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Identifying factors important for the survival of Neisseria gonorrhoeae in the presence of neutrophils

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Background

Gonorrhea is the second most common sexually transmitted disease in the world. It is caused by a human-specific pathogen, the Gram-negative diplococcus Neisseria gonorrhoeae. The infection usually takes place on the mucosal surfaces of the urogenital tract, with neutrophils being the first responders. However, bacteria can survive the engulfment by neutrophils and even propagate within these innate immune cells. How gonococci achieve this is not fully understood.

Aim/Methods

With the aim of investigating bacterial factors important for the survival of N. gonorrhoeae in the presence of neutrophils, we have generated a library of knockouts using transposon mutagenesis. Primary human neutrophils were infected with this library and surviving bacteria were isolated. After three rounds of infection, we sequenced the output and compared it with the input library to identify underrepresented transposon insertion sites, which would help us determine the genes important for gonococcal survival within neutrophils.

Results

We identified several genes that might play a role in N. gonorrhoeae survival in the presence of neutrophils. We generated knockout strains of selected targets and could generally confirm the results of the transposon library screen. Some of the gene deletions impaired gonococcal growth, and we observed variability in results dependent on the neutrophil donor. However, for some of the targets we obtained a consistent reduction in survival upon exposure to neutrophils, qualifying them as the focus of future research.

Conclusions

The transposon library of N. gonorrhoeae mutants is a promising tool for studying the requirement of bacterial genes for infection processes. Besides proteins involved in pilus assembly and lactate metabolism, we also identified a transcriptional regulator and an uncharacterized membrane protein as factors that determine gonococcal survival in neutrophils.