plans for continued engagement around dissemination of results. Accurate measurement of sensitive or stigmatized behavior presents a challenge to the validity of nearly all STI research. Maximizing the acceptability, feasibility and validity of network studies will lead to more accurate estimates of the drivers of STI transmission and will provide more valid insights about the opportunities for interventions to prevent and control STI outbreaks.

Disclosure No significant relationships.

S14.4 THE ROLE OF SEXUAL NETWORKS IN THE GLOBAL SPREAD OF ANTIMICROBIAL-RESISTANCE ENTERIC INFECTIONS

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In high-income countries, enteric pathogens have typically affected returning travellers or children, or spread from contaminated point sources. However, sexually transmitted enteric infections (STEI) are now well documented, particularly among men who have sex with men (MSM). The phenomenon was recognised in patients with HIV/AIDS in the early 1970's as arising from direct/indirect ingestion of faecal matter via sexual contact. Bacteria (*Shigella* spp., *Salmonella* spp., *Campylobacter* spp., *Escherichia coli*), viruses (Hepatitis A), and protozoa (*Giardia* spp., *Cryptosporidium* spp., *Entamoeba histolytica*) have all been implicated. Following a nadir during the 90's and early-2000's, new epidemics of enteric pathogens affecting MSM have been reported internationally. Facilitated by global travel, these have familiar characteristics (oral-anal behaviours and HIV-associations), but also important new features (associations with 'chemsex', social media use, PrEP, syndemic STIs, and transmission in the absence of HIV). For some STEIs, notably Shigellosis, a worrying new feature is resistance to multiple antimicrobial classes found in most isolates from MSM. This may be collateral to frequent antibiotic exposure acting as a selection pressure among the sexual networks affected. Understanding of these sexual networks has been informed by a wide range of approaches, from qualitative patient interviews, through scrutiny of national surveillance trends (male-to-female ratios, gender excess, geographical distributions) and electronic data linkage, to population-level pathogen phylogenomics. These are challenging infections to study, not least due to being sometimes asymptomatic, as well as patient and clinician unawareness about sexual transmission leading to missed or mis-diagnoses, the hidden nature of the affected population, and stigma. Moreover, many questions remain about the prevalence, transmission, duration of infection, clinical implications, drivers of antimicrobial resistance, and effective public health and clinical interventions. Embracing transdisciplinary approaches to understand the sexual networks affected and the behavioural and pathogen-associated drivers seems essential if we are to move from observation to control.

Disclosure No significant relationships.

S15 – NEW APPROACHES TO STI DIAGNOSIS AND PREVENTION

Wednesday, July 17, 2019

10:45 AM – 12:15 PM

S15.1 FOUR *TREPONEMA PALLIDUM* PROTEINS DETECTED IN URINE FROM SYPHILIS-INFECTED INDIVIDUALS USING MASS SPECTROMETRY

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Background The direct detection of *Treponema pallidum* peptides in bodily fluids could facilitate the early diagnosis of initial-, repeat-, congenital- and neuro-syphilis.

Methods To this end, we prospectively recruited 54 individuals with a new diagnosis of syphilis and 6 controls. Their urine specimens were pooled according to disease stage and assessed using complementary mass spectrometry techniques (MALDI-TOF-TOFMS/MS, LC/ESI-IM-Q-TOF/HDMS^E) to uncover potential syphilis biomarkers.

Results In total, 26 unique peptides were uncovered corresponding to four unique *T. pallidum* proteins (Tp0486, Tp0742, Tp0804 and Tp0369) that have no, or minimal, genetic sequence similarity to other known proteins, including prokaryotes and human proteins.

Conclusion This is the first study reporting direct detection of *T. pallidum* proteins in human biofluid samples using MS-based proteomics methods. These could be promising diagnostic test targets.

Disclosure No significant relationships.

S15.2 CRISPR DIAGNOSTICS: EXPANDING THE NUCLEIC ACID DETECTION TOOLBOX BY HARNESSING MICROBIAL DIVERSITY

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10.1136/sextrans-2019-sti.70

Versatile, rapid, and portable sensing of nucleic acids is vital for applications in human health. The RNA-targeting CRISPR-associated enzyme Cas13 has recently been adapted for such purpose. This detection platform, termed SHERLOCK (Specific High Sensitivity Enzymatic Reporter UNLOCKing), can discriminate between inputs that differ by a single nucleotide at very low concentrations and can be lyophilized for portable deployment. However, this technology has several limitations, including the lack of quantitation and reliance on fluorescent detection equipment for readout. Here, we extend the SHERLOCK technology to address these limitations and further develop the utility of this platform. Many applications require detection of more than one target molecule in a single reaction, and we therefore sought to create a multiplex platform that relies on unique cleavage preferences of Cas enzymes. To identify possible candidate enzymes compatible with multiplexing, we biochemically characterized three members of the

CRISPR-Cas13a family and fourteen members of the CRISPR-Cas13b family.

We next focused on tuning the output of the SHERLOCK signal to make it more quantitative, sensitive, and robust to broaden the utility of the technology, testing optimizations of the amplification to enable quantitative and able to accept larger input volumes for increased sensitivity.

