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Development of a broadly protective Neisseria gonorrhoeae vaccine candidate

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Background

The increasing prevalence of antibiotic-resistant N. gonorrhoeae (Ng) highlights the pressing need for effective vaccines. While the N. meningitidis vaccine 4CMenB (BEXSERO) has shown some cross-protection against Ng, the identification of protective antigens for an effective gonococcal vaccine remains challenging.

Aim/Methods

We employed the EDEN (Efficacy Discriminating Educated Network) artificial intelligence antigen discovery platform (EVAXION Biotech) to analyze ten phylogenetically distinct gonococcal proteomes to identify highly conserved novel potentially protective antigens against a wide range of Ng strains. We identified, expressed and tested the efficacy of 26 antigens against Ng experimentally. Parameters for efficacy included human complement-dependent bactericidal activity and reduction in duration and burden of Ng in the mouse vaginal colonization model.

Results

Two unique EDEN candidates, involved in cell division, demonstrated exceptional efficacy against N. gonorrhoeae colonization in vivo against all three strains tested, as well as the ability to induce antisera with high bactericidal activity (>50% killing) against 41 of 50 Ng strains in vitro. To advance vaccine development, we designed the two antigens as a single fusion protein for optimal manufacturability and reduced production costs. The preclinical evaluation of our novel vaccine candidate either formulated as recombinant protein adjuvanted with GLA-SE or expressed from a nucleotide vaccine vector, showed robust immunogenicity to both antigenic components. Efficacy in vivo relied on killing by the membrane attack complex (C5b-9) of complement, evidenced by loss of efficacy in complement C9-/- mice, which have intact opsonophagocytic mechanisms. Finally, delivery of our fused antigens as a DNA vaccine induced a strong antigen-specific IFNγ CD4+ T cell response.

Conclusions

The fusion protein candidate vaccine induces high immunogenicity, broad anti-Ng bactericidal activity and efficacy against vaginal Ng colonization in mice. Specifically, we have identified antibody-mediated complement-dependent killing as mode of action and have shown the induction of strong Th1 responses using GLA-SE adjuvant or through DNA vaccine delivery. We conclude that a chimeric derivative of these two ubiquitously expressed and conserved proteins is a promising Ng vaccine candidate.