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Diverse Role of bla_{CTX-M} and Porins in Mediating Ertapenem Resistance Among Carbapenem Resistant Enterobacterales

Cody Black¹, Cody A. Black^{2,3}, Raymond Benavides^{2,3}, Sarah M. Bandy^{2,3}, Steven S. Dallas^{3,5}, Gerard Gawrys^{2,3,5}, Wonhee So⁶, Alvaro G. Moreira^{3,7}, Samantha Aguilar^{2,3,5}, Kevin Quidilla^{2,3}, Dan F. Smelter^{2,3}, Kelly R. Reveles^{2,3}, Christopher R. Frej^{2,3,5}, Jim M. Koeller^{2,3} and Grace C. Lee^{2,3,7}

¹The University of Texas Health Science Center at San Antonio;

²College of Pharmacy, The University of Texas at Austin, Austin, USA;

³Joe R. and Teresa Lozano Long School of Medicine, The University of Texas Health at San Antonio, San Antonio, USA;

⁴Department of Pathology and Laboratory Medicine, The University of Texas Health at San Antonio, San Antonio, USA;

⁵University Health System, San Antonio, USA; ⁶College of Pharmacy, Western University of Health Sciences, Pomona, USA and ⁷Veterans Administration Research Center for AIDS and HIV-1 Infection and Center for Personalized Medicine, South Texas Veterans Health Care System, San Antonio, USA

OBJECTIVES/GOALS: In this study, we aim to report the role of porins and bla_{CTX-M} β-lactamases among *Escherichia coli* and *Klebsiella pneumoniae*, focusing on emerging carbapenem resistant Enterobacterales (CRE) subtypes, including non-carbapenemase producing Enterobacterales (NCPE) and ertapenem-resistant but meropenem-susceptible (ErMs) strains. **METHODS/STUDY POPULATION:** Whole genome sequencing was conducted on 76 carbapenem-resistant isolates across 5 hospitals in San Antonio, U.S. Among these, NCP isolates accounted for the majority of CRE (41/76). Identification and antimicrobial susceptibility testing (AST) results were collected from the clinical charts. Repeat speciation was determined through whole genome sequencing (WGS) analysis and repeat AST, performed with microdilution or ETEST[®]. Minimum inhibitory concentrations (MIC) were consistent with Clinical and Laboratory Standards Institute (CLSI M100, ED33). WGS and qPCR were used to characterize the resistome of all clinical CRE subtypes, while western blotting and liquid chromatography with tandem mass spectrometry (LC-MS-MS) were used to determine porin expression and carbapenem hydrolysis, respectively. **RESULTS/ANTICIPATED RESULTS:** bla_{CTX-M} was found to be most prevalent among NCP isolates (p = 0.02). LC-MS/MS analysis of carbapenem hydrolysis revealed that bla_{CTX-M}-mediated carbapenem hydrolysis, indicating the need to reappraise the term, “non-carbapenemase (NCP)”[®] for quantitatively uncharacterized CRE strains harboring bla_{CTX-M}. Susceptibility results showed that 56% of all NCPE isolates had an ErMs phenotype (NCPE vs. CPE, p < 0.001), with *E. coli* driving the phenotype (*E. coli* vs. *K. pneumoniae*, p < 0.001). ErMs strains carrying bla_{CTX-M} had 4-fold more copies of bla_{CTX-M} than ceftriaxone-resistant but ertapenem-susceptible isolates (3.7 v. 0.9, p < 0.001). Immunoblot analysis demonstrated the absence of OmpC expression in NCP-ErMs *E. coli*, with 92% of strains lacking full contig coverage of ompC. **DISCUSSION/SIGNIFICANCE:** Overall, this work provides evidence of a collaborative effort between bla_{CTX-M} and OmpC in NCP strains that confer resistance to ertapenem but not meropenem. Clinically, CRE subtypes are not readily

appreciated, potentially leading to mismanagement of CRE infected patients. A greater focus on optimal treatments for CRE subtypes is needed.

