

Extensive recombination in a population can also limit inferences about phylogenetic history. Here, we investigate the impact of recombination in the study of isolates with reduced susceptibility to cefixime (cef^{RS}; cefixime MICs ≥ 0.25 $\mu\text{g/ml}$) in the United States.

Methods We generated draught genome sequences for 242 gonococcal isolates collected by CDC's Gonococcal Isolate Surveillance Program (GISP). These isolates comprise all 141 cef^{RS} isolates from GISP in 2009–10 and 141 susceptible isolates matched by location, collection date, and sexual orientation of the infected individual. We predicted recombinant regions and generated a maximum likelihood phylogenetic tree from core SNPs. We performed *in silico* MLST and NG-MAST typing, and compared phylogenies of antibiotic resistance loci to whole genome-based phylogenies.

Results Per site *r/m* ratios (relative likelihood that a polymorphism was introduced through recombination rather than mutation) of recent branches in the phylogenetic tree are higher and fraction of homoplasious sites much lower than for the overall tree, suggesting that extensive recombination reduces confidence in the phylogeny's deep branches. Comparison with *in silico* MLST and NG-MAST reveals that traditional typing-based phylogenetic inferences, even for recent events, are confounded by recombination. Of the 21 penA alleles in this dataset, mosaic PBP2 pattern XXXIV was the most common (present in 116/121 cef^{RS} isolates). We find several recombination events introducing this allele into distinct lineages, and an event within the *dcw* gene cluster, which includes the penA allele, associated with reversion from cef^{RS} to cefixime susceptibility.

Conclusions Genomic methods reveal the impact of recombination on phylogenetic history, spread of resistance elements, and genome evolution, and offer a superior approach to traditional typing schemes in understanding population structure and dynamics.

Y1.5 SEXUAL RISK FACTORS AMONGST WOMEN WHO HAVE SEX WITH MEN AND WOMEN: THE WOMEN IN INDIANA SEXUAL HEALTH AND EXPERIENCE STUDY (WISHES)

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V R Schick, B Van Der Pol, B Dodge, A Bell, C Neal. *Indiana University, Bloomington, IN, United States*

Background Previous research suggests that women who have sex with women and men (WSWM) may be at a higher risk for STI than women with exclusively male (WSM) or female (WSW) partners. In contrast to previous research which has compared WSWM to WSW/WSM, the present study explored risk factors which may be unique to WSWM.

Methods Local women aged 18 or older who reported genital contact with a male and female partner within the past year were invited to participate in the study. Upon completion of an internet-based baseline survey about their sexual and STI history, participants were invited to participate in an in-person interview. During the meeting, participants engaged in a semi-structured interview followed by completion of a sexual event history calendar (SEHC). Participants were then asked to self-collect oral, vaginal and anal samples to screen for Chlamydia, Gonorrhea and Trichomoniasis.

Results Eighty participants with a mean age of 26.74 (SD = 7.97) completed the survey. The majority of the participants reported genital contact at an earlier age with a male partner (M = 16.02, SD = 3.31) than with a female partner (M = 18.93, N = 5.13). The most common type of genital contact was external genital rubbing with a male (97.5%, N = 78) and/or female (93.5%, N = 74) partner. Most participants reported a wide variety of sexual behaviours. Over half of the participants (57.5%, N = 44) reported engaging in a threesome/orgy within the past year. Data on the sequence of sexual acts was captured using the SEHC. Most participants self-collected a sample for STI screening. Approximately 30% (N = 25) of the participants reported an STI diagnosis within their lifetime and close to 10% of the participants tested positive for Chlamydia.

Discussion The study was successful in recruiting a sizable number of participants with a range of sexual experiences. The majority of participants opted to participate in all phases of the study.

Oral sessions

0.01 - Microbial virulence and host response

001.1 ASSOCIATION OF GENETIC VARIANTS WITH CHLAMYDIA TRACHOMATIS REINFECTION

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R Kapil, J Tang, C G Press, W M Geisler. *University of Alabama at Birmingham, Birmingham, AL, United States*

Background Up to 20% of *Chlamydia trachomatis* (CT)-infected patients are reinfected within months after treatment, suggesting some fail to develop protective immunity. Genetic determinants influencing CT reinfection risk have not been fully elucidated. Our primary research objective is to identify genetic determinants of CT reinfection. Based on previously reported associations of HLA class II alleles with CT complications, our initial investigations focus on HLA class II genes.

Methods In an ongoing prospective natural history study, CT-infected subjects are enrolled, treated with azithromycin 1 g single dose, and return for a 6-month follow-up visit for repeat CT testing using the Gen-Probe APTIMA Combo 2 assay (Gen-Probe, Inc., San Diego, CA). HLA class II alleles are resolved by a combination of PCR-based techniques. Genomic DNA is stored for further genotyping.

