Partner services are a longstanding component of public health efforts to control sexually transmitted infections (STI). However, they have not been a consistent part of HIV prevention efforts either in high-or lower-income nations. In many areas, partner services for HIV and other STIs have been administratively separated, and the goals of partner services have usually been narrowly conceived to concentrate exclusively on the diagnosis and treatment of sex partners. This is now beginning to change. New evidence suggests that HIV PS in high income nations may be less effective at finding new cases of HIV than previously believed, but could play an important role in linkage to care. In sub-Saharan Africa, HIV PS appears to be highly acceptable and effective.

This session will focus on new opportunities in the area of HIV PS. The speaker will review the following issues: (1) data supporting the efficacy of HIV partner services as an HIV case-finding tool in both in high and low-income nations; (2) cost and cost-effectiveness data on HIV PS; (3) evidence that PS for bacterial STIs can be used to promote HIV case-finding and engagement in care among persons with previously diagnosed HIV infection; and (4) outstanding research questions related to HIV PS.

S.07 - Bacterial virulence and host response

**S07.1 INSIGHTS INTO MATERNAL GONORRHOEA: HUMAN PRIMARY CERVICAL AND AMNIOCHORIONIC EPITHELIAL CELL RESPONSES TO NEISSERIA GONORRHOEAE INFECTION**


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Bacterial infection is widely recognised as a factor contributing to adverse pregnancy outcomes (APOs). *Neisseria gonorrhoeae* infections continue to be a universal and intractable problem. In this regard, maternal gonorrhoea increases a woman’s risk for APO by 6.5-fold. Bacterial infection is thought to trigger a pro-inflammatory response that initiates those processes involved in (preterm) delivery of the organism. Further, we found a direct correlation between the effectiveness of Sap transporter, which takes up periplasmic LL37 for cytoplasmic degradation and the contribution of the trans-envelope to virulence in humans. Further, we find that the maintenance of two discrete exit mechanisms underscores the fundamental importance of this process for intracellular pathogens such as *Chlamydia*. Extrusions are novel pathogenic structures that we hypothesise confer unique means of interacting with the host’s innate immune system, enabling immune evasion and promoting tissue dissemination. To this end, we have recently illuminated key characteristics of chlamydial extrusions that allow direct infection of new cells and their engulfment by professional phagocytes. Bacteria within phagocytosed extrusions are protected from macrophage killing mechanisms for at least 8 h. These results have important implications for *Chlamydia* pathogenesis in *vivo*, including dissemination, transmission and the elicitation of immune responses.

**S07.2 THE EXTRUSION PARADIGM OF CHLAMYDIA PATHOGENESIS**


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*Chlamydia* is the most commonly reported bacterial disease in the United States, and remains the leading bacterial cause of sexually transmitted infection, responsible for approximately 90 million new STI cases annually worldwide. Of particular concern is that infections with *C. trachomatis* can lead to severe medical complications in women, such as pelvic inflammatory disease and ectopic pregnancy. Alarmingly, there remain fundamental gaps in our understanding of *Chlamydia* pathogenesis in *vivo*, for example their natural course of infection in humans and why protective immunity is not established. To help address these questions, our laboratory has been interested in determining how *Chlamydia* disseminate within the host. Our original discoveries elucidated the mechanisms by which *Chlamydia* exit host cells *in vitro*. Surprisingly, *Chlamydia* possess two mechanisms for cellular escape that are mutually exclusive: (i) Extrusion, a packaged release of *Chlamydia* in which the vacuole pinches off and exits the cell within a membrane-encased compartment; this leaves the original host cell intact, often with a residual chlamydial inclusion. (ii) Lysis, a destructive process that is mediated by proteases and the sequential rupture of vacuole, nuclear and plasma membranes, culminating in the release of free bacteria. The maintenance of two discrete exit mechanisms underscores the fundamental importance of this process for intracellular pathogens such as *Chlamydia*. Extrusions are novel pathogenic structures that we hypothesise confer unique means of interacting with the host’s innate immune system, enabling immune evasion and promoting tissue dissemination. To this end, we have recently illuminated key characteristics of chlamydial extrusions that allow direct infection of new cells and their engulfment by professional phagocytes. Bacteria within phagocytosed extrusions are protected from macrophage killing mechanisms for at least 8 h. These results have important implications for *Chlamydia* pathogenesis in *vivo*, including dissemination, transmission and the elicitation of immune responses.

