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