

**LB1.68 VAGINAL LACTIC ACID ELICITS AN ANTI-INFLAMMATORY RESPONSE FROM HUMAN CERVICOVAGINAL EPITHELIAL CELLS AND INHIBITS PRODUCTION OF PRO-INFLAMMATORY MEDIATORS ASSOCIATED WITH HIV ACQUISITION**

<sup>1</sup>G Tachedjian, <sup>1</sup>Hearps AC, <sup>1</sup>D Tyssen, <sup>1</sup>D Sribnoski, <sup>2</sup>L Bayigga, <sup>1</sup>Diaz Dj, <sup>1</sup>M Aldunate, <sup>3</sup>Cone Ra, <sup>1</sup>R Gugasyan, <sup>2</sup>Anderson Dj. <sup>1</sup>Burnet Institute, Melbourne, Australia; <sup>2</sup>Boston University, Boston, USA; <sup>3</sup>Johns Hopkins University, Baltimore, USA

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**Introduction** Inflammation in the female reproductive tract (FRT) promotes while *Lactobacillus* spp. protect women from HIV acquisition. We assessed if lactic acid (LA), a major acid metabolite produced by lactobacilli, decreases inflammatory mediators produced by cervicovaginal epithelium.

**Methods** LA at physiological levels and pH were added apically to human vaginal or cervical epithelial cells and an organotypic tissue model cultured in transwells. Cells were stimulated apically with bacterial or viral mimicking TLR agonists, TNF or genital fluids (data collected in 2017). Cytokines and chemokines were quantified by luminex-based assays.

**Results** LA (pH 3.9) treatment of epithelial cell lines elicited significant increases in the anti-inflammatory cytokine IL-1RA. When added simultaneously to stimulation, LA inhibited the TLR agonist-induced production of inflammatory mediators IL-6, IL-8, TNF $\alpha$ , RANTES and MIP3 $\alpha$ . The same LA anti-inflammatory effects were not recapitulated with media acidified to the same pH with HCl, and was mediated by the protonated form of LA present at pH  $\leq$ 3.9. Both l- and d-isomers of LA elicited similar anti-inflammatory effects. LA pretreatment of cells for 1 hour, followed by cell washing and TLR agonist stimulation, inhibited pro-inflammatory production indicating a direct effect on cells. A similar anti-inflammatory effect of LA was observed in primary cervicovaginal cells and in an organotypic epithelial tissue model, and when FRT epithelial cells were exposed to either cervicovaginal or seminal fluids. Immune mediators were elicited by LA at physiological levels and pH that had little impact on cell viability or monolayer/tissue integrity.

**Conclusion** LA acts on FRT epithelial cells to inhibit inflammation that might explain in part the HIV protective properties of LA producing lactobacilli. This study highlights the potential use of LA-containing agents or LA-producing probiotics as adjuncts to female-initiated HIV prevention strategies

**LB1.69 CLINICAL AND ANALYTICAL EVALUATION OF THE NEW APTIMA MYCOPLASMA GENITALIUM ASSAY ON THE PANTHER INSTRUMENT (HOLOGIC), M. GENITALIUM PREVALENCE, AND ANTIMICROBIAL RESISTANCE IN M. GENITALIUM IN SWEDEN, DENMARK AND NORWAY IN 2016**

<sup>1</sup>Magnus Unemo, <sup>2</sup>Kirsten Salado-Rasmussen, <sup>1</sup>Marit Hansen, <sup>3</sup>Anne Olaug Olsen, <sup>4</sup>My Falk, <sup>1</sup>Daniel Golparian, <sup>1</sup>Johan Ringlander, <sup>4</sup>Christian Steczko Nilsson, <sup>3</sup>Harald Moi, <sup>5</sup>Henrik Westh, <sup>6</sup>Jörgen Skov Jensen. <sup>1</sup>Who Collaborating Centre for Gonorrhoea and Other Stis, Örebro University Hospital, Örebro – Sweden; <sup>2</sup>Bispebjerg Hospital, Copenhagen – Denmark; <sup>3</sup>Olafia Clinic, Oslo – Norway; <sup>4</sup>Örebro University Hospital, Örebro – Sweden; <sup>5</sup>Hvidovre University Hospital, Copenhagen – Denmark; <sup>6</sup>Statens Serum Institut, Copenhagen – Denmark

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**Introduction:** *Mycoplasma genitalium* (MG) is a frequent aetiology of urethritis and cervicitis, which can result in severe reproductive complications. Resistance in MG to first-line (azithromycin) and second-line (moxifloxacin) treatment has rapidly increased. The new CE-marked APTIMA MG assay (Hologic) is now commercially available. Our aims were to evaluate the clinical and analytical sensitivity and specificity of the new APTIMA MG assay and an APTIMA MG RUO assay, and describe the prevalence of MG, *N. gonorrhoeae*, *C. trachomatis* and resistance to azithromycin and moxifloxacin in Sweden, Denmark and Norway in 2016.

