



**3rd Annual Texas
Medical Center
Antimicrobial
Resistance and
Stewardship
Conference**

January 22-24, 2020

**Abstract
Guide**

The Gulf Coast Consortia (GCC), located in Houston, Texas, is a dynamic, multi-institution collaboration of basic and translational scientists, researchers, clinicians and students in the quantitative biomedical sciences, who benefit from joint training programs, topic-focused research consortia, shared facilities and equipment, and exchange of scientific knowledge. Working together, GCC member institutions provide a cutting-edge collaborative training environment and research infrastructure beyond the capability of any single institution. GCC training programs currently focus on Biomedical Informatics, Computational Cancer Biology, Molecular Biophysics, Neuroengineering, Pharmacological Sciences, Precision Environmental Health Sciences and Antimicrobial Resistance. GCC research consortia gather interested faculty around research foci within the quantitative biomedical sciences, and currently include Antimicrobial Resistance, Nanox, Mental Health, Innovative Drug Discovery and Development, Translational Pain Research, Theoretical and Computational Neuroscience, Single Cell Omics, Regenerative Medicine, Translational Imaging and Cellular and Molecular Biophysics. Current members include Baylor College of Medicine, Rice University, University of Houston, The University of Texas Health Science Center at Houston, The University of Texas Medical Branch at Galveston, The University of Texas M. D. Anderson Cancer Center, and the Institute of Biosciences and Technology of Texas A&M Health Science Center.

GCC for Antimicrobial Resistance Executive Steering Committee

Cesar Arias, UTHealth, Chair

Ashok Chopra, UTMB

Kevin Garey, UH

Magnus Hook, TAMHSC IBT

Julian Hurdle, TAMHSC IBT

Tim Palzkill, BCM

Trish Perl, UTSW

George Phillips, Rice U.

Lynn Zechiedrich, BCM, Co-Chair

Adriana Rosato, HMRI

Tor Savidge, BCM

**Ed Septimus, Harvard Med.
School & TAMU**

Yousif Shamoo, Rice U.

Samuel Shelburne, MDACC

Suzanne Tomlinson, GCC

Vincent Tam, UH

Center for Antimicrobial Resistance and Microbial Genomics (CARMiG)

MISSION

The Mission of the Center for Antimicrobial Resistance and Microbial Genomics is to develop a comprehensive research and educational program to study the complex factors that contribute to the development of resistance and create an environment where specific actions can be taken to tackle this important public health problem. We seek to develop research in a variety of areas that involve, i) mechanisms of antimicrobial resistance, ii) epidemiology of antibiotic resistance organisms, iii) clinical impact of antibiotic resistance, iv) antibiotic stewardship and iv) the influence of antibiotic resistance in the environment (including in animals for human consumption). Primarily, we seek to develop innovative clinical and therapeutic approaches to deal with multi-drug resistant organisms.

CORE ACTIVITIES

Clinical and antibiotic stewardship cores – understanding the clinical aspects of antibiotic resistance and launching programs on surveillance, antibiotic stewardship, and interventional studies

Basic science – elucidation of the molecular mechanisms of antibiotic resistance and identification of potentially novel targets for drug discovery

Genomics – performing and analyzing bacterial genome sequencing to develop rapid diagnostic tools, evaluate antimicrobial resistance profiles, and study the molecular epidemiology of resistant pathogens

Pharmacology and animal models – development of animal models to study therapeutics and pharmacological aspects of antibiotics

Training and education – supporting the development of young investigators interested in antimicrobial resistance and launching educational training programs for clinicians and scientists at the graduate, postgraduate, and assistant professor level

Clinical trials – provide the ideal location and expertise to lead and conduct robust, large-scale clinical trials.

For additional information, please visit us at

<https://www.carmig.net/>



As the 4th largest city in the United States and home to the largest medical center in the world, The Houston Health Department has made it a priority to address Healthcare Associated Infections (HAI) and Antibiotic Resistant and Stewardship (AR AS) in the Houston area. This involves a multifaceted approach that entails coordination with members of the healthcare community, public health, academia and other stakeholders. Through a CDC grant awarded to the city, the HAI program has been able to strengthen local capacity to perform epidemiological and laboratory work by detecting, tracking and responding to infectious disease threats. With this funding the program has been able to implement the below activities:

- Participation in the CDC's Antibiotic Resistance and Laboratory Network (ARLN) that involves HHD's laboratory collecting, confirming and characterizing carbapenem resistant isolates. In 2018 HHD's laboratory collected and characterized resistance of 412 Carbapenem resistant Enterobacteriaceae (CRE) and Carbapenem resistant Pseudomonas aeruginosa (CRPA) isolates from facilities within Houston and 16 surrounding counties.
- Responding to investigations of multidrug resistant organisms with a focus on containment and preventing transmission.
- Performing Infection Control Assessments (ICARs) to identify strengths and mitigate potential infection control gaps in healthcare facilities. Currently HHD's HAI program is working with facilities on identified needs in the areas of 1) staff training in infection prevention and control 2) education in environmental cleaning, injection safety, and PPE and 3) drug expertise in the core elements of antibiotic stewardship.
- Promotion and implementation of CDC's core elements of Antibiotic Stewardship Programs in healthcare facilities. The goal is to develop activities with facilities that reduce adverse events, prevent antimicrobial resistance and produce better outcomes for patients.
- Continue partnering with CARMIG to host its Annual Antimicrobial Resistance and Stewardship Symposium.
- Improving surveillance to drive public health action.
- Coordinated communications and partnerships that focus on developing AR AS activities that will benefit the Houston community.

**UT Center for Antimicrobial Resistance and Microbial Genomics (CARMiG)
Gulf Coast Consortia Antimicrobial Resistance Consortium**

Special Thanks to Rice University Creative Ventures Fund for their sponsorship of this year's conference.

**3rd Annual Texas Medical Center Antimicrobial Resistance
and Stewardship Conference
BRC Building
January 22-24, 2020**

Day 1 – Wednesday, January 22, 2020

7:00-8:00 *Career Mentoring: Women in Infectious Disease Research (Event Space, Includes light breakfast)*
Natasha Kirienko, PhD, Assistant Professor, Rice University
Barbara Wells Trautner, MD, PhD, Professor and Director, Baylor College of Medicine
Helen Boucher, MD, Professor, Tufts Medical Center

8:00-8:30 Registration and light breakfast

8:30-8:35 Welcome
Cesar Arias, MD, PhD, Professor, University of Texas Health Science Center

8:35-9:00 *Drowning of the Antibiotic Pipeline: How to Save it*
Helen Boucher, MD, Professor, Tufts Medical Center

Session 1

Conveners: William Miller, MD, Assistant Professor, University of Texas Health Science Center
Adriana Rosato, PhD, Associate Professor, Houston Methodist Research Institute

9:00-9:25 *Cell Envelope of Gram-Negative Bacteria: An Antibacterial Target*
Anna Konovalova, PhD, Assistant Professor, University of Texas Health Science Center

9:25-9:50 *Antibiotic Resistance and the Gonococcus: Regulation of Gene Expression*
William Shafer, PhD, Professor, Emory University

9:50-10:15 *Emergence of Antibiotic Resistance in Streptococci*
Anthony Flores, MD, PhD, Associate Professor, University of Texas Health Science Center

10:15-10:45 Break and Vendor Show

Session 2

Conveners: Jourdan Andersson, PhD, Postdoctoral Associate, Baylor College of Medicine
Luis Vega, PhD, Postdoctoral Research Fellow, University of Texas Health Science Center

- 10:45-11:10 *Antivirulence Approaches Against Pseudomonas aeruginosa*
Natasha Kirienko, PhD, Assistant Professor, Rice University
- 11:10-11:35 *Mining Fungal Genomes for Concealed Natural Product Antimicrobials*
Gerald Bills, PhD, Professor, University of Texas Health Science Center
- 11:35-12:00 *Revisiting Therapeutics Against MDR Gram-negative Bacteria*
David Greenberg, MD, Associate Professor, University of Texas Southwestern
- 12:00 Pick up lunches (Event Space)
- 12:30-1:00 Rapid Fire Session (Event Space)
Samuel Aitken, MDACC, *Microbiome and Cumulative Antibiotic use as Predictors of Stenotrophomonas Maltophilia Infection in Patients with Acute Myeloid Leukemia Receiving Remission-induction Chemotherapy*, Poster #1
Amira Bhalodi, Accelerate Diagnostics, Inc., *Improving Outcomes and Antibiotic Stewardship for Patients with Bloodstream Infections (IOAS): A Quasi-Experimental Multicenter Analysis of Time to Optimal Therapy*, Poster #4
Larissa Grigoryan, BCM, *Effectiveness of Antibiotic Stewardship Intervention for Urinary Tract Infections in Primary Care: a Difference in Differences Study*, Poster #10
Jinhee Jo, UH, *A Single-Center Surveillance Study of Cystic Fibrosis Microbiological Culture*, Poster #13
Heer Mehta, RU, *Evolution of Resistance to Doxycycline and Ciprofloxacin in the Category A Bioterrorism Agent, Francisella tularensis*, Poster #18
Christine Pybus, UT Southwestern, *Cefiderocol Retains Anti-Biofilm Activity in Gram-Negative Pathogens*, Poster #24
David Reynoso, UTMB, *A User-Friendly QlikSense® Application To Track & Report Essential Stewardship Metrics*, Poster #25
- 1:00-2:00 Poster session and lunch (Event Space) Poster Numbers 1-32
- Session 3**
- Conveners: Andrew Chou, MD, Assistant Professor, Baylor College of Medicine
Barbara W. Trautner, MD, PhD, Professor, Baylor College of Medicine
- 2:00-2:25 *Non-antibiotic Host-targeted Therapeutics and Antimicrobial Peptides to Combat Multiple Drug Resistant Microbes*
Ashok Chopra, PhD, Professor, University of Texas Medical Branch
- 2:25-2:50 *Antibiotic Resistance in Clostridium difficile Drives the Need for Alternate Therapeutic Strategies*
Julian Hurdle, PhD, Associate Professor, Texas A&M Health Science Center
- 2:50-3:15 *Emergence Resistance Against New β -lactam/ β -lactamase Inhibitors: Epidemiology and Mechanisms*
Ryan Shields, PharmD, Associate Professor, University of Pittsburgh
- 3:15-3:30 Break

Session 4

- Conveners: Truc T. Tran, PharmD, Assistant Professor, University of Texas Health Science Center
Yousif Shamoo, PhD, Professor and Vice-Provost for Research, Rice University
- 3:30-3:55 *Toward Understanding how Positive Supercoiling Drives Fluoroquinolone Efficacy*
Lynn Zechiedrich, PhD, Professor, Baylor College of Medicine
- 3:55-4:20 *Leveraging Regulation and Genetic Bases of Ceftaroline Resistance in MRSA: Role of Carbapenems*
Adriana Rosato, PhD, Associate Professor, Houston Methodist Research Institute
- 4:20-4:45 *Cell Membrane Changes Associated with Daptomycin Resistance*
Brian Werth, PharmD, Associate Professor, University of Washington
- 4:45-5:10 *Microbiome and Worsening Glycemia Among Mexican Americans in Starr County, Texas*
Eric Brown, PhD, Associate Professor, University of Texas Health Science Center
- 5:10-5:25 Selected abstract
Genetic and Phenotypic Signatures Predictive of 'Bicarbonate [NaHCO₃]-Responsiveness' and β-Lactam Sensitization Among Methicillin-Resistant Staphylococcus aureus (MRSA)
Selvi Ersoy, University of California Los Angeles
- 5:25-5:40 Selected abstract
Emergence of Unusual Carbapenemase-producing Carbapenem Resistant Organisms in Houston, Texas
Ifrah Chaudhary, Houston Health Dept.
-

Day 2 - Thursday, January 23, 2020

Translational and Clinical Aspects of Antibiotic Resistance

- 7:00-8:00 *Career Mentoring: Meet the Professors Basic Scientist Track (Event Space, Includes light breakfast)*
Ashok Chopra, PhD, Professor, University of Texas Medical Branch
Lynn Zechiedrich, PhD, Professor, Baylor College of Medicine
Tim Palzkill, PhD, Professor, Baylor College of Medicine

8:00-8:30 Registration and light breakfast

Session 5

- Conveners: William Miller, MD, Assistant Professor, University of Texas Health Science Center
Luis Ostrosky-Zeichner, MD, Professor, University of Texas Health Science Center
- 8:30-8:55 *Catheter Associated Bloodstream Infections and Resistance*
Isaam Raad, MD, Professor, University of Texas MD Anderson Cancer Center

- 8:55-9:20 *Clinical Impact of Antibiotic Resistance in Pediatric Infections*
Sheldon Kaplan, MD, Professor, Texas Children's Hospital
- 9:20-9:45 *New Insights into the Development of Carbapenem Resistance in Non-carbapenemase Producing Enterobacteriaceae*
Sam Shelburne, MD, PhD, Professor, University of Texas MD Anderson Cancer Center
- 9:45-10:15 Vendor Show and Networking
- Session 6**
- Conveners: Norma Perez, DO, Associate Professor, University of Texas Health Science Center
Jennifer Walker, PhD, Assistant Professor, University of Texas Health Science Center
- 10:15-10:40 *The Carbapenem-resistant Enterobacteriaceae Epidemic in the United States*
David van Duin, MD, PhD, Associate Professor of Medicine, University of North Carolina
- 10:40-11:05 *Antibiotic Use and Prevention of Resistance*
Sara Cosgrove, MD, Professor, Johns Hopkins Medicine
- 11:05-12:00 *Keynote: The Interaction Between the Immune System and Antimicrobials*
Victor Nizet, MD, PhD, Professor and Vice-Chair for Basic Research, University of California San Diego
- 12:00 Lunch (pick up lunches and be seated for rapid fire session)
- 12:30-1:00 Rapid Fire Session (Event Space)
Sam Erickson, UTHSCH, *The YxdJK System is a Targeted Stress Response that Mediates Specific Protection Against the Human Antimicrobial Peptide LL-37 in Enterococcus faecalis*, Poster #42
Ravikanthreddy Marreddy, Texas A&M IBT, *Antimicrobial Mode of Action of Ebselen Against Clostridium difficile*, Poster #52
April Nguyen, UTHSCH, *Cardiolipin Synthase Mediates Daptomycin Resistance in Enterococcus faecalis*, Poster #53
Rudo Simeon, Texas A&M, *Engineering Protease-Stable DARPin Inhibitors of Clostridium Difficile Toxin B*, Poster #58
Doris Taylor, BCM, *Use of a DNA-Encoded Chemical Library Approach to Identify Inhibitors For Use of a DNA-Encoded Chemical Library Approach to Identify Inhibitors For*, Poster #61
Jessica Galloway-Pena, MDACC, *Oral and Stool Microbiome Community Coalescence is Driven by Antibiotic Exposure in Acute Leukemia Patients*, Poster #66
- 1:00-2:00 Poster session and Lunch (Event Space) Poster Numbers 33-68
- Session 7**
- Conveners: Cesar Arias, MD, PhD, Professor, University of Texas Health Science Center
- 2:00-3:00 *Challenging Clinical Cases on Antimicrobial Resistance*
Vance Fowler, MD, Professor, Duke University

David van Duin, MD, PhD, Associate Professor, University of North Carolina
Luis Ostrosky-Zeichner MD, Professor, University of Texas Health Science Center

3:00-4:00 *T32 Trainee Symposium: Texas Medical Center Training Program on Antimicrobial Resistance (TP-AMR) and Emory Training Program on Antimicrobial Resistance*

Conveners: Lynn Zechiedrich, PhD, Professor, Baylor College of Medicine
Kevin Garey, PharmD, Professor, University of Houston

3:00-3:15 *Association of Antimicrobial Resistance-encoding Mobile Genetic Elements with Enhanced Bacterial Pathogen Fitness and Transmissibility*
Luis Vega, PhD, Postdoctoral Research Fellow, University of Texas Health Science Center

3:15-3:30 *Utilizing Host Targeted, Immunomodulating Drugs to Combat Clostridioides Difficile Infection*
Jourdan Andersson, PhD, Associate Fellow, Baylor College of Medicine

3:30-3:45 *Aminoglycoside Heteroresistance in Gram-Negative Pathogens*
Edgar Sherman, Graduate Student, Emory University

Session 8 Microbiome session: Sponsored by the Kelsey Research Foundation
Conveners: Herbert Dupont, MD, Professor, University of Texas Health Science Center
Blake Hanson, PhD, Assistant Professor, University of Texas Health Science Center

4:00-4:25 *Microbiome Changes and Clinical Outcomes in Bone Marrow Transplant Patients*
Ying Taur, MD, MPH, Infectious Disease Specialist, Memorial Sloan Kettering Cancer Center

4:25-4:50 *Gut Metabolomics in Graft vs Host Disease*
Andrew Koh, MD, Associate Professor, University of Texas Southwestern

4:50-5:35 *Keynote: Superbugs and The Gut Microbiome*
Cynthia Sears, MD, Professor, Johns Hopkins University

Day 3 – Friday, January 24, 2020

Antibiotic Stewardship

7:00-8:30 Career Mentoring: Meet the Professors, Clinical Scientist Track, MDs and PharmDs
(Event Space, Includes light breakfast)
Edward Septimus, MD, Professor, Harvard Medical School and Texas A&M College of Medicine
Trish Perl-DeLisle, MD, Professor, University of Texas Southwestern
Vincent Tam, PharmD, Professor, University of Houston

8:00-8:30 Registration and light breakfast

Session 9

Convener: Charlene Offiong, PharmD, HAI Coordinator, Houston Health Department

8:30-9:15 *Keynote: Tennessee Experience*

Christopher Evans, PharmD, BCPS, Pharmacist, Healthcare Associated Infections and Antimicrobial Resistance Program, Tennessee Department of Health

9:15-9:45 *Sepsis Quality Measures: Balancing Timely Care, Antibiotic Stewardship, and Reliability*

Chanu Rhee, MD, MPH, Assistant Professor, Harvard Medical School

9:45-10:15 *Diagnostic Testing C. difficile*

Kevin Garey, PharmD, Professor, University of Houston College of Pharmacy

10:15-10:45 Vendor show and networking

Session 10

Conveners: Kristi Kuper, PharmD, Director of Clinical Pharmacy, TabulaRasa Healthcare/DoseMe

10:45-11:15 *Transition of Care*

Christy Su, PharmD, Clinical Pharmacy Specialist, Memorial Hermann Greater Heights

11:15-11:45 *Penicillin Allergy Evaluation as Antibiotic Stewardship*

Kimberly Blumenthal, MD, Assistant Professor, Harvard Medical School/Massachusetts General Hospital

11:45-12:15 *Panel: Clinical Cases*

Ed Septimus, MD, Professor, Harvard Medical School and Texas A&M College of Medicine

Sara Cosgrove, MD, Professor, Johns Hopkins Medicine

Lilian Abbo, MD, Professor, Jackson Health System and University of Miami Miller School of Medicine

12:15-1:00 Panel: *Houston Stewardship Best Practices*

Moderator: Frank Tverdek, PharmD, Clinical Pharmacy Manager, MD Anderson Cancer Center

Mandelin Cooper, PharmD, Director of Clinical Pharmacy, HCA Clinical Services Group

Chase Janak, PharmD, Clinical Specialist, Houston Methodist Hospital

Andrea L. Mora, PharmD, Clinical Associate Professor and Vice Chair, Texas A&M College of Pharmacy

1:00-2:00 Poster viewing and Lunch (Event Space)

Session 11

Conveners: Samuel Aitken, Pharm D, Clinical Pharmacy Specialist, MD Anderson Cancer Center
José Munita, MD, Associate Professor, Clinica Alemana, Universidad del Desarrollo, Chile

- 2:00-2:30 *Organ Transplant Stewardship*
Lilian Abbo, MD, Professor, Jackson Health System and University of Miami Miller School of Medicine
- 2:30-3:00 *CAP Guideline Update*
Daniel Musher, MD, Professor, Baylor College of Medicine
- 3:00-3:30 *Immunization Panel Discussion*
Carol Baker, MD, Professor, University of Texas Health Science Center
Flor M. Munoz-Rivas, MD, Associate Professor, Texas Children's Hospital
Robert Atmar, MD, Professor, Baylor College of Medicine
- 3:30-3:45 Closing Remarks
Cesar Arias, MD, PhD, Professor, University of Texas Health Science Center

Speakers
(in alphabetical order)



Lilian M. Abbo, MD, FIDSA
Professor
Clinical Infectious Diseases
Organ Transplant Stewardship
Panel: *Clinical Cases*

Dr. Lilian Abbo, is the Chief for Infection Prevention and Antimicrobial Stewardship at Jackson Health System and a Professor of Clinical Infectious Diseases at the University of Miami Miller School of Medicine. She oversees three acute care hospitals licensed with 2,240 beds, two long term care facilities and infection prevention for the four Miami Dade County corrections department. She is core faculty of the Miami Transplant Institute and is involved in the management of complex immunocompromised patients with multidrug resistant infections.

Dr. Abbo graduated from the Universidad Central de Venezuela, “Luis Razetti” Medical School followed by a fellowship in Infectious Diseases at Jackson Memorial Hospital/ University of Miami. She has co-authored over 80 peer-reviewed publications, several book chapters, has been an invited speaker in national and international meetings in the fields of antimicrobial stewardship, transplant associated infections and infection prevention.

Dr. Abbo is a Fellow of the Infectious Diseases Society of America (IDSA) and is actively involved in several committees for IDSA and the American Society of Transplantation. Her research is focused on antimicrobial resistance, transplantation, infection prevention and antibiotic stewardship.

Lilian is the past president of Women in Academic Medicine at the University of Miami Miller School of Medicine and currently a Fellow of the 25th Hedwig van Ameringen Executive Leadership in Academic Medicine (ELAM) Program for Women at Drexel University College of Medicine class of 2019-2020.



