resistance in gonococcus remain to be identified. These findings have implications for the development of molecular diagnostics and for understanding the mechanistic basis of cephalosporin resistance.

Disclosure No significant relationships.

004.2 PHYLOGENOMIC ANALYSIS REVEALS PERSISTENCE OF *NEISSERIA GONORRHOEA* CLADES WITH REDUCED SUSCEPTIBILITY TO CEPHALOSPORINS

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Background The emergence of *Neisseria gonorrhoeae* strains with reduced susceptibility to the extended-spectrum cephalosporins (ESCs) cefixime and ceftriaxone has raised concerns over a future of untreatable gonorrhea. In 2015, a treatment regimen consisting of ceftriaxone and azithromycin were recommended to assist in delaying the further selection of resistant strains, including those with elevated cephalosporin minimum inhibitory concentrations (MICs) (ESC^{em}). Recently, we conducted a retrospective study to assess the genetic relatedness of isolates in the United States from 2006–2017, and describe the emergence and dissemination of ESC^{em} lineages over time.

Methods We examined the genomes of 637 *N. gonorrhoeae* isolates collected through the Gonococcal Isolate Surveillance Project (GISP), including 317 isolates with elevated cefixime MICs (CFX^{em}; MIC $\geq$ 0.25 μ g/mL), 96 isolates with elevated ceftriaxone MICs (CRO^{em}; MIC $\geq$ 0.125 μ g/mL), and 224 accompanying cephalosporin-susceptible isolates matched by region and collection date. We generated a core-genome SNP phylogeny, and examined the distribution of antimicrobial determinants known to be associated with cephalosporin resistance.

Results The majority of gonococcal isolates with elevated MICs to either cephalosporin or both (n = 337) possessed the mosaic *penA* XXXIV allele (cefixime: 87%, 276/317, P < 0.001; ceftriaxone: 61%, 59/96, P < 0.001). SNP analysis revealed that there were two major clades containing ESC^{em} isolates that appear to have arisen independently. Notably, Clade A (MLST ST1580; 2009–2011) contained 30, primarily CFX^{em} isolates, while the largest clade in the study (Clade B, MLST ST1901; 2006–2017) contained 224 ESC^{em} isolates. A third clade (Clade C, MLST ST1600; 2014–2017) contained 6 ESC^{em} isolates with a novel *penA* LXXI.

Conclusion The prevalence of mosaic *penA* XXXIV alleles was highest among gonococcal isolates with reduced susceptibility to ESCs over a 12-year period. Genomic methods can aid in efforts to monitor antimicrobial resistance markers of concern and ultimately slow the emergence and spread of circulating ESC^{em} strains.

Disclosure No significant relationships.

004.3 PRIORITIZING NOVEL DRUG TARGETS BASED ON GENOMICS AND PROTEOMICS APPROACH IN *NEISSERIA GONORRHOEA*

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Background *N. gonorrhoeae*, a major causative agent of STI, has acquired resistance to most of the commonly used drugs. Hence there is an urgent need to look for novel drug targets and new drugs to combat this disease. Although a large number of prokaryotic genomes have been sequenced, only a small percentage is completely annotated. Structure-function annotation of hypothetical proteins (HPs) can be exploited to identify novel drug targets.

Methods Various web tools were used under stringent condition to predict the function of different HPs and to identify novel drug targets based on their cellular localization, domains, motifs and by using STRING (<http://string-db.org/>) to identify their potential interactions with other proteins. To predict drug targets, essential genes were identified using DEG database and BLASTed against proteome of *Homo sapiens* to exclude homologous proteins.

Results Using bioinformatics tools, 206 HPs were analyzed for their subcellular localization. 140 HPs were predicted as cytoplasmic proteins and 10 as extracellular. Nine proteins in the outer membrane, seven as inner membrane whereas three in the periplasmic area. Using available tools, function to 32 HPs was assigned with high confidence; 11 proteins showed signal peptide whereas 21 proteins showed transmembrane helices. We predicted 19 proteins as putative enzymes crucial for the survival of *Neisseria*. These 19HPs were sub-classified as DNA modification system (5), transferases (3), hydrolase (3), FAD/NAD binding enzymes (5) and others (3). Other 12 HPs were characterized as transporter proteins including autotransporter (8), TonB dependent receptor (2), members of TAT pathway (1) and branched chain amino acid transporter (1). Two transporter proteins were predicted as adhesins and further classified as drug targets whereas five were predicted as vaccine candidates. We also predict five cytoplasmic and 4HPs localized in outer membrane as potential drug targets.

Conclusion These results are expected to be helpful in the development of improved therapeutics.

Disclosure No significant relationships.

004.4 MYCOPLASMA GENITALIUM *parC* AND *gyrA* MUTATIONS ASSOCIATED WITH MOXIFLOXACIN AND SITAFLOXACIN TREATMENT FAILURE

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Background There has been a rapid increase in the resistance of *Mycoplasma genitalium* to first line (azithromycin) and second line (fluoroquinolone) therapy, particularly in the Asia-Pacific

region. While mutations conferring resistance to azithromycin are well established, this is not the case for fluoroquinolones. We aimed to define mutations associated with fluoroquinolone failure to inform next generation resistance assays.