**S07.3 SURVIVAL STRATEGIES OF HAEMOPHILUS DUCREYI: ROLE OF TRANSPORTERS**


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During human disease, *Haemophilus ducreyi* leads a primarily extracellular lifestyle, in which the organism is under constant pressure from the immune system. To survive in this environment, *H. ducreyi* expresses multiple mechanisms that counteract various antimicrobial activities of innate immunity. Key among these is secretion of LspA proteins to prevent phagocytosis, allowing *H. ducreyi* to reside extracellularly. When phagocytes cannot engulf bacteria, they secrete granule contents, including antimicrobial peptides (APs) such as cathelicidin and defensins, to kill the pathogens extracellularly. APs bind and destabilise cell membranes to lyse bacteria. Our laboratory is studying two transporter systems that protect *H. ducreyi* from human APs, including cathelicidin LL37 and beta-defensins. To prevent lethal interactions between LL37 and the inner membrane, *H. ducreyi* utilises the Sap (sensitive to antimicrobial peptides) transporter, which takes up periplasmic LL37 for cytoplasmic degradation. By mutating structural components of the Sap transporter, we have found a direct correlation between the effectiveness of Sap-mediated LL37 resistance *in vitro* and the contribution of the transporter to virulence in humans. Further, we found that *H. ducreyi*
OppA (oligopeptide binding protein A), the periplasmic component of another uptake transporter, appears to cooperate with the Sap transporter for LL37 uptake. For beta-defensin resistance, H. ducreyi utilises the MTR efflux transporter. MTR is a member of the resistance-nodulation-division family of multidrug resistance transporters that pump hydrophobic agents from the periplasm and cytoplasm out of the cell. Our data demonstrate that the H. ducreyi MTR transporter confers resistance to both LL37 and beta-defensins. Interestingly, we also found that the MTR transporter affects activation of CpxRA, which globally regulates virulence factors in H. ducreyi. The role of MTR in human virulence is under investigation. Together, these studies highlight the significance of AP resistance mechanisms to pathogen survival in the human host.

S07.4 IDENTIFICATION OF DETERMINANTS TRIGGERING ANTIGENIC VARIATION IN MYCOPLASMA GENITALITUM


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Mycoplasma genitalium (MG) is an emerging sexually transmitted pathogen associated with reproductive tract disease in men and women. Despite the development of a robust antibody response, MG can persist for months to years, potentially increasing the risk for sexual transmission and serious upper reproductive tract infection in women. The molecular basis of MG pathogenesis is poorly understood, in part due to its fastidious nature, extremely small genome lacking known virulence genes, and the limited genetic tools available for molecular investigations. Nevertheless, previous studies have linked MG virulence to its unique terminal organelle, a complex structure that mediates adherence, motility, and cell division. The terminal organelle is composed of a complex array of unique proteins, including MgpB and MgpC which serve as major adhesins and are required for terminal organelle biogenesis. Remarkably, these two surface-exposed proteins also undergo phase and antigenic variation through a unique process of segmental recombination between discreet variable regions within mgpB and mgpC and multiple homologous archived sequences, termed MgPa repeats (MgpPar). Our goal is to identify the molecular factors required to promote this genetic diversity, a mechanism which likely contributes to the ability of MG to adapt to different host conditions and maintain persistent infections. Recently, we have shown that RecA is required for mgpB/C gene variation and that this protein is expressed in several isoforms. We have now expanded these studies by showing that these RecA isoforms originate from different translational start sites and that specific recA upstream sequences regulate the expression ratio of these isoforms and mgpB/C-MgPar recombination. Together, these studies suggest the presence of novel regulatory mechanisms that may allow this genetically challenged organism to cause disease, evade the host immune response, and persist in infected individuals.

S07.5 UNDERSTANDING DISSEMINATION OF TREPONEMA PALLIDUM WITHIN THE HOST - IS THERE HOPE FOR A SYPHILIS VACCINE?


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mata pallidum is a highly invasive spirochete that disseminates to organ sites distal to the site of primary infection and is able to cross both the blood-brain and placental barriers during the course of infection. The corkscrew motility used by T. pallidum is able to contribute to its invasive nature. However, this signature motility is shared with other spirochetes and thus the factors responsible for the widespread dissemination capability that is unique to T. pallidum remain unknown. We have identified the treponemal-specific, surface-localised protein pallilysin as a dual functioning adhesin/metalloprotease that exhibits specific attachment to, and degradation of, multiple extracellular matrix components. Pallilysin is produced as an inactive proprotease that can be activated via either autocatalytic cleavage or host-originating thrombin cleavage. Purified recombinant pallilysin, as well as a non-invasive model treponeme heterologously expressing pallilysin on its surface, exhibit specific degradation of fibrin clots. Pallilysin immunisation alters the course of T. pallidum dissemination following challenge within the rabbit model of syphilis infection, with immunised rabbits exhibiting a reduced bacterial burden within organs distal to the site of challenge compared to unimmunized control rabbits. Further, rabbit infectivity tests (RIT) showed that rabbits receiving lymph nodes from challenged, immunized rabbits exhibited a reduced bacterial burden compared to non-immunized rabbits. RIT of pallilysin-expressing T. pallidum in a T. pallidum-specific metalloprotease that (1) exploits the host coagulation cascade to facilitate protease activation, (2) plays a central role in treponemal dissemination and (3) shows promise as a novel syphilis vaccine candidate.