Jourdan Andersson, PhD
Associate Fellow
TCH Pathology

Utilizing Host Targeted, Immunomodulating Drugs to Combat Clostridioides Difficile Infection

Dr. Jourdan Andersson is a postdoctoral fellow in the laboratory of Dr. Tor Savidge at Baylor College of Medicine in Houston, TX. She is also part of the first cohort of trainees in the Texas Medical Center Training Program in Antimicrobial Resistance (TPAMR). She received her B.S in Biochemistry and Biophysics from Rensselaer Polytechnic Institute in Troy, NY and her PhD in Human Pathophysiology and Translational Medicine from the University of Texas Medical Branch in Galveston, TX. Her research has focused on identifying host-targeted therapeutics to combat antibiotic resistant pathogens, particularly members of the Enterobacteriaceae family and *Clostridioides difficile*.



Cesar A. Arias, MD, MSc, PhD, FIDSA
Professor
Infectious Disease

Cesar A. Arias, M.D. MSc, Ph.D. is the Margaret and Herbert Dupont Chair in Infectious Diseases and holds the Laurel and Robert H. Graham Faculty Fellowship at McGovern Medical School. He is the director and founder of the Center of Antimicrobial Resistance and Microbial Genomics (CARMiG) at McGovern Medical School and the Center for Infectious Diseases at the UTHealth School of Public Health. Dr. Arias obtained his medical degree from Universidad El Bosque, Bogota, Colombia (first in class) and then spent 6 years in the United Kingdom where he obtained Masters in Clinical Microbiology at The University of London and a PhD in Microbial Biochemistry and Molecular Microbiology at University of Cambridge. He then was awarded a Wellcome Trust International Fellowship to develop antimicrobial resistance research in Colombia, where he founded (and still directs) the Molecular Genetics and Antimicrobial Resistance Unit and International Center for Microbial Genomics at Universidad El Bosque, Bogota. In 2002, he moved to Houston for training in Internal Medicine and Infectious Diseases at UTHealth McGovern Medical School and MD Anderson Cancer Center. He joined the UTHealth faculty as assistant professor in 2008 and became professor in 2016.

Dr. Arias is a nationally and internationally recognized expert conducting NIH-funded basic, translational and clinical research on mechanisms of antibiotic resistance with emphasis on Gram-positive organisms (in particular enterococci). His expertise also includes the clinical impact of resistance and the molecular epidemiology of antibiotic-resistant organisms, using state-of-the-art genomic analyses. He was one of the first recipients of the NIH K99/R00 Pathway to Independence Award and has also been the recipient of the American Society of Clinical Microbiology Young Investigator Award and the Infectious Diseases Society Oswald Avery Award for early achievement, among others. Dr Arias was a standing member of the NIH/NIAID Microbiology and Infectious Diseases study section since 2012 and has served a reviewer for the European Union Joint Program Initiative for Antimicrobial Resistance (JPIAMR). He has been active in professional societies including serving in the Program Planning Committee of IDWeek since 2014, serving as Vice-Chair (2018) and Chair (2019). He was inducted to the American Society for Clinical Investigation in 2015. Dr. Arias is an adjunct professor at Universidad El Bosque in Bogota, Colombia and visiting professor at Universidad De Desarrollo/ Clinica Alemana in Santiago, Chile. He is the founder and co-chair of the International Symposium of Antimicrobial Resistance. He serves as editor of Antimicrobial Agents and Chemotherapy and is the Chair of the Gulf Coast Consortium on Antimicrobial Resistance in Houston (a partnership between 7 institutions in the Texas Medical Center). Dr. Arias carries out projects with a network of collaborators across the Texas Medical Center and international sites using multidisciplinary approaches. His research has resulted in more than 150 publications.



Robert L. Atmar, MD
Professor
Medicine

Panel: *Immunization Panel Discussion*

Robert L. Atmar, M.D., is the John S. Dunn Research Foundation Clinical Professor in Infectious Diseases in the Departments of Medicine and Molecular Virology & Microbiology at Baylor College of Medicine. He received a Bachelors of Science degree in Biology from Texas A&M University in 1978 and his medical degree from Baylor College of Medicine in 1981. He completed an internship and residency in Internal Medicine and fellowship in Infectious Diseases at Baylor College of Medicine. He is a member of BCM's Vaccine Treatment & Evaluation Unit and the Digestive Diseases Center, and he also serves as the chief of the Infectious Diseases Service at Ben Taub General Hospital. Dr. Atmar's research interests include the epidemiology, pathogenesis, diagnosis, treatment and prevention of viral respiratory and enteric infections. He has studied influenza and noroviruses for more than 25 years, with a special emphasis on the diagnosis, clinical evaluation, and immunology of these viral infection and on the evaluation of vaccine candidates and strategies to prevent disease caused by these viruses. He is a Fellow in the IDSA, ACP and SHEA, and he serves as the North American editor for the Journal of Infection. He is also a member of the Advisory Committee on Immunization Practices (ACIP).



Carol J. Baker, MD

Professor
Pediatrics

Panel: *Immunization Panel Discussion*

Dr. Baker is professor of pediatrics at University of Texas Medical School in Houston, and formerly professor of pediatrics, molecular virology and microbiology at Baylor College of Medicine (BCM) from 1975-2018.

Dr. Baker made groundbreaking recognition of neonatal and young infant group B streptococcal disease and its correlation of lack to maternal antibodies to the GBS capsular polysaccharide during her infectious diseases fellowship training at BCM and Harvard Medical School. She subsequently expanded knowledge of changing epidemiology of neonatal sepsis, and GBS pathogenesis and prevention strategies. Her work with Dennis L. Kasper led to NIH-funded research of candidate GBS vaccines and clinical trials, and her advocacy work first with the American Academy of Pediatrics in 1992 and then with the U.S. Centers for Disease Control and Prevention (CDC) in 1996 led to routine culture screening of pregnant women for GBS colonization and intrapartum antibiotic prophylaxis, a policy that has implemented in several European countries and resulted in a more than 80% reduction GBS disease in the U.S.. A pioneer in advocating for maternal immunization, the recommendation for routine pertussis booster immunization during every pregnancy was made during her time as Chair of the Advisory Committee for Immunization Practices to the CDC, 2009-2012.

Dr. Baker is the author or co-author of more than 400 peer reviewed publications, book chapters, reviews and editorials. She was an editor of 5 editions of the AAP Red Book. A committed clinician and teacher, she has received several awards and mentored dozens of pediatric infectious diseases trainees. A few of her many awards include the Mentor and Alexander Fleming Lifetime Achievement Awards from the Infectious Diseases Society of America, the Distinguished Physician and Distinguished Research Awards from the Pediatric Infectious Diseases Society, and the Albert Sabin Gold Medal Award from the Sabin Vaccine Institute.



Gerald Bills, PhD
Professor
Molecular Medicine

Mining Fungal Genomes for Concealed Natural Product Antimicrobials

Gerald Bills is professor in the Institute of Molecular Medicine, University of Texas Health Science Center at Houston. His lab studies how and why fungi produce bioactive natural products in order to deliver molecules that can intervene in human diseases and infections. His lab has characterized the biosynthesis of pneumocandin B0, the starting molecule for the antifungal drug, CANGIDAS, and has worked on reprogramming pneumocandin biosynthesis to produce new derivatives with improved potency, spectrum and pharmacokinetics. His lab has identified the biosynthetic pathway for enfumafungin, the starting natural product for the clinical candidate, Ibrexifungerp. His lab is also searching for new antifungal compounds against *Cryptococcus meningitis*. Previously he worked at Merck Research Laboratories in the USA and Spain (1988-2008) where he established new strategies for generating fungal and other microbial metabolites for drug discovery. He was a member of teams that discovered some of the most significant fungal natural products of the past two decades, including enfumafungin, precursor of an antifungal agent (Ibrexifungerp) now in phase III trials, and other molecules that entered major medicinal chemistry projects at Merck. Before returning to the USA in 2012, he was the head of Microbiology at the Fundación MEDINA, Granada, Spain (2009-2012), an institute devoted to the discovery of antiinfective and therapeutic agents from microbial metabolites.



Kimberly Blumenthal, MD, MSc
Assistant Professor
Medicine

Penicillin Allergy Evaluation as Antibiotic Stewardship

Kimberly Blumenthal, MD, MSc is an Allergist/Immunologist and drug allergy researcher at Massachusetts General Hospital and Assistant Professor of Medicine at Harvard Medical School. She is the Co-Director of the Clinical Epidemiology Program within the Division of Rheumatology Allergy and Immunology and the Quality and Safety Officer for Allergy at the Edward P. Lawrence Center for Quality and Safety. Dr. Blumenthal performs drug allergy research that uses methods of epidemiology, informatics, economics, and decision science. Her research is funded by the NIH/NIAID, AHRQ, and foundations, including the American Academy of Allergy, Asthma, and Immunology Foundation and CRICO, the risk management foundation. Dr. Blumenthal is recognized nationally for having identified the morbidity and mortality associated with unverified penicillin allergy labels and creating innovative approaches to the evaluation of penicillin and cephalosporin antibiotic allergies in the hospital setting. Dr. Blumenthal has authored more than 60 peer-reviewed publications including manuscripts published in high-impact journals such as Lancet, JAMA, and the BMJ.

Dr. Blumenthal graduated from Columbia University with a BA in Economics. She studied medicine at Yale University School of Medicine, before training at the Massachusetts General Hospital for Internal Medicine and Allergy and Immunology. She completed a Master of Science in Clinical Epidemiology at the Harvard T.H. Chan School of Public Health in 2017.



Helen W. Boucher, MD, FACP, FIDSA
Professor
Medicine

Drowning of the Antibiotic Pipeline: How to Save it

Helen Boucher is the Chief of the Division of Geographic Medicine and Infectious Diseases and Director of the Tufts Center for Integrated Management of Antimicrobial Resistance (CIMAR), a collaborative, cross-disciplinary initiative between Tufts University and Tufts Medical Center with a mission of innovating to protect humanity from the global threat of antimicrobial resistance by integrating solutions across human and veterinary medicine, stewardship and awareness. She is Director of TMC's Heart Transplant and Ventricular Assist Device Infectious Diseases Program, and Professor of Medicine at Tufts University School of Medicine.

Dr. Boucher's clinical interests include infections in immunocompromised patients and *S. aureus* infections. Her research interests focus on *S. aureus* and the development of new anti-infective agents. She is the author or coauthor of numerous abstracts, chapters, and peer-reviewed articles, which have been published in such journals as *The New England Journal of Medicine*, *Antimicrobial Agents and Chemotherapy*, *Clinical Infectious Diseases*, and *The Annals of Internal Medicine*; she is Associate Editor of *Antimicrobial Agents and Chemotherapy*.

In 2015, Dr. Boucher was appointed a voting member of the Presidential Advisory Council on Combating Antibiotic-Resistant Bacteria, and elected Treasurer of the Infectious Diseases Society of America. She was awarded the IDSA Society Citation Award in October, 2015. Dr. Boucher serves on the Board of Trustees of The College of the Holy Cross and as Chair of the Board of Trustees of the Physicians of Tufts Medical Center.



Eric L. Brown, PhD
Associate Professor
Infectious Disease

Microbiome and Worsening Glycemia Among Mexican Americans in Starr County, Texas

Dr. Eric L. Brown received his undergraduate degree in Biology from Texas A&M University and Ph.D. in Immunology from the University of Texas Graduate School of Biomedical Sciences in Houston, TX. His graduate work focused on the immunosuppressive effects of ultraviolet radiation on numerous infectious agents including *Schistosoma mansoni*, *Candida albicans*, and Lyme spirochete *Borrelia burgdorferi*. During his postdoctoral fellowship at the Institute of Biosciences and Technology, he received two grants from the Centers of Disease control to study mechanisms of bacterial attachment to host matrix components and for the development of a second-generation Lyme vaccine. He is currently an Associate Professor of Infectious Disease at the University of Texas Health Science Center School of Public Health. His research projects involve studying immune evasion strategies employed by *Staphylococcus aureus*, the impact of the gut microbiome on changing glycemia status, and developing vaccination strategies for the prevention of diseases caused the causative agent of Chagas disease, *Trypanosoma cruzi*. His areas of expertise include recombinant protein technology, cell biology, molecular biology, immunology, vaccine design, microbiome research, and animal models of infectious disease. He teaches Parasitology, Medical Microbiology and Immunology and is listed as a co-inventor on three U.S. and international patents.



Ifrah Chaudhary
Epidemiologist
Arbovirus Coordinator

Emergence of Unusual Carbapenemase-producing Carbapenem Resistant Organisms in Houston, Texas

Ifrah has a Master of Public Health degree with an emphasis in Epidemiology from New York University College of Global Public Health, and a Bachelor of Arts degree in Psychology from the University of Colorado Boulder. Currently, Ifrah works as an Epidemiologist at the Houston Health Department (HHD) where she serves as the Arbovirus Coordinator and assists the HHD Healthcare-Associated Infections Program with investigating and containing unusual multidrug-resistant organisms. Additionally, she investigates Texas' notifiable conditions and works alongside with the Centers for Disease Control and Prevention to understand the health impact of Hurricane Harvey among pregnant women and infants.

Before starting at the Houston Health Department, Ifrah focused her thesis on investigating the associations between ovarian hormones and periodontitis in U.S. Hispanic women and was nominated to present at the 2017 National Oral Health Conference. She continues her research endeavors in women's health, and other research topics of interest including social epidemiology, big data in health sciences and infectious diseases, by furthering her educational career and pursuing a doctorate in epidemiology.



Ashok K Chopra, PhD, CSc

Professor

Microbiology & Immunology

Non-antibiotic Host-targeted Therapeutics and Antimicrobial Peptides to Combat Multiple Drug Resistant Microbes

Senior Scientist, WHO Collaborating Sealy Center for Vaccine Research and Sealy Institute for Vaccine Sciences, Centers for Tropical, Biodefense and Emerging Infectious Diseases, Institute for Human Infections & Immunity, Institute for Translational Sciences, and Shriners Burns Hospitals for Children

Assistant Director-Microbiology & Immunology Graduate Program, Director-Center for Antibiotic Resistance and Microbiome, Program Director-NIH T32 “Biodefense Training Program.” University of Texas Medical Branch, Galveston, TX, USA

My research interests during the past two decades have been on identifying virulence factors/mechanisms from several Gram-negative and Gram-positive bacteria and to demonstrate their roles in causing human diseases. Specifically, my group has focused on type 2-, -3, and -6 secretion systems and quorum sensing, and we have used molecular/genomics/proteomics tools to better understand mechanisms of action of the selected virulence factors. Our emphasis is on gastrointestinal and respiratory diseases as well as necrotizing fasciitis with a focus on bacterial-host cell interactions. In addition, we are developing and testing new vaccines and therapeutics against Tier-1 select agents, such as *Yersinia pestis*, the causative agent of plague. We are testing new platforms to display antigens from biodefense-related and emerging pathogens that are protective. My laboratory has made a startling discovery by characterizing a novel host regulatory molecule which acts as a double-edged sword, being involved in modulating inflammation and playing a pivotal role in causing neurodegenerative disorders, in humans. Finally, we are examining new therapeutics other than antibiotics (both host directed and antimicrobials) that could be used to combat diseases caused by antibiotic-resistant bacteria and their potential effects on microbiota.

Mandelin Cooper, PharmD, BCPS
Director
Clinical Pharmacy

Panel: *Houston Stewardship Best Practices*

Mandelin Cooper, PharmD, BCPS is the Director of Clinical Pharmacy for the Clinical Services Group of HCA Healthcare. Dr. Cooper's areas of focus include the Antimicrobial Stewardship Program (AMP), Clinical Pharmacy Workflow (CPW), clinical pharmacy program and metrics. Dr. Cooper serves on the Antibiotic Stewardship Committee for the Society of Infectious Diseases Pharmacist (SIDP), the ID-PRN Programming Committee for American College of Clinical Pharmacy (ACCP), and is part of an Advisory Panel for the SAAR. She is a research team member for the CDC and Harvard Pilgrim group leading the INSPIRE trial for antibiotic smart decision prompts for prescribers. She was part of the team that won the Institute for Safe Medication Practices (ISMP) Cheers Award for the Clinical Pharmacist Workflow Model.

Dr. Cooper received her Doctor of Pharmacy degree from the University of Houston. She completed a PGY-1 Pharmacy Practice Residency at Thomas Jefferson University Hospital in Philadelphia, PA and a PGY-2 Residency in Infectious Diseases at Mayo Clinic in Rochester, MN. She is a Board Certified Pharmacotherapy Specialist who has been with HCA since 2008.



Sara E. Cosgrove, MD, MS
Professor
Medicine

Antibiotic Use and Prevention of Resistance

Sara E. Cosgrove, MD, MS, is a Professor of Medicine in the Division of Infectious Disease at Johns Hopkins University School of Medicine and has a joint appointment in the Department of Epidemiology at the Johns Hopkins Bloomberg School of Public Health. She serves as the Director of the Department of Antimicrobial Stewardship and the Associate Hospital Epidemiologist at The Johns Hopkins Hospital. Dr. Cosgrove's research interests include the epidemiology and outcomes of antimicrobial resistance, the development of tools and programs to promote the rational use of antimicrobials, the prevention of hospital-acquired infections and the epidemiology and management of *S. aureus* bacteremia. Her recent research focuses on strategies for implementation of antimicrobial stewardship activities across all healthcare settings via a large project funded by the Agency for Healthcare Research and Quality. She was member of the President's Council of Advisors on Science and Technology Working Group on Antimicrobial Resistance and is a voting member to the Presidential Advisory Council on Combating Antibiotic-Resistant Bacteria. She is a Past President of the Society for Healthcare Epidemiology's Board of Directors. Dr. Cosgrove received her undergraduate degree from Columbia College in New York, New York, her medical degree from Baylor College of Medicine in Houston, Texas, and her master of science degree in epidemiology from Harvard School of Public Health in Boston, Massachusetts. She completed her postgraduate training in internal medicine at The Johns Hopkins Hospital and underwent subsequent training in infectious disease at Beth Israel Deaconess Medical Center in Boston.



Selvi Ersoy, PhD
Postdoctoral Research Fellow
Infectious Disease

Genetic and Phenotypic Signatures Predictive of 'Bicarbonate [NaHCO₃]-Responsiveness' and β -Lactam Sensitization Among Methicillin-Resistant Staphylococcus aureus (MRSA)

Dr. Selvi Ersoy is a Postdoctoral Research Fellow at the Lundquist Institute for Biomedical Innovation (formerly LA Biomed) at the Harbor-UCLA Medical Center, working in the lab of Dr. Arnold Bayer, MD in the Division of Infectious Disease. She earned her B.S. in Genetics with a minor in Medical Anthropology at the University of California Irvine in 2010. She attended the University of California Santa Barbara for her graduate studies, where she earned her PhD in Molecular, Cellular, and Developmental Biology with an emphasis in Microbiology in the lab of Dr. Michael Mahan, PhD. There, she studied the influence of host microenvironments on antibiotic susceptibility in a variety of Gram-negative and Gram-positive microbial pathogens. Dr. Ersoy joined the Bayer Lab in 2017, where she has focused her research on the influence of bicarbonate, our body's primary biological buffer, on β -lactam susceptibility in methicillin-resistant Staphylococcus aureus (MRSA). Her research investigates genetic and phenotypic mechanisms through which bicarbonate alters MRSA susceptibility to clinically relevant β -lactams, the in vivo relevance of this phenomenon in a rabbit model of infective endocarditis, and the scope of this phenotype among clinical MRSA isolates. The aim of her research is to improve antimicrobial susceptibility testing procedures and standard treatment practices for MRSA infection.

Christopher Evans, PharmD, BCPS
Pharmacist
Healthcare Associated Infections and Antimicrobial
Resistance Program
Tennessee Experience

Dr. Christopher Evans is a pharmacist with the Healthcare Associated Infections and Antimicrobial Resistance Program at the Tennessee Department of Health. He received his Doctor of Pharmacy degree from the Campbell University School of Pharmacy in Buies Creek, NC, and completed a general pharmacy practice residency at Vidant Health (formerly Pitt County Memorial Hospital) in Greenville, NC. He also completed an infectious diseases pharmacy residency at the University of Rochester Medical Center in Rochester, NY, where he later served as the Antimicrobial Stewardship Pharmacist for seven years.

His research interests include the clinical impact and metrics of antimicrobial stewardship programs and antibiotic use and resistance tracking. He maintains active memberships in the American College of Clinical Pharmacy (ACCP), the Society of Infectious Diseases Pharmacists (SIDP), and the Council for State and Territorial Epidemiologists.



Anthony Flores, MD PhD
Associate Professor
Pediatrics

Emergence of Antibiotic Resistance in Streptococci

Dr. Flores completed his MD, PhD, and MPH in 2006 as part of the Medical Scientist Training Program at the University of Rochester School of Medicine and Dentistry. He moved to Houston, TX for his pediatric residency and subsequent fellowship in infectious diseases at Baylor College of Medicine (BCM) and Texas Children's Hospital (TCH). During his fellowship, Dr. Flores initiated investigative studies into the mechanisms of group A Streptococcus (GAS) carriage and pathogenesis under the mentorship of Dr. James Musser, a leader in bacterial pathogenesis and genomics. Dr. Flores completed his post-graduate training in 2012 and was a faculty member at BCM/TCH until 2017 when he moved to UTHealth/McGovern Medical School to join the Division of Pediatric Infectious Diseases and CARMiG. Dr. Flores' research was funded during his training years by St. Jude Children's Research Hospital/Pediatric Infectious Diseases Society and Robert Wood Johnson Foundation. Currently, Dr. Flores' research is supported by grants from the NIH/NIAID toward gene regulation and contribution to asymptomatic carriage in GAS (R01) and epidemic GAS clone emergence (R21).