Another goal of SHERLOCKv2 was engineering a visual readout of activity requiring no additional instrumentation. We designed a lateral-flow readout that was based on the destruction of a FAM-biotin reporter, allowing for detection on commercial lateral flow strips. Abundant reporter accumulates anti-FAM antibody-gold nanoparticle conjugates at the first line on the strip, preventing binding of the antibody-gold conjugates to protein A on the second line; cleavage of reporter would reduce accumulation at the first line and result in signal on the second line. We profiled Cas13 cleavage preferences on homopolymer reporters, and found that most orthologs preferred either uridine, a combination of bases, or adenine. We refined the cleavage sequence preferences by evaluating collateral activity across di-nucleotide motifs, finding a large diversity of di-nucleotide cleavage motif preferences.). From these di-nucleotide cleavage screens, we found that the activities of LwaCas13a, CcaCas13b, LbaCas13a and PsmCas13b could all be independently measured with the four di-nucleotide reporters AU, UC, AC, and GA, respectively. Additionally, using a random in vitro RNA library motif cleavage screen, we identified numerous RNA 6-mers that allowed for further orthogonality between Cas13 enzymes. When combined with RPA, we detected two DNA targets (the *P. aeruginosa* acyl-transferase gene and the *S. aureus* thermonuclease gene) down to the attomolar range. These advances in in-sample multiplexing via orthogonal base preferences allow for many targets to be detected at scale and for cheaper cost.

We tested a range of primer concentrations and found that 240nM exhibited the greatest correlation between signal and input, and quantification was sustainable across a large range of sample concentrations down to the attomolar range. By scaling up the pre-amplification RPA step, we found that Lwa-Cas13a could give detection signal for 200, 80, and 8zM input samples and allow for single-molecule volume inputs of 250µL and 540µL.

We tested lateral flow with Cas13 for instrument-free detection of ZIKV or DENV ssRNA, and found that detection was possible in under 90 minutes with sensitivities down to the 2 aM condition. Moreover, we found that we could do rapid genomic DNA extraction from human saliva (<10min) and input this directly into SHERLOCK without purification for rapid genotyping in under 23 minutes by fluorescence and 2 hours by lateral flow. The additional refinements presented here for Cas13-based detection allow for quantitative, visual, more sensitive, and multiplexed readouts, enabling additional applications for nucleic acid detection, especially in settings where portable and instrument-free analysis are necessary. SHERLOCKv2 can be used for multiplexed genotyping to inform pharmacogenomic therapeutic development and application, detecting genetically modified organisms in the field, or determining the presence of co-occurring pathogens. Moreover, the rapid, isothermal readout of SHERLOCKv2, enabled by lateral flow and Csm6, provides an opportunity for detection in settings where power or portable readers are unavailable, even for rare species like circulating DNA. In the future, it might be possible to make solution-based colorimetric readouts and multiplex lateral flow assays containing multiple test

strips for different targets. Improved CRISPR-dx nucleic acid tests make it easier to detect the presence of nucleic acids in a range of applications across biotechnology and health and are now field-ready for rapid and portable deployment.

Disclosure No significant relationships.

S15.3

REDUCING THE GLOBAL BURDEN OF INFECTIOUS DISEASES THROUGH PRECISION INFECTION MANAGEMENT (PIM)

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10.1136/sextrans-2019-sti.71

The global rise in the prevalence of antibiotic resistant bacteria is a problem so serious that it threatens all modern medicine. One major factor contributing to the problem is the limited information available to clinicians regarding the risks posed by individual strains of pathogens. Titrating clinical interventions according to these risks would enable the more judicious use of antibiotics, would reduce the time necessary to control serious infections, and would minimize antibiotic-associated treatment complications. We are developing a new Precision Infection Management (PIM) strategy for achieving these objectives. Our approach links the complete proteomic, metabolomic, and genomic sequences of 50,000 microbial isolates to birth-to-death medical records and integrates microbial risk-factors into a hand-held smartphone app for clinicians. 50,000 isolates spanning two decades of clinical diagnostic work in southern Alberta are being cultured in 96-well format and DNA, protein, and metabolites are being extracted using an automated workflow. Full genome sequences are being collected by the Broad Institute, quantitative proteomics analyses are being acquired using a TMT11plex workflow, and metabolomics data are being acquired using our metabolic preference assay. De-identified patient data have been collected from Alberta Health Services and these records are being linked to each clinical isolate to enable microbe/clinical outcome association studies. All data are being stored on a new secure data hub, ResistanceDB, which supports complex multi-omics data mining, machine learning, and microbial risk assignment. We are currently establishing the microbiology, analytical, and informatics pipelines necessary to support the comprehensive analyses of 50,000 microbial isolates. We have recently launched our pilot ResistanceDB hub, and have collected genomics, proteomics, and metabolomics data on a pilot set of 1,000 clinically-linked microbial isolates. We have established automated data capture and archival systems to collect data from each of the 'omics pipelines and have invested significant time in evaluating practical methods for analyzing thousands of microbial samples. We are currently using our computational resources to survey the current state of microbial populations and document their evolution over the last decade. Our preliminary analyses show a dramatic rise in the prevalence of resistant organisms over this time. We have developed several new visualization tools for projecting microbial population-level changes over time and we are currently working to understand how these microbial dynamics have affected patient outcome. Our quantitative proteomics methods are currently capturing over 1,000 microbial proteins, including most of the known virulence factors and our metabolomics assay is capturing more than 250 metabolites from a transect of central carbon metabolism. We are currently transitioning