Results *Treponema pallidum* binds both the rounded and spread morphologies of activated platelets via a polar tip structure, maintaining a firm tether under fluidic conditions. A lack of interaction between heat-killed *T. pallidum* and platelets confirmed specificity and identified heat-labile *T. pallidum* surface components as mediators of this interaction. Viability assays illustrated *T. pallidum* retained viability in platelet rich plasma for >3 days under these conditions.
Conclusion The demonstration in this study of (1) prolonged *T. pallidum* survival within human platelet rich plasma and (2) *T. pallidum*-platelet interactions indicates that platelets do not exhibit a direct antimicrobial effect on *T. pallidum* and that *T. pallidum* mediates a strong and specific interaction with human platelets. These findings may reveal a novel mechanism of host survival employed by this elusive pathogen.

O06.2 INITIAL INTERACTIONS OF HERPES SIMPLEX VIRUS WITH HUMAN SKIN DENDRITIC CELLS

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Introduction HSV2 initially infects the stratified squamous epithelium of the anogenital mucosa prior to entering nerve endings, resulting in lifelong latent infection of neurons in the dorsal root ganglia. We have recently reported that topical application of HSV-1 to the inner surface of human foreskin explants, simulating *in vivo* infection, infects epidermal Langerhans cells (LCs) which then emigrate into the dermis. Here they formed large cell clusters with dermal dendritic cells (DCs). HSV-expressing LC fragments were observed inside the dermal DCs/macrophages.
Methods To define the mechanism of this interaction, we isolated LCs and dermal DCs from large human abdominal skin specimens by flow sorting. LCs were infected with HSV2 and co-cultured with dermal DCs.
Results All infected LCs developed apoptosis and fragments of them were observed within the dermal DC cytoplasm. HSV infected LCs expressed several chemokines as RNA and protein, with corresponding receptors expressed on dermal DC subsets. These DCs also expressed several phagocytic/apoptotic receptors for phosphatidylserine. In genital herpes lesions the selective contact of CD8 T cells with one of three dermal DC subsets was observed. The distribution of CD4 T cells and contact with these DC subsets is eventually being studied.
Conclusion Thus, we conclude that a viral antigen relay takes place whereby HSV infected LCs undergo apoptosis and are taken up by dermal DCs by phagocytosis for subsequent antigen presentation, probably via different pathways for CD4 and CD8 T cells. As dendritic cells are key targets for the new generation of vaccine adjuvants these studies define potential cellular targets for mucosal vaccines.

O06.3 ANALYSIS OF THE *TREPONEMA PALLIDUM* PROTEOME FOR EVIDENCE OF HOST PROTEIN MIMICRY; IDENTIFICATION OF A MECHANISM FOR BACTERIAL PERSISTENCE AND ESTABLISHMENT OF LATENCY DURING SYPHILIS INFECTION?

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Introduction The causative agent of syphilis, *Treponema pallidum*, is a highly invasive pathogen that can establish lifelong latency. Experimental evidence generated by our laboratory demonstrates a subset of *T. pallidum* proteins exhibits mimicry of host proteins, a strategy that may be used by *T. pallidum* to evade detection by the immune system and establishment of latency. Here we analysed all *T. pallidum* proteins of unknown function to assess the complete repertoire of potential host protein mimics expressed by this stealthy and highly successful pathogen.
Methods Amino acid sequences of 327 functionally unannotated protein-coding genes from *T. pallidum ssp. pallidum* (Nichols strain) were submitted to the protein fold recognition server, Phyre2. For each *T. pallidum* protein, the 20 top-ranked template matches and structural models were obtained. To identify potential *T. pallidum* host protein mimics, we analysed the source organism and functions of all high-confidence template proteins used for modelling (confidence scores/90%; alignment coverage/10%).
Results High-confidence structural predictions were generated for 51% of *T. pallidum* proteins with no assigned function (167/327). Analysis of these 167 functionally unannotated proteins identified a range of *T. pallidum* proteins predicted to adopt structural folds similar to domains from host proteins central to the processes of homeostasis and self-recognition, including Toll-like receptors, extracellular matrix components, and proteins involved in cell-signalling, complement and blood coagulation pathways.
Conclusion Our analyses have identified a complement of potential host protein mimics within *T. pallidum*. This novel finding will provide significant insight into *T. pallidum* virulence mechanisms for mediating host attachment and subverting host recognition, thereby aiding establishment of persistent infection. Our results also illustrate the power of molecular modelling for enhancing our understanding of microbial pathogenesis and disease establishment for bacterial pathogens with unique proteomes.

O06.4 HIGHER LEVELS OF A CYTOTOXIC PROTEIN, VAGINOLYSIN, IN LACTOBACILLUS-DEFICIENT COMMUNITY STATE TYPES IN THE VAGINAL MUCOSA

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Introduction Bacterial cytotoxic proteins, such as vaginolysin (VLY) produced by *Gardnerella vaginalis*, are thought to be virulence factors that *in vitro* alter cell integrity and local immunity. VLY may play a significant role in bacterial vaginosis (BV), therefore we assessed whether *G. vaginalis* dominant

vaginal microbiota and immune markers were associated with higher concentrations of VLY in reproductive-age women.