Vance Fowler, MD, MHS

Professor

Medicine and Molecular Genetics & Microbiology

Challenging Clinical Cases on Antimicrobial Resistance

Vance Fowler, MD, MHS, Professor, Departments of Medicine and Molecular Genetics & Microbiology, Duke University Medical Center. Dr. Fowler has over 2 decades of continuous support as PI from the NIH for clinical and translational research in *Staphylococcus aureus* and other bacterial infections. Dr. Fowler created the *S. aureus* Bacteremia Group, co-founded the International Collaboration on Endocarditis, and is the Communicating PI of the Antibacterial Resistance Leadership Group. He has over 250 peer-reviewed publications with > 19,000 citations.



Kevin Garey, PharmD, MS
Professor
Pharmacy Practice
Diagnostic Testing C. difficile

Kevin Garey, Pharm.D., M.S., is Chair of the Department of Clinical Sciences and Administration and Professor of Pharmacy Practice at the University of Houston College of Pharmacy in Houston, Texas. He also serves as Division Head, Experiential Therapeutics and Clinical Pharmacology. Additionally, he holds an academic appointment as Adjunct Associate Professor at the University of Texas School of Public Health in Houston.

Dr. Garey earned his Bachelor of Science in Pharmacy from Dalhousie University in Halifax, Nova Scotia, Canada. He earned his Doctor of Pharmacy degree from the State University of New York at Buffalo, in Buffalo, New York and a Master of Science in Biometry from the University of Texas School of Public Health, Houston. He completed a Pharmacy Practice Residency at the Mary Imogene Bassett Hospital in Cooperstown, New York. He also completed an Infectious Disease Residency and Fellowship in Infectious Diseases at the University of Illinois at Chicago, Illinois.

Dr. Garey is an active member of the Society of Infectious Diseases Pharmacists and the American Society of Health-Systems Pharmacists (ASHP). His research interests include antimicrobial stewardship activities to prevent and treat *Clostridium difficile* infection, surgical site infections, and systemic candidiasis. He has received numerous national awards recognizing excellence in research, teaching, and publications. In 2010, Dr. Garey received the ASHP Best Practices Award in Health-System Pharmacy for implementation and validation of an antimicrobial stewardship program.



David Greenberg, MD
Associate Professor
Infectious Diseases and Geographic Medicine
Revisiting Therapeutics Against MDR Gram-negative Bacteria

Dr. Greenberg is an Associate Professor of Infectious Diseases and Microbiology at University of Texas Southwestern (UTSW). After finishing his Infectious Diseases training at the National Institutes of Health, he became an Assistant Clinical Investigator in the Laboratory of Clinical Infectious Diseases at NIAID where he studied host-pathogen interactions in immunocompromised patients. This is where he first started his work on utilizing antisense molecules as novel therapeutics. They are studying whether silencing different pathogens in a gene-specific way can inhibit growth in vitro and in vivo. They are utilizing peptide-conjugated phosphorodiamidate morpholino oligomers (PPMOs) to block mRNA and prevent translation of target genes in both essential cellular pathways as well as antibiotic resistance genes themselves. They are currently studying these in a number of pathogens including *Escherichia coli*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae* and the *Burkholderia cepacia* complex. In addition, they have begun to investigate using PPMOs to block virulence mechanisms such as biofilm formation. Finally, he has experience in the sequencing of bacterial pathogens and have worked with our bioinformatics group to develop robust, automated pathways to search for the presence of antibiotic resistance genes in both single and metagenomic bacterial samples. They are currently utilizing these algorithms to better understand the emergence of resistance in particular patient populations such as those with hematologic malignancies.



Julian G. Hurdle, PhD

Associate Professor

Molecular Microbiology/Infectious Diseases

Antibiotic Resistance in Clostridium difficile Drives the Need for Alternate Therapeutic Strategies

Dr. Hurdle's laboratory has a translational focus that impacts human health through the discovery and development of antimicrobials, antibiotic action and target validation, mechanisms of antibiotic resistance, and effects of resistance genes on bacterial fitness and pathogenesis. He has a particular focus on natural products, given the large diversity of molecules found in nature that can be harnessed for therapeutic development. Having worked in this area for more than 10 years, he considers himself to be a growing expert in the anti-infective field, stemming from leading multi-disciplinary collaborations that bridge the gap between microbiology and pharmaceutical sciences, postdoctoral work with Sandoz Pharmaceuticals and Novacta Biosystems at University of Leeds, UK, consultancy on the development of antibacterials in preclinical development, and leading the microbiology component of an inter-disciplinary drug discovery team at St. Jude Research Children's Hospital resulting in agents in advanced pre-clinical studies for TB disease. Notably, his lab is leading an interdisciplinary discovery of novel agents to prevent or treat *C. difficile* infection (CDI) and other drug-resistant bacterial infections and use both in vitro and animal models for PK and efficacy to progress lead compounds, and understanding novel mechanisms of resistance in *Clostridium difficile*.



Chase Janak, PharmD, BCPS
Clinical Specialist
ID/Antimicrobial Stewardship
Panel: Houston Stewardship Best Practices

Chase Janak obtained his Doctor of Pharmacy from the University of Houston College of Pharmacy in 2009. He completed his PGY1 Pharmacy Practice Residency and PGY2 Infectious Diseases Residency at Houston Methodist Hospital in Houston, TX. After residency, he began practice at Baylor University Medical Center in Dallas, TX, working as an Emergency Department Clinical Pharmacist and assisted with the development of their newly formed Antimicrobial Stewardship Program. In 2013, he returned to Houston Methodist Hospital to take a position as a Clinical Pharmacist and is now the pharmacist lead for the Antimicrobial Stewardship Program at Houston Methodist Hospital.



Sheldon L. Kaplan, MD

Professor

Pediatric Medicine

Clinical Impact of Antibiotic Resistance in Pediatric Infections

Born and raised in Missouri, Dr. Kaplan is board certified in Pediatrics and Pediatric Infectious Diseases. Dr. Kaplan is a graduate of the University of Missouri-Columbia and the University of Missouri School of Medicine-Columbia. He was a resident in Pediatrics and a fellow in Pediatric Infectious Diseases at St. Louis Children's Hospital and Washington University School of Medicine, St. Louis, MO.

Dr. Kaplan is currently Professor and Executive Vice-Chair and Head of the Section of Infectious Diseases in the Department of Pediatrics at the Baylor College of Medicine and Chief of the Infectious Disease Service as well as the Head of the Department of Pediatric Medicine at Texas Children's Hospital in Houston, TX.

Dr. Kaplan has published over 250 peer-reviewed articles, over 140 invited articles, chapters, or reviews and is a co-editor of the Feigin and Cherry's Textbook of Pediatric Infectious Diseases, 5th, 6th, 7th and 8th Editions. He is Editor-in-Chief--Pediatrics as well as the Co-Editor of the Pediatric Infectious Diseases section of UpToDate®. His current research interests include infections in children caused by *Staphylococcus aureus* and *Streptococcus pneumoniae*. Dr. Kaplan is a Past President of the Pediatric Infectious Diseases Society and a past member of the Anti-Infectives Advisory Committee of the FDA and served for 7 years on the Subboard of Pediatric Infectious Diseases of The American Board of Pediatrics including 2 years as chair. In 2011 he received the Arnold J. Rudolph Baylor Pediatric Award For Lifetime Excellence In Teaching. In 2019 he received the European Society for Paediatric Infectious Diseases Distinguished Award for Education and also had an Endowed Chair in the Department of Pediatrics at the Baylor College of Medicine named in his honor.

Dr. Kaplan, his wife, two daughters, son-in-law and grandchildren all live in Houston.



Natasha Kirienko, PhD
Assistant Professor
BioSciences

Antivirulence Approaches Against Pseudomonas aeruginosa

Natasha Kirienko is a molecular biologist and geneticist who received her BS and MS degrees in biology and biochemistry at Rostov State University in Russia, and her PhD in molecular biology at the University of Wyoming. After an appointment as a postdoctoral researcher at Harvard Medical School and Massachusetts General Hospital, she joined the faculty of the BioSciences department at Rice University in 2015 as a CPRIT Scholar in Cancer Research.



Andrew Y. Koh, MD
Associate Professor
Pediatrics, Microbiology
Gut Metabolomics in Graft vs Host Disease

Andrew Y. Koh, M.D. is Associate Professor in Pediatrics, Microbiology, and Harold C. Simmons Comprehensive Cancer Center at the University of Texas Southwestern Medical Center and Director of Pediatric Hematopoietic Stem Cell Transplantation at Children's Health Dallas. Dr. Koh is dually trained in Pediatric Hematology/Oncology (Dana Farber Cancer Institute) and Pediatric Infectious Diseases (Boston Children's Hospital). The Koh Lab focuses on understanding how the gut microbiome influences host immune responses in cancer and stem cell transplant patients. Specific projects include bacterial/fungal infections originating from the gut, graft-versus host disease, the evolution of antibiotic resistance in the mammalian gut, and host immune anti-tumor response.



Anna Konovalova, PhD

Assistant Professor

Microbiology and Molecular Genetics

Cell Envelope of Gram-Negative Bacteria: An Antibacterial Target

Dr. Konovalova received her Ph.D. in 2011 from the Max-Planck Institute in Marburg, Germany. She joined UTHealth in 2017 after completing her postdoctoral training with Professor Thomas J. Silhavy at Princeton University, USA. The Konovalova lab is focused on how Gram-negative bacteria build and maintain the integrity of their cell envelope, the hallmark of which is the outer membrane (OM). The OM is an essential organelle and a major factor of intrinsic antibiotic resistance. Her research team combines classic genetics, state-of-the-art biochemistry and innovative -omics approaches to provide deep functional understanding of the OM assembly and homeostasis pathways and their interconnectivity as the first step in the scientific roadmap for antibiotic discovery.

McGovern Medical School

The University of Texas Health Science Center at Houston



Andrea Mora, PharmD
Clinical Associate Professor and Vice Chair
Pharmacy Practice

Panel: *Houston Stewardship Best Practices*

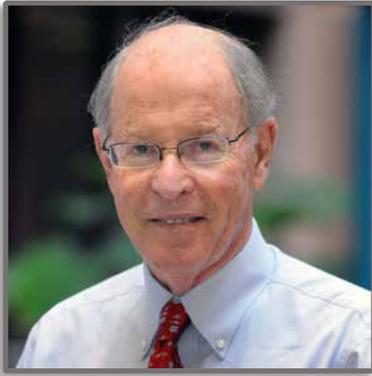
Dr. Andrea Mora is a Clinical Associate Professor and Associate Department Head of Pharmacy Practice at the Texas A&M Rangel College of Pharmacy. She earned her PharmD from the University of Houston College of Pharmacy and subsequently completed a general practice residency at St. Luke's Episcopal Hospital in Houston followed by an infectious diseases PGY2 residency at the South Texas Veterans Health Care System in San Antonio. In her ten years at the Rangel College of Pharmacy she has received over fifteen teaching awards including the Texas A&M Association of Former Students Distinguished Achievement Award for College-Level Teaching in 2015. She also served as the faculty advisor for the Student Society of Health System Pharmacy. In her clinical practice she serves as the Infectious Diseases Clinical Pharmacist at Lyndon B. Johnson Hospital in Houston, TX and works alongside the infectious disease faculty of UT McGovern Medical School.



Flor M. Munoz-Rivas, MD
Associate Professor
Infectious Diseases

Panel: *Immunization Panel Discussion*

Dr. Munoz-Rivas has over 20 years of experience in conducting clinical research focusing on the epidemiology of infectious diseases and vaccines in special populations including infants, children, adolescents, pregnant women and immunocompromised hosts. Her particular interest and expertise is in respiratory pathogens, vaccinology and maternal immunization. She has been principal investigator or co-investigator in studies describing the epidemiology of various pathogens (eg. influenza, pertussis, RSV, pneumococcus, CMV and norovirus), and phase I-IV clinical trials studying novel treatment options or vaccines for the prevention of viral and bacterial infections in infants, children and pregnant women. I collaborate with clinicians and investigators through National Institutes of Health (NIH) and Centers for Disease Control (CDC) and Prevention research networks (e.g. VTEU), and globally. She is a site PI for 3 CDC pandemic preparedness influenza projects that focus on surveillance, vaccine and antiviral effectiveness in hospitalized and ambulatory patients, and pregnant women; lead PI for a NIH sponsored study of post-natal Zika virus infection in young children rural Guatemala; and co-investigator for the CDC NVSN ARI/AGE Surveillance Network, a CDC funded five year project to establish illness surveillance sites in Central America, and a NIH study of high dose influenza vaccine in bone marrow transplant recipients. She is a member of the Committee of Infectious Diseases (COID) of the AAP, the influenza and pertussis working groups of the ACIP/CDC, and of special interest groups of the WHO, NIH, CDC, NVAC, and BMGF maternal immunization initiatives, including the GAIA project for the development of case definitions for the assessment of safety of vaccines in pregnancy. At BCM she serves as Chair of the Institutional Review Board. At Texas Children's Hospital, she is a consultant in pediatric infectious diseases and Director of the Transplant Infectious Diseases program. She mentors learners (MS, MD, PA, NP, PhD) at her and other institutions, and teaches at the Institut Pasteur and International Vaccine Institute (IVI) Vaccinology courses in Paris and Seoul, respectively.



Daniel Musher, MD

Professor

Microbiology and Molecular Biology

CAP Guideline Update

Dr. Daniel Musher is Distinguished Service Professor of Medicine, Professor of Molecular Virology and Microbiology and, formerly, Professor of Immunology at Baylor College of Medicine. His principal areas of interest have been bacterial infections and host response, but in recent years he has studied the etiology of community acquired pneumonia due to bacteria or viruses. He has coauthored more than 560 publications in the medical literature and has received the DeBakey medal for his research. The Infectious Diseases Society of America recognized him with its Outstanding Clinician and Teacher Award in 2009.



Victor Nizet, MD
Professor and Vice-Chair
Basic Research

The Interaction Between the Immune System and Antimicrobials

Victor Nizet, MD is Distinguished Professor and Vice Chair for Basic Research in the Department of Pediatrics, Distinguished Professor of Pharmacy & Pharmaceutical Sciences, and Chief of the Division of Host-Microbe Systems and Therapeutics at the University of California, San Diego (UCSD). Dr. Nizet is a graduate of Reed College, received his medical training at Stanford University School of Medicine, completed a Residency and Chief Residency in Pediatrics at Harvard University's Children's Hospital in Boston, Massachusetts, and then a Fellowship in Pediatric Infectious Diseases at the University of Washington's Children's Hospital in Seattle. Dr. Nizet leads a large basic and translational research laboratory focused on discovering virulence factors of invasive bacterial pathogens, elucidating mechanisms of host innate immunity, and novel approaches to infectious disease therapy. He is also spearheading the for the UCSD Collaborative to Halt Antibiotic-Resistant Microbes (CHARM) which will debut in Fall 2019. Dr. Nizet has authored over 440 peer-reviewed publications and collaborated with several biotechnology interests in developing new antibiotic and immune-based therapies against drug-resistant pathogens. Dr. Nizet's work has been recognized by an American Heart Association Established Investigator Award, the American Lung Association Career Investigator Award, the American Asthma Foundation Senior Investigator Award, the E. Mead Johnson Award for Research in Pediatrics, and the 2016-17 UCSD Chancellor's Associates Award for Faculty Excellence in Research in Science and Engineering. Dr. Nizet has been elected to the American Society for Clinical Investigation, the Association of American Physicians, and the American Academy of Microbiology. Details of his research program can be found on the laboratory website: <http://nizetlab.ucsd.edu>



Luis Ostrosky-Zeichner, MD, FACP, FIDSA, FSHEA,
FECMM, CMQ

Professor

Medicine and Epidemiology

Challenging Clinical Cases on Antimicrobial Resistance

Dr. Ostrosky-Zeichner is a professor of medicine and epidemiology, the Vice-Chair of Medicine for Healthcare Quality, and the director of the Laboratory of Mycology Research, at the Division of Infectious Diseases of the McGovern Medical School (a part of UTHealth). He also serves medical director for epidemiology and antimicrobial stewardship for Memorial Hermann Texas Medical Center, UT Physicians, and Cornerstone TMC. He is a fellow of the American College of Physicians, the Infectious Diseases Society of America, the Society of Healthcare Epidemiology of America, and the Academy of the European Confederation of Medical Mycology. He is a Senior Editor for Journal of Antimicrobial Chemotherapy, as well as an editorial board member of Antimicrobial Agents and Chemotherapy. He is a board member of the Mycoses Study Group and Educational Consortium and the International Immunocompromised Host Society. He is also a past chair of the Infectious Diseases Society of America Standards and Practice Guidelines Committee and has been a consultant to the US FDA and CDC. He has advanced training and experience in medical mycology, healthcare epidemiology, antimicrobial stewardship, general and transplant infectious diseases, and healthcare quality and has published over 140 peer-reviewed articles on those topics.

Dr. Ostrosky-Zeichner obtained his medical degree from Universidad Nacional Autonoma de Mexico. He completed his internal medicine residency at Instituto Nacional de Ciencias Medicas y Nutricion Salvador Zubiran, and his infectious diseases fellowship at the University of Texas Medical School at Houston and MD Anderson Cancer Center combined fellowship program.



Issam I. Raad, MD, FACP, FIDSA, FSHEA
Department Chair
Department of Infectious Diseases, Infection Control
and Employee Health
Catheter Associated Bloodstream Infections and Resistance

Dr. Raad is considered one of the world's leading experts in the field of healthcare related infections and infections in cancer. As an Endowed Distinguished Professor of Medicine, Dr. Raad has chaired MD Anderson's Department of Infectious Diseases, Infection Control and Employee Health since 2005. During his 30 years at The University of Texas M. D. Anderson Cancer Center, Dr. Issam I. Raad has made numerous outstanding clinical research contributions that have led to significant improvements in controlling life-threatening bloodstream infections in patients with cancer and other serious illnesses throughout the world. His research includes development of innovative antimicrobial central venous catheters devices and antimicrobial catheter lock solutions that have significantly reduced the risk of bloodstream infections worldwide. In the most recent CDC Guidelines, Dr. Raad's innovations have been recommended at the highest level (Category 1A) for the prevention of healthcare associated bloodstream infections.

Dr. Raad received his medical degree (1982) from the American University of Beirut School of Medicine in Lebanon and completed specialty training in internal medicine and infectious diseases at the University of Florida College of Medicine in Gainesville.

In 1992, he had an inspired idea to impregnate the catheters with antibiotics and initiated laboratory studies to design such a catheter, and then demonstrated in pre-clinical animal studies that antibiotic-coated catheters decrease the rate of infection. The first multicenter clinical trial in 1995 to assess the antimicrobial catheters showed more than a five-fold decrease in the bloodstream infections (Raad et al., *Ann Intern Med*, 1997), and a second clinical trial (Darouiche R, Raad I et al., *N Engl J Med*, 1999) found that antibiotic catheters could significantly reduce life-threatening infections resulting in their worldwide use. In addition to antimicrobial vascular catheters, Dr. Raad also developed similar antimicrobial devices to prevent ventriculitis/meningitis, pacemaker infections and urologic infections. He also developed novel antimicrobial agents to prevent microbial biofilm and related resistance discovering that chelators are bioenhancers of antimicrobial agents in preventing biofilm. He has multiple patents on this novel technology which has also been recommended by the CDC through the use of catheter lock solutions in high-risk patients.

Dr. Raad has published more than 450 scientific articles in peer-reviewed journals and 40 book chapters. Dr. Raad's studies have been highly cited (H-index score of 84 with 33,700 citations/Scopus 2004-2019) and holds over 72 issued patents and 94 provisional patents. Most of this technology has been transferred from the bench to bedside and is already applied to patient care. He, therefore, ranks high among the leading inventors at M.D. Anderson in terms of patent productivity and ability to transfer his inventions to patient care.

Dr. Raad has been widely honored for his research, patient care, mentorship and education. His recent awards and honors include the following: 2019 MD Anderson Distinguished Educator and Expertscape's algorithms top 0.1% of scholars writing about bacteremia as well as tetracycline antibiotics; 2018 Charles A. LeMaistre, M.D., Outstanding Achievement Award in Cancer, which is one of the highest achievement awards at MD Anderson; 2016: The University of Texas Regents' Outstanding Teaching Award, the MD Anderson Division of Internal Medicine's Robert F. Gagel Lifetime Achievement Award and the highly prestigious Ellis Island Medal of Honor whereby previous recipients included seven past presidents, Nobel Prize winners, and leading physician scientists; 2015 Society of Healthcare Epidemiology of America Mentor Scholar Award for mentoring fellows and junior faculty. Previously in 2004 received the Houston Intellectual Property Law Association's Outstanding Inventor Award and was commissioned by the Governor of Texas as an Admiral in the Texas Navy.

In 1995 he served as an Advisory Reviewer of the United States Congress report on antibiotic-resistant bacteria and co-authored the CDC and Prevention Guidelines on Prevention of Intravascular Catheter-Related Infections in 2002, 2009, and 2011. He also co-authored the Infectious Diseases Society of America Guidelines in 2001, 2009, 2011 and 2020.



