016.3 CYTOKINE IMMUNE RESPONSE AGAINST NATURAL HUMAN PAPILLOMAVIRUS INFECTION AMONG MEN IN KISUMU, KENYA

¹Raphael Ondondo*, ²Elizabeth Bukusi, ³Zipporah Nganga, ²Michael Kiptoo, ²Solomon Mpoke. ¹Masinde Muliro University of Science and Technology, Kakamega, Kenya; ²Kenya Medical Research Institute, Nairobi, Kenya; ³Jomo Kenyatta University of Agriculture and Technology, Nairobi, Kenya

10.1136/sextrans-2019-sti.195

Background Human papillomavirus (HPV) is strongly associated with ano-genital and cervical cancer. Persistence of oncogenic HPV genotypes is required for development and progression of HPV-associated malignancies. Although, >70% of women clear incident HPV infections, data on natural history and HPV immunology among men is limited.

Methods To evaluate cell-mediated immune response against natural HPV infection among men, we assessed cytokine (IFN- γ , TNF- α , IL-2, IL-4, IL-6, IL-10 and IL-13) responses in peripheral-blood-mononuclear cells (PBMCs) collected from 135 men enrolled in a prospective HPV cohort study. PBMCs were stimulated by HPV L1 gene viral-like-particles (VLP) and cytokine responses measured using a multiplex Luminex assay.

Results Of 135 men included in this analysis, 41 men had persistent HPV infection, 44 men cleared HPV infection and 50 were HPV uninfected. Their mean (SD) ages were 28.9 (6.79), 27.6 (6.49) and 26.4 (4.81) years respectively. Immune response was induced in 22% (95% CI: 12.8–35.2) of HPV uninfected men, 64% (95% CI: 48.9–76.2) of men with HPV clearance and 51% (95% CI: 36.5–65.8) of men with HPV persistence. Men with HPV clearance and HPV persistence were significantly ($p < 0.01$) at increased odds [OR = 6.20 (95% CI: 2.29–17.19) and OR = 3.72 (95% CI: 1.37–10.25) respectively] of mounting cytokine responses compared to HPV uninfected men. T-helper type 1 (Th1) cytokines IFN- γ (5.1 mean-fold increase) and IL-2 (4.2-fold) were significantly ($p < 0.0001$) upregulated among men with HPV clearance and not in men with HPV persistence, compared to HPV uninfected men. Among men with HPV clearance compared to those with persistent HPV infection, IFN- γ (2.4-fold) and IL-2 (3.0-fold) were the only cytokines significantly ($p < 0.0001$) upregulated. In the three groups of men, there were no significant changes in Th1 cytokine TNF- α , and Th2 cytokines: IL-4, IL-6, IL-10 and IL-13.

Conclusion In this study, Th1 cell-mediated cytokine immune response was associated with HPV clearance in men.

Disclosure No significant relationships.

016.4 STRUCTURAL SIMILARITY OF *TREPONEMA PALLIDUM* PROTEIN TP0225 WITH HUMAN TOLL-LIKE RECEPTOR 2

Simon Houston*, Raghavendran Ramaswamy, Bianca Loveless, Martin Boulanger, Caroline Cameron*. University of Victoria, Biochemistry and Microbiology, Victoria, Canada

10.1136/sextrans-2019-sti.196

Background The causative agent of syphilis, *Treponema pallidum*, is a highly invasive chronic pathogen. Here we used bioinformatics and structural biology to characterize the sole LRR-containing protein in *T. pallidum*, Tp0225. In other bacterial pathogens, Leucine-Rich Repeat (LRR)-containing proteins contribute to chronicity by mediating attachment, invasion and immune evasion.

Methods A phylogenetic tree was constructed to determine the evolutionary relationship between Tp0225 and LRR homologs from pathogenic and non-pathogenic treponemes. The size and organization of Tp0225 protein domains were analyzed by comparing them to the domains of the treponemal homologs. For structure determination, the full-length recombinant protein was purified, crystallized, and the three dimensional structure determined using X-ray crystallography.

Results Bioinformatic analyses showed that Tp0225 has diverged more from non-pathogens compared to pathogens during evolution. The structure of Tp0225 demonstrated that the protein adopts a non-classical LRR fold and contains a hydrophobic pocket on the surface of the structure. This unusual LRR characteristic is similar to the hydrophobic pocket found on the surface of the human Toll-like Receptor 2 (TLR2) LRR domain that recognizes *T. pallidum* during infection.

