O01.4 RABBIT IMMUNIZATION WITH *B. BURGDORFERI* EXPRESSING *T. PALLIDUM* TPRK AND TP0435 AS A NOVEL VACCINE DESIGN FOR SYPHILIS

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Background Syphilis is resurgent in many developed countries, including the United States, and still prevalent in developing nations, where it causes significant morbidity in adults and mortality when infection is congenital. Such evidence highlights the need for novel control strategies to curtail syphilis spread, including the development of a vaccine. Although some of the most promising vaccine candidates have been identified among the putative surface-exposed integral outer membrane antigens of the syphilis spirochete, immunization/challenge experiments using denatured/refolded recombinants did not fully protect animals against infection in the rabbit model of syphilis. We speculated that immunizing with antigens in their native structure and with a delivery approach that simulates the antigen cellular compartment could increase the protective ability of these vaccine candidates.
Methods To test our hypothesis, we engineered a lab-derived non-pathogenic *Borrelia burgdorferi* strain to express the *tp0897* and *tp0435* genes of *Treponema pallidum* subsp. *pallidum* and immunized rabbits by injecting recombinant strain intramuscularly without adjuvant. The *tp0897* and *tp0435* genes encode the putative integral outer membrane protein TprK, and the abundantly expressed periplasmic/surface 17-kDa lipoprotein (Tp0435) of the syphilis agent, respectively. Following the development of a specific response to these treponemal antigens in immunized animals, rabbits were challenged with the Nichols strain of *Treponema pallidum*. Primary lesion development and treponemal burden within lesions were measured using dark-field microscopy and real time RT-qPCR, while serology was used to assess establishment of the infection.
Results No protection was seen in rabbits immunized with *Borrelia* expressing Tp0435 and only partial protection in animals immunized with *Borrelia* expressing TprK.
Conclusion Our surrogate *Borrelia* system is an effective delivery system to elicit a specific response to *Treponema pallidum* antigens. This novel approach will help assess the efficacy of syphilis vaccine candidates
Disclosure No significant relationships.

O01.5 A MENINGOCOCCAL NATIVE OUTER MEMBRANE VESICLE VACCINE AS A PLATFORM FOR PRESENTING CONSERVED GONOCOCCAL ANTIGENS

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Background *Neisseria meningitidis* (Nm) outer membrane vesicles (OMV) are treated with detergents to decrease endotoxin activity, which removes lipoproteins and may result in non-native protein structures. Previously, we prepared native OMV (NOMV) vaccines from mutant Nm with genetically attenuated endotoxin and over-expressed Factor H binding protein (FHbp) mutants with reduced binding to human FH. Mice immunized with NOMV-FHbp developed higher and broader meningococcal SBA responses than a control recombinant FHbp vaccine. The NOMV-FHbp also elicited SBA against *Neisseria gonorrhoeae* (Ng) strain FA1090, which expresses many outer membrane proteins that are highly conserved in both pathogens. In this study, we identify antigens in NOMV-FHbp that elicit SBA against Ng as well as those that elicit blocking antibodies in rhesus macaques to develop a NOMV vaccine with the potential to provide protection against both pathogens.
Methods Antiserum from mice immunized with NOMV-FHbp were used to immunoprecipitate antigens from FA1090. The antigens were identified by LC-MS/MS. Antigens that elicit blocking antibodies in macaques were identified by comparing antibody responses that were positive for SBA in mice and macaques with those in macaques that also had antibodies to conserved antigens but lacked SBA against FA1090.
Results Antibodies elicited by NOMV-FHbp were reactive with four integral membrane proteins and one lipoprotein in FA1090 that are highly conserved in Nm (≥87% identity), essential for bacterial survival humans, and are known to mediate SBA against Nm and Ng. One of the proteins also mediates Ng adhesion to human cervical cells, which can be blocked by vaccine-elicited antibodies. Blocking antibodies elicited by NOMV-FHbp appear to be directed to Rmp, which is known for this effect.
Conclusion An engineered NOMV vaccine containing a few conserved overexpressed antigens and lacking antigens having the potential to elicit blocking antibodies, such as Rmp, may provide broad protection against disease caused by pathogenic Nm and Ng.
Disclosure No significant relationships.

O01.6 MENINGOCOCCAL VESICLE VACCINES DELETED FOR MAJOR OUTER MEMBRANE PROTEINS ENHANCE GONOCOCCAL CLEARANCE IN A MURINE MODEL

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Background With an incidence rate of 106 million infections a year, *Neisseria gonorrhoeae* has a significant effect on global morbidity. Rapid development of gonococcal antibiotic resistance, and reports of treatment failures with last-line cephalosporins, has caused the Centers for Disease Control and Prevention to label *N. gonorrhoeae* as an urgent threat and has sparked renewed interest in development of a gonococcal vaccine.
Methods In this study, we immunized mice with detoxified outer membrane vesicles (dOMVs) isolated from the closely-related pathogen *Neisseria meningitidis* and examined the effect on gonococcal clearance in a murine vaginal colonization model. dOMV vaccines were derived from (1) wild type (WT) bacteria, (2) an isogenic strain (ΔABR) deleted for expression of the major outer membrane proteins PorA, PorB, and RmpM, or (3) an isogenic strain (OCh) deleted for PorA and expressing a varying PorB sequence type relative to the parental strain. ELISAs were used to evaluate anti-dOMV IgG and IgA antibody titers present in sera and vaginal washes. Sera were also used to identify potential gonococcal vaccine