Chanu Rhee, MD, MPH
Assistant Professor
Population Medicine

Sepsis Quality Measures: Balancing Timely Care, Antibiotic Stewardship, and Reliability

Dr. Rhee is an Assistant Professor of Population Medicine at Harvard Medical School and an intensivist, infectious disease physician, and Assistant Hospital Epidemiologist at Brigham and Women's Hospital. His clinical and research interest is the epidemiology, diagnosis, treatment, and prevention of sepsis and infections in critically ill patients, with a particular focus on using electronic health record data to improve disease surveillance and quality of care. He is the clinical co-lead for the Partners Sepsis Collaborative and has been an institutional leader in improving sepsis recognition and management across the Partners HealthCare System. As an investigator in the CDC Prevention Epicenters Program, he has led several multicenter projects focusing on sepsis epidemiology, including the work that led to the development of CDC's Adult Sepsis Event surveillance paradigm. He is a member of the Massachusetts Sepsis Consortium, the American College of Emergency Physicians' Sepsis Guidelines Panel, and the IDSA Sepsis Task Force.



Adriana Rosato, PhD
Associate Professor
Pathology and Genomic Medicine

Leveraging Regulation and Genetic Bases of Ceftaroline Resistance in MRSA: Role of Carbapenems

Dr. Adriana Rosato is an Associate Professor of Houston Methodist Research Institute (HMRI) with affiliated position at Weill Cornell College of Medicine (New York, NY). Dr. Rosato has 25 years of commitment to different aspects in the field of Infectious Diseases, Clinical Microbiology and antimicrobial resistance (AMR) expanding from basic research to clinical and translational medicine. Specifically, her research goals have been to characterize evolutionary and molecular mechanisms of multidrug resistant (MDR) pathogens underlying antibiotic resistance and the dynamic process of host/pathogen infections. MDR organisms are important human pathogens responsible for infections to which antimicrobial options are limited. Dr. Rosato's works have been recognized worldwide; she has extensively published and received multiple awards. She is a reviewer and have participated in the discussion and decision of funding at NIH/NIAID and European agencies. She is an advisor/consultant of WHO, division antimicrobial resistance and PAHO and has deeply participated in the implementation of the National Plan of Action of antimicrobial resistance, addressing and implementing innovative AMR research and stewardship initiatives while increasing the awareness, training and educational activities in the field of AMR. Moreover, Dr. Rosato has a strong interest of service to the medical, scientific, public health communities and training of young investigators/Pharm D and MD/PhD fellows.



Cynthia L. Sears, MD

Professor

Medicine, Oncology and Molecular Microbiology and
Immunology

Superbugs and The Gut Microbiome

Cynthia L. Sears, M.D. is Professor of Medicine, Oncology and Molecular Microbiology and Immunology at the Johns Hopkins University School of Medicine and the Bloomberg School of Public Health. She is the Microbiome Program Leader of the Bloomberg-Kimmel Institute for Cancer Immunotherapy at Johns Hopkins and is Director of the Johns Hopkins Germfree Murine Facility. She is an infectious diseases expert who has focused on enteric infections for her career. In particular, she has studied the pathogenesis of enterotoxigenic *Bacteroides fragilis* (ETBF), both in the laboratory and in clinical settings, over the past 25 years. The current focus of the Sears laboratory is to determine how the microbiota and specific bacteria contribute to colon carcinogenesis. The Sears laboratory integrates studies in humans and mouse models, employing microbiology, bioinformatics and immunologic methods. Dr. Sears served as Associate Editor of *Clinical Infectious Diseases* from 2000 to 2016. She has been an active member of the Infectious Diseases Society of America (IDSA) for more than 20 years, serving the Society in numerous capacities. She is currently President of IDSA from October, 2018-October, 2019.



Edward Septimus, MD, FIDSA, FACP, FSHEA
Professor

Panel: *Clinical Cases*

Dr. Ed Septimus received his medical degree from Baylor College of Medicine in Houston in 1972. Dr. Septimus went on to complete his postgraduate training in internal medicine and infectious diseases at Baylor College of Medicine in Houston. Dr. Ed Septimus is board certified in both internal medicine and infectious diseases. He was VP Research and Infectious Diseases HCA Healthcare until 2018. He has served on the Board of Directors of the Infectious Diseases Society of America (IDSA) and was on the IDSA Antimicrobial Resistance Committee, the SHEA Antimicrobial Stewardship Committee, and the IDSA Quality Measurement Committee. He was the first recipient of the IDSA Annual Clinician Award. In 2011 he was appointed to the Healthcare-Associated Infections/Preventable Adverse Events Advisory Panel for the Texas Department of State Health Services. He was awarded the John S Dunn Sr. Outstanding Teacher Award in 2010, 2011, 2013 and 2014. He is on the FDA Anti-Infective Drug Advisory Group and is co-chair of the NQF Patient Safety Steering Committee. He holds a faculty position as Clinical Professor at Texas A&M College of Medicine, Senior Lecturer Department of Population Medicine Harvard Medical School, and Professor Distinguished Senior Fellow, School of Public Health, George Mason University. He has published over 100 articles and chapters.

Texas A&M College of Medicine
Harvard Medical School
George Mason University



William M. Shafer, PhD

Professor

Microbiology and Immunology

Antibiotic Resistance and the Gonococcus: Regulation of Gene Expression

Dr. Shafer received his Ph.D. degree in Microbiology from Kansas State University in 1979 under the mentorship of John J. Iandolo, Ph.D. He then performed post-doctoral studies at the University of North Carolina-Chapel Hill, NC. Under the mentorship of P.F. Sparling, M.D. he studied the mechanisms by which *Neisseria gonorrhoeae* can develop resistance to killing by human serum. In 1982 he moved to Emory University School of Medicine where he is now Professor of Microbiology and Immunology as well as Senior Research Career Scientist at the Atlanta VA Hospital. He is also Director of the Antimicrobial Resistance and Therapeutic Discovery Training Program and Co-director of the Emory Antibiotic Resistance Center. His laboratory is engaged in research dealing with the mechanisms used by the sexually transmitted pathogen *Neisseria gonorrhoeae* to develop resistance to antibiotics used by clinicians in the treatment of gonorrhea and antimicrobial compounds produced by the host during infection. The gonococcus causes over 87 million cases of gonorrhea worldwide each year and many strains causing disease are now resistant to multiple antibiotics. There is now considerable concern that unless new antibiotics are developed, gonorrhea may become an untreatable disease in the not too distant future. With grant support from the NIH and VA since 1984, his group studies how gonococci avoid the antibacterial action of cationic antimicrobial peptides that participate in innate host defense and how they employ a drug efflux pump to export antimicrobials including antibiotics.



Samuel Shelburne, MD, PhD

Professor

Infectious Diseases and Genomic Medicine

New Insights into the Development of Carbapenem Resistance in Non-carbapenemase Producing Enterobacteriaceae

Dr. Shelburne did his undergraduate work at Princeton University, his medical school training at the University of Texas Medical Branch, and his residency, chief medical residency, and infectious diseases training at Baylor College of Medicine in Houston, TX. He did a research fellowship (T32 and K08) under Dr. Jim Musser at the Methodist Hospital Research Institute in Houston, TX.

He is the Deputy Chair for Scholarly Activity in the Department of Infectious Diseases at the MD Anderson Cancer Center. His laboratory is interested in factors that determine the incidence and clinical outcomes of bacterial infections. His work mainly focuses on the genomics and signal transduction of group A *Streptococcus* to cause serious human infections.

The Shelburne laboratory also researches:

- The epidemiology of invasive staphylococcal and group B streptococcal infections in adults
- The impact of the microbiome on infections in immunocompromised patients
- Genetic factors driving antimicrobial resistance amongst bacteria causing human infections



Edgar Sherman, BS
Graduate Student/Trainee
Antimicrobial Resistance and therapeutic Discovery
Training Program

Aminoglycoside Heteroresistance in Gram-Negative Pathogens

I am a first-generation Hispanic student pursuing my Ph.D. in the Microbiology and Molecular Genetics program at Emory University and a recent graduate of the Antimicrobial Resistance and Therapeutic Discovery Training Program. My long-term research interests are to characterize the genetic pathways of antibiotic resistance in pathogenic bacteria to understand how resistance develops and to discover novel drug targets. For my research at Emory University, I am working in the laboratory of Dr. David Weiss to identify mechanisms of antibiotic resistance in Gram-negative pathogens. Specifically, I am interested in the genetic processes involved in antibiotic heteroresistance to aminoglycosides.



Ryan Shields, PharmD
Associate Professor
Medicine

*Emergence Resistance Against New β -lactam/ β -lactamase Inhibitors:
Epidemiology and Mechanisms*

Ryan Shields is an Associate Professor in the Departments of Medicine and Clinical and Translation Research at the University of Pittsburgh, and Co-Director of UPMC's Antibiotic Management Program. He is actively engaged in the management of patients infected by multi-drug resistant bacteria and fungi. His laboratory focuses on the characterization and suppression of antimicrobial resistance by using molecular markers to predict patient responses and PK-PD pre-clinical models to study antibiotic combination approaches. Using these techniques, Dr. Shields's clinical and research roles have focused on clinical utilization and emergence of resistance of novel antimicrobial agents against CRE, and innovative stewardship approaches to implement new diagnostic tests.



Christy Su, PharmD, BCPS
Infectious Diseases Clinical Pharmacy Specialist
Transition of Care

Christy Su PharmD, BCPS is the Infectious Diseases Clinical Pharmacy Specialist at Memorial Hermann Greater Heights Hospital. She received her pharmacy degree at the University of Houston College of Pharmacy and completed her Infectious Diseases Pharmacy Residency Training at The Brooklyn Hospital Center in Brooklyn, NY. Currently, Dr. Su leads her hospital Antimicrobial Stewardship Program as well as collaborative efforts across Memorial Hermann Health System. Dr. Su is an active member of the Society of Infectious Diseases Pharmacists and reviews content for the Antimicrobial Stewardship Certification Program. Additionally, Dr. Su serves as a peer-reviewer for the Journal of Pharmacy Practice.



Ying Taur, MD, MPH

Infectious Disease Specialist

Microbiome Changes and Clinical Outcomes in Bone Marrow Transplant Patients

Dr. Taur is interested in the epidemiology of infections that occur in patients who have complex conditions, such as those with cancer. Patients who have a number of pre-existing conditions are challenging to treat, and we are engaged in clinical research to study these complex conditions and find better way to treat them. He is investigating new methods designed to examine infections in their natural clinical setting and to provide unbiased estimates of their impact on patient outcomes.



David van Duin, MD, PhD
Associate Professor
Medicine

The Carbapenem-resistant Enterobacteriaceae Epidemic in the United States

Dr. van Duin is an Associate Professor in the Infectious Diseases Division at the University of North Carolina. Dr. van Duin is the founding Director of the Immunocompromised Host ID service. His main research interests are multi-drug resistant Gram-negative bacteria, and infections in immunocompromised patients.



Luis Alberto Vega, PhD
Postdoctoral Research Fellow
Antimicrobial Resistance

Association of Antimicrobial Resistance-encoding Mobile Genetic Elements with Enhanced Bacterial Pathogen Fitness and Transmissibility

Dr. Luis Alberto Vega was born in Mexico City, Mexico. He came to the United States as a high school student, and subsequently obtained degrees from Rice University and Washington University in St. Louis. The majority of his research career has been devoted to the investigation of Group A Streptococcus pathogenesis. He is currently a postdoctoral trainee in the Texas Medical Center Training Program in Antimicrobial Resistance under the mentorship of Dr. Anthony Flores, Dr. Cesar Arias and Dr. Sam Shelburne.



Brian Werth, PharmD
Associate Professor
Pharmacy

Cell Membrane Changes Associated with Daptomycin Resistance

Dr. Werth is an Associate Professor of Pharmacy at the University of Washington with a background in acute care pharmacy and infectious diseases pharmacotherapy. His research broadly focuses on optimizing antimicrobial pharmacodynamics against multi-drug resistant bacteria such as MRSA. His currently funded projects are focused on the resistance selection potential of long-acting lipoglycopeptides and the mechanisms of cross-resistance among glycopeptides, lipopeptides, and lipoglycopeptides as well as the beta-lactam seesaw effect in *S. aureus*. Dr. Werth's team of interdisciplinary collaborators are interested in bringing multi-omics mass-spectrometric approaches to interrogate the mechanisms of antimicrobial resistance and they are currently focused on using ion-mobility mass spectrometry to quantify changes in bacterial membrane composition associated with antimicrobial exposure and resistance.



Lynn Zechiedrich, PhD
Professor
Microbiology

Toward Understanding how Positive Supercoiling Drives Fluoroquinolone Efficacy

Lynn Zechiedrich, Ph.D. holds the Kyle and Josephine Morrow Chair and is a Professor in Microbiology at Baylor College of Medicine. The Zechiedrich laboratory takes a multidisciplinary approach to study how DNA supercoiling affects the enzymes that act on DNA and the antibiotics that inhibit these enzymes. The work has branched into understanding DNA activity for gene therapy delivery. Among other honors, she won a New Investigator Award from the Burroughs Wellcome Fund, a Curtis Hankamer Research Award, and funding from the Human Frontier Science Program. She is a Fellow of the National Academy of Inventors. She was Baylor College of Medicine's BRASS Mentor of the Year in 2013. She holds four issued U.S. patents and three issued foreign patents that are licensed to Twister Biotech, Inc., a company she founded in 2011, and has multiple patents pending. She served or is serving on numerous grant review committees, reviews for 47 different peer-reviewed journals, ranging from mathematics and physics to microbiology and gene therapy, and has served or is serving on multiple editorial boards.

Rapid Fire Speakers

Day 1



Samuel Aitken, MDACC, *Microbiome and cumulative antibiotic use as predictors of *Stenotrophomonas maltophilia* infection in patients with acute myeloid leukemia receiving remission-induction chemotherapy*, Poster #1



Amira Bhalodi, Accelerate Diagnostics, Inc., *Improving Outcomes and Antibiotic Stewardship for Patients with Bloodstream Infections (IOAS): A Quasi-Experimental Multicenter Analysis of Time to Optimal Therapy*, Poster #4



Larissa Grigoryan, BCM, *Effectiveness of Antibiotic Stewardship Intervention for Urinary Tract Infections in Primary Care: a Difference in Differences Study*, Poster #10



Jinhee Jo, UH, *A Single-Center Surveillance Study of Cystic Fibrosis Microbiological Culture*, Poster #13



Heer Mehta, RU, *Evolution of Resistance to Doxycycline and Ciprofloxacin in the Category A Bioterrorism Agent, *Francisella tularensis**, Poster #18



Christine Pybus, UT Southwestern, *Cefiderocol Retains Anti-Biofilm Activity in Gram-Negative Pathogens*, Poster #24



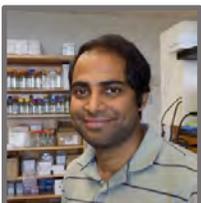
David Reynoso, UTMB, *A User-Friendly Qliksense® Application To Track & Report Essential Stewardship Metrics*, Poster #25

Rapid Fire Speakers

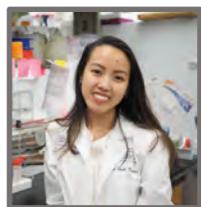
Day 2



Sam Erickson, UTHSCH, *The YxdJK System is a Targeted Stress Response that Mediates Specific Protection Against the Human Antimicrobial Peptide LL-37 in Enterococcus faecalis*, Poster #42



Ravikanthreddy Marreddy, Texas A&M IBT, *Antimicrobial Mode of Action of Ebselen Against Clostridium difficile*, Poster #52



April Nguyen, UTHSCH, *Cardiolipin Synthase Mediates Daptomycin Resistance in Enterococcus faecalis*, Poster #53



Rudo Simeon, Texas A&M, *Engineering Protease-Stable DARPIn Inhibitors of Clostridium Difficile Toxin B*, Poster #58



Doris Taylor, BCM, *Use of a DNA-Encoded Chemical Library Approach to Identify Inhibitors For*, Poster #61



Jessica Galloway-Pena, MDACC, *Oral and Stool Microbiome Community Coalescence is Driven by Antibiotic Exposure in Acute Leukemia Patients*, Poster #66

Poster Presenters*(alphabetical order)*

First	Last	Institution	Abstract Title	Poster #
Samuel	Aitken	MDACC	<i>Microbiome and Cumulative Antibiotic use as Predictors of Stenotrophomonas Maltophilia Infection in Patients with Acute Myeloid Leukemia Receiving Remission-induction Chemotherapy</i>	1
Samuel	Aitken	MDACC	<i>Prevalence of Ceftriaxone Sensitive, Piperacillin-tazobactam Resistant Escherichia coli Bacteremia in Patients with Hematologic Malignancy</i>	33
Zain	Alamarat	UTHSCH	<i>Long Term Compassionate Use of Cefiderocol to Treat Chronic Osteomyelitis Caused by XDR-Pseudomonas aeruginosa and ESBL-producing Klebsiella pneumoniae in a Pediatric Patient</i>	34
Masaad	Almutairi	UH	<i>Clinical Outcomes of Ribotype 106 Clostridioides difficile in a Tertiary Hospital</i>	35
Faris	Alnezary	UH	<i>Indomethacin Decreases Survival in a Galleria mellonella insect Clostridioides difficile model</i>	2
Oswaldo	Alquicira	BCM	<i>A Conceptual Framework for Understanding How and Why People Take Antibiotics Without a Prescription</i>	36
Jourdan	Andersson	BCM	<i>Utilizing Host-Targeted, Immunomodulating Drugs to Combat Clostridioides difficile Infection</i>	3
Dierdre	Axell-House	BCM	<i>LiaX As A Surrogate Marker of Daptomycin Susceptibility In Multidrug-Resistant Enterococcus faecium Recovered From Cancer Patients</i>	37
Amira	Bhalodi	Accelerate Diagnostics, Inc.	<i>Improving Outcomes and Antibiotic Stewardship for Patients with Bloodstream Infections (IOAS): A Quasi-Experimental Multicenter Analysis of Time to Optimal</i>	4

Poster Presenters*(alphabetical order)*

First	Last	Institution	Abstract Title	Poster #
David	Boragine	BCM	<i>Directed Evolution of a Potent Inhibitor of the Methicillin-Resistant Staphylococcus aureus (MRSA) Resistance Enzyme, PBP2a</i>	38
Jovan	Borjan	MCACC	<i>Improved Outcomes for Cancer Patients Treated with Ceftazidime-Avibactam Versus Polymyxin-Containing Regimens for Carbapenem-Resistant Enterobacteriaceae Bacteremia</i>	5
Amy	Butcher	BCM	<i>Comparison of Pediatric Staphylococcus aureus Cervical Lymphadenitis from 2015-2018</i>	39
Nicolo	Cabrera	UTHSCH	<i>Efficacy of Ceftolozane/Tazobactam for Multidrug-Resistant Gram-Negative Infections in Multiple</i>	40
Katrina	Chan	UH	<i>Developing a Liquid Chromatography Tandem Mass Spectrometry Method for the Quantification of Amikacin in Different Biological Matrices</i>	6
Ifrah	Chaudhary	Houston Health Dept	<i>Emergence of Unusual Carbapenemase-producing Carbapenem Resistant Organisms in Houston, Texas</i>	31
Vikas	Chonira	Texas A&M	<i>Protein Engineering of Anti-TcdB DARPins with Protease Stability</i>	7
Sam	Erickson	UTHSCH	<i>The YxdJK System is a Targeted Stress Response that Mediates Specific Protection Against the Human Antimicrobial Peptide LL-37 in Enterococcus faecalis</i>	42
Selvi	Ersoy	UCLA	<i>Genetic and Phenotypic Signatures Predictive of 'Bicarbonate [NaHCO₃]-Responsiveness' and β-Lactam Sensitization Among Methicillin-Resistant Staphylococcus aureus (MRSA)</i>	8
Anthony	Flores	UTHSCH	<i>Evolution of Group B Streptococcal Capsular Type V Invasive Infections in Neonates and Young Infants: A Whole Genome Sequencing Study</i>	43

Poster Presenters*(alphabetical order)*

First	Last	Institution	Abstract Title	Poster #
Ian	Furey	BCM	<i>KPC-2 Variants Reveal Active Site Requirements for Carbapenem Hydrolysis</i>	9
Jessica	Galloway-Pena	MDACC	<i>Oral and Stool Microbiome Community Coalescence is Driven by Antibiotic Exposure in Acute Leukemia Patients</i>	66
Jessica	Galloway-Pena	MDACC	<i>Oral Mycobioime and Inter-kingdom Interactions Over the Course of Induction Therapy for Leukemia: An Observational</i>	67
Ramya	Ganiga Prabhakar	RU	<i>Demonstrate Emulsion Droplets as a Culturing Platform for Antibiotic Discovery</i>	44
Melanie	Goebel	BCM	<i>It's a Whale of a Problem: The ORCA (Organizational Readiness to Change Assessment) Highlights Differential Readiness for Antibiotic Stewardship Across</i>	45
Sarah	Gomez-Villegas	UTHSCH	<i>A New Classification Of The Staphylococcus aureus B-lactamase Based On Unique Amino Acid Sequences And Its Role in the Cefazolin Inoculum Effect</i>	46
Larissa	Grigoryan	BCM	<i>Effectiveness of Antibiotic Stewardship Intervention for Urinary Tract Infections in Primary Care: a Difference in Differences</i>	10
Larissa	Grigoryan	BCM	<i>Creating an Outpatient-Specific Antibioqram to Guide Treatment for Urinary Tract Infections</i>	56
Joseph	Hornak	UTMB	<i>Ceftaroline Combination Therapy with Daptomycin or Vancomycin for Methicillin-Resistant Staphylococcus aureus Bacteremia after Monotherapy Failure: A Single-Center Experience</i>	47
Thomas	Horvath	BCM	<i>Bioanalytical Capabilities of the Texas Children's Microbiome Center – Mass Spectrometry Laboratory (TCMC-MSL).</i>	12
Nicholas	Hummel	RU	<i>Repurposing Bioactive Compounds for Treatment of Multidrug-Resistant Pathogens</i>	65

