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Discovery and immune characterization of novel N. gonorrhoeae vaccine targets

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Background

A worldwide alarming trend of increased antibiotic resistance development has been reported for Neisseria gonorrhoeae, which has compromised treatment of this sexually transmitted infection. New therapeutic strategies against this pathogen are needed, including development of a gonococcal vaccine. Our group has previously designed an immunobioinformatics-based strategy to discover potential new vaccine candidate antigens based on transcriptomic analysis of the N. gonorrhoeae genes expressed during natural human mucosal infections in men and women.

Aim/Methods

By coupling gonococcal gene expression with bioinformatics analyses and focusing on hypothetical proteins, we have identified 36 potential novel vaccine candidates. Our strategy, which we called CASS (Candidate Antigen Selection Strategy), takes into account predicted proteins' characteristics including immunogenicity, membrane localization and structure features favorable for recombinant expression, among other criteria. So far, we have examined 10 candidates from our pool of 36 hypothetical proteins in mouse immunization experiments using alum alone or alum+MPLA as adjuvants.

Results

We have previously reported that NGO0690, NGO0948 and NGO1701 induce robust and cross-reactive antibodies with bactericidal activity. Preliminary in vivo studies indicated a promising trend of protection from N. gonorrhoeae vaginal colonization in mice immunized with these antigens and alum. NGO0690, NGO0948 and NGO1701 are also recognized by sera from N. gonorrhoeae infected women. Characterization of the

function of NGO1701, an hypothetical membrane protein with holomogy to a four-helix bundle copper-binding protein, in N. gonorrhoeae F62 indicates that deletion of this gene leads to increased sensitivity to copper, nickel, cobalt, and manganese toxicity. N. gonorrhoeae F62 ΔNGO1701 also appears more resistant to H_2O_2 killing, an effect that has been observed for other gonococcal deletion mutants (poster from A. Sunkavalli). Continuing our analysis of CASS antigens, here we show a robust antibody response also in sera from mice immunized with NGO0861, NGO1438 and NGO1802 and alum+MPLA, with bactericidal titers between 1/20-1/80.

Conclusions

Our results support the CASS as a tool for discovery of new vaccine candidates and potential novel virulence factors. Further analyses of growth restrictions for the ΔNGO1701 deletion mutant and the corresponding complemented strain will provide more details of this gene's function.