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Utility of targeting the bacterial transferrin receptor for a gonococcal vaccine

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Background

Neisseria gonorrhoeae (Ngo) is exquisitely adapted to its human host and, as such, utilizes numerous host proteins to allow for survival and growth during infection. The bacterial transferrin receptor, composed of the integral membrane protein transferrin binding protein A (TbpA) and the membrane-anchored surface lipoprotein transferrin binding protein B (TbpB), allows the gonococcus to scavenge the essential micronutrient iron from the host protein transferrin in vivo. These proteins have both been considered attractive candidate vaccine targets due to their surface accessibility and important role in pathogenesis.

Aim/Methods

TbpB offers benefits as an immunogen due to stability, full surface accessibility, and ease of production, however antigenic variability remains a challenge towards a broadly protective vaccine. To contend with this, we utilized the novel software Navargator to select representative variants from the known TbpB diversity.

Results

From these, we identified a bivalent TbpB formulation that elicited broad cross-reactivity, elicited bactericidal antibodies against a panel of gonococcal strains, and elicited protection in the lower genital tract colonization model of infection against two heterologous strains of Ngo. In comparison to TbpB, TbpA exhibits far less variability, however only some regions of the protein are accessible to antibody when expressed by the gonococcus. Therefore, we sought to determine whether a combination vaccine targeting both TbpA and TbpB would be more efficacious than targeting either component individually. TbpA, TbpB, or TbpA+TbpB were formulated and immunized into mice. Sera from mice was evaluated against strains of Ngo expressing either only TbpA, only TbpB, or both to determine the relative immunogenicity of each strategy in the context of the whole bacterial cell. The combination of TbpA and TbpB elicited higher levels of bactericidal antibodies compared to sera from animals immunized with either immunogen individually when tested against MS11. Finally, mice were challenged in the lower genital tract colonization model, where all formulations reduced the duration of colonization compared to adjuvant alone, and the combination of TbpA and TbpB led to more rapid clearance of Ngo compared to individual protein vaccines.

Conclusions

Together, these data suggest that targeting the bacterial transferrin receptor for a gonococcal vaccine is a compelling strategy.