Poster Presenters*(alphabetical order)*

First	Last	Institution	Abstract Title	Poster #
Jinhee	Jo	UH	<i>A Single-Center Surveillance Study of Cystic Fibrosis Microbiological Culture</i>	13
Allison	Judge	BCM	<i>Mapping the Determinants of Antibiotic Catalysis and Substrate Specificity of CTX-M β-lactamases</i>	14
Alex	Kang	RU	<i>Pyoverdine Production Drives Gallium Nitrate Persistence in <i>Pseudomonas aeruginosa</i></i>	15
Iordanis	Kesisoglou	UH	<i>Mathematical Modeling of Bacterial Population Size Measurements Produced by an</i>	48
Ayesha	Khan	UTHSCH	<i>Resensitization to β-lactams in Daptomycin (DAP) Resistant Enterococci is Caused by Multifaceted Penicillin-Binding Protein (PBP) Alterations and Cell Membrane (CM) Remodeling, Mediated by a Single Protein</i>	16
Julie	Kuo	UH	<i>Epidemiologic Surveillance of Carbapenem-resistant Enterobacteriaceae in a Large Academic Teaching Hospital in Houston, Texas Update 2020</i>	50
Sarah	Lach	UTHSCH	<i>Rcs Envelope Stress Response Detects and Counteracts Cationic Antimicrobial Peptides</i>	51
Shuo	Lu	BCM	<i>Development And Evaluation Of A Novel Protein-based Assay For Specific Detection Of KPC β-lactamases From <i>Klebsiella pneumoniae</i> Clinical Isolates</i>	17
Ravikanthreddy	Marreddy	Texas A&M IBT	<i>Antimicrobial Mode of Action of Ebselen Against <i>Clostridium</i></i>	52
Heer	Mehta	RU	<i>Evolution of Resistance to Doxycycline and Ciprofloxacin in the Category A Bioterrorism Agent, <i>Francisella tularensis</i></i>	18

Poster Presenters

(alphabetical order)

First	Last	Institution	Abstract Title	Poster #
María Fernanda	Mojica	Universidad El Bosque	<i>Population Structure of CTX-M-Producing Extraintestinal Pathogenic E. coli (ExPEC) from Patients with Urinary Tract Infections (UTI) and Bloodstream Infections from Colombia</i>	19
Marguerite	Monogue	UT Southwestern	<i>Evaluating the Unnecessary Use of Intravenous Broad-Spectrum Antibiotics in Presumed Sepsis and Septic Shock Patients in the Emergency Department</i>	20
April	Nguyen	UTHSCH	<i>Cardiolipin Synthase Mediates Daptomycin Resistance in Enterococcus faecalis</i>	53
Michael	Nikolaou	UH	<i>A General In Vitro Model for Simultaneous Simulation of the Dynamics of an Arbitrary Number of Drugs with Different Half-Lives</i>	21
Niels	Oppermann	Accelerate Diagnostics, Inc.	<i>Evaluation of an Updated Antimicrobial Susceptibility Testing Assay for Enterobacterales and Meropenem Directly from Positive Blood Culture on the Accelerate Pheno™ System</i>	22
Niels	Oppermann	Accelerate Diagnostics, Inc.	<i>Evaluation of Updated Antimicrobial Susceptibility Testing Assays for P. aeruginosa and Aztreonam, Ceftazidime, Cefepime, Meropenem, and Piperacillin/Tazobactam Directly from Positive Blood Culture on the Accelerate Pheno™ System</i>	54
Diana	Panesso	UTHSCH	<i>LiaF might have a an Activator role of the LiaR-Mediated Response Against daptomycin and Antimicrobial Peptides in Multidrug-Resistant Enterococcus</i>	55
Orville	Pemberton	RU	<i>Deciphering The Role of Enterococcus faecium PBP5 In The See-saw Effect</i>	23
Christine	Pybus	UT Southwestern	<i>Cefiderocol Retains Anti-Biofilm Activity in Gram-Negative</i>	24

Poster Presenters*(alphabetical order)*

First	Last	Institution	Abstract Title	Poster #
David	Reynoso	UTMB	<i>A User-Friendly QlikSense® Application To Track & Report Essential Stewardship Metrics</i>	25
Nick	Rutter	Populus Global Solutions	<i>An Academic-Information Technology Partnership to Create an Infectious Diseases Translational Science Database</i>	11
Keiko	Salazar	MDACC	<i>Countermeasures to Viral Infection Reveal Therapeutically Exploitable Bacterial Compromises</i>	49
William	Shropshire	UTHSCH	<i>Plasmidome in Co-Circulating, Carbapenem Resistant Klebsiella pneumoniae ST258 and ST307 Strains in Houston, TX</i>	26
Shelby	Simar	UTHSCH	<i>The Role of the Accessory Genome in Enterococcal Bacteremia: Results from the Vancomycin-Resistant Enterococcal Bacteremia Outcomes Study (VENOUS)</i>	57
Sabona	Simbassa	Texas A*M HSC Bryan	<i>Bacteria-Specific Drug Delivery: Hetero-multivalent Targeted Liposomes for Treatment of Pseudomonas aeruginosa</i>	27
Rudo	Simeon	Texas A&M	<i>Engineering Protease-Stable DARPin Inhibitors of Clostridium Difficile Toxin B</i>	58
Xinhao	Song	RU	<i>Using Synthetic Ecology to Explore the Evolution of Social Interactions among Streptomyces</i>	59
Zhizeng	Sun	BCM	<i>Deep Sequencing of Combinatorial Libraries Reveals the Active Site Requirements for the Function of the Colistin Resistance Enzyme MCR-1</i>	60
Adeline	Supandy	RU	<i>Comparing Mechanisms of Enterococcus Faecium and Enterococcus Faecalis' Adaptation to Daptomycin-Fosfomycin Combination Therapy</i>	28
Doris	Taylor	BCM	<i>Use of a DNA-Encoded Chemical Library Approach to Identify Inhibitors For Use of a DNA-Encoded Chemical Library Approach to Identify Inhibitors For</i>	61

Poster Presenters*(alphabetical order)*

First	Last	Institution	Abstract Title	Poster #
Austen	Terwilliger	BCM	<i>Progress on the Development of a Field-To-Practice Phage Therapy Pipeline</i>	68
Truc	Tran	UTHSCH	<i>Cardiolipin Synthase is Localized in Cell Membrane Anionic Phospholipid Microdomains in Enterococcus Faecalis</i>	29
Jennifer	Walker	UTHSCH	<i>Deposition of Host Proteins on Medical Devices Provide a Bed for MRSA Biofilms</i>	62
Jia	Wang	UTMB	<i>Identification of FDA-approved Drugs That Inhibit Survival of Mycobacterium Bovis BCG in Macrophages</i>	30
Xu	Wang	RU	<i>Development of Antivirulence Compounds Targeting Pyoverdine</i>	63
Qingbin	Yuan	RU	<i>Nano-Metal Oxides as a Switch-hitter: Killing Antibiotic Resistant Bacteria by Dissolution and Decrease Antibiotic Tolerance by Attachment</i>	41
Yue	Zhou	RU	<i>Structural and Biochemical Studies of MurAA, an Enolpyruvate Transferase that Contributes to Daptomycin Resistance in Enterococcus faecium</i>	64
Ayesha	Zuberi	MCACC	<i>Whole Genome Analysis of Antimicrobial Resistance Genotypes of Invasive Group B Streptococci in Cancer Patients</i>	32

Prevalence of Ceftriaxone Sensitive, Piperacillin-tazobactam Resistant *Escherichia coli* Bacteremia in Patients with Hematologic Malignancy

Sarah L. Spitznogle, PharmD¹; Caitlin R. Rausch, PharmD¹; Samuel A. Shelburne, MD, PhD^{2,3}; Samuel L. Aitken, PharmD^{1,3}

¹Division of Pharmacy; The University of Texas MD Anderson Cancer Center

²Department of Infectious Diseases, Infection Control, and Employee Health; The University of Texas MD Anderson Cancer Center

³Center for Antimicrobial Resistance and Microbial Genomics (CARMiG); The University of Texas MD Anderson Cancer Center

Corresponding author: Samuel L. Aitken, PharmD, Department of Pharmacy, The University of Texas MD Anderson Cancer Center, 1400 Holcombe Blvd, Houston, TX 77030, slaitken@mdanderson.org

Background

Piperacillin-tazobactam (TZP) is commonly used in the treatment of proven or suspected bacteremia in patients with hematologic malignancy. While TZP resistance is common in ceftriaxone (CRO)-resistant *E. coli* isolates, the prevalence of TZP resistance in CRO-sensitive *E. coli* in patients with hematologic malignancy is unknown. Thus, we sought to determine the prevalence of TZP resistance in *E. coli* bloodstream isolates from patients with hematologic malignancy and various CRO sensitivity phenotypes.

Methods

This is a retrospective cohort study of adult (age ≥ 18) patients with *E. coli* bacteremia on either the leukemia or stem cell transplant (SCT) services at The University of Texas MD Anderson Cancer Center (MDACC) between 8/2016 and 7/2019. Isolates were categorized according to current CLSI resistance breakpoints. A first isolate was defined as the first positive blood culture, subsequent episodes were defined as any isolate obtained at least 24 hours after the first negative blood culture.

Results

409 *E. coli* isolates were identified and 21 isolates were excluded due to unavailable TZP susceptibility data; thus, 388 *E. coli* isolates were included in the analysis. The overall prevalence of TZP resistant CRO susceptible *E. coli* was 7.7% and varied by service: 9.5% in patients with leukemia vs 3.5% in patients post SCT ($p = 0.06$). 46.9% of isolates were CRO-resistant, of which 97.1% were extended-spectrum beta-lactamase (ESBL) producers. The TZP MIC₅₀ was 4ug/ml, MIC₉₀ was 128ug/ml, with an MIC range of 3ug/ml to ≥ 256 ug/ml. Based on CRO sensitivity, the TZP MIC distribution varied significantly. In CRO-sensitive isolates the MIC₅₀ and MIC₉₀ were 4ug/ml and 64ug/ml, respectively, compared to 8ug/ml and 128ug/ml in CRO-resistant isolates ($p < 0.01$). TZP resistance was more common in CRO-resistant isolates (35.2% vs 14.6%, $p < 0.01$). Additionally, TZP resistance was more common in subsequent episodes of bacteremia than first episodes (38.3% vs 21.3%, $p = 0.02$) and, overall, 7 patients with initially TZP-sensitive isolates developed TZP resistance in their second episode.

Conclusion

TZP resistance is common in patients with hematologic malignancy and *E. coli* bacteremia, with significant variations by CRO resistance phenotype. TZP resistance becomes more common with subsequent episodes of bacteremia compared to the first. The clinical implications and genetic cause of this phenotype is currently unknown and warrants further investigation.

Microbiome and cumulative antibiotic use as predictors of *Stenotrophomonas maltophilia* infection in patients with acute myeloid leukemia receiving remission-induction chemotherapy

Samuel L. Aitken, Pranoti V. Sahasrabhojane, Dimitrios P. Kontoyiannis, Tor C. Savidge, Cesar A. Arias, Samuel A. Shelburne, Jessica R. Galloway-Peña

Corresponding author: Samuel L. Aitken, PharmD, Department of Pharmacy, The University of Texas MD Anderson Cancer Center, 1400 Holcombe Blvd, Houston, TX 77030, slaitken@mdanderson.org

Background: *S. maltophilia* infections are increasingly common in patients with acute myeloid leukemia (AML) and associated with high mortality. *S. maltophilia* is a frequent colonizer in AML patients but relatively little is known about factors that drive *S. maltophilia* infection. We sought to evaluate the utility of cumulative antibiotic use and the microbiome as predictors of *S. maltophilia* infection in AML patients receiving remission induction chemotherapy (RIC).

Methods: We performed a subanalysis of a prospective, observational cohort study between 9/2013 and 8/2015 of adult patients with AML receiving RIC. In this study, fecal and oral microbiome samples collected every 96 hours from the start of RIC until neutrophil recovery were assessed for the relative abundance of *S. maltophilia* via 16s rRNA quantitation. The primary outcome, microbiologically proven *S. maltophilia* infection, was analyzed using a time-varying Cox proportional hazards model accounting for *S. maltophilia* relative abundance and cumulative antibiotic exposure. Patients were censored at neutrophil recovery or death.

Results: 90 patient were included, of whom 8 (9%) developed *S. maltophilia* infection (pneumonia, n=6; skin/soft-tissue infection, n=2). 4/8 (50%) patients were bacteremic. 7/8 (88%) patients with *S. maltophilia* infection had detectable oral 16s oral reads mapping to *S. maltophilia* vs 22/82 (27%) without infection ($p < 0.01$). An oral *S. maltophilia* relative abundance of 36% predicted infection (sensitivity: 96%, specificity 93%, likelihood ratio +: 17.08). No association of *S. maltophilia* infection with the fecal relative abundance was seen. Cumulative meropenem exposure was associated with increased infection risk (hazard ratio [HR] 1.17, 95% CI 1.01 – 1.35, $p = 0.03$), while levofloxacin was associated with decreased infection risk (HR 0.83, 95% CI 0.66 – 1.04, $p = 0.10$).

Conclusions: The oral microbiome may play an important role in *S. maltophilia* pathogenesis in AML patients. Cumulative antibiotic exposure likely modifies *S. maltophilia* infection risk. These data suggest that real-time molecular monitoring of the oral cavity for *S. maltophilia* in AML patients could identify patients at high risk for *S. maltophilia* infection and improve targeted therapy.

Funding: None

Long Term Compassionate Use of Cefiderocol to Treat Chronic Osteomyelitis Caused by XDR-*Pseudomonas aeruginosa* and ESBL-producing *Klebsiella pneumoniae* in a Pediatric Patient

Zain I. Alamarat^a, Jessica Babic^b, Truc T. Tran^c, Susan H. Wootton^a, An Q. Dinh^c, William R. Miller^{c,d}, Blake Hanson^{c,d}, Audrey Wanger^f, Joshua L. Gary^g, Cesar A. Arias^{c,d,e}, Norma Pérez^{a#}

^aDepartment of Pediatrics, Division of Pediatric Infectious Diseases, UTHealth, McGovern Medical School, Houston, TX

^bDepartment of Pharmacy, Memorial Hermann Texas Medical Center, Houston, TX

^cDivision of Infectious Diseases and Center for Antimicrobial Resistance and Microbial Genomics (CARMiG), UTHealth, McGovern Medical School, Houston, TX

^dCenter for Infectious Diseases, UTHealth, School of Public Health, Houston, TX.

^eMolecular Genetics and Antimicrobial Resistance Unit and International Center for Microbial Genomics, Universidad El Bosque, Bogota, Colombia

^fDepartment of Pathology and Laboratory Medicine, UTHealth, McGovern Medical School, Houston, TX

^gDepartment of Orthopaedic Surgery, UTHealth, McGovern Medical School, Houston, TX

Corresponding Author: Norma Pérez, Department of Pediatrics, Division of Pediatric Infectious Diseases, UTHealth, McGovern Medical School, Houston, TX

Address correspondence to norma.perez@uth.tmc.edu

ABSTRACT

We report a 15 year-old Nigerian adolescent male with chronic osteomyelitis caused by extensively drug-resistant (XDR) *Pseudomonas aeruginosa* ST773 carrying bla_{NDM-1} and an extended spectrum β -lactamase (ESBL)-producing *Klebsiella pneumoniae*. The patient developed neurological side effects in the form of circumoral paresthesia with polymyxin B and asymptomatic elevation of transaminases with aztreonam (used in combination with ceftazidime/avibactam). Cefiderocol treatment for 14 weeks plus bone implant resulted in apparent cure and avoided amputation.

Clinical Outcomes of Ribotype 106 *Clostridioides difficile* in a Tertiary Hospital

Almutairi MS, Gonzales-Luna AJ, Alam MJ, Fallatah SB, Alnezary FS, Begum K, Garey KW

Department of Pharmacy Practice and Translational Research, University of Houston College of Pharmacy

Corresponding author: Masaad Almutairi, Department of Pharmacy Practice and Translational Research, University of Houston College of Pharmacy, 4849 Calhoun Rd #3044, Houston, TX, E-mail: malmutai3@central.uh.edu

Introduction: *Clostridioides difficile* is an anaerobic, Gram-positive bacillus that causes gastrointestinal infection with symptoms ranging from diarrhea to life-threatening colitis. *C. difficile* ribotype (RT) 106 has been identified as one of the most prevalent isolates in the United States, yet there are few studies regarding its associated clinical outcomes. It has been shown to produce more spores than several other ribotypes, which we hypothesized may lead to higher rates of recurrence than seen with other ribotypes. This study aimed to study clinical outcomes associated with *C. difficile* infection (CDI) caused by ribotype 106, including severity of disease, mortality rate, and recurrence rate.

Methods: We conducted a descriptive, retrospective study of patients infected with *C. difficile* RT 106 at a single center in Houston, Texas between 2016 and 2018. Isolates were ribotyped using fragment analysis PCR, and a convenience sample was selected for inclusion in this study. Minimum inhibitory concentrations (MICs) were tested against four clinically relevant antibiotics using broth microdilution and measured at 48 hours. Electronic medical records were reviewed for demographic data, laboratory values, exposure to several risk factors, recurrence rate, and mortality. Severity of disease was calculated using definitions provided in the 2017 Infectious Disease Society of America (IDSA)/Society for Healthcare Epidemiology of America (SHEA) guidelines.

Results: A total of 29 patients were included with a mean age of 64 (± 19) years old. The majority were female (n=15, 52%) and 66% (n=19) were white. Fifty-two percent of the population was classified as having severe CDI. The MICs for vancomycin, eravacycline, metronidazole and fidaxomicin were tested, and the medians (IQRs) were 2 $\mu\text{g}/\text{ml}$, (2-4) 1 $\mu\text{g}/\text{ml}$ (1-1), 0.25 $\mu\text{g}/\text{ml}$ (0.125-0.5), and 0.065 $\mu\text{g}/\text{ml}$ (0.03125-0.0625), respectively. Eleven isolates showed a vancomycin MIC $> 2\mu\text{g}/\text{ml}$. Most patients experienced an initial clinical cure, with 74% of patients experiencing resolution of *C. difficile* symptoms by day 6 of treatment and 78% with complete resolution of symptoms by day 14. The 30-day CDI recurrence rate was 10%, while the 90-day recurrence rate was 17%. The 30-day mortality rate was 10%, and no additional deaths were observed following day 30.

Conclusion: In our small, single-center, convenience sample, patients infected with *C. difficile* RT 106 demonstrated similar recurrence rates to those reported in the literature with other ribotypes. Approximately half of the patients experienced a severe episode of CDI, with 10% of infections resulting in death within 30-days of infection. Although this represents the first clinical outcomes study dedicated to *C. difficile* RT 106, larger, comparative studies are needed to help elucidate consequences of its widespread dissemination.

Keywords. *Clostridioides difficile*, Ribotype 106

Poster #35

Disclosure: No relevant financial relationship exists.

Indomethacin Decreases Survival in a *Galleria mellonella* insect *Clostridioides difficile* model

Alnezary FS, Alam MJ, Almutairi MS, Fallatah SB, Loveall C, Lancaster C, Gonzales-Luna AJ, Garey KW

Department of Pharmacy Practice and Translational Research, University of Houston College of Pharmacy

Corresponding author: Faris Alnezary, Department of Pharmacy Practice and Translational Research, University of Houston College of Pharmacy, 4849 Calhoun Rd #3044, Houston, TX, E-mail: falnezar@central.uh.edu

Introduction: *Clostridioides difficile* infection (CDI) is an urgent public health threat worldwide. Previous experimental rodent studies have shown that the use of nonsteroidal anti-inflammatory drugs (NSAIDs) is associated with enhanced severity of CDI. *Galleria mellonella* provides an invertebrate model that is inexpensive, easy to maintain, and does not require specialized equipment. This study investigated the feasibility of using *G. mellonella* as a surrogate insect model to evaluate the effect of NSAIDs on CDI severity and survival.

Methods: *G. mellonella* larvae were gavaged with 1×10^6 - 8 colony forming units (CFU) of using two *C. difficile* ribotype 027 strains (R20291 and CD 196) and one ribotype 014-020 strain (MT-5313). Larvae were infected with or without (control) pretreatment via gavage with indomethacin (5 μ g/larva) 24 hours prior to *C. difficile* inoculation. At least 10 larvae were used for each experiment. After inoculation, the larvae were kept at 37°C post-infection and monitored daily for 120 hours for activity, extent of cocoon formation/growth, melanization, and survival.

Results: Seventeen of thirty (57%) control larvae survived compared to 6 of 30 (20%) given indomethacin ($p=0.0002$). For individual *C. difficile* strains, the survival rates in control larvae were 50% and 45% for ribotype 027 strains and 65% for the ribotype 014-020 strain. Survival with indomethacin-treated larvae decreased to 15%, 15%, and 25%, respectively.

Conclusion: Indomethacin increased mortality in a *G. mellonella* CDI model. This high-throughput insect model could complement and expand upon other vertebrate models of CDI.

Keywords. *Galleria mellonella*, indomethacin, *Clostridioides difficile*

Disclosure: No relevant financial relationship exists.