Results A total of 199 African American subjects have been studied to date: 90% women and median age 23. CT reinfection at follow-up was noted in 18%. Subjects with *HLA-DQB1*05* more often had reinfection (20 [26%] vs. 16 [13%], *P* = 0.018), which remained significant after controlling for age and gender (OR 2.6, 95% CI 1.2–5.6, *P* = 0.012). Other *HLA-DQB1* alleles were not significantly associated with reinfection (*P* ≥ 0.1).

Conclusion *HLA-DQB1*05* was associated with CT reinfection, suggesting it could influence protective immunity. More comprehensive genotyping from larger prospectively studied cohorts should help confirm or refine this observation. Analysis of additional HLA class II genes and genes beyond the human MHC is in progress.

001.2 INNATE IMMUNITY MODULATION BY TRICHOMONAS VAGINALIS GALECTIN-BINDING GLYCOLIPID DOMAINS

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^{1,2}R N Fichorova, ¹H S Yamamoto, ¹T Fashemi, ¹O R Buck, ¹E Foley, ³G R Hayes, ⁴S Sato, ³B N Singh. ¹Laboratory of Genital Tract Biology, Department of Obstetrics, Gynecology and Reproductive Biology, Brigham and Women's Hospital, Boston, MA, United States; ²Harvard Medical School, Boston, MA, United States; ³Department of Biochemistry and Molecular Biology and Department of Obstetrics and Gynecology, SUNY Upstate Medical University, Syracuse, NY, United States; ⁴Research Centre for Infectious Diseases, Faculty of Medicine, Laval University, Quebec, QC, Canada

Background *Trichomonas vaginalis* is a protozoan extracellular parasite causing long-lasting and recurrent vaginitis with a wide range of symptoms and increased risk of HIV and other viral STIs. The protozoan virulence factors that subvert the mucosal immune response are poorly understood. Here we investigate the role of the ceramide-phosphatidyl-inositol glycolipid core (CPI-GC) of the protozoan lipophosphoglycan (LPG), which is the major glycoconjugate on the trichomonad surface (2–3 million copies/parasite). We have previously determined that CPI-GC lacks mannose but

contains poly lactosamine repeats representing potential ligands for animal lectins called galectins, implicated in HIV pathogenesis.

Methods CPI-GC was isolated from *T. vaginalis* LPG by mild acid hydrolysis and C18-SepPak separation. Binding to galectin-1 and -3 (Gal-1 and -3) was determined by Biolayer Interferometry. Inflammation-related proteins and Gal-1 and 3 were measured by a multiplex immunoassay in supernatants from human cervical and vaginal epithelial cells infected with *T. vaginalis* or exposed to CPI-GC from different clinical isolates.

Results CPI-GC activated NF- κ B and upregulated cFos, COX-2, IL-8, MIP-3 α , IL-6, IL-1 β and VEGF in a MEK1/2 dependent manner. In addition, IL-6, ICAM-1 and VEGF up-regulation was mediated by p38 while IL-8 and MIP-3 α were ERK 1/2 mediated. CPI-GC from different clinical isolates varied in their ability to bind Gal-1 and Gal-3, which were constitutively expressed by vaginal and cervical epithelial cells and released at higher levels in the extracellular space during exposure to live trichomonas and CPI-GC. CPI-GC from all isolates invariably reduced levels of the natural microbicide SLPI. Mutant trichomonads that failed to bind Gal-1 and Gal-3 showed higher proinflammatory activity suggesting a role for the CPI-GC –galectin binding in suppressing innate immune responses.

Conclusion Interventions targeting CPI-GC or restoring the balance of natural immune defences represent a promising strategy for preventing adverse outcomes from *T. vaginalis* infection.

001.3 REGULATORY T CELLS IN PERIPHERAL BLOOD AND CEREBROSPINAL FLUID OF SYPHILIS PATIENTS WITH AND WITHOUT NEUROLOGICAL INVOLVEMENT: A COMPREHENSIVE AND COMPARATIVE STUDY

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Li K, C Wang, H Lu, X Gu, Z Guan, P Zhou. Shanghai Skin Disease Hospital, Shanghai, China

Background Syphilis, a sexually transmitted disease caused by spirochetal bacterium *Treponema pallidum*, can progress to affect central nervous system, causing neurosyphilis. While many neurosyphilis patients may be asymptomatic, some patients can develop severe neurological and psychiatric symptoms. Accumulating evidence suggest that skin lesions and clinical symptoms of early syphilis patients result from host immune and inflammatory responses. However, very little is known about the immune components in neurosyphilis.

