## P1.31 THE COSTS OF TARGETED CIPROFLOXACIN THERAPY VS. EMPIRIC THERAPY FOR *NEISSERIA GONORRHOEAE* INFECTIONS OVER A THIRTEEN-MONTH STUDY PERIOD

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**Introduction** Novel approaches to combating drug-resistant *N. gonorrhoeae* infections are urgently needed. Targeted therapy with ciprofloxacin for susceptible infections has been made possible by the development of a rapid molecular assay for the determination of mutation in the gyrase A gene of *N. gonorrheoae*, which reliably predicts susceptibility to ciprofloxacin.
**Methods** Using previously collected data over a thirteen-month study period of all *N. gonorrhoeae* cases diagnosed to UCLA Health System, we determined the costs per-test of running the rapid genotypic gyrase A assay and treatment with 500 mg of ciprofloxacin for wild-type infections and compared these estimations with the costs of the standard of care treatment, which is empiric dual therapy with 250 mg ceftriaxone injection and 1000 mg azithromycin. Cost estimates for non-empiric therapy included assay reagents, labour, refrigerator space, and ciprofloxacin 500 mg. Cost estimates for empiric therapy included costs of ceftriaxone 250 mg, injection, azithromycin 1000 g, needle, syringe, and clinic space.
**Results** There were 167 non-empirically treated anatomic site-specific *N. gonorrhoeae* infections during the thirteen month study period, 51 (30.5%) of which were wild-type, and 49 (29.3%) were mutant. Using the total number of specimens tested (167) we calculated the cost of running the assay per specimen to be $97.4. With an additional cost of $2.2 per pill of ciprofloxacin, the total cost of non-empiric therapy for wild-type infections was estimated to be $99.6. The cost of empiric treatment with ceftriaxone and azithromycin was estimated to be $141, however there may be additional costs of up to $300 based on the clinic facility fees, which vary greatly by location.
**Conclusion** We found that the genotypic assay with ciprofloxacin therapy among wild-type infections is less costly than empiric therapy. Furthermore, given the consequences ceftriaxone resistance, including continued transmission and the sequela of untreated infection, the true difference in cost may be even greater.

## P1.32 HAND-HELD RAPID WHOLE GENOME NANOPORE SEQUENCING TO PREDICT *NEISSERIA GONORRHOEAE* ANTIBIOTIC SUSCEPTIBILITY: STEPS TOWARDS CLINIC BASED TAILORED ANTIMICROBIAL THERAPY

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**Introduction** Next generation sequencing can accurately predict antibiotic susceptibility in *Neisseria gonorrhoeae* (NG) allowing preservation of first-line treatments in the face of widespread antimicrobial resistance (AMR). The rapid nature of novel hand-held nanopore sequencing (NPS) gives promise for utility at the point of care. We evaluated time to result post DNA extraction, and accuracy of MinION (Oxford Nanopore Technologies) NPS to predict phenotypic antimicrobial susceptibility (PAMS) of NG to ciprofloxacin and azithromycin.
**Methods** One-directional (1-D) NPS using bar-coded DNA library preparations from 48 NG isolates, prospectively collected from a London clinic, were run on NPS flow cells (3 per R9.0 flow cell) and illumina MiSeq as a comparator. NPS raw sequences were transferred to the cloud for base-calling, alignment, and variant calling using standard tools.
**Results** Mean time for 1-D library preparation was roughly 1 hour; NPS and alignment took <40 min per sample with single nucleotide polymorphism (SNP) calling adding little extra time. NPS genome coverage was >30X per isolate. Of 48 samples, PAMS to ciprofloxacin, and azithromycin was 74% and 87% respectively. Accuracy of NPS-based genotypic susceptibility, defined as absence of any known AMR-associated SNP's, to predict PAMS for ciprofloxacin and azithromycin, was 34/34 (100%; 95% CI 89.8%–100%) and 35/40 (87.5%; 95% CI 73.9%–94.5%) respectively. Accuracies improved significantly for azithromycin when only high quality reads were included, and with Illumina sequencing. 30 of the 34 isolates susceptible to azithromycin were also susceptible to ciprofloxacin, and 3 of 6 isolates resistant to azithromycin were also resistant to Ciprofloxacin.
**Conclusion** NPS accurately predicted ciprofloxacin PAMS but was less accurate for azithromycin. With new iterations of the technology, imminent rapid barcoded library preparation (10 min) and rapid DNA extraction from clinical samples, NPS may allow accurate ceftriaxone-adjunctive treatment combinations, for a substantial proportion of patients.

## P1.33 MULTIPLEX ASSAY FOR THE DETECTION OF SYPHILIS AND OTHER PATHOGENS ASSOCIATED WITH GENITAL LESIONS USING PLEXPCR

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**Introduction** Syphilis is a well-known STI caused by the bacterium *Treponema pallidum*. It can result in genital lesions and substantial morbidity and mortality. Recently, there has been an alarming global resurgence of syphilis with infections rising to unprecedented rates. As such, it is increasingly pertinent to test genital lesions for syphilis.Herpes simplex virus types 1 and 2 (HSV-1 and HSV-2) and Varicella zoster virus (VZV) cause lesions in cutaneous and mucocutaneous sites. While HSV-1 and HSV-2 are commonly known to cause genital lesions, recent publications have also found VZV in genital specimens. This unexpected finding suggests that reactivation of VZV in this atypical presentation is not as uncommon as previously believed. Using our highly specific PlexZyme technology that enables efficient multiplexing in real-time PCR (qPCR), we have developed a genital lesion assay for the detection of syphilis, HSV-1, HSV-2 and VZV to facilitate prompt and correct treatment of these STI pathogens.