**Methods** From January 2016 to March 2017, first-void urine (from males) and vaginal swabs were collected from consecutive attendees at 3 STD clinics in Sweden, Denmark and Norway. All samples were tested with the APTIMA MG assay, APTIMA MG RUO assay, APTIMA CT/NG assay, and a quantitative *mgpB* PCR. Resistance was determined by sequencing of the 23S rRNA gene and *parC*. For analytical evaluation, isolates of diverse genome-sequenced MG and other mycoplasma species in different concentration were tested.

**Results** In total, 5269 patients were included. The rate of MG infected patients was 7.3%, however, the rate significantly varied in the different countries. The sensitivity of the APTIMA MG assay, APTIMA MG RUO assay and *mgpB* PCR ranged between 95.8%–100%, 95.8%–100%, and 73.2%–81.6%, respectively, in the countries. The specificity of the APTIMA MG assay, APTIMA MG RUO assay and *mgpB* PCR ranged between 99.6%–100%, 100%, and 99.7%–100%, respectively. The resistance level to azithromycin was 40% (18%–56% in the countries) and multidrug resistance (to both azithromycin and moxifloxacin) was found in all countries.

**Conclusion** Both the APTIMA MG assays had a significantly superior sensitivity compared to the *mgpB* PCR. The prevalence of MG as well as azithromycin resistance was high. Increased testing using validated and quality assured molecular tests for MG, antimicrobial resistance surveillance and routine resistance testing in MG-positive samples is crucial.

**LB1.70 ABERRANT HUMORAL IMMUNE RESPONSES IN NEUROSYPHILIS: CXCL13/CXCR5 PLAY A PIVOTAL ROLE FOR B CELL RECRUITMENT TO THE CSF**

Pingyu Zhou. Shanghai Skin Disease Hospital, Shanghai – China Popular Republic

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**Introduction** Previous studies have documented that humoral immune responses participated in neurological damage in neurosyphilis patients. However, the mechanisms that trigger and maintain humoral immunity involved in neurosyphilis remain unknown.

**Methods** Using flow cytometry expression of B cells was measured in neurosyphilis and non-neurosyphilis. Expression of immunoglobulin indices and CXCL13 was detected by ELISA. A modified chamber assays were used to migration and inhibition assays. The presence of CXCL13<sup>+</sup> cells, CD20<sup>+</sup> B cells, CD3<sup>+</sup> T cells, CD138<sup>+</sup> plasma cells and CD35<sup>+</sup> follicular dendritic cells was studied by immunohistochemistry.

**Results** We found that enrichment of B cells were observed and activated in the cerebrospinal fluid (CSF) of NS patients. Immunoglobulin indices were increased and associated with

the progress to neurosyphilis. Moreover, high expression of CSF CXCL13 mediated B cells migration both *in vitro* and *in vivo*. More importantly, there was a positive correlation between the CSF B cells, immunoglobulin indices, and CSF CXCL13 levels. Interestingly, ectopic germinal centres (EGCs), the important structures for the maintenance of humoral immunity, were observed in the intracranial syphilitic gumma. **Conclusion** CXCL13/CXCR5 mediated the aggregation of B cells, which directed the aberrant humoral immune responses via the formation of EGCs. Our observations suggest a molecular mechanism of neurological damage in neurosyphilis.

#### LB1.71 VAGINAL MICROBIOTA CONTROLS EPITHELIAL CELL PROLIFERATION AND SUSCEPTIBILITY TO *C. TRACHOMATIS* INFECTION

Steven Smith, Jacques Ravel. University of Maryland, Baltimore, USA

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**Introduction** Dysbiotic states of the vaginal microbiota, including bacterial vaginosis (BV), are characterised by a paucity of *Lactobacillus* spp., the presence of an array of anaerobes, a pH >4.5, and are associated with increased susceptibility to STIs. The mechanisms by which vaginal microbiota protect or increase the risk to STIs remain unknown. By characterising the *in vivo* host miRNA response to different types of vaginal microbiota, we gained insight into functions that play a role in epithelial homeostasis. Understanding the molecular mechanisms driving vaginal dysbiosis may help develop strategies reduce the risk of STIs.