A Conceptual Framework for Understanding How and Why People Take Antibiotics Without a Prescription

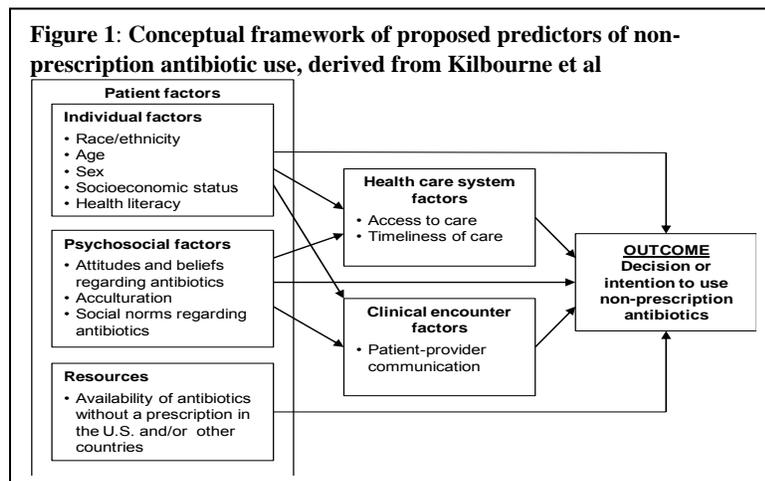
Osvaldo Alquicira¹, Barbara W. Trautner^{2,3}, Susan Nash¹, Juanita Salinas¹, Melanie Goebel,⁴ and Larissa Grigoryan¹

1. Department of Family and Community Medicine, Baylor College of Medicine, 3701 Kirby Drive, Houston, TX 77098 (Corresponding Author Address *)
2. VA Center for Innovations in Quality, Effectiveness and Safety (IQuEST), Michael E. DeBakey Veterans Affairs Medical Center, Houston, TX
3. Section of Health Services Research, Departments of Medicine and Surgery, Baylor College of Medicine, Houston, TX
4. Section of Infectious Diseases, Department of Medicine, Baylor College of Medicine, Houston, TX

*Corresponding Author: Osvaldo Alquicira¹, E-mail:Osvaldo.Alquicira@bcm.edu

Objectives: The prevalence of non-prescription antibiotic use in the U.S. varies from 5% among socioeconomically and ethnically diverse primary care patients to 66% among Latino migrant workers. Respondents obtained antibiotics from stores or flea markets in the U.S., friends or relatives, and leftover antibiotics from previous prescriptions. This unsafe practice may lead to increased antibiotic resistance. As groundwork to develop an intervention to decrease non-prescription use, we mapped reported drivers of non-prescription use to the Kilbourne conceptual framework for advancing health disparities research.

Methods: The Kilbourne framework consists of three phases: detection of health disparities and identification of vulnerable populations, understanding why disparities exist, and reducing disparities through interventions. We focused on the first two phases and mapped the identified drivers of non-prescription use onto the key domains of the Kilbourne conceptual framework: patient, health care system, and clinical encounter factors. We also conducted brief field research to explore anecdotal reports regarding availability of non-prescription antibiotics in our community.



Results: Figure 1 shows the proposed factors that may directly or indirectly predict non-prescription antibiotic use based on published studies. Key potential factors are individual factors, psychosocial factors, resources, healthcare system factors, and clinical encounter factors. The relevance of resources (availability) to non-prescription use was supported by our research team’s purchase of amoxicillin, tetracycline and metronidazole without prescriptions from a flea market in

Houston, TX.

Conclusions: The Kilbourne conceptual framework provides a strong, comprehensive basis for research and intervention in the challenging problem of non-prescription use. Our current research will test the proposed relationships between patient, health care system and clinical encounter factors and non-

prescription use. We are conducting a survey among indigent and insured patient populations to identify the relative importance of these factors and validate our proposed framework of non-prescription use.

Funding Source: This project was supported by grant number R01HS026901 from the Agency for Healthcare Research and Quality. The content is solely the responsibility of the authors and does not necessarily represent the official views of the Agency for Healthcare Research and Quality.

Utilizing Host-Targeted, Immunomodulating Drugs to Combat *Clostridioides difficile* Infection

Andersson JA^{1,2,3}, Peniche AG⁴, Galindo CL⁵, Boonma P⁶, Sha J³, Luna RA^{1,2}, Savidge TC^{1,2}, Chopra AK³, Dann SM³

1. Department of Pathology and Immunology, Baylor College of Medicine, 2. Texas Children's Microbiome Center, Texas Children's Hospital, 3. Department of Microbiology and Immunology, University of Texas Medical Branch, 4. Department of Internal Medicine, University of Texas Medical Branch, 5. Division of Cardiology, Vanderbilt University Medical Center, 6. Faculty of Medicine, King Mongkut's Institute of Technology

Corresponding Author: Jourdan A. Andersson, Department of Pathology and Immunology, Baylor College of Medicine; Texas Children's Microbiome Center, Texas Children's Hospital, 1102 Bates Avenue, Houston, TX, Email: jourdan.andersson@bcm.edu

Clostridioides difficile is the leading cause of antibiotic-associated colitis. With limited therapeutic options currently available and high rates of recurrence, the need to develop new treatment options is urgent. Previously, we utilized a drug repurposing approach and identified 3 drugs, amoxapine (AXPN, anti-depressant), doxapram (DXP, breathing stimulant), and trifluoperazine (TFP, anti-psychotic), with efficacy in mouse models across a broad range of human pathogens. However the protective mechanism(s) of action of these drugs remained unknown. Utilizing a murine model of lethal CDI, we evaluated the efficacy of AXPN, DXP, and TFP as standalone therapy and found that all three drugs offered mice partial protection. While treatment with each drug resulted in reduced *C. difficile* burden and toxin production *in vivo*, the drugs were found to not be bacteriostatic or bactericidal. Additionally, drug treatment had little influence on microbiota composition and did not restore antibiotic and infection induced dysbiosis. Interestingly, drug efficacy was dependent on the presence of the microbiota, indicating crosstalk between the microbiota and immune system may be responsible for drug-mediated protection. Subsequent RNA-seq analysis revealed shared enhancement of innate immune responses, including promotion of neutrophil recruitment, upregulation of *IL33*, and activation of the IL-22 signaling pathway. Focusing on AXPN, we demonstrate that neutralization of IL-33 or depletion of neutrophils results in a loss of drug efficacy. Overall, this data indicates that drug efficacy is related to elicitation of a controlled immune response that effectively combats infection without causing collateral host damage. This data also provides further support of the early influx of neutrophils as well as upregulation of IL-33 being protective against severe CDI.

This work was supported by: NIH R56 grant AI132682 (to AKC and SMD); Pilot Awards from the UTMB Institute for Human Infections and Immunity (to SMD and AKC) and John S. Dunn Foundation (to AKC and TCS); and NIAID U01-AI124290, NIDDK P30-DK56338 and Texas Children's Hospital (to TCS). JAA was supported in part by the Jeane B. Kempner Postdoctoral Fellowship and the Texas Medical Center Training Program in Antimicrobial Resistance T32, NIH grant T32-AI141349.

LiaX As A Surrogate Marker of Daptomycin Susceptibility In Multidrug-Resistant *Enterococcus faecium* Recovered From Cancer Patients

Axell-House DB¹, Khan A², Shelburne SA³, Shamooy Y⁴, Tran TT⁵, Arias CA^{5,6}

1. Department of Infectious Diseases, Baylor College of Medicine
2. McGovern Medical School, University of Texas Health Science Center
3. Department of Infectious Diseases, The University of Texas MD Anderson Cancer Center
4. Institute of Biosciences and Bioengineering, Rice University
5. Center for Antimicrobial Resistance & Microbial Genomics, University of Texas Health Science Center
6. Center for Infectious Diseases, University of Texas School of Public Health

Corresponding Author: Dierdre Axell-House, Department of Infectious Diseases, Baylor College of Medicine, One Baylor Plaza, Houston, TX. Email: axellhou@bcm.edu

Background: Vancomycin-resistant *Enterococcus faecium* (VRE_{fm}) are leading causes of bloodstream infections (BSI) in patients with hematological malignancies. Daptomycin (DAP) is commonly used to treat VRE BSI, but rates of DAP non-susceptibility (DAP-NS) in this population are reported up to 20-40%. Current DAP minimum inhibitory concentration (MICs) have poor reproducibility. We recently reported that LiaX is a key effector of the LiaFSR cell membrane stress response pathway triggered by DAP. LiaX is novel extracellular protein released to the milieu upon exposure to DAP, functioning as an *in situ* regulator of the membrane response. LiaX also serves as a sentinel molecule detecting the presence of DAP and antimicrobial peptides, such as LL-37 in *E. faecalis*. We postulated that detection of extracellular LiaX correlates with DAP non-susceptibility in clinical strains of VRE_{fm}

Methods: We initially used six well-characterized VRE_{fm} BSI isolates (two DAP-S, four DAP-NS) as reference strains to optimize a whole-cell indirect enzyme-linked immunosorbent assay (ELISA) method for LiaX detection. We assessed limit of detection and reproducibility of the ELISA LiaX method. Subsequently, we applied the method to 57 clinical VRE_{fm} BSI isolates from patients with cancer to perform a validation stage. Broth microdilution (BMD) was used to determine DAP MICs for all isolates. Colony forming units per ELISA well were calculated to control ELISA A₄₀₅ readings for organism quantity.

Results: The six reference strains demonstrated high reproducibility with coefficient of variation between separate assays of <15%. The ELISA showed excellent detection of ~10⁸ CFUs per well, within the tested limits of detection of 10⁶ and 10⁹ CFUs per well. All DAP-NS reference strains had increased detection of LiaX (p<0.0001) compared to DAP-S reference strains. In the 57 isolates used for validation, six were DAP-NS by BMD MIC, a prevalence of 10.5% (95% CI: 4.4-22.2%). The LiaX test and MIC had categorical agreement on 56% of isolates. Of the isolates with categorical disagreement, 19 isolates were susceptible by MIC but non-susceptible by LiaX ELISA, and 5 isolates were non-susceptible by MIC but susceptible by LiaX ELISA.

Conclusions: Detection of extracellular LiaX has important discrepancies with routine DAP MIC and may be a more accurate marker of the DAP-mediated cell membrane response to DAP. Further characterization of the discrepant isolates by time-kill assays is warranted to fully validate the performance of LiaX ELISA, and has the potential to replace MICs in routine clinical practice.

Funding: NIH/NIAID R01AI134637, K24AI121296 to CAA

Improving Outcomes and Antibiotic Stewardship for Patients with Bloodstream Infections (IOAS): A Quasi-Experimental Multicenter Analysis of Time to Optimal Therapy

Bhalodi AA¹, MacVane SH¹, Morgan MA², Ben-Aderet MA³, Madhusudhan M⁴, Kolev J³, Dare RK⁵, Rosenbaum ER⁶, Wolfe K⁵, Ford B⁷, Dilek I⁸, Kinn PM⁹, Percival KM⁹, Humphries RM¹.

¹Scientific Affairs, Accelerate Diagnostics Inc

²Department of Pathology and Laboratory Medicine, Cedars-Sinai Medical Center

³Department of Medicine, Cedars-Sinai Medical Center

⁴Department of Hospital Epidemiology, Cedars-Sinai Medical Center

⁵Department of Internal Medicine, University of Arkansas for Medical Sciences

⁶Department of Pathology, University of Arkansas for Medical Sciences

⁷Department of Pathology, University of Iowa Hospitals and Clinics

⁸Department of Internal Medicine, University of Iowa Hospitals and Clinics

⁹Department of Pharmaceutical Care, University of Iowa Hospitals and Clinics

Corresponding author: Amira A Bhalodi, Scientific Affairs, Accelerate Diagnostics, Inc. 3950 South Country Club Road #470, Tucson, AZ Email: abhalodi@axdx.com

Objective: Measuring impact of diagnostic technologies on patient care can be complex. Effect of antibiotic optimization for patients with bloodstream infections (BSI) was evaluated in the Accelerate PhenoTest™ BC kit (AXDX) registry program, with emphasis on time to optimal therapy (TTOT).

Methods: This multicenter, quasi-experimental study compares clinical and antimicrobial stewardship metrics, prior to and after implementation of AXDX, to evaluate the impact this technology has on patients with BSI. Laboratory and clinical data from hospitalized patients with BSI (excluding contaminants) were compared between two groups, one that underwent testing on AXDX (post-AXDX) and one that underwent alternative microorganism identification and susceptibility testing (pre-AXDX). Interim analysis of data collected from 3 centers was performed. Pre-AXDX methods for each of the 3 sites were: Verigene®, MALDI-TOF MS, and BD Phoenix™ at Hospital A; MALDI-TOF MS and VITEK® 2 at Hospital B; and MALDI-TOF MS, VITEK® 2, and Sensititre™ at Hospital C. All institutions had active antimicrobial stewardship programs throughout the study period. Primary outcome was TTOT; multiple linear regression analysis was performed to identify clinical factors associated with TTOT.

Results: 407 patients with BSI (208 pre-AXDX, 199 post-AXDX) were included in this analysis. Patient demographics, comorbidities, and severity of illness (median Pitt bacteremia score of 2) were similar between groups, as were distributions of gram negative (~60%), gram positive (~30%), and polymicrobial (~10%) BSI. The most prevalent gram-negative and gram-positive organisms were *E. coli* and *S. aureus*, respectively. Median TTOT was 41.7 hours (interquartile range [IQR], 19.2-71.4) in the pre-AXDX group and 28.9 hours (IQR, 13.3-51.4) in the post-AXDX group (P=0.02). Independent factors associated with shorter TTOT were BSI with AXDX on-panel organisms (P=0.002), absence of intravenous vasopressors (P=0.01), and post-AXDX group (P=0.05).

Conclusion: Implementation of AXDX improves antimicrobial stewardship in patients with BSI reducing both TTOT and unnecessary antimicrobial exposure.

Directed Evolution of a Potent Inhibitor of the Methicillin-Resistant *Staphylococcus aureus* (MRSA) Resistance Enzyme, PBP2a

Boragine D¹, Adamski C¹, Mehta S², Palzkill T^{1,2}

1. Department of Biochemistry and Molecular Biology, Baylor College of Medicine
2. Department of Pharmacology and Chemical Biology, Baylor College of Medicine

Corresponding Author: Timothy Palzkill, Department of Pharmacology and Chemical Biology, Baylor College of Medicine, One Baylor Plaza, Houston, Tx, timothy@bcm.edu

Abstract:

Antibiotic resistance has manifested into a global health epidemic. One of the most widespread human pathogens, Methicillin-resistant *Staphylococcus aureus* (MRSA) encodes a novel penicillin-binding-protein, PBP2a. Production of PBP2a by MRSA confers resistance to nearly all β -lactam antibiotics by continued peptidoglycan cell wall synthesis, even at high concentrations of antibiotic. The transpeptidase domain of PBP2a shares structural homology with class A β -lactamases, bacterial enzymes that inactivate β -lactam antibiotics. Class A β -lactamases, such as TEM-1, are inhibited by protein-based inhibitors named β -lactamase inhibitory proteins (BLIPs) and BLIP-II potently inhibits TEM-1 with a K_D 0.48pM. It was previously found that BLIP-II also weakly binds to PBP2a in the low micromolar range (K_D 1.5 μ M), in contrast to BLIP-II's potent inhibition of TEM-1. We hypothesize that through directed evolution, we can re-engineer BLIP-II for altered specificity to potently bind PBP2a. A directed evolution approach using phage display affinity selection was used to identify a BLIP-II double mutant, N50A:Y113H, that enhanced the binding affinity to PBP2a 30-fold to a K_D of 50nM. An additional directed evolution cycle, starting with the tighter binding BLIP-II^{N50A:Y113H} template, was then performed to select for PBP2a binding while driving the binding affinity down to low nanomolar range. To date, we have identified several BLIP-II^{N50A:Y113H} mutants that exhibit an additional ~3-5-fold enhancement in binding affinity to PBP2a and have also identified a G205W mutant that improved binding an additional 50-fold with a K_D ~1nM. This is a >1,000-fold enhancement in binding affinity to PBP2a compared to wild-type BLIP-II. However, the BLIP-II^{N50A:Y113H} mutants resulted in >5,000-fold loss in binding to TEM-1, K_i 0.09nM, thereby indicating a change in selectivity compared to wild-type BLIP-II. Each BLIP-II mutant resulted in enhanced binding affinity to PBP2a, while simultaneously weakening the binding affinity to TEM-1. Thus, the evolved BLIP-II variants have shifted from high affinity for β -lactamases and low affinity towards PBPs, towards high affinity for PBPs with reduced affinity for β -lactamases. These results suggest that BLIP-II can be further optimized and serve as a scaffold for developing potential PBP2a inhibitors.

Funding by:

NIH RO1 AI32956-25 to TP

Gulf Coast Consortia: HAMBP T32 GM008280-29 to DB

Improved outcomes for cancer patients treated with ceftazidime-avibactam versus polymyxin-containing regimens for carbapenem-resistant *Enterobacteriaceae* bacteremia

Borjan J¹, Shelburne SA^{2,3}, Bhatti MM⁴, Aitken SL^{1,3}

1. Division of Pharmacy, The University of Texas MD Anderson Cancer Center, Houston, TX, USA.
2. Department of Infectious Diseases, Infection Control, and Employee Health, The University of Texas MD Anderson Cancer Center, Houston, TX, USA.
3. Center for Antimicrobial Resistance and Microbial Genomics (CARMiG), UTHealth McGovern Medical School, Houston, TX, USA.
4. Department of Laboratory Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX, USA

Objective

Outcomes are improved with ceftazidime-avibactam (CZA) compared to polymyxin-based regimens (PBR) for carbapenemase-producing carbapenem-resistant *Enterobacteriaceae*. It is unclear if this finding is true in non-carbapenemase (non-CP) producing CRE. The purpose of this study was to compare the efficacy and safety of CZA-based and PBR for CRE bacteremia in cancer patients with a high prevalence of non-CP CRE.

Methods

Adult cancer patients with first occurrence of CRE (i.e., meropenem non-susceptible) bacteremia treated with either CZA or PBR as directed therapy were included. Day 14 integrated benefit-risk outcomes based on desirability of outcome ranking (DOOR; 1 - cured and discharged home, 2 - cured and hospitalized, 3 - cured and hospitalized with renal failure, 4 - not cured, 5 - dead) were used. DOOR is a recently developed statistical approach designed to unify important patient and clinician outcomes. Inverse probability of treatment weighting (IPTW) ordered logistic regression was used to model the odds of moving down ranked DOOR categories (i.e., having a worse outcome). The probability of a patient treated with CZA or a PBR having a worse DOOR category was also calculated. IPTW logistic regression was used to model the odds of 14-day mortality.

Results

43 patients (CZA, n = 24; PBR, n = 19) with similar demographics and relative illness were included. *Klebsiella pneumoniae* (n = 21) and *Escherichia coli* (n = 16) were most common. 16/43 (37%) were CP CRE, 19/43 (44%) were non-CP CRE, and the remainder were unknown. The probability of a better DOOR for patients treated with CZA was 58% (95% CI 53% - 62%). Patients treated with CZA had an 81% reduction in IPTW-adjusted odds of a worse DOOR (OR 0.19, 95% CI 0.05 – 0.76; p = 0.02). 14-day mortality was 2/24 (8%) for patients receiving CZA vs 5/19 (26%) for patients treated with PBR (IPTW-adjusted OR 0.12, 95% CI 0.02 – 0.82, p = 0.03).

Conclusion

These data suggest that CZA-based treatment, compared to PBR, has a superior integrated benefit-risk profile for the treatment of CRE bacteremia in cancer patients with a high burden of non-CP CRE. These

Poster #5

findings build upon available data and suggest that CZA is preferred to PBR for CRE with heterogenous resistance mechanisms.

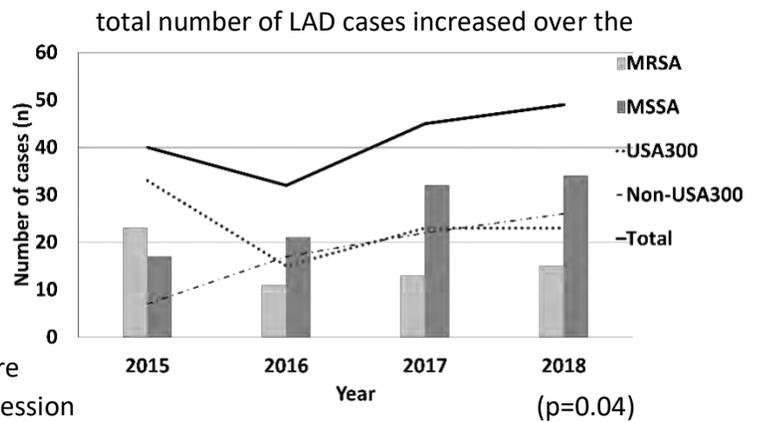
Comparison of Pediatric *Staphylococcus aureus* Cervical Lymphadenitis from 2015-2018

Butcher A1, Funck A1, Sommer L1,2, Lamberth LB2, Vallejo JG1,2, Kaplan SL1,2, Hultén, KG 1,2. 1. Department of Pediatrics, Baylor College of Medicine 2. Infectious Disease Section, Texas Children’s Hospital.

Objectives: Methicillin resistant *S. aureus* (MRSA) is declining as a cause of both invasive and skin and soft tissue infections at Texas Children’s Hospital (TCH) while increasing clindamycin resistance has been observed among both MRSA and methicillin susceptible SA (MSSA). This study was designed to describe the patient and *S. aureus* isolate characteristics associated with cervical lymphadenitis (LAD) cases at Texas Children’s Hospital from 2015-2018.

Methods: Cases were identified from an ongoing surveillance study on *S. aureus* in which patients and isolates were prospectively identified and added to a database. Patients <18 years old with *S. aureus* LAD and available isolates from 2015-2018 were identified. Chart review was performed. The patient isolates were characterized by pulsed-field gel electrophoresis (USA300 vs. non-USA300), *agr* group (I-IV), and analyzed for presence of *pvl* (*lukSF-PV*). Antimicrobial susceptibilities were obtained. Statistical analysis was performed using STATA11. A $p < 0.05$ was considered statistically significant. This study was approved by the Institutional Review Board at Baylor College of Medicine.

