S11 - Molecular aspects of antimicrobial resistant *Neisseria gonorrhoeae*

S11.1 REAL-TIME PCR DETECTION OF *N. GONORRHOEAE* RESISTANCE: WHERE ARE WE NOW?

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Ongoing emergence and spread of *Neisseria gonorrhoeae* antimicrobial resistance is of global concern and was recently designated an "urgent threat" by the United States Centres for Disease Control and Prevention. Australia is not immune to the *N. gonorrhoeae* resistance problem as highlighted by the first report of a ceftriaxone-resistant strain from Australia in 2014. Enhancing antimicrobial resistance (AMR) surveillance strategies to advance detection of gonococcal AMR is a priority. Whilst bacterial culture-based methods remain the most definitive means of assessing *N. gonorrhoeae* AMR, there has been decreasing availability of cultured isolates for AMR susceptibility testing owing to increased use of nucleic acid amplification test (NAAT)-based methods for gonorrhoea diagnosis. Molecular AMR surveillance tools have the potential to overcome these problems. In particular, polymerase chain reaction (PCR)-based methods targeting key genetic markers of resistance can facilitate rapid, more intense sampling, for *N. gonorrhoeae* strains of public health importance following NAAT-based diagnosis. This presentation will discuss the development of real-time PCR methods for *N. gonorrhoeae* AMR detection and in doing so will highlight potential technical obstacles that may impinge upon assay design and performance.

S11.2 EFFLUX PUMPS IN *NEISSERIA GONORRHOEAE* – CAUSE OF RESISTANCE AND TARGETS FOR THERAPEUTICS AND VACCINE?

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Neisseria gonorrhoeae is the cause of the sexually transmitted infection termed gonorrhoea, which afflicts over 100 million people worldwide each year. Since the mid-1940s, beginning with the availability of penicillin (Pen), antibiotic therapy has been the mainstay for curing infection and halting the spread of the gonococcus in the community. Unfortunately, gonococci developed resistance to Pen and many other antibiotics that were brought into clinical practice to counter act the growing problem of Pen (and other antibiotics) resistance. With the recent emergence of strains expressing resistance to the third-generation cephalosporins (cefixime and ceftriaxone) or other important antibiotics (macrolides and fluoroquinolones) there is considerable fear that without new antibiotics, gonorrhoea will become more difficult to treat; indeed, some have warned of the possibility of untreatable infections. In order to address this public health crisis of antibiotic resistant gonococci, it is essential that new bacterial targets are identified so as to facilitate the development of novel therapeutic drugs. I will discuss the role of the MtrC-MtrD-MtrE efflux pump in the development of gonococcal resistance to antibiotics and host-derived antimicrobials (e.g., cationic antimicrobial peptides). These phenotypes are augmented in gonococcal strains that have mutations that result in enhanced transcription of the *mtrCDE* efflux pump gene complex. I will provide evidence that this efflux pump is critical for the ability of gonococci to resist certain antibiotics as well as surviving during infection. Against this background, I will propose that this pump offers new targets for drug development (efflux pump inhibitors) and vaccine development to combat antibiotic resistant gonococcal strains and to prevent infections.

S11.3 USE OF WHOLE GENOME SEQUENCING TO DETERMINE THE PROBABILITY OF ANTIMICROBIAL RESISTANCE IN *NEISSERIA GONORRHOEAE*

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Neisseria gonorrhoeae has demonstrated remarkable ability to rapidly develop antimicrobial resistance to each antimicrobial class used for therapy including the currently recommended class of antimicrobials, the cephalosporins. Emerging resistance to cephalosporins will severely complicate treatment of gonorrhoea. Advanced Molecular Detection approaches, such as whole genome sequencing to determine mechanisms of resistance, have the potential to advance our understanding of gonorrhoea. To date, we have sequenced >1,000 genomes from *N. gonorrhoeae* isolates with elevated cefixime or azithromycin minimum inhibitory concentrations (MICs) or resistance to previously recommended antimicrobials, and isolates collected from multiple geographic sites to accomplish the following objectives: (1) to identify mutations that confer antimicrobial resistance or increased MICs; (2) to inform the development of molecular assays for resistance determinants through insights gleaned from WG from which point-of-care assays for resistance markers will be developed. Such assays will change the paradigm of gonorrhoea treatment. Use of real-time results on the presence or absence of resistance determinants will allow clinicians to personalise treatment for patients, and prevent inadvertent use of agents that are no longer routinely recommended because of resistance. Such assays can also substantially expand the reach of surveillance of antimicrobial resistance and allow public health officials to rapidly detect and respond to outbreaks of resistant strains; and (3) to develop and maintain a microbial library, a web-accessible and searchable database that will include bacterial and viral genomic sequences and associated meta-data, such as basic de-identified demographic characteristics of patients and phenotypic susceptibility data. In the long term, knowledge of the genetic mechanisms responsible for resistance or deceased susceptibility in *N. gonorrhoeae* gained from sequencing may translate into the identification or development of new therapeutic agents.

S12 – Sexual health issues for Indigenous youth in Australia and New Zealand

Indigenous peoples worldwide suffer disproportionately poor sexual and reproductive health. This symposium will describe the sexual and reproductive health issues for Indigenous youth in Australia and New Zealand. Given that both Indigenous populations are demographically young in age compared to other ethnic groups, they require strategies that address their unique developmental and cultural needs. We will draw on data from

two national sexual behavioural surveys among Indigenous youth conducted in Australia and New Zealand, as well as summarise the evidence, the gaps and challenges with a social determinants lens. We will discuss opportunities and explore innovative ideas that may address these disparities via an interactive panel and group discussions.

