1440. The Genetic Basis for a Neisseria gonorrhoeae Clinical Isolate That Contains mtrR$_{-79}$ Mutation But Is Highly Susceptible to Antibiotics Effluxed by the Mtr Pump System

Jianzhong Huang, PhD[1]; Karen Ingraham, MS[1]; [1]GlaxoSmithKline, Collegeville, Pennsylvania

Session: P-66. Resistance Mechanisms

Background. *Neisseria gonorrhoeae* (NG) possesses multiple drug efflux systems that play an important role in evading antibiotics in the treatment for gonorrhea and in helping this pathogen to evade innate antimicrobial defenses during infection. The *mtrR*$_{-79}$ and *mtr*$_{120}$ mutations in the promoter region between *mtrR* and *mtrCDE* are common mutations contributing to overexpression of the MtrCDE efflux pump resulting in increased efflux to multiple antibiotics including macrolides, β-lactams and tetracycline. However, we found a NG clinical isolate that contains the *mtrR*$_{-79}$ mutation but is highly susceptible to antibiotics effluxed by the MtrCDE pump system.

Methods. PCR amplification, DNA sequencing and natural transformation were used to investigate the genetic basis responsible for the increased susceptibility by this isolate.

Results. We amplified by PCR the individual genes of *mtrCDE*, respectively, from this susceptible isolate as well as a NG isolate that contains the *mtrR*$_{-79}$ mutation with increased efflux; there was no difference in the size of PCR products between the susceptible isolate and the isolate with increased efflux, indicating there was no large deletion/insertion in these genes. DNA sequence analysis of *mtrCDE* revealed the susceptible isolate also contained a loss-of-function mutation ΔGC from a 6 GC repeat GCGCGCGCGCGC in *mtrC* resulting in MtrC A117 frameshift predicted to produce a truncated MtrC protein that results in a low efflux phenotype. Natural transformation of the susceptible isolate with a wild type *mtrC* and selection with ciprofloxacin generated transformants that corrected the ΔGC mutation and restored the increased efflux phenotype.

Conclusion. Our results indicate that genotyping of *mtrR* and the promoter region between *mtrR* and *mtrCDE* is insufficient to predict increased efflux phenotype and provide direct evidence that NG isolates with elevated efflux is able to genetically revert to low efflux via loss-of-function mutations in the coding region of the efflux pump genes.

Disclosures. Jianzhong Huang, PhD, GlaxoSmithKline (Employee, Shareholder) Karen Ingraham, MS, GlaxoSmithKline (Employee, Shareholder)

1441. Using Carbapenem Resistance Levels to Discriminate Between Carbapenemase Producing and Non-Carbapenemase Producing Carbapenem Resistant Enterobacteriaceae

William J. Koehne, III, MPH[1]; Tiina Peritz, MS, BSN, RN, CIC[2]; Kristin Privette, MPH[3]; Jane Gould, MD[3]; [1]Philadelphia Department of Public Health, Philadelphia, PA, USA; Council of State and Territorial Epidemiologists, Atlanta, GA, USA, Philadelphia, Pennsylvania; [2]Philadelphia Department of Public Health, Philadelphia, Pennsylvania; [3]1Philadelphia Department of Public Health, Philadelphia, PA, USA, Philadelphia, Pennsylvania

Session: P-66. Resistance Mechanisms

Background. Carbapenem-resistant *Enterobacteriaceae* (CRE) are a growing threat globally. Many CRE organisms carry plasmids that produce a carbapenemase enzyme (CP-CRE). Early detection of CP-CRE and aggressive infection prevention and control (IPC) measures are necessary to reduce transmission of resistant organisms and their plasmids. Many hospital laboratories do not test CRE for carbapenemase production. In Apr '18, the Philadelphia Department for Public Health (PDPH) established mandatory CRE reporting including isolate submission for mechanism testing at public health laboratories.

Methods. We analyzed trends of carbapenem resistance in CP and non-CP-CRE. We calculated sensitivity (Sen), specificity (Spe), positive and negative predictive values (PPV, NPV) at each level of carbapenem resistance to develop a predictive model with goal of effectively discriminating CP and non-CP CRE. ROC curves were plotted.

Results. From June,'18-Feb,'20, 351 CRE had genetic mechanism testing. 192 (54.7%) were *Klebsiella pneumoniae*, 53 (15.1%) were *Enterobacter cloacae,* 52 (14.8%) were *E. coli*, and the remaining 54 (15.4%) other *Enterobacteriaceae.*186 (53.0%) had a recorded minimum inhibitory concentration (MIC) for ertapenem, 191 (54.4%) for meropenem, 116 (33.0%) for imipenem, and 9 (2.6%) for doripenem. Doripenem was not further analyzed. The odds of being CP-CRE increased with increasing MIC. One standard dilution increase in MIC was associated with the following odds ratios (OR) of being CP-CRE: ertapenem OR 1.43 (95% CI: 1.11–1.83), imipenem OR 2.52 (95% CI: 1.7–3.793), meropenem, OR 2.20 (95% CI: 1.72–2.81). For each carbapenem, we calculated Sen, Spe, PPV, and NPV values for five MIC cut points; 0.5, 1, 2, 4, and 8 ug/ml, non-CP CRE defined as ≤ MIC cut point, CP-CRE defined as > cut point.