Results: A total of 166 patients with cervical chain lymph node isolates were identified; 104 (62.7%) were MSSA and 94 (56.6%) were USA300. The study period due to an increase of MSSA infections ($p=0.001$). 73.5% of patients had no underlying conditions and 86.7% were community acquired infections ($n=144$, 86.7%). MRSA (vs. MSSA) infections were associated with fever ($p=0.01$) and higher absolute neutrophil count (ANC) ($p=0.008$). Patients with USA300 LAD (vs. non-USA300 LAD) had higher ANC counts ($p < 0.0001$) and more frequently displayed internal jugular vein compression on ultrasound.



The majority (74.7%) of isolates were *agr* group I and *pvl* was present in 63.9% of the isolates. Clindamycin resistance (CR) was 19.9% (18% MLS_B resistance) with 24% CR among MSSA vs. 12.9% CR among MRSA. The majority of patients had surgical incision and drainage ($n=154$, 92.8%) and were started on empiric clindamycin ($n=111$, 66.9%) or clindamycin plus another agent ($n=36$, 21.7%). All patients with CR isolates were switched to an alternative antibiotic. There were 11 documented recurrences, 4 of which had US-guided needle aspiration as part of their treatment.

Conclusions: MSSA caused the majority of *S. aureus* cervical LAD at TCH. USA300 isolates caused more compressive and inflammatory findings. CR was greater among MSSA isolates which are increasing as a cause of LAD infections. Given the high CR rate, clindamycin may not be the optimal choice for the empiric treatment of LAD infections in this patient population.

Poster #39

Funding: No funding to disclose

Efficacy of Ceftolozane/Tazobactam for Multidrug-Resistant Gram-Negative Infections in Multiple Urban Hospitals

Nicolo L. Cabrera^{1,2}, Truc T. Tran^{1,3}, Anne Gonzales-Luna^{4,5}, Travis Carlson⁶, Faris Alnezary^{4,5}, William R. Miller^{1,3}, An Q. Dinh^{1,3}, Blake Hanson⁷, Jose M. Munita^{3,8}, Samuel A. Shelburne², Samuel L. Aitken², Kevin W. Garey^{4,5}, Laura Puzniak⁹, Cesar A. Arias^{1,3,7}

¹Department of Internal Medicine and ³Center for Antimicrobial Resistance and Microbial Genomics, University of Texas Health Science Center McGovern Medical School, Houston, Texas

²University of Texas MD Anderson Cancer Center, Houston, Texas

⁴CHI St. Luke's Health-Baylor St. Luke's Medical Center, Houston, Texas

⁵University of Houston College of Pharmacy, Houston, Texas

⁶High Point University, High Point, North Carolina

⁷Center for Infectious Diseases, University of Texas Health Science Center School of Public Health, Houston, Texas

⁸Genomics and Resistant Microbes Group, Universidad del Desarrollo, Santiago, Chile

⁹Merck & Co., Inc.

Corresponding Author: Nicolo L. Cabrera, Department of Internal Medicine, University of Texas Health Science Center McGovern Medical School, 6431 Fannin St, Houston, Texas, Email: Nicolo.L.Cabrera@uth.tmc.edu

Background: Ceftolozane/tazobactam (C/T) is a novel cephalosporin/beta-lactamase inhibitor combination developed for use against multidrug-resistant (MDR) Gram-negative infections, particularly *Pseudomonas aeruginosa* (PA). C/T is approved for complicated urinary tract and intraabdominal infections as well as hospital-acquired/ventilator-associated bacterial pneumonias. However, comprehensive clinical characterization of patients treated with C/T in non-FDA-approved indications is limited.

Materials/methods: Patients ≥ 18 years who received C/T for ≥ 48 hours while hospitalized in 9 acute care centers in Houston, TX from January 2016 through September 2018 were included. Demographic, microbiologic, treatment and clinical outcome data were retrospectively collected by chart review. In patients who received multiple inpatient courses of C/T, only the first course with C/T was assessed.

Results: 210 patients met inclusion criteria: 58% were non-white, 35% were female and 13% were immunocompromised. Median age was 61 years (IQR, 48 to 69). Median Charlson comorbidity index was 5 (IQR, 2 to 6). At the onset of the index episode, a significant proportion of patients required intensive care unit admission (44%), mechanical ventilation (37%) and pressor support (22%). Respiratory sources were the most common (50%) followed by urine (15%). Positive cultures were documented in 93% of the cases and PA was found in 86%. Majority (95%) of PA which were MDR. C/T use was guided by susceptibility testing of the index isolate in ca. 52%. In 5.7% of cases, C/T was used to escalate therapy without any documented C/T-susceptible organism. Half (51%) of the cohort received initial dosing appropriate for renal function while 36% receiving a lower than recommended dose. Clinical success (i.e., recovery from infection-related signs and symptoms) occurred in 77%. The in-hospital mortality rate in our cohort was 15% with 26 of 31 deaths deemed infection-related.

Conclusions: We report a large multicenter observational cohort that received C/T. A 77% clinical success with the use of C/T was documented. These data support the use of C/T in critically ill patients infected with MDR PA.

Developing a Liquid Chromatography Tandem Mass Spectrometry Method for the Quantification of Amikacin in Different Biological Matrices

Chan K¹, Wang W¹, Ledesma K², Yin T¹, Tam VH^{1,2}

¹Department of Pharmacological and Pharmaceutical Sciences, University of Houston

²Department of Pharmacy Practice and Translational Research, University of Houston

Corresponding author: Vincent H. Tam, Department of Pharmacy Practice and Translational Research, University of Houston, 4849 Calhoun Road, Houston, TX, E-mail: vtam@uh.edu

Objectives: Amikacin is an antibiotic from the aminoglycoside class which are used to treat gram-negative multi-drug resistant bacterial infections. Conventional quantification assays such as immunoassays do not provide satisfactory specificity or sensitivity (1-3 ug/mL). Such assays have limited reliability because the antibodies used may bind to compounds with similar chemical structures. In contrast, chromatographic assays coupled with mass spectrometry can separate and identify structurally similar compounds. Additionally, mass spectrometry used with different ion modes can significantly expand the detectable range of quantification.

Methods: A Waters UPLC Acquity™ liquid chromatography system coupled with an API 5500 QTrap Triple-Quadrupole mass spectrometer were used to develop this assay. An Acquity™ UPLC BEH C18 column (2.1 x 150 mm, internal diameter, 1.7 μm) was used with the mass spectrometer. For the aqueous mobile phase, 60 mM ammonium hydroxide in water was prepared. For the organic mobile phase, a similar concentration of ammonium hydroxide was prepared in acetonitrile. To optimize the quantifiable range of different biological matrices, both positive and negative ion modes were tested and optimized. To prepare cell lysate samples, protein precipitation by acetonitrile was used. To prepare serum samples, solid phase extraction was used. Tobramycin was used as the internal standard.

Results: The assay was able to quantify lower concentrations of amikacin in positive mode (0.016 - 8 μg/mL) and higher concentrations of amikacin in negative mode (0.25 – 80 μg/mL). In positive mode, while the range is narrower, the ability to detect such low concentrations of amikacin is ideal for cell lysate samples. In negative mode, while the lower limit is higher, the ability to detect in a broader range is ideal for serum samples. The assay was validated in both ion modes, with $R^2 > 0.997$ and inter/intraday variability < 15% in both modes.

Conclusions: An assay to quantify amikacin that is more specific and more sensitive than conventional assays was successfully developed. Mass spectrometry allowed for specific identification of amikacin. Additionally, using positive ion mode significantly decreased the lower limit of detection, and using negative ion mode significantly increased the range of detection as compared to conventional assays. This assay will be used for future cellular uptake and animal pharmacokinetic studies.

Funding: Defense Advanced Research Projects Agency (DARPA) under Contract No. 140D6318C0026

Emergence of Unusual Carbapenemase-producing Carbapenem Resistant Organisms in Houston, Texas

Offiong C¹, Olumuyiwa T², Chaudhary I³, Nwachukwu P⁴, Brown P⁵, Foster R⁶, Sumpter J⁷

1. Division of Disease Prevention and Control, Houston Health Department
2. Division of Disease Prevention and Control, Houston Health Department
3. Division of Disease Prevention and Control, Houston Health Department
4. Division of Disease Prevention and Control, Houston Health Department
5. Bureau of Laboratory Services, Houston Health Department
6. Bureau of Laboratory Services, Houston Health Department
7. Bureau of Laboratory Services, Houston Health Department

Objectives: The emergence of carbapenemase-producing carbapenem resistant organisms (CP-CROs) has become of great concern as these pathogens are easily transmissible and are shown to be spreading worldwide as a result of several factors including cross-border patient transfer between healthcare facilities, lack of optimal inter-facility communication, and gaps in infection control practices. The Houston Health Department's Healthcare-Associated Infection (HHD HAI) Program played a key role in leading the Centers for Disease Control and Prevention's (CDC) guidance on detecting and containing unusual CP-CROs. As Houston is the fourth largest city in the U.S. and home to the world's largest medical center, the purpose of this analysis is to examine the wide-reaching spread of these CP-CROs.

Methods: From August 2018 to August 2019, CP-CRO samples were collected and sent in to the HHD Antibiotic Resistance Laboratory Network (ARLN). These isolates were examined for patient carrying CP-CROs (i.e. verona integron-mediated metallo- β -lactamase (VIM), klebsiella pneumoniae carbapenemase (KPC), new delhi metallo- β -lactamase (NDM), imipenem resistance metallo- β -lactamase (IMP), oxacillin metallo- β -lactamases (OXA-23, OXA 24/40, OXA-48)). A bivariate analysis was conducted to determine the rate of resistance mechanism(s) detected by organism.

Results: The analytic sample sent into the HHD ARLN consisted of 164 samples carrying CP-CROs from 59 clinical laboratories and healthcare facilities in the Houston Area (Table 1) including: (1) carbapenem resistant Enterobacteriaceae (CRE) with the KPC gene (68.3%), (2) CROs carrying the NDM gene, including CRE-Escherichia coli (1.8%) and CRE-Enterobacter cloacae complex (2.4%), (3) carbapenem resistant Pseudomonas aeruginosa (CRPA) carrying the VIM gene (4.9%), and (4) carbapenem resistant Acinetobacter baumannii (CRAB) detected with OXA-23 (1.2%) and OXA-24/48 (0.6%) genes. Reports also detected two isolates (i.e., CRE-Klebsiella pneumoniae, CRPA) carrying dual-resistance genes (1.2%), with CRPA demonstrating as pan-resistant (0.6%).

Conclusions: Many challenges remain for the HHD ARLN in detecting CP-CROs in the Houston area. For example, while the KPC gene has been documented to be endemic in the U.S., a rise in other unusual resistance mechanisms not native to the Houston region, such as the NDM and VIM genes, dual-resistance genes, and pan-resistance have been documented due to many factors including international healthcare visits, misuse of antibiotics, and infection control gaps. The information found is critical to containing the growing transmission of unusual resistance genes in Houston, Texas.

Funding Sources:

Agency: Centers for Disease Control and Prevention

Grant: Epidemiology and Laboratory Capacity for Prevention and Control of Emerging Diseases

Table 1. Sample characteristics of carbapenemase-producing carbapenem resistant organisms; HHD ARLN Data, Houston, Texas, August 2018-August 2019 (n=164)

Organism	Total (N=164) N (%)	VIM (n=8) n (%)	KPC (n=136) n (%)	NDM (n=10) n (%)	IMP (n=2) n (%)	OXA- 23 (n=2) n (%)	OXA- 24/40 (n=1) n (%)	OXA- 48 (n=3) n (%)	IMP & NDM (n=1) n (%)	NDM & OXA-48 (n=1) n (%)
CRE- Escherichia coli	17 (10.4)	0 (0.0)	14 (8.5)	3 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
CRE- Enterobacter cloacae complex	9 (5.5)	0 (0.0)	5 (3.0)	4 (2.4)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
CRE-Klebsiella oxytoca	1 (0.6)	0 (0.0)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
CRE-Klebsiella pneumoniae	118 (72.0)	0 (0.0)	112 (68.3)	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	3 (1.8)	0 (0.0)	1 (0.6)
CRPA	16 (9.8)	8 (4.9)	4 (2.4)	1 (0.6)	2 (1.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
CRAB	3 (1.8)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (1.2)	1 (0.6)	0 (0.0)	0 (0.0)	0 (0.0)

N = number of samples; HHD ARLN = Houston Health Department Antibiotic Resistance Laboratory Network; CRE = carbapenem resistant Enterobacteriaceae; CRPA = carbapenem resistant Pseudomonas aeruginosa; CRAB = carbapenem resistant Acinetobacter baumannii; VIM = verona integron-mediated metallo- β -lactamase; KPC = klebsiella pneumoniae carbapenemase; NDM = new delhi metallo- β -lactamase; IMP = imipenem resistance metallo- β -lactamase; OXA-48 = oxacillin metallo- β -lactamase

Protein Engineering of Anti-TcdB DARPins with Protease Stability

Chonira V¹, Simeon R¹, Chen Z¹

1. Department of Microbial Pathogenesis and Immunology, Texas A&M University

Corresponding author: Zhilei Chen, Department of Microbial Pathogenesis and Immunology, Texas A&M University, 8447 Riverside Parkway, Bryan, Texas 77807, E-mail: zchen4@tamu.edu

Each year, *Clostridium difficile* causes over a quarter million infections, 14000 deaths and over ~\$1 billion in treatment-associated costs in the United States. The pathology of *C. difficile* infection (CDI) is mainly due to its two secreted exotoxins, TcdA and TcdB, which target small GTPases and disrupt tight junctions in the colonic epithelium resulting in bloody diarrhea.

The current paradigm for treating CDI mainly entails administration of antibiotics or intravenous delivery of anti-TcdB antibody bezlotoxumab. Unfortunately, antibiotics treatment suffers from a high CDI recurrence rate, in part due to the emergence of antibiotic-resistant bacteria in recent decades, while the antibody therapy neither lessens the disease severity nor shortens the disease duration albeit it reduces the CDI recurrence rate from 28% to 16% in a phase III clinical trial. We postulate that, since the toxins are secreted within the colon, an anti-toxin therapeutic that can be delivered directly to the colon may provide a more effective treatment for CDI.

Previously, our lab engineered a panel of anti-TcdB designed ankyrin repeat proteins (DARPins) with potent toxin neutralization activity. The best DARPin, DLD-4, neutralized TcdB with $EC_{50} \sim 4$ pM. DLD-4 is a dimer DARPin consists of 1.4E and U3. However, DLD-4 was found to be sensitive to digestion by proteases (i.e. trypsin, chymotrypsin) that are abundant in the GI tract, limiting its therapeutic potential. The protease stability of 1.4E was improved via rational design and directed evolution. The best DARPin, T10-2, showed strong stability against trypsin digestion but remained susceptible to chymotrypsin digestion.

Since protease digestion requires that the substrate be docked in the protease active site, we hypothesized that rigid proteins should exhibit higher protease stability due to steric hindrance. In this study, to further improve the protease stability of T10-2, four different pairs of disulfide bonds were introduced into T10-2 between adjacent α - helices to increase the scaffold rigidity.

The YxdJK System is a Targeted Stress Response that Mediates Specific Protection Against the Human Antimicrobial Peptide LL-37 in *Enterococcus faecalis*

Erickson SG¹, Khan A^{1,2}, Pettaway C^{1,2}, Arias CA^{1,2,3,4}, Miller WR^{1,2}

1. Division of Infectious Diseases, Department of Internal Medicine, McGovern Medical School, Houston, TX 2. Center for Antimicrobial Resistance and Microbial Genomics, McGovern Medical School, Houston, TX 3. Center for Infectious Diseases, University of Texas Health Science Center, School of Public Health, Houston, TX 4. Molecular Genetics and Antimicrobial Resistance Unit, Universidad El Bosque, Bogota, Colombia

Corresponding Author: William Miller, Division of Infectious Diseases, McGovern Medical School, 6431 Fannin, MSB 2.112, Houston, Texas 77030. Email: William.R.Miller@uth.tmc.edu

Background: Enterococci are opportunistic pathogens with a wide array of intrinsic and acquired antimicrobial resistance determinants. As commensals of the human gastrointestinal tract, enterococci have evolved a network of two component-signaling systems (TCS), to evade killing by cationic antimicrobial peptides (CAMPs) of the host innate immune response. Activation of these pathways can also lead to resistance to the innate immunity and AMP-like antibiotics such as daptomycin, complicating treatment of severe enterococcal infections. Our previous work implicated the YxdJK cell envelope TCS in resistance to daptomycin independent of the LiaFSR stress response, specifically through activating mutations in the YxdK histidine kinase. The aim of this study was to characterize the contributions of the YxdJK system to protection from host derived CAMPs, namely, a cathelicidin and an α -defensin.

Methods: Knockouts of the genes encoding the YxdJ response regulator and YxdK histidine kinase responsible for system activation, and an allelic exchange of the YxdK_{A202E} allele from a daptomycin resistant *E. faecalis* isolate, were constructed in the laboratory strain *E. faecalis* OG1RF using a p-chloro-phenylalanine counterselection system. The strain OG1RF Δ liaX (resistant to CAMP killing) and OG1RF Δ liaR (susceptible to CAMP killing) were controls. Killing assays were performed in triplicate for LL-37 in RPMI+5% LB broth in the presence and absence of 80nM LiaX, an extracellular mediator of CAMP resistance in *E. faecalis* and for hNP-1 in 10mM K₂PO₄ buffer. Strains were grown to mid-logarithmic phase in brain heart infusion (BHI) broth, and diluted to a final inoculum of 10³ cells/mL. LL-37 (50 μ g/mL) and hNP-1 (50, 75, 100 μ g/mL) were added, and cells were incubated for 2 hours at 37° C followed by colony counts. Percent survival was calculated as the ratio of viable bacteria after treatment with CAMPs compared to untreated controls.

Results: LL-37 killed OG1RF with a mean survival of 12% and addition of exogenous LiaX mediated resistance with an increase to 57% survival. Both OG1RF Δ yxdJ and OG1RF Δ yxdK had significantly reduced survival (< 5%) compared to OG1RF (p < 0.05), even though the strains retain an active LiaFSR system. This phenotype was not rescued by the addition of LiaX. Further, the introduction of the YxdK_{A202E} allele was sufficient to confer resistance to LL-37 killing (mean survival 57%) even in the CAMP sensitive OG1RF Δ liaR mutant (mean survival 53%, p < 0.001). HNP-1 killed OG1RF in a dose-dependent manner at 50, 75, and 100 μ g/mL (mean survival 76, 69, 34%, respectively). However, even at 50 μ g/mL, the LL-37 resistant OG1RF Δ liaX and OG1RF YxdK_{A202E} showed no increased resistance to hNP-1.

Conclusions: The YxdJK system plays an important role in mediating specific resistance to the CAMP and human cathelicidin, LL-37, but not to the α -defensin, hNP-1. Absence of either YxdJ or YxdK abolished LiaX

Poster #42

mediated resistance to LL-37, and a mutation in the histidine kinase that activates the system is sufficient to increase resistance to LL-37 killing independent of LiaFSR. Thus, enterococci likely have specific stress response systems that mediate increased resistance to each family of CAMPs.

Genetic and Phenotypic Signatures Predictive of 'Bicarbonate [NaHCO₃]-Responsiveness' and β-Lactam Sensitization Among Methicillin-Resistant *Staphylococcus aureus* (MRSA)

Ersoy SC^{1*}, Otmishi M², Milan VT¹, Li L¹, Pak Y¹, Mediavilla J³, Chen L³, Kreiswirth B³, Chambers HF⁴, Proctor RA⁵, Xiong YQ^{1,6}, Fowler VG⁷, Bayer AS^{1,6}

¹The Lundquist Institute at Harbor-UCLA, Torrance, CA, USA; ²California State University-Dominguez Hills, Carson, CA, USA; ³Meridian Health, Nutley, NJ, USA; ⁴UCSF School of Medicine, San Francisco, CA, USA; ⁵University of Wisconsin School of Medicine and Public Health, Madison, WI, USA; ⁶Geffen School of Medicine at UCLA, Los Angeles, CA, USA; ⁷Duke University Medical Center and School of Medicine, Durham, NC, USA

*Presenting Author: Selvi Ersoy, The Lundquist Institute at Harbor-UCLA, 1124 West Carson Street Torrance, CA, E-mail: selvi.ersoy@lundquist.org

Background: Selected prototype MRSA strains exhibit *in vitro* susceptibility to standard β-lactams (e.g., oxacillin [OXA]; cefazolin [CFZ]) when tested in cation-adjusted Mueller-Hinton Broth (CA-MHB) supplemented with NaHCO₃ ("NaHCO₃-responsiveness"). *In vivo* activity of these same two β-lactams has been previously demonstrated for NaHCO₃-responsive MRSA strains in experimental endocarditis (Ersoy et al *Antimicrob Agents Chemother* 2019). When screening a larger cohort of 58 clinical MRSA strains, ~75% and ~36% were identified as responsive to CFZ and OXA, respectively, in NaHCO₃-supplemented CA-MHB. The current study was designed to identify potential phenotypic and genetic predictors of the NaHCO₃-responsive phenotype in this larger MRSA cohort.

Methods: 58 recent MRSA bloodstream isolates, identified as either NaHCO₃-responsive or non-responsive to CFZ and OXA *in vitro*, were used in this study. The following *in vitro* phenotypic analyses were performed: i) population analysis profiles (PAPs); and ii) NaHCO₃ + β-lactam synergy. Also, we analyzed the correlation between: the intrinsic β-lactam MICs in standard CA-MHB; NaHCO₃ responsiveness; and co-responsiveness to both β-lactams. Genotypically, the linkage between CC, *agr*, and *spa* genotypes and NaHCO₃-responsiveness was determined.