Methods Forty women self-collected mid-vaginal swabs in a cross-sectional study. Microbial communities were characterised by 16S rRNA gene amplicon sequence analysis. VLY (ng/ml) was detected by ELISA and normalised by a cube root transformation. Absolute bacterial abundance of *G. vaginalis* (log_{10} transformed) was estimated by multiplying its relative abundance by the sample total bacterial burden estimated by qPCR. Pro-inflammatory immune markers were quantified by Luminex and categorised above and below the median. Multivariate linear regression models evaluated factors associated with VLY abundance and controlled for confounders, including smoking and history of vaginal douching.

Results Vaginal microbiota clustered into 3 community state types (CSTs); 2 dominated by *Lactobacillus* spp. (*Lactibacillus iners* (CST-III) or *L. crispatus* (CST-I)), and one lacking *Lactobacillus* spp. and characterised by BV-associated bacteria including *G. vaginalis* and *Atopobium vaginae* (CST-IV). In the multivariate analysis, CST-IV, *G. vaginalis* bacterial load, a high Nugent Gram stain score, and a more basic vaginal pH (all $p<0.03$) were positively associated with increasing concentrations of VLY. TNF-α, TGF-β and IL-8 were inversely associated with VLY but only TNF-α remained significant in multivariate analysis ($p=0.01$).

Conclusion This study confirms that vaginal microbiota lacking lactobacilli, as well as other clinical indicators of BV, were associated with higher concentrations of VLY *in vivo*. Inflammatory markers were inversely associated with VLY. Because VLY may alter the vaginal microbiota and local inflammation, the role of VLY in BV warrants further evaluation.

O06.5 DEVELOPMENT OF A HUMAN URETHRAL EQUIVALENT TO STUDY *CHLAMYDIA TRACHOMATIS* INVASION

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Introduction *Chlamydia trachomatis* (Ct) genovars D-K cause non-invasive urogenital infections, which often remain asymptomatic. Little is known about the invasion of the epithelial layer and the subsequent effects of Ct on the epithelium in humans. The objective of this study was to develop a human urethral 3D *in vitro* equivalent to gain a better insight into the invasiveness of Ct in host tissue.

Methods Human urethral equivalents were constructed by seeding primary urethral keratinocytes and fibroblasts on top of and into a collagen matrix. Urethral cells were isolated from urethral clinical specimens of transgender patients undergoing gender surgery at VUMC. Urethral equivalents were incubated with a Ct genovar D strain, by placing a Ct impregnated nylon gauze on top of each model. Standard Ct cell culture, existing of HeLa cells grown on coverslips, were used as a control to assess growth of Ct strains used for infections of the urethral equivalents. Ct invasion was assessed after 2, 4 and 6 days of incubation.

Results Urethral equivalents consisted of a fully differentiated urethral epithelium on a urethral fibroblast populated collagen hydrogel. The epithelium consisted of multiple differentiated cell layers resembling native urethral tissue. We successfully infected urethral equivalents with a Ct genovar D strain. Ct invasion and expansion was detected in the epithelial layer, but not in the underlying collagen matrix, at 2, 4 and 6 days post infection. Morphological changes of the urethral equivalent could be observed at 2, 4 and 6 days post infection compared to non-infected urethral equivalents, whereby it appeared that the epithelial layer grows around the invaded Ct bacteria.

Conclusion We were able to construct a urethral equivalent resembling native urethral tissue. Moreover, these urethral equivalents could successfully be infected by a Ct genovar D strain, making this a promising life model to investigate the human pathogenesis of urogenital Ct infections.

O06.6 THE URETHRAL MICROBIOTA IN NONGONOCOCCAL URETHRITIS

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Introduction There is no known aetiology for up to half of all nongonococcal urethritis (NGU) cases. We sought to characterise the bacterial communities in men with (NGU+) and without (NGU-) NGU among men who have sex with men (MSM) and men who have sex with women (MSW), to determine if the urethral microbiota is associated with NGU status.

Methods From December 2014 to December 2015, urine samples were collected from 49 MSM (23 NGU+; 26 NGU-) and 48 MSW (21 NGU+; 27 NGU-) attending the Seattle STD Clinic. NGU was defined as urethral symptoms and/or visible discharge, and >5 PMNs per high powered field. *Chlamydia trachomatis* (CT) and *Mycoplasma genitalium* (MG) were detected by transcription mediated amplification (TMA). The urethral microbiota was characterised using broad-range 16S rRNA gene PCR with deep sequencing. Bacterial diversity was calculated using the Shannon index.

Results Mean urethral bacterial diversity in NGU+ MSM (0.82) was lower than in NGU- MSM (1.48), *Streptococcus* (n=7), *Corynebacterium* (n=5), *Haemophilus* (n=3), *Mycoplasma* (n=3), and *Lactobacillus iners* (n=2). Urethral microbiotas with dominant taxa were more common in NGU+ MSM (95.7%), while NGU+ MSW (61.9%) had microbiotas characterised by the presence of several vaginal bacteria. Among NGU- men, 53.8% MSM and 48.1% MSW had microbiotas with dominant taxa, including *Streptococcus* (n=19), *L. iners* (n=5), and *Gardnerella vaginalis* (n=4).

Conclusion The urethral microbiota in NGU is heterogeneous. NGU- MSM had more diverse urethral bacterial communities than NGU+ MSM, and presence of vaginal bacteria in MSW suggests sharing or acquisition from female partners. Future longitudinal studies may help inform if key bacteria predict incident NGU.