

## (1) Submission ID#1539682

Protection against *N. gonorrhoeae* induced by OMV-based Meningococcal Vaccines are associated with cross-species directed humoral and cellular immune responses

---

### Author(s)

Weiyan Zhu, PhD

Postdoctoral Research Associate

University of North Carolina at Chapel Hill

Kristie L. Connolly, PhD

Senior Staff Scientist

Uniformed Services University

Andreea Waltmann, PhD

Assistant Professor

University of North Carolina at Chapel Hill

Andrew MacIntyre, PhD

Assistant Professor

Duke University

Ann Jerse, n/a

Professor

Uniformed Services University of the Health Sciences

Margaret Bash, n/a

Principal Investigator

US Food and Drug Administration

Kathryn A. Matthias, n/a

Staff Scientist

US Food and Drug Administration

J. Alex Duncan, MD PhD

Professor, Program Director

University of North Carolina Chapel Hill

### Background

Limited protective immunologic responses to natural *N. gonorrhoeae* infection and a lack of knowledge have

hampered development of a gonococcal vaccine. Recent studies in humans and mice have found meningococcal outer membrane vesicle-containing vaccines induce cross species immune responses against gonococci and are associated with protection. The exact protective mechanisms remain unclear.

#### Aim/Methods

We immunized mice with two *N. meningitidis* OMV-containing vaccines previously shown to induce accelerated clearance of *N. gonorrhoeae* in a murine infection model and assessed the immune signatures associated with bacterial clearance.

#### Results

Mice immunized with 4CMenB or MC58 $\Delta$ ABR significantly shortened bacterial colonization after bacterial challenge compared with Alum controls. Vaccination with either 4CMenB (a commercially available FDA-approved MenB vaccine) or MC58  $\Delta$ ABR dOMV (OMV prepared from an engineered strain of *N. meningitidis* lacking PorA, PorB, and RmpM) elicited robust sera and mild mucosal cross-reactive anti-*N. gonorrhoeae*-OMV antibodies as measured by ELISA titer. Splenocytes from both 4CMenB- and MC58  $\Delta$ ABR dOMV-immunized mice exhibited elevated IL2, IL4 and IL5 production after restimulation with *N. gonorrhoeae* OMV, when compared to splenocytes from alum immunized control mice. Interestingly, splenocytes from MC58  $\Delta$ ABR dOMV-vaccinated mice also exhibited enhanced *N. gonorrhoeae* OMV-stimulated secretion of Interferon-gamma, IL17, and IL18 when compared to responses from splenocytes from alum- or 4MenB-immunized animals. Interestingly, increased anti-*N. gonorrhoeae* OMV IgG2a titers in response to *N. gonorrhoeae* challenge was strongly correlated with accelerated bacterial clearance in MC58  $\Delta$ ABR-immunized mice. Other vaccine induced serologic responses to *N. gonorrhoeae* OMV in either 4CMenB- or MC58  $\Delta$ ABR dOMV-immunized mice were not linked with bacterial clearance. There was no significant correlation between any single measured *N. gonorrhoeae* OMV-stimulated cellular cytokine response and bacterial clearance observed.

#### Conclusions

Our data suggest the immunologic mechanism of cross-species protection against *N. gonorrhoeae* in mice induced by these two meningococcal OMV-containing vaccines likely involves both humoral and cellular responses to vaccine and is different between the two vaccines.