Conclusion We have determined the structure of the only LRR-containing protein in *T. pallidum* and have shown that it contains an unusual LRR structural feature that is shared with the host innate immune signaling molecule TLR2. This structural mimicry may be involved in subversion of normal host processes during *T. pallidum* infection.

Disclosure No significant relationships.

016.5 TARGETING COMPLEMENT RECEPTOR 3 ON PRIMARY HUMAN CERVICAL CELLS HAS THE POTENTIAL TO CURE *NEISSERIA GONORRHOEA* INFECTION

¹Jennifer Edwards*, ²Christopher Day, ²Michael Jennings. ¹The Research Institute at Nationwide Children's Hospital and The Ohio State University, Department of Pediatrics, The Center for Microbial Pathogenesis, Columbus, USA; ²Griffith University, Gold Coast Campus, Institute for Glycomics, Southport, Australia

10.1136/sextrans-2019-sti.197

Background Complement receptor 3 (CR3) is a leukocytic, pattern recognition receptor that plays a pivotal role in innate immunity. CR3 is also uniquely expressed by human cervical epithelial cells where it is the key receptor mediating *Neisseria gonorrhoeae* (Ng) cervicitis. Binding of the Ng surface appendage, pilus, to the I-domain region of CR3 (CR3ID) is critical to cervical cell adherence and modulates the host response to infection. Thus, the pilus-CR3ID interaction may pose a novel target for critically-needed, new strategies to treat or prevent Ng disease in women.

Methods To identify potential inhibitors of the Ng-CR3 interaction, recombinant human I-domain or purified CR3 were immobilized on biosensor chips. Interactions between these immobilized proteins and a library of 3141 drugs were investigated by surface plasmon resonance (SPR). Drugs that bound the CR3ID were further examined by competitive SPR studies and in Ng, primary human cervical epithelial (Pex) cell infection assays.

Results Using SPR, we identified fourteen drugs that bound to the CR3ID with disassociation constants in the nanomolar range. Competitive SPR analysis demonstrated that six of these fourteen drugs blocked the pilus-CR3ID interaction. Moreover, these drugs also blocked Ng adherence to Pex cells as well as to Chinese hamster ovary cells expressing CR3 (CHO-CR3). One drug, carbamazepine, was chosen for further analysis using a panel of low-passage and multidrug-resistant Ng strains. Carbamazepine blocked adherence to Pex and CHO-CR3 cells for all strains tested and also could cure Pex cells

that had an established *Ng* infection. In this regard, a single dose of carbamazepine was effective in curing ($\geq 99\%$ *Ng* killing by 24h post-treatment) Pex cells infected with multidrug-resistant *Ng* strains, including the ceftriaxone-resistant strains WHO-X (H041) and WHO-Y (F89).

Conclusion Our data identify safe, repurposed, drugs that may have efficacy in preventing and treating *Ng* cervical infection in women.

Disclosure No significant relationships.

016.6 BASIC SCIENCE AIDS SYPHILIS VACCINE DEVELOPMENT: BLOODSTREAM SPREADING BY THE SYPHILIS SPIROCHETE *TREPONEMA PALLIDUM*

¹Karen Lithgow*, ¹Brigitte Church, ¹Jenny Moon, ¹Simon Houston, ¹John Burke, ³Leigh Anne Swayne, ²Leonard Foster, ¹Caroline Cameron. ¹University of Victoria, Biochemistry and Microbiology, Victoria, Canada; ²University of British Columbia, Biochemistry and Molecular Biology, Vancouver, Canada; ³University of Victoria, Division of Medical Sciences, Victoria, Canada

10.1136/sextrans-2019-sti.198

Background *Treponema pallidum* ssp. *pallidum* (*Tp*) causes syphilis, a sexually transmitted infection characterized by multi-stage disease and diverse symptoms. *Tp* undergoes rapid vascular dissemination, penetrating tissue, placental, and blood-brain barriers to access secondary infection sites via a process that is incompletely understood. The protein Tp0751 is an adhesin on the host-facing surface of *Tp* that mediates adherence to endothelial cells (ECs) lining blood vessel walls. This study explores *Tp* movement across endothelial barriers to enhance our understanding of *Tp* dissemination and identify host interactions that could be targeted for vaccine development.