Figure 1. ROC Curves

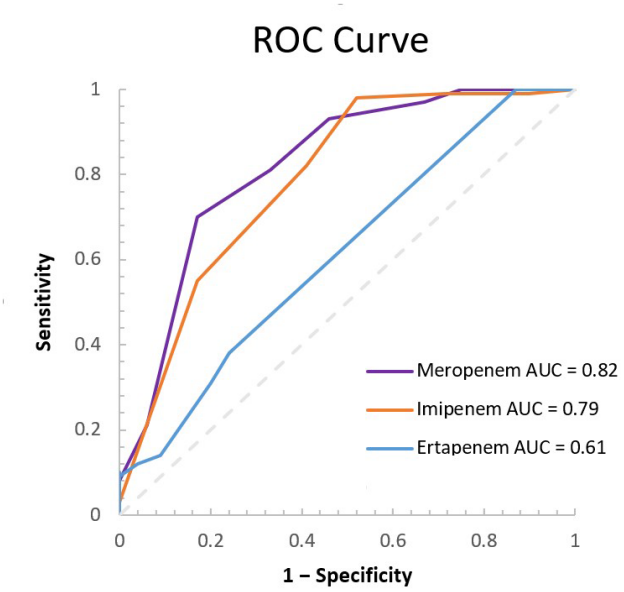

Table 1. Sensitivity, Specificity, PPV, NPV of MIC Cut Points

	Meropenem Resistance to identify CP-CRE				
	0.5 ug/ml	1 ug/ml	2 ug/ml	4 ug/ml	8 ug/ml
Sensitivity (95% CI)	97% (94-100)	94% (89-89)	81% (75-88)	70% (62-77)	21% (14-28)
Specificity (95% CI)	33% (20-45)	54% (40-67)	67% (55-80)	83% (72-93)	94% (89-100)
PPV (95% CI)	79% (73-85)	84% (79-90)	87% (81-93)	92% (86-97)	91% (81-100)
NPV (95% CI)	81% (64-98)	76% (62-90)	57% (45-70)	51% (40-61)	31% (34-38)
	Imipenem Resistance to identify CP-CRE				
	0.5 ug/ml	1 ug/ml	2 ug/ml	4 ug/ml	8 ug/ml
Sensitivity (95% CI)	99% (97-100)	98% (95-100)	82% (73-90)	55% (45-66)	3% (0-7)
Specificity (95% CI)	28% (11-44)	48% (30-66)	59% (41-77)	83% (69-97)	100% (100-100)
PPV (95% CI)	80% (73-88)	**85% (78-92)**	86% (80-93)	91% (83-98)	100% (100-100)
NPV (95% CI)	89% (68-100)	**88% (71-100)**	52% (34-69)	38% (26-50)	26% (18-34)
	Ertapenem Resistance to identify CP-CRE				
	0.5 ug/ml	1 ug/ml	2 ug/ml	4 ug/ml	8 ug/ml
Sensitivity (95% CI)	100% (100-100)	38% (30-46)	31% (24-40)	14% (8-20)	12% (7-18)
Specificity (95% CI)	13% (4-22)	76% (65-87)	80% (69-90)	91% (83-98)	96% (91-100)
PPV (95% CI)	74% (67-80)	79% (69-89)	79% (68-90)	79% (63-95)	89% (74-100)
NPV (95% CI)	100% (100-100)	33% (25-42)	32% (24-40)	30% (23-37)	31% (24-38)

Conclusion: There were no MIC cut points that performed well in both Sen and Spe, however, for the purposes of IPC, correctly classifying CP CRE (Sen) is more important than correctly classifying non-CP CRE (Spe). MIC cut points that performed best were imipenem MIC of 1 ug/ml and meropenem MIC of 1 ug/ml, with Sen 98%, 94% respectively, PPV 85%, 84% respectively and NPV 88%, 76% respectively. When further testing is not available, MIC cut points may be used to infer CP production.

Disclosures. **All Authors**: No reported disclosures

1442. Acquisition and Transferability Mechanisms of Mercury Resistance Genes in Latin-American Staphylococcus aureus Strains

Oscar Ortega-Recalde, MD, MSc, PhD[1]; Aura M. Echeverri, n/a[1]; Rafael Rios, MSc[1]; Lina Carvajal, BCh[1]; Angie K. Hernandez, BSc[1]; Catalina Espitia-Acero, n/a[2]; Sebastian Solano-Gutierrez, n/a[3]; William C. Shropshire, MPH[4]; Cesar A. Arias, MD, MSc, PhD, FIDSA[5]; Lorena Diaz, PhD[6]; Sandra Rincon, PhD[2]; Jinnethe Reyes, MSc, PhD[6]; [1]Universidad El Bosque, Bogota, Distrito Capital de Bogota, Colombia; [2]Universidad el Bosque, Bogota, Distrito Capital de Bogota, Colombia; [3]CIB, Bogota, Distrito Capital de Bogota, Colombia; [4]UTHealth School of Public Health, Houston, TX; [5]CARMiG, UTHealth and Center for Infectious Diseases, UTHealth School of Public Health, HOU, TX; Molecular Genetics and Antimicrobial Resistance Unit and International Center for Microbial Genomics, Universidad El Bosque, BOG, COL, Houston, Texas; [6]Molecular Genetics and Antimicrobial Resistance Unit and International Center for Microbial Genomics, Universidad El Bosque, Bogota, Colombia, Bogota, Distrito Capital de Bogota, Colombia

Session: P-66. Resistance Mechanisms

Background. Latin-American (LA) countries are among the largest mercury (Hg) polluters in the world. Fittingly, a significant high frequency (>50%) of Hg resistance genes (MRG) has been observed in LA MRSA genomes, including USA300-LV clone, which contains the genomic element COMER, encoding for copper and Hg resistance genes adjacent to SCC*mec*IVc/E. Co-selection of MRG and antibiotic resistance genes