The gonococcal FHbp was predicted as not being surface-expressed, while NadA was absent in all the Ng isolates. The immunodominant OMV protein PorA was present in nearly all Ng isolates, but harbored deletions in the promoter regions, preventing its transcription. Noteworthy, OMPs including FetA, PilQ, Omp85, RmpM, LbpA and TonB-dependent receptors, previously identified and abundantly expressed in the NZ98/254 OMV, displayed ≥93% sequence identity between Nm and Ng, and were highly conserved within Ng.
Conclusion Our results provide a better understanding of the OMPs present in the OMV of the 4CMenB vaccine. These OMPs may contribute to the observed cross-protection, and can serve as potential antigen targets for guiding the next steps of gonorrhea vaccine development.
Disclosure No significant relationships.

O01.2 GENETIC, STRUCTURAL, AND SURFACE ANTIGENIC VARIATION OF *TREPONEMA PALLIDUM'S* OMPEOME: STEPS TOWARDS A GLOBAL SYPHILIS VACCINE

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10.1136/sextrans-2019-sti.105

Background The failure of current prevention strategies to curtail the spread of syphilis, including mother-to-child transmission, underscores the need for a vaccine with worldwide efficacy. Characterization of variation within *T. pallidum* (*TPA*) outer membrane proteins (OMPs) is critical for this goal.
Methods ClustalW identified polymorphisms within 21 β-barrel forming OMPs (*TPA*'s OMPeome) of 15 unique *TPA* strains. Structural models and conformational B-cell epitopes (BCEs) were predicted. Clade assignments were made using *tp0548* and *tp0558* sequences.
Results *TPA* OMPeomes contain four paralogous families (Tpr, FadL, OmpW, and efflux pump OMPs) and orthologs for BamA and LptD. The Tprs group into Subfamilies I (C/D/I), II (E/G/J) and III (B/H/L); Tpr β-barrel domains contain 10 β-strands and five extracellular loops (ECLs) harboring BCEs. TprI is invariant, while TprC and TprD have variability located predominantly in ECLs. The closely related TprE and TprJ β-barrels exhibit extremely low variability. TprG β-barrels variants contain a 23 aa insertion derived from TprE or TprJ. The TprB and TprH β-barrels are fully conserved; there are two TprL β-barrels variants. The FadL orthologs (TP0548, TP0856, TP0858, TP0859, TP0865) consist of 14-stranded β-barrels with seven ECLs harboring predicted BCEs. Variability among FadLs range between fully conserved (TP0856) to highly variable (TP0548). Both OmpWs are fully conserved and consist of 8-stranded β-barrels with four ECLs containing BCEs. The highly conserved efflux pump OMPs (OprJ/TP0966, OprN/TP0967, TolC/TP0969) likely form homotrimeric 12-stranded β-barrels. The 18-stranded BamA/TP0326 β-barrel contains a single aa substitution in ECL4. The LptD/TP0515 β-barrel contains 24 β-strands, 12 ECLs and numerous BCEs, which cluster primarily into two variants. Most OMPs do not align with clade designations.
Conclusion 1.) *TPA* OMPs display variable degrees of sequence and surface antigenic variation. 2.) *TPA* OMPeomes are mosaics likely resulting from recombination among circulating strains. 3.) Our analysis enables selection of variable and non-variable OMPs for assessment of protective capacity.
Disclosure No significant relationships.

O01.3 ENGINEERING HYBRID BACTERIAL TRANSFERRIN RECEPTOR-BASED VACCINES TO CONFER BROAD PROTECTION AGAINST *NEISSERIA GONORRHOEAE*

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10.1136/sextrans-2019-sti.106

Background The bacterial transferrin receptor has long been considered an outstanding vaccine target against pathogenic Neisseria species as it is surface-exposed and essential for bacterial survival and virulence *in vivo*. Required for iron uptake from the human protein transferrin (hTf), this receptor is composed of two proteins, an integral membrane channel (transferrin binding protein A; TbpA), and a surface anchored lipoprotein (TbpB). Vaccine development has predominantly focused on TbpB as it is a soluble, stable antigen that is highly immunogenic and easy to produce in large quantities. However, TbpB is also highly variable and so achieving broad cross-protection in a vaccine has been considered challenging. In comparison, TbpA is highly conserved but the production of this integral membrane protein is technically challenging and not considered practicable for large-scale development.
Methods We performed protein structure-based engineering to remove variable unstructured surface loops on TbpB to provide a soluble, stable and immunologically cross-protective scaffold upon which surface-exposed loops of TbpA have been displayed. These chimeric immunogens have been used to immunize rabbits and mice, including 'humanized' transgenic mice that express human hTf. Immunological cross-reactivity against a broad panel of *N. gonorrhoeae* isolates and the presence of functional antibodies targeting the gonococcal transferrin receptor were monitored by ELISA, hTf-binding and growth-based analyses, and immunized mice were challenged with genital *N. gonorrhoeae* infection.
Results The chimeric immunogens elicit antibodies against both TbpA and TbpB. The antisera is broadly cross-reactive against the gonococcal strain panel, is bactericidal, blocks transferrin-based iron acquisition and growth, and protects mice against gonococcal infection. While wild type TbpB-based immunogens have reduced functional antibody in hTf-expressing mice, the binding-defective Tbp-based immunogens are equally efficacious in both wild type and hTf-transgenic animals.
Conclusion Our rationally-designed hybrid immunogens simultaneously target two components of an essential iron acquisition pathway, eliciting broad cross-protection against gonococcal colonization and disease.
Disclosure No significant relationships.