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Associations with gene-transcript expressions in cocaine use disorder reveal genetic predispositions with other substance use and cardio-neurovascular disease.

Chinwe Nwaneshiudu¹, Kiran Girdhar^{1,2}, Rita Z. Goldstein³, Eduardo Butelman⁴, Nelly Alia-Klein³, Panos Roussos^{2,5} and James J. Peters⁶

¹Icahn School of Medicine at Mount Sinai Hospital; ²Center for Disease Neurogenomics, Friedman Brain Institute, Icahn Institute for Data Science and Genomic Technology Department of Psychiatry, Department of Genetics and Genomic Science;

³Department of Psychiatry, Department of Neuroscience, Icahn School of Medicine at Mount Sinai, New York, USA; ⁴Department of Psychiatry, Icahn School of Medicine at Mount Sinai, New York, USA;

⁵Center for Dementia Research, Nathan Kline Institute for Psychiatric Research, Orangeburg, USA, Mental Illness Research Education and Clinical Center (MIRECC) and ⁶VA Medical Center, Bronx, New York, USA, Hess Center for Science and Medicine, New York

¹Icahn School of Medicine at Mount Sinai Hospital; ²Center for Disease Neurogenomics, Friedman Brain Institute, Icahn Institute for Data Science and Genomic Technology Department of Psychiatry, Department of Genetics and Genomic Science;

³Department of Psychiatry, Department of Neuroscience, Icahn School of Medicine at Mount Sinai, New York, USA; ⁴Department of Psychiatry, Icahn School of Medicine at Mount Sinai, New York, USA;

⁵Center for Dementia Research, Nathan Kline Institute for Psychiatric Research, Orangeburg, USA, Mental Illness Research Education and Clinical Center (MIRECC) and ⁶VA Medical Center, Bronx, New York, USA, Hess Center for Science and Medicine, New York

OBJECTIVES/GOALS: Using biomarkers to identify vulnerabilities from cocaine use disorder (CUD) is a focus of recent investigations. Current clinical efforts focus on psychiatric recovery in CUD, however other body systems are missed. Applying blood-based transcriptomics to investigate how clinical conditions relate to CUD can alter current treatment approaches. **METHODS/STUDY POPULATION:** We conducted a comprehensive longitudinal study of 12 individuals (mean 53 yrs.; M/F ratio 9: 3) with CUD abstinent from cocaine. 44 blood samples collected repeatedly every 3 months for 9 months were bulk RNA sequenced. We began with phenotype harmonization grouping individuals with the following metrics; cocaine withdrawal, cue craving, generalized craving, perceived stress, and days of abstinence. We ran differential gene and transcript expression with time across grouping of metrics using the dream software and used the multivariate test to examine their associations. We used the association of gene-transcripts to determine genetic predispositions with clinical traits using the Multi-marker Analysis of GenoMic Annotation assessing their overlap to a reference GWAS database. **RESULTS/ANTICIPATED RESULTS:** Individuals were grouped in 2 clusters based on scores of cue craving, generalized craving, cocaine withdrawal, and 3 clusters based on days of abstinence from cocaine use. Gene-transcript(s) associations revealed genetic predisposition towards certain clinical conditions and substance use traits. Cannabis use disorder showed significant enrichment between the greater vs. lesser abstinent days, and lesser vs. least abstinent days at 9 months. The “drinks per week” trait showed significant gene enrichment between greater vs. lesser abstinent days at 9 months. Coronary artery disease was also enriched with greater vs. least abstinent days at 3 months. Lastly, significant baseline differences in predisposition to small vessel ischemic stroke were seen in responders with high vs low perceived stress. **DISCUSSION/SIGNIFICANCE:** These results from a robust and feasible pipeline suggest genetic predisposition in CUD for other substances and cardio-neurovascular