfate via the conventional reduction pathway.

Aim/Methods

The aim of this research is to uncover the unconventional pathway by which N. gonorrhoeae reduces inorganic thiosulfate for cysteine biosynthesis. The pspE and str genes of N. gonorrhoeae encode single-domain thiosulfate sulfurtransferases which catalyze the reduction of thiosulfate to sulfite and sulfide in the presence of thiophilic acceptors. Recombinant Str and PspE proteins have been expressed and purified to determine Michaelis-Menten kinetics via a continuous spectrophotometric assay measuring the production of lead sulfide.

Results

Kinetic characterization of both Str and PspE confirms thiosulfate reductase activity in the presence of an array of thiol acceptor substrates including glutathione, cysteine, and dithiothreitol.

Conclusions

Future work is aimed to elucidate the physiological function of these enzymes. N. gonorrhoeae MS11 ΔpspE and Δstr strains will undergo phenotypic characterization, assessing their ability to grow in the presence of different sulfur sources, resist oxidative stress, and infect ME-180 cells. Our proposed pathway of thiosulfate reduction via sulfurtransferase enzymes could be pivotal in advancing our understanding of how pathogens

fulfill their sulfur requirements. Herein, we offer insight into the versatility and function of sulfurtransferases within N. gonorrhoeae.