**Methods** Leveraging prospectively collected daily vaginal swab samples, miRNA-seq profiling was used to gain insight into host regulatory mechanisms controlled by vaginal microbial communities. Random Forest miRNA feature ranking was used to identify miRNAs expressed in response to different types of vaginal microbiota. *In vitro*, VK2 epithelial cells were exposed to vaginal bacteria culture supernatants, and miRNA expression was measured by qPCR, while cyclin D1 was measured by Western blot. Cell proliferation was quantified using scratch and EdU assays. Cell proliferation's effect on *C. trachomatis* infection was performed on cervical A2EN epithelial cells.

**Results** We leveraged daily collected vaginal samples in conjunction with a machine learning approach to discover eight miRNAs differently controlled by vaginal microbiota. Of these, expression of miR-193b, known to regulate host cell proliferation, was increased by *Lactobacillus* spp.-dominated microbiota. Recently, *in vitro*, VK2 cells exposed to *Lactobacillus*-conditioned supernatants exhibited reduced proliferation, high miRNA-193b expression and decreased abundance of cyclin D1. Importantly, epithelial cell proliferation was required for efficient *C. trachomatis* infection.

**Conclusion** These findings contribute to the vaginal microbiota's role in cellular homeostasis and susceptibility to STIs, which may lead to improved preventive strategies by modulating vaginal microbiota composition.

#### LB1.72 PREVALENCE OF HUMAN PAPILLOMA VIRUS INFECTION AND DETECTION OF HPV TYPES IN HIV- POSITIVE MALE PATIENTS FOLLOWED BY ANAL CYTOLOGICAL ABNORMALITIES IN EASTERN INDIA

Abhilasha; Jaya Chakravarty, Shyam Sundar, Madhukar Rai. Banaras Hindu University, India

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**Introduction** India has a third large population of people living with Human Immunodeficiency Virus (HIV) in the world. Incidence of Human papilloma virus (HPV) infection anal cancer is high among People Living with HIV/AIDS (PLHIV). However, there are very few studies among HIV positive men in India. Thus this cross-sectional study was performed to assess the prevalence and risk factors of anal HPV infection and anal HPV types in HIV positive males attending the Anti-retroviral therapy (ART) centre.

**Method** We screened HIV positive men with Anal Papanicolaou smear cytology and HPV testing. HPV DNA was detected by Consensus Polymerase Chain Reaction (PCR) using dissimilar E6 consensus and MY09/11 consensus primers followed by sequencing for confirmation the type of HPV.

**Results** 126 HIV-positive men were included in the study. Mean age was 35.37±8.2 years. Median CD4+T cell counts were 253/μL. Mean weight and mean Haemoglobin was 49.53 ±8.45 Kg and 11.2±1.73 g/dl respectively. 74 patients were treatment naive and 52 were on Anti-Retroviral Therapy (ART) 48 (38%) gave positive for history of anal intercourse with other men although 91% were married. Anal cytology was done in 95 patients, out of which 61 (64.2%) had cytological abnormalities, of which 28 (29.4%) cases had LSIL, 33 (34.7%), had ASCUS. In multivariate analysis, an only risk factor for cytological abnormality was a history of anal intercourse Odds Ratio (OR) 0.122 (95% 0.036–0.410). HPV DNA was detected in 25.21% patients. The most prevalent HPV type in the study group was HPV-16 (10%) followed by HPV-18,31,35,17,66,72,52,68 and 107 (15.21%) genotypes were detected in anal pap samples.

**Conclusion** In our study, the prevalence of HPV infection was 25.21% and anal cytological abnormality was 64.2%, which is high. Anal Pap smear screening should be done especially in HIV positive males with the history of bisexuality. HPV DNA screening by using consensus PCR method followed by sequencing more beneficial and cost-effective for HPV genotyping HIV infected men on antiretroviral therapy.

## Clinical Science

#### P2.01 ASSESSING THE IMPACT OF INDIVIDUALISED TREATMENT: AN INDIVIDUAL-BASED MATHEMATICAL MODELLING STUDY OF ANTIMICROBIAL RESISTANT *NEISSERIA GONORRHOEAE* TRANSMISSION, DIAGNOSIS AND TREATMENT IN MEN WHO HAVE SEX WITH MEN

<sup>1</sup>Adam Zienkiewicz, <sup>1</sup>Martin Homer, <sup>1</sup>Hannah Christensen, <sup>1</sup>Darryl Hill, <sup>2</sup>Neil Woodford, <sup>2</sup>Helen Fifer, <sup>2</sup>Gwenda Hughes, <sup>1</sup>Katherine Turner. <sup>1</sup>University of Bristol, UK; <sup>2</sup>Public Health UK

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**Introduction** Antimicrobial resistant (AMR) gonorrhoea is a global public health threat. In London, diagnoses in men who have sex with men (MSM) have more than quadrupled from