Methods The methods of affinity chromatography and proteomics were used to identify receptor proteins on host ECs that are bound by Tp0751. Antibody inhibition studies revealed specific receptor regions required for binding. Endothelial barrier traversal was investigated with immunofluorescence and barrier permeability assays. Phosphoproteomics identified endothelial intracellular signaling pathways initiated by Tp0751 by exploring gain/loss of phosphoryl groups on proteins.

Results Here we show *Tp* uses Tp0751 to bind the 67 kDa laminin receptor (LamR) on human EC surfaces. Importantly, the same region of LamR is also targeted by meningitis-causing bacteria including *Neisseria meningitidis* and *Streptococcus pneumoniae*. Further molecular analyses reveal that *Tp* and Tp0751 disrupt the architecture of human cell-cell junctions in blood vessel walls without altering overall barrier integrity. Phosphoproteomics demonstrates that ECs exposed to Tp0751 exhibit differential phosphorylation on proteins known to promote endothelial barrier traversal by leukocytes and pathogens.

Conclusion These studies suggest a common tissue invasion strategy exists for neuroinvasive pathogens and identifies an interaction that can guide vaccine development for syphilis and other neuroinvasive diseases. Further, exploring *Tp* barrier traversal reveals that *Tp* uses similar mechanisms as immune

cells and neurotropic pathogens to invade tissues and cause the detrimental sequelae associated with syphilis. These studies enhance our understanding of *Tp* infection and facilitate targeted syphilis vaccine development.

Disclosure No significant relationships.

017 – SCREENING AND VACCINATION

Wednesday, July 17, 2019

1:45 PM – 3:15 PM

017.1 HPV FOCAL 48 MONTH EXIT RESULTS BY AGE FOR WOMEN HPV OR LBC NEGATIVE AT BASELINE SCREENING

¹Gina Ogilvie*, ²Dirk Van Niekerk, ³Mel Krajden, ²Laurie Smith, ³Darrel Cook, ¹Ruth Martin, ¹Gavin Stuart, ²Kathy Ceballos, ²Marette Lee, ⁴Stuart Peacock, ⁵Eduardo Franco, ⁴Andrew Coldman. ¹University of British Columbia, Vancouver, Canada; ²BC Cancer, Vancouver, Canada; ³BC Centre for Disease Control, Vancouver, Canada; ⁴BC Cancer Research Centre, Vancouver, Canada; ⁵McGill University, Montreal, Canada

10.1136/sextrans-2019-sti.199

Background HPV FOCAL, a large clinical trial conducted within an organized screening program setting, compared high-risk human papillomavirus (HPV) testing (Liquid based cytology (LBC) triage for HPV positives) to LBC for primary screening for cervical cancer. Primary endpoints included detection of high grade cervical intraepithelial neoplasia (CIN) grade 2 or greater (CIN2+) or grade 3 or greater (CIN3+) over 48 months in women 25–65 yrs of age.

Methods Over 18,000 women were randomized into the HPV and LBC arms. HPV arm: baseline HPV testing; if HPV negative, exit at 48 months with HPV/LBC co-testing. LBC arm: baseline LBC testing; if LBC negative, screen at 24 months with LBC and exit at 48 months with HPV/LBC co-testing (in LBC arm, 48 months disease detection includes disease found at 24 months). We present 48 month exit CIN2+ results by age for baseline negative women.

Results At baseline, in the HPV arm, 8769 were HPV negative and in the cytology arm, 9074 were cytology negative. For all ages, at 48 months significantly more CIN2+ was detected in the LBC vs. HPV arm (10/1000 [95%CI: 8, 12] vs 4/1000 [95% CI: 3,5], respectively, $p < 0.01$). In both groups, CIN2+ exit screen detection rates were highest in the women 25–29 yrs of age at baseline screening (LBC 30.8/1,000 & HPV 19.5/1,000) and lowest in women 50+ at baseline (LBC 3.5/1,000 & HPV 1.8/1,000).

Conclusion At FOCAL exit where women were co-tested with LBC and HPV, less CIN2+ was detected across all age strata in women who were baseline HPV negative, than in baseline cytology negative women, confirming the safety of a 48 month interval for HPV negative women. In addition, the highest CIN2+ rates were detected in women who were 25–29 yrs at baseline and lowest in those 50+ at baseline, informing for age appropriate HPV-based program planning.

Disclosure No significant relationships.