Methodology/Principal Findings In the present study, we perform a comprehensive and comparative analysis of regulatory T cells (Tregs) between 102 neurosyphilis patients and 431 syphilis patients without neurological involvement. We found secondary and serofast patients had increased Treg percentage, suppressive function and TGF- β levels in peripheral blood compared to healthy donors and serum Rapid Plasma Reagin (RPR) titers were positively correlated with Treg numbers in these patients. Neurosyphilis patients had higher Treg frequency in peripheral blood than those of syphilis patients without neurological involvement. Importantly, CD4+ T cells were increased and predominated in cerebrospinal fluid (CSF) of both asymptomatic and symptomatic neurosyphilis patients. Interestingly, a significant decrease in CSF CD4+ CD25 high Treg percentage was observed in symptomatic neurosyphilis patients compared to those of asymptomatic neurosyphilis patients, which may be associated with low CSF TGF- β levels.

Conclusions Our findings suggest that neurological progression in syphilis patients may be associated with an enhanced systemic Treg response and an increased local CD4+ T cell infiltration. A decrease in Treg frequency in CSF of symptomatic neurosyphilis patients indicates that immune-mediate tissue damage might be involved in the development of neurological symptoms.

001.4 BLOOD TRANSCRIPTIONAL PROFILING OF WOMEN WITH CHLAMYDIA TRACHOMATIS IDENTIFIES A PELVIC INFLAMMATORY DISEASE (PID) SIGNATURE

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T Darville, X Zheng, C O'Connell, U Nagarajan, I Macio, H Wiesenfeld, L Rabe, S Hillier. University of Pittsburgh, Pittsburgh, PA, United States

Objective Most women with Chlamydia trachomatis (CT) infection are asymptomatic, while ~3% progress to pelvic inflammatory disease (PID) within two weeks of untreated infection. The identification of biomarkers that predict development of PID would aid in identification of women at risk for complications of infertility and ectopic pregnancy. The specific aim of this study was to identify a whole blood transcript signature for acute PID due to chlamydial infection.

Methods We performed gene expression microarrays using whole blood from 79 women who had a gynecologic exam, and cervical and endometrial microbiologic testing. Samples were divided into five groups: Group 1, women with acute PID who were CT+ at endometrium (PID+, CT+, and E+); Group 2, asymptomatic women who were CT+ at endometrium (PID-, CT+, E+); Group 3, asymptomatic women who were CT+ at cervix (PID-, CT+, E-); Group 4, asymptomatic women who were CT- at cervix and endometrium (PID-, CT-, E-); Group 5, women with symptoms of PID who were negative for CT or other sexually transmitted pathogens (PID+, STI-, E-).

Results We identified a transcript signature that discriminated women with chlamydial PID from all other groups. Pathway analysis revealed that the chlamydial PID signature contained genes from interferon response pathways. Gene transcription in a subset of women with chlamydial endometrial infection clustered with women with chlamydial PID.

Conclusions Our study raises the possibility that transcriptional biomarkers with potential as diagnostic and prognostic tools can be identified to combat chlamydial reproductive tract disease in women.

001.5 EFFICACY OF RG1-VLP VACCINATION AGAINST GENITAL AND CUTANEOUS HUMAN PAPILLOMAVIRUSES IN VITRO AND IN VIVO

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¹C Schellenbacher, ²K Kwak, ³D Fink, ¹S Shafiti-Keramat, ¹B Huber, ¹C Jindra, ²R Roden, ¹R Kimbauer. ¹Medical University Vienna, Division of Immunology, Allergy and Infectious Diseases (DIAID), Vienna, Austria; ²Johns Hopkins University, Baltimore, MD, United States; ³Institute of Laboratory Animal Science, Veterinary University Vienna, Austria, Vienna, Austria

Licensed human papillomavirus (HPV) vaccines, based on virus-like particles (VLP) self-assembled from major capsid protein L1, afford type-restricted protection against types 16/18/6/11 (or 16/18 for the bivalent vaccine), which cause 70% of cervical carcinomas (Cxca) and 90% of genital warts. However, they do not protect against less prevalent high-risk types causing 30% of CxCa, or cutaneous HPV. The minor capsid protein L2 confers low-level immunity to type-common epitopes.

Chimeric RG1-VLP presenting HPV16L2 amino acids 17–36 (RG1 epitope) within the DE-surface loop of HPV16L1 induce cross-neutralisation *in vitro*. We hypothesised, that RG1-VLP vaccination protects against a large spectrum of mucosal and cutaneous HPV infections *in vivo*.

L2-specific antibody and CTL responses in RG1-VLP vaccinated rabbits were determined by ELISA and ELISPOT assays. Cross-neutralisation was analysed using native or pseudovirion (PsV) assays. Vaccine efficacy *in vivo* was determined in a mouse genital challenge model.