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Anti-NHBA antibodies elicited by MenB-4C vaccination are key to the serum bactericidal activity against Neisseria gonorrhoeae

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Author(s)

Yih-Ling Tzeng, Ph.D.

Research Associate Professor

Emory University School of Medicine

Soma Sannigrahi, n/a

Senior Research Specialist

Emory University School of Medicine

Ray Borrow, Ph.D.

Professor

Meningococcal Reference Unit, UK Health Security Agency

Nadine Rouphael, M.D.

Professor

Emory University School of Medicine

Varun Phadke, M.D.

Assistant Professor

Emory University School of Medicine

David Stephens, M.D.

Professor

Emory University School of Medicine

Background

The MenB-4C (Bexsero) vaccine contains detergent-extracted outer membrane vesicles (OMVs) from a group B Neisseria meningitidis (Nm) strain NZ98/254 and three recombinant Nm protein antigens (NadA, GNA2091-FHbp fusion and NHBA-GNA1030 fusion). Previous work has shown that MenB-4C generates serum antibodies to Nm and Ng OMV proteins. Mounting evidence indicates MenB-4C can protect against infections with N. gonorrhoeae (Ng). The immunologic basis for this cross protection remains to be elucidated.

Aim/Methods

The aim of this work was to characterize human serum antibody response elicited by MenB-4C. Ten paired human sera obtained pre- and post-immunization with MenB-4C (one month after a third vaccine dose, Vaccine 2015;33(29):3322-30) were used in ELISAs and Western blots to probe IgG and IgA responses to

OMVs from NZ98/254 and Ng strain CNG20, and a purified Ng recombinant NHBA (rNHBA Ng1291) protein. NHBA variants 542 (Ng1291) and 475 (CNG20) differing by three amino acids and are the dominant variants, found in > 60% of Ng strains. Both variants contain identical ~ 60 aa deletions when compared to the NHBA variant 2 of NZ98/254. The contribution of MenB-4C elicited anti-NHBA antibodies to serum bactericidal activity (SBA) against Ng was evaluated by SBA assays.

Results

All post (not pre) MenB-4C sera showed strong IgG, but variable IgA, responses to native OMVNZ98/254 and lower reactivities to Ng OMVCNG20 by ELISA. All post (not pre) MenB-4C sera showed strong IgG recognition of gonococcal rNHBA1291. The lower IgG antibodies captured by OMVCNG20 relative to rNHBANg1291 implied a low abundance of NHBA in the gonococcal OMVs. SBA (10% v/v post sera) against Ng1291 demonstrated ~30% killing compared to > 90% killing of Nm vaccine strain NZ98/254, consistent with the absence or divergence of NadA, FHbp and PorA in Ng. In competitive SBA assays, in which sera were pre-incubated with rNHBA Ng1291, only ~10% of SBA against NZ98/254 was titrated away. However, the majority (~80%) of SBA against Ng1291 was attributed to NHBA-specific antibodies and an Δnhba mutant was serum resistant.

Conclusions

While NHBA expression is low in Ng, anti-NHBA antibodies cross react robustly with Ng NHBA and account for most of the serum bactericidal activity toward Ng.