**Methods** To develop a genital lesion assay, the syphilis target was added to our existing HSV-1, HSV-2 and VZV assay (also containing a DNA extraction/amplification control) in a single-well multiplex qPCR. The performance of the assay was evaluated on 90 genital specimens for which in-house PCR results for syphilis had been determined.
**Results** The genital lesion assay showed robust performance in multiplex with sensitive detection to 10 copies for all targets. The multiplexed assay detected 54/57 syphilis positives, corresponding to a sensitivity and specificity of 94.7% and 100.0%, respectively. The assay also detected 4 HSV-1 and 2 HSV-2 infections (2 and 1 syphilis co-infections, respectively).
**Conclusion** The lesion assay offers simultaneous detection and differentiation of pathogens that cause genital lesions. In response to the current emerging syphilis outbreak, this assay could provide a rapid and effective method of determining the infectious agent responsible for genital lesions, supporting earlier detection and rapid treatment to reduce morbidity or worse outcomes.

## P1.34 DONOR OF MOSAIC PENA GENE OF CEFTRIAXONE RESISTANT *NEISSERIA GONORRHOEAE* FC428 AND GU140106

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**Introduction** Gonorrhoea is a global health concern because *N. gonorrhoeae* has now acquired resistance to antibiotics including the 3rd generation cephalosporin, ceftriaxone. Mosaic structure in penicillin-binding protein 2 gene (*penA*) is the main cause of ceftriaxone resistance which is formed by natural transformation of DNA of ceftriaxone-resistant ($CRO^R$) commensal *Neisseria* spp. However, none of the previous studies has fully elucidated the source of transformed DNA. In this study, we show that genetic comparison between $CRO^R$-*N. gonorrhoeae* strains (GU140106 and FC428) and $CRO^R$ – *Neisseria* commensals.
**Methods** $CRO^R$-*Neisseria* commensals were isolated from pharyngeal swabs. Genome sequence was obtained by MiSeq, Illumina, and the sequence of *penA* flanking region (*mraW-NGO*1540-*penA-murE-dcaA*) was obtained using the *N. gonorrhoeae* FA1090 as a reference sequence. Alignment of the compared sequences were prepared by CLUSTALW. Species identification of *Neisseria* commensals was performed using phylogeny constructed by 53 ribosomal proteins (*rps*) sequences.
**Results** Based on the sequence similarity of *penA* gene, two $CRO^R$-*Neisseria* commensals were speculated to be the origin of each mosaic *penA* of GU140106 and FC428. Both of the candidates were *N. cinerea* according to the *rps* phylogeny. The DNA region including *penA* originated from *N. cinerea* which consist the part of mosaic *penA* in the $CRO^R$-*N. gonorrhoeae* was about 1.3 kb including of parts of *penA* and *murE*. Further analysis revealed that mosaic *penA* of GU140106 occurred by recombination between $CRO^R$-*N. cinerea* and $CRO^S$ -*N. gonorrhoeae* which the NG-MAST type was same with GU140106. The mosaic *penA* of FC428 was also thought to emerged in the same way with GU140106. However, there was a limitation because of the lack of $CRO^S$-*N. gonorrhoeae* that has the same NG-MAST type with FC428.
**Conclusion** The two $CRO^R$-*N. gonorrhoeae*, GU140106 and FC428, might acquire resistance by homologous recombination with *Neisseria* commensals, and *N. cinerea* might be the donor of mosaic *penA* which causes resistance to ceftriaxone in *N. gonorrhoeae*.

## P1.35 SURFACE MODIFIED SOLID LIPID NANOPARTICLES FOR THE TARGETED DELIVERY TO BRAIN: MANAGEMENT OF HIV-1 ASSOCIATED DEMENTIA

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**Introduction** HIV-Associated Dementia (HAD) is a significant neurological complication which occurs years after the acute viral sero-conversion reaction responsible for progressive Immuno-suppression and high viral loads. Many patients infected with HIV-1 suffer cognitive impairment ranging from mild to severe HAD. With Present available treatment system, there is no satisfactory treatment for HAD available.
**Methods** In this study, nifedipine loaded solid lipid nanoparticles (SLN) were developed for targeting drug into CNS, to block the apoptosis by HIV-1 virus. This would decrease the process of neurodegeneration and increase survival time of neuronal cells. Also, this targeted delivery to brain will minimise the systemic effect of nifedipine, avoiding its delivery peripherally.The uncoated SLN were prepared by Solvent Injection Method and coated with tween 80 and Lyophylized. Shape and surface morphological studies were done by Scanning and Transmission Electron Microscopy (TEM). The *in-vitro* release profile of entrapped drug was studied using dialysis membrane. *Ex-vivo* studies consisted of DNA fragmentation followed by *in-vivo* studies.
**Results** The SEM and TEM images show smooth and spherical surface of SLN. I*n-vitro* release profile of drug shows more than 90% of drug release in 48 hours. DNA fragmentation was determined in presence and in absence of gp120 mimicking agent which shows no DNA fragmentation thus developed carrier system works properly in releasing drug and blocking apoptosis in cortical cells. Fluorescence microscopy shows qualitative uptake and localization pattern of coated SLNs in brain.
**Conclusion:** *In-vitro* and *in-vivo* studies results shows more specific delivery of Nifedipine to Brain. DNA Fragmentation and Cell Viability studies shows dementia blocking activity on brain cells. Brain specific delivery of Nifedipine could reduce the dose and potential systemic side effects, thus providing site specific delivery to brain. Thus, CNS delivery of these Nifedipine loaded SLNs via Intra-venous delivery will also open new opportunities for other Anti-Retroviral drug delivery to brain.