S12.1 SEXUAL HEALTH OF MAORI ADOLESCENTS, FINDINGS FROM THE YOUTH'12 NATIONAL YOUTH HEALTH AND WELLBEING SURVEY IN SECONDARY SCHOOLS THROUGHOUT NEW ZEALAND

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Aim To describe the prevalence and trends of sexual health behaviours for Māori youth in New Zealand.
Method The Youth 2000 survey series are anonymous, representative, cross-sectional, self-administered surveys undertaken in 2001, 2007 and 2012 with over 27,000 New Zealand secondary school students aged 12–18 years.
Results Data from the surveys highlight that in 2012, 36% of Māori had ever had sex. This was significantly lower than in previous waves of the survey (47.6% in 2001, 55.8% in 2007). Similarly those who report being currently sexually active has declined over time (33.5% in 2001, 41.8% in 2007 and 26.5% in 2012). Despite the trends to fewer Māori youth engaging in sexual behaviour in secondary school, the use of contraception (51.3% in 2001, 52.2% in 2007 and 48.4% in 2012) and condoms (46.4% in 2001, 36.1% in 2007 and 43.8% in 2012) has not improved. Compared to New Zealand European (NZE) students, Māori are significantly more likely to be sexually active (OR 1.50, 95% CI 1.24, 1.83) and less likely to use contraception (OR 0.50, 95% CI 0.38, 0.66). There was no difference in condom use between Māori and NZE. Māori also reported that they were less able to access primary care (GP) they required in the previous 12 months (OR 0.84, 95% CI 0.72, 0.99).
Conclusion Māori youth in New Zealand are delaying sexual activity, but those who are sexually active are particularly vulnerable to STIs. Specific strategies are required that improve access to appropriate contraception and condom use for Māori.

S13 - Microbiome of the genital tract, host immune responses and STI interactions

S13.1 THE MANY FACETS OF THE VAGINAL MICROBIOME IN HEALTH AND DISEASE

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The vaginal microbiota forms the first line of defense against sexually transmitted infection (STIs). Population-based surveys of the bacteria inhabiting the vagina have shown that several kinds of vaginal microbiota exist, that differs in bacterial composition and abundance. Further, in some women, these communities are dynamic and can change over short period of time, while in other, they are highly stable and do not change. The impact of both composition and dynamic of the vaginal microbiota on the susceptibility to diseases is still poorly understood. The application of modern genomic technologies, ecological principles and *in vitro* modelling affords a better understanding of the role of vaginal microbiome in health and diseases. Metagenomic sequencing provides a comprehensive view of the genetic make up of the bacterial species comprising the vaginal microbiome, and highlights associations between different genomic species of the same genus, or strains of the same species and their contribution to the protective properties of the vaginal microbiome. For example, the genomic make up of certain vaginal bacteria correlates with their ability to maintain a stable and protective vaginal microbiome. Further, the use of *in vitro* three-dimensional models of cervical epithelial cell lines is a good surrogate to evaluate the contribution of microbial products to the function of the vaginal microbiome. Using a 3D model of cervical epithelial cells, we have shown that the production of different isomers of lactic acid by *Lactobacillus* spp. is associated with protection against chlamydial infection in a pH dependent manner. Understanding the vaginal microbiome structure and functions is critical to devise novel and personalised strategies to maximise women's health.

S13.2 GENITAL IMMUNOLOGY, THE MICROBIOTA AND HIV TRANSMISSION

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Background The probability of HIV acquisition after a sexual exposure is low, but surprisingly heterogeneous. Key mucosal immune determinants of susceptibility include genital epithelial disruption and/or the presence of activated $CD4^+$ T cell in the genital mucosa, both of which have been linked to mucosal inflammation. We hypothesise that the genital microbiota may alter mucosal immunology and hence HIV susceptibility.
Methods We have carried out *ex vivo* studies of cervical, foreskin and semen mucosal immunology and *in vivo* studies of HIV acquisition in participant cohorts from Canada and East Africa. Studies use endocervical cytobrush samples and ectocervical biopsies from female participants, as well as foreskin tissues obtained during elective penile circumcision and semen samples from male participants. Mucosal T cell parameters and soluble genital immune factors associated with HIV transmission are assessed, co-infection diagnostics performed and the bacterial microflora assayed using 16S rRNA gene-based pyrosequencing and quantitative PCR.
Results In HIV-uninfected individuals, asymptomatic herpes infection was characterised by mucosal T cell immune activation and increased CD4 expression of the HIV co-receptor CCR5 and/or a4b7, in the absence of any local elevation in pro-inflammatory cytokines. However, while a vaginal microbiome characterised by bacterial diversity was not associated with mucosal cellular alterations, microbiota alterations in both the vagina and foreskin were associated with elevated pro-inflammatory cytokines, and the latter with a proteomic profile suggestive of epithelial disruption. In HIV-infected men, the semen microbiome was altered and linked to levels of HIV RNA in the seminal plasma, as well as to local levels of pro-inflammatory cytokines.
Conclusion The microbiota of the vagina and foreskin are associated with HIV susceptibility, and with important alterations in mucosal immunology that appear to be quite distinct to those induced by the HIV-enhancing co-infection HSV-2. This may lead to new clinical HIV prevention strategies.