Methods Samples from patients undergoing resistance-guided therapy with either moxifloxacin (Apr-2017–Jun-2018, 202 cases: 21 moxifloxacin failures) or sitafloxacin (Jun-2016–May-2017, 125 cases: 12 sitafloxacin failures) were sequenced for key regions of *parC* and *gyrA* genes. Chi-square or Fisher's exact tests were used to examine prevalence of each mutation and treatment outcome.

Results In an interim analysis the most common *parC* mutations were G248T (amino acid change S83I; 16%), G259A (D87N; 4%), G248A (S83N; 1%) and mutations effecting S83R (1%). G248T (S83I) mutation was more common among patients that failed moxifloxacin [15/21 failures (71%) vs 11/181 cures (6%), $p < 0.001$] and sitafloxacin [6/12 failures (50%) vs 19/113 cures (17%), $p = 0.0063$]. Notably, sitafloxacin cured a higher proportion of infections carrying the S83I mutation than moxifloxacin (76% vs 42%; $p = 0.015$). *ParC* D87N was not associated with failure of moxifloxacin [1/21 failures (5%) vs 11/181 cures (6%)]. The most common *gyrA* mutations were G285A (M95I; 5%) and G295T (D99Y; 1%). An infection with an S83I mutation was more likely to fail treatment when combined with a *gyrA* mutation (M95I or D99N) (4/6 sitafloxacin failures with *parC* S83I also had *gyrA* mutation, compared to 1/16 cures; $p = 0.0093$), suggesting an additive effect.

Conclusion This study provides compelling evidence that *parC* G248T (S83I) mutations contribute to failure of moxifloxacin and sitafloxacin used for macrolide-resistant *M. genitalium*. These data will inform the development of quinolone resistance assays needed to ensure optimal selection of antimicrobials in *M. genitalium*.

Disclosure No significant relationships.

004.5 POINT-OF-CARE MAGNETOFLUIDIC ASSAY CARTRIDGE FOR *NEISSERIA GONORRHOEAE* DETECTION AND ANTIMICROBIAL RESISTANCE DETERMINATION

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Background The rise of antimicrobial resistant (AMR) *Neisseria gonorrhoeae* (NG) has prompted worldwide concern over the looming possibility of untreatable gonococcal infections. A reduction of antimicrobial use by transitioning from generalized prescriptions to targeted pathogen-specific treatments would aid in treatment efficacy and reduce the risk of AMR NG development. However, actual implementation of such targeted treatments has been limited by the lack of rapid diagnostic tools that can provide antimicrobial susceptibility results at the point-of-care (POC).

Methods To address the need for a rapid NG screening test, we have developed a portable magnetofluidic instrument and corresponding assay cartridge. The assay cartridges use functionalized magnetic beads to couple nucleic acid extraction directly to a PCR-based duplexed nucleic acid amplification test (NAAT). The NAAT targets the *opa* gene for NG identification and the *gyrA* gene for characterization of ciprofloxacin

susceptibility. In order to assess assay performance, we analyzed 27 well characterized NG strains and 29 swabs (20 urethral, 9 penile meatal) previously tested by culture.

Results The instrument has a compact footprint (5'x5.3'x3.3') and runs on a 5V, 2A power supply that can be provided by a small portable battery pack. Detection of NG and genotypic characterization of ciprofloxacin susceptibility was completed in <40 minutes. The cartridge-based assay correctly identified 100% (27/27) of the NG isolates as well as 100% (10/10) of the ciprofloxacin-resistant NG strains. All urethral and penile swabs were correctly identified as well (15/15 positive, 14/14 negative).

Conclusion Magnetofluidic assay cartridges allow automation of NAAT-based testing for NG and assessment of antimicrobial susceptibility. The portability, low power consumption, and ease-of-use of our platform has potential for enabling rapid diagnostics at the POC and in low-resource settings to guide targeted use of antimicrobials. Further studies with clinical samples are warranted.

Disclosure No significant relationships.

004.6 PREDICTION OF AVAILABLE DRUG TARGETS OF *NEISSERIA GONORRHOEAE* BASED ON CODON USAGE PARAMETER

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Background *Neisseria gonorrhoeae* is a gram negative diplococcus bacterium and the causative agent of the sexually transmitted disease Gonorrhea. It has been recently given the status of 'superbug' by World Health Organization because of the increasing antibiotic resistance and unavailability of a viable vaccine candidate targeted against this bacterium. Over the recent years, there have been increasing reports about the use of subtractive genomics to identify potential drug and vaccine targets.

Methods Hence, present study utilizes the knowledge of Codon biasing, a tool to identify the essential genes in *N. gonorrhoeae* that could be novel therapeutic targets for drug or vaccine development. Through the screening of a total of 2350 genes, we could shortlist 29 'essential' genes from the complete gene set. This selection process was done through calculating CAI scores for individual genes. Through the data-mining of BLAST2GO and InterProScan databases, we could predict the function of these 29 genes.

Results All the selected 29 genes were involved in important cellular functions like DNA replication, energy synthesis and metabolites production. This study also shortlists the essential genes of *N. gonorrhoeae* that could be used to target *Neisseria*. We identified a molecule/drug which can be used as a target against essential protein DapD (succinyltransferase).

Conclusion To conclude, through subtractive genomics, we could identify 29 genes that seem to be essential for the survival of the bacteria *Neisseria gonorrhoeae*. Identification of these genes can be helpful in understanding the pathogenesis of the bacteria as well. Moreover some of these genes are excellent drug targets as these are essential for the growth of bacteria. The selected molecule ZINC06311339 promises hope