Results: Of four selected MRSA (two NaHCO₃-responsive and two NaHCO₃-non-responsive strains), each displayed homo-resistant PAPs in standard media; additionally, the resistant sub-populations of only the two NaHCO₃-responsive strains were repressible by NaHCO₃ exposure. A synergistic bactericidal interaction between NaHCO₃ and β-lactams was only found in NaHCO₃-responsive (but not in non-responsive) strains. Of the 21 OXA-susceptible strains, 20 were also susceptible to CFZ in the presence of NaHCO₃, indicating that OXA-responsiveness is a good predictor of CFZ-responsiveness. A low baseline β-lactam MIC (i.e., MICs in CA-MHB alone < 64 μg/mL) was not predictive of NaHCO₃-responsiveness to either β-lactam. Genotypically, CC8, *agr* I, and *spa* 1 genotypes were all significantly linked to the β-lactam:NaHCO₃-responsive phenotype for OX, but not for CFZ (p < 0.05).

Conclusion: The NaHCO₃-responsive phenotype is common for both OX, and especially for CFZ among clinical MRSA isolates. Phenotypically, PAPs and intrinsic MICs determined in standard media are not predictive of NaHCO₃-responsiveness. In contrast, genotypically, CC, *agr* and *spa* types may be useful biomarkers for β-lactam:NaHCO₃-responsiveness *in vitro*. Current animal model studies are in-progress to verify the *in vivo* predictability of the above genotypic markers for effective β-lactam therapy among NaHCO₃-responsive MRSA strains.

Poster #8

Funding Sources: NIH-NIAID (to ASB): RO1 AI 146078

Evolution of Group B Streptococcal Capsular Type V Invasive Infections in Neonates and Young Infants: A Whole Genome Sequencing Study

Flores AR^{1,2}, Sanson MA¹, Shah BJ¹, Rench M³, Shelburne SA⁴, and Baker CJ¹

1. Division of Infectious Diseases, Department of Pediatrics, UTHSC/McGovern Medical School, Houston, TX
2. Center for Antimicrobial Resistance and Microbial Genomics, UTHSC/McGovern Medical School, Houston, TX
3. Division of Infectious Diseases, Department of Pediatrics, Baylor College of Medicine and Texas Children's Hospital, Houston, TX
4. Departments of Infectious Diseases and Genomic Medicine, MD Anderson Cancer Center, Houston, TX

Corresponding author: Anthony R. Flores, McGovern Medical School, 6431 Fannin St MSB 3.130, Houston, TX, 77030, Email: anthony.r.flores@uth.tmc.edu

BACKGROUND: Since 1970 group B *Streptococcus* (GBS) has been a frequent cause of sepsis or meningitis in young infants. Capsular polysaccharide type V was first recognized in 1990 and has increased to the point where it now causes ~15% of GBS infections. GBS type V strains are almost entirely sequence type 1 (ST1) in adult infections. To understand the emergence of type V GBS, we compared infant strains before 1990 to more contemporary isolates from young infants and adults.

METHODS: 35 strains isolated from blood or CSF of infants <90 days of age (Houston, 1979-1996) were compared to the following previously sequenced type V, ST1 strains: (1) 14 from infant blood or CSF from Center for Disease Control and Prevention (CDC) (2015-2017), (2) 193 blood ST1 isolates from adults (Houston, 1992-2013), and (3) 516 invasive isolates from the CDC (2015-2017). Isolates were sequenced using an Illumina MiSeq instrument followed by molecular typing, antimicrobial resistance gene determination and phylogenetic analysis. Antimicrobial susceptibility testing (AST) was performed using disk diffusion and E-test.

RESULTS: The majority (29/35) of Houston young infant strains were ST1. Type V GBS strains isolated prior to 1990 were more likely to be of ST-2 or ST-26 (5/10) compared to those from 1990 or later (24/25 and 14/14 CDC infant invasive type V). Tetracycline resistance was identified in 83% (29/35) while macrolide resistance (MR) occurred in only 23% (8/35) of the strains. Compared to early neonatal isolates, MR was significantly more frequent among contemporary neonatal (12/14, 86%, $P < 0.0001$) and adult (502/710, 71%, $P < 0.0001$) ST1 GBS. Phylogenetic analysis showed two distinct clades defined, in part, by MR. A high-frequency MR (340/360, 94%) clade was defined by the presence of *erm(B)* on Tn3872 while the low-frequency MR clade (159/350, 45%) was more diverse in mobile elements contributing to MR. The majority (27/29) of early neonatal ST1 GBS strains were observed in the low-frequency MR clade.

CONCLUSIONS: Infant invasive disease due to type V GBS before 1990 consisted of more diverse STs but is now almost exclusively ST1. Differences in the frequency of MR between early neonatal and contemporary type V ST1 GBS suggest MR may, at least in part, have driven the expansion of type V ST1 GBS.

Kpc-2 Variants Reveal Active Site Requirements for Carbapenem Hydrolysis

Furey IM¹, Mehta SC¹, Sankaran B², Hu L³, Prasad B.V.V.³, Palzkill T¹

1 Department of Pharmacology and Chemical Biology, Baylor College of Medicine, Houston TX

2 Lawrence Berkeley National Laboratory, Berkeley CA

3 Department of Biochemistry and Molecular Biology, Baylor College of Medicine, Houston TX

Klebsiella pneumoniae carbapenemase (KPC-2) is a serine β -lactamase that is able to hydrolyze and inactivate nearly all available β -lactam antibiotics. In addition to its ability to hydrolyze penicillins (ampicillin) and cephalosporins (cefotaxime), it can also hydrolyze carbapenems (imipenem, meropenem), which are used to treat serious clinical infections. Structural and sequence analysis of KPC-2 compared to other closely related β -lactamases does not reveal a basis for the unique ability of KPC-2 to hydrolyze carbapenems in addition to penicillins and cephalosporins. We hypothesize that compared to closely related β -lactamases, subtle amino acid differences throughout KPC-2 contribute specifically to confer carbapenem resistance. To identify the molecular basis of carbapenem hydrolysis by KPC-2, we used a genetic approach with a library of randomly mutagenized KPC-2 genes to select for penicillin-resistant/carbapenem-sensitive clones. Biochemical and structural analyses were employed to characterize selected KPC-2 mutant enzymes. Two such mutants, KPC-2(F72Y) and KPC-2(T215P) exhibit an impaired ability to hydrolyze carbapenem antibiotics while retaining high activity towards ampicillin. Steady-state kinetic analysis of each purified enzyme showed both the F72Y and T215P mutations result in a >10-fold reduction in k_{cat} towards carbapenems imipenem and meropenem. Because k_{cat} is the product/sum of two steps during catalysis, we next used pre-steady state kinetics to determine the rate-limiting step in hydrolysis. Pre-steady state kinetics determined that deacylation, the second step of hydrolysis, was rate limiting for both mutants. X-ray crystallography was then used to determine the structures of these two enzymes. The structures of F72Y and T215P reveal deacylation of carbapenems was impaired by separate mechanisms in each mutant. KPC-2(F72Y) exhibits a change in the coordination of the catalytic water molecule involved in deacylation, while KPC-2(T215P) undergoes a conformational change that alters the carboxylate binding pocket used to bind β -lactam antibiotics. Together, these data suggest KPC-2 has evolved to hydrolyze carbapenems through increased coordination of both its catalytic water molecule and the ability to bind and position substrate in the active site.

Funding

5T32AI055449-13 to IF

R01 AI32956-28 to TP

Oral Mycobiome and Inter-kingdom Interactions Over the Course of Induction Therapy for Leukemia: An Observational Cohort Study

Robinson S¹, Peterson CB², Sahasrabhojane P³, Shelburne SA^{3,4}, Kontoyiannis DP³, and Galloway-Peña JR^{3,4}

1. The Department of Statistics, Rice University Houston, TX
2. The Department of Biostatistics, The University of Texas MD Anderson Cancer Center Houston, TX
3. The Department Infectious Diseases, Infection Control, and Employee Health, The University of Texas MD Anderson Cancer Center Houston, TX
4. The Department Genomic Medicine, The University of Texas MD Anderson Cancer Center Houston, TX USA

Corresponding author: Jessica Galloway-Peña, Department of Genomic Medicine, The University of Texas MD Anderson Cancer Center, 1901 East Rd 4SCR4.1336, Houston, TX 77054 E-mail: jrgalloway@mdanderson.org

Background: Although the term “microbiome” technically refers to all microorganisms, the majority of microbiome studies to date have focused on the bacteriome. To begin to investigate the role of the mycobiome in patients with hematologic malignancy, we sought to characterize the oral mycobiome including mycobiome-bacteriome interactions in the setting of remission-induction chemotherapy (RIC) for acute myeloid leukemia (AML).

Methods: Oral samples (n=299) were prospectively collected twice weekly from 39 AML patients during RIC until neutrophil recovery. Illumina MiSeq 16S rRNA V4 and ITS2 sequencing were used to determine bacterial and fungal diversity and community composition, respectively. Intra- and inter-kingdom network connectivity (the total number of edges) at baseline (T1), a midpoint (T3), and a later time point (T6), were assessed via SPIEC-EASI.

Results: In this exploratory study, we found that mycobiome α -diversity was not significantly associated with antibiotic or antifungal exposures. However, we observed that post-chemotherapy mycobiome α -diversity was lower in subjects receiving high intensity chemotherapy, and certain fungal taxa had differing abundance trends for patients receiving low vs. high intensity chemotherapy regimens. When analyzing specific fungal taxa, greater decreases in *Malassezia* were seen over time among patients on high intensity RIC compared low intensity RIC (P=0.003). We also identified aspects of the fungal community compositions that were associated with the incidence of microbiologically or clinically defined infections. Analyses of intra- and inter-kingdom relationships at T1, T3, and T6 indicated that inter-kingdom connectivity increased over the course of IC as bacterial α -diversity was diminished.

Conclusions: In the first longitudinal study of the mycobiome during RIC for AML, we found that mycobiome-bacteriome interactions are highly dynamic, interconnected and may have clinical implications. Including mycobiome analysis in microbiome studies may be necessary to optimally understand how the microbiome impacts clinical outcomes, and should be considered in the design of studies aimed at confirming the ecological and clinical role of fungal communities.

Funding: This work was supported by MDACC Knowledge GAP and MRP grants to D.P.K and S.A.S. and the National Institute of Allergy and Infectious Disease [1 K01 AI143881-01 to J.G.P.].

Oral and Stool Microbiome Community Coalescence is Driven by Antibiotic Exposure in Acute Leukemia Patients

Galloway-Peña JR^{1,2}, Aitken SL³, Sahasrabhojane PV², Shelburne SA^{1,2}

1. Department of Genomic Medicine, The University of Texas MD Anderson Cancer Center
2. Department of Infectious Disease, Infection Control and Employee Health, The University of Texas MD Anderson Cancer Center
3. Division of Pharmacy, The University of Texas MD Anderson Cancer Center

Corresponding author: Jessica Galloway-Peña, Department of Genomic Medicine, The University of Texas MD Anderson Cancer Center, 1901 East Rd 4SCR4.1336, Houston, TX 77054 E-mail:

jrgalloway@mdanderson.org

Objectives: Community coalescence is defined as “a joining of previously separate communities, forming a new entity that is not easily separable into parts again”. Although this terminology has been proposed to describe ecological community interchange usually in an environmental context (i.e. the mixing of population in aquatic environments, or rhizosphere communities), there is evidence that community coalescence occurs within the human body with important consequences. We sought to characterize and define oral-fecal community coalescence, the likely clinical variables attributing to this phenomenon, and clinical consequences in acute leukemia patient receiving induction remission chemotherapy (RIC).

Methods: Longitudinal fecal (n=566) and oral (n=769) samples and respective 16S V4 sequences were derived from 93 adult AML patients undergoing RIC. Differences in community structure were visualized using PCoA of Bray-Curtis distances or hierarchical clustering. A time-varying Cox proportional hazards model was used to assess the risk of coalescence associated with each additional day of antibiotic exposure. Differential enrichment of bacterial taxa was estimated using pairwise Mann-Whitney test with FDR-adjustment. Associations with infection were determined using chi-squared analysis.

Results: Although most samples clustered by body site, some of the samples bridged habitats, where some oral and stool samples clustered together via principal coordinates plot as well as hierarchical clustering. In order to objectively quantify coalescence, we plotted the minimum Unifrac distance between any longitudinally collected stool and oral sample pair within a single patient. Upon determining the interquartile range of those distances (Mean: 0.34, IQR: 0.26-0.44), we defined a patient exhibiting microbial community coalescence between oral and stool sites as any patient falling below the interquartile range (n=23). When treated as a time-varying covariate, each additional day of linezolid (HR 1.15, 95% CI 1.06 – 1.24, P < 0.001), meropenem (HR 1.13, 95% CI 1.05 – 1.21, P = 0.001) metronidazole (HR 1.13, 95% CI 1.05 – 1.21, P = 0.001), and cefepime (HR 1.10, 95% CI 1.01 – 1.18, P = 0.021) increased the hazard oral-stool microbial community coalescence. Levofloxacin (HR 0.75, 95% CI 0.61 – 0.93, P = 0.009) appeared to have protective effects against microbiome community coalescence. By the time of neutrophil recovery (after coalescence and antibiotic exposure occurred) the relative abundance of Bacteroidia (P < 0.001), Fusobacteriia (P = 0.012), and Clostridia (P = 0.013) in the stool were significantly lower in those that exhibited oral-gut community coalescence versus those who did not. Exhibiting oral-stool community coalescence was associated with the occurrence of infections prior to neutrophil recovery (P = 0.002), as well as infections during the 90 days post neutrophil recovery (P = 0.027).

Conclusions: Although it is known that antimicrobial interventions have significant effects on the gut microbiota, this work elucidates specific effects on microbial ecology and biogeography. Additionally, we have furthered the understanding of the links between oral and intestinal microbiota and their relationship with infection.

Poster #66

Funding: This work was supported by the National Institute of Allergy and Infectious Disease [1 K01 AI143881-01 to J.G.P.].

Demonstrate Emulsion Droplets as a Culturing Platform for Antibiotic Discovery

Ganiga Prabhakar R, Hirning A, Alnahhas R, Seo S, Song X, Coleman T, Bennett M, Shamoo Y
Department of Biosciences, Rice University

Corresponding author: Yousif Shamoo, Department of Biosciences, Rice University, 6100 Main Street, Houston, Texas, E-mail: shamoo@rice.edu

Members of a microbial community compete for limited nutrients. To gain competitive advantage, few microbes produce specialized metabolites with antibiotic properties. Some of these metabolites are produced only under certain stress conditions and therefore remain largely silent in traditional lab cultures. By activating these silent pathways, we gain insights into how microbial communities interact as well as gain access to novel metabolites with potential activity against multidrug resistant (MDR) pathogens.

Streptomyces roseosporus produces daptomycin to kill sensitive strain of *Enterococcus faecalis*. Yet, we need daptomycin variants or novel metabolites to treat daptomycin-resistant *E. faecalis* infections. Therefore, we encapsulate *S. roseosporus* and MDR *E. faecalis* as predator and prey respectively, to study how environmental stress can activate cryptic pathways in a predator.

As a proof of principle, we designed a model predator-prey system in *Escherichia coli*, such that each droplet contains a 'defective-predator' and a 'prey'. A defective-predator has a single nucleotide polymorphism (SNP) to knockout production of quorum sensing (QS) molecules. An evolved predator activates the engineered cryptic pathway to produce QS molecules required for killing the prey. Therefore, an evolved predator can grow to a higher density compared to a defective-predator within the droplets.

Quorum sensing molecules must be spatially segregated for efficient enrichment of the evolved predator. However, we observe a controlled diffusion of the QS molecules between the droplets. We are currently testing sink droplets — filled with quorum quenching enzymes — to establish spatial segregation between evolved and defective-predators. By iterating the growth of evolved predator in emulsion, we could increase its population density to detectable level. Thus, competition based directed evolution can harness the evolutionary power of predators to produce specialized metabolites under defined co-culture conditions.

Funding: National Institutes of Health Grant [R01AI080714 to Y.S.]

It's a Whale of a Problem: The ORCA (Organizational Readiness to Change Assessment) Highlights Differential Readiness for Antibiotic Stewardship Across Organizations

Melanie C. Goebel MD^{1*}, Barbara W. Trautner MD, PhD^{2,3}, Less is More Group, Larissa Grigoryan MD, PhD⁴

1. Division of Infectious Diseases, Department of Medicine, Baylor College of Medicine, One Baylor Plaza, BCM 285, Room 672E, Houston, TX 77030, USA (*address for corresponding author)

2. Center for Innovations in Quality, Effectiveness, and Safety (IQuEst), Michael E. DeBakey Veterans Affairs Medical Center, Houston, TX USA

3. Section of Health Services Research, Department of Medicine, Baylor College of Medicine, Houston, TX USA

4. Department of Family and Community Medicine, Baylor College of Medicine, 3701 Kirby, Houston, TX 77098, USA

*Corresponding author: Melanie C. Goebel, Email: mcgoebel@bcm.edu

Objectives: Targeted antibiotic stewardship interventions are needed to reduce unnecessary treatment of asymptomatic bacteriuria (ASB). The Organizational Readiness to Change Assessment (ORCA) is a validated survey instrument that has been used to detect potential obstacles to change and tailor interventions. In an outpatient stewardship study, primary care practices with high readiness to change trended toward greater improvements in antibiotic prescribing. We used the ORCA to assess barriers to change before implementing a multicenter inpatient stewardship intervention for ASB.

Methods: Surveys were self-administered by healthcare professionals in inpatient medicine and long-term care units at 4 geographically diverse Veterans Affairs facilities during January-December 2018. Participants included providers (physicians, physician assistants, and nurse practitioners), nurses, and pharmacists. The survey included seven subscales: evidence (perceived evidence strength) and six context subscales (favorability of the organizational context to support change). Responses were scored on a 5-point Likert scale, with 1 meaning very weak or strongly disagree. Scores were compared between professional types and sites. We also measured allocated employee effort for stewardship at each site.

Results: 104 surveys were completed, with an overall response rate of 69.3%. For all sites combined, the evidence subscale had the highest score of the seven subscales (mean 4, SD 0.9); the resources subscale was significantly lower than other subscales (mean 2.8, SD 0.9, $P < 0.001$). Scores for budget and staffing resources were lower than scores for training and facility resources ($P < 0.001$ for both comparisons). Pharmacists had lower scores than providers for the staff culture subscale ($P = 0.04$). Comparing subscales between sites, ORCA scores were significantly different for leadership behavior (communication and management), measurement (goal setting and accountability), and general resources. The site with the lowest scores for resources (mean 2.4) also had lower scores for leadership behavior and measurement, and lower pharmacist effort devoted to antibiotic stewardship.

Conclusions: Although healthcare professionals endorsed the evidence about non-treatment of ASB, perceived barriers to antibiotic stewardship included inadequate resources and lack of leadership support. These findings provide targets for tailoring the intervention to maximize the success of our stewardship program. Our support to sites with lower leadership scores will include training of local champions who are dedicated to supporting the intervention. For sites with low scores for resources, our targeted implementation strategies include analyzing local needs and avoiding increased workload for existing personnel.

Funding sources: This work was supported by the Veterans' Affairs Health Services Research and Development Service (grant no. IIR 16-025) and by the Center for Innovations in Quality, Effectiveness and Safety (grant no. CIN 13-413) at the Michael E. DeBakey VA Medical Center, Houston, Texas.

A New Classification of the *Staphylococcus aureus* B-lactamase Based on Unique Amino Acid Sequences and its Role in the Cefazolin Inoculum Effect

Gomez-Villegas S¹, Carvajal-Ortiz LP², Rincon-Nuñez S², Rios-Nieto R², Diaz-Ortiz L², Porras-Guzman J², Sigh KV¹, Panesso D¹, Reyes MI², Murray BE¹, Arias CA^{1,2}, Reyes J¹.

1.CARMiG. McGovern Medical School. The University of Texas, Health science center at Houston.

2.Molecular Genetics and Antimicrobial Resistance Unit, Universidad El Bosque, Bogotá, Colombia

Corresponding author: Jinnethe Reyes, Molecular Genetics and Antimicrobial Resistance Unit, Universidad El Bosque, Av Carrera 9 #131a-2. Bogota, Colombia. E-mail: jinnethereyes@yahoo.com

Background: Cefazolin (Cz) has become one of the first-line agents in the treatment of severe MSSA infections due to its benign toxicity profile. Yet, the Cefazolin Inoculum effect (CzIE) is a big caveat in this approach. This phenomenon is defined as MSSA strain with a Cefazolin MIC >16 µg/ml when an Inoculum of 10⁷ CFU/ml is present and has been linked to failure in the treatment of deep-seated MSSA infections. It depends on the presence of the B-Lactamase of *S. aureus* (BlaZ), which is classified in A, B, C and D, based on serologic characteristics of the enzyme and the amino acid residues in the position 128 and 216. Yet, this classification fails to accurately predict which strains will display this phenomenon. Thus, we aimed to report a new classification of the BlaZ that considers the full amino acid sequence, and that could potentially be more accurate in predicting the presence of the CzIE. Furthermore, we also tested the role of different types of Beta-lactamase in this phenomenon by expressing *in trans* the *blaZ* gene from a CzIE+ strain and the CzIE – strain.

Methodology: 690 contemporary MSSA bloodstream isolates from Latin America were included in this study. Standard (5 x 10⁵ CFU/ml) and High Inoculum (5 x 10⁷ CFU/ml) were determined by broth microdilution. The CzIE was defined as a MIC ≥ to 16µg/ml when high inoculum was tested. gDNA was extracted using the DNAeasy Blood and Tissue kit (Qiagen), DNA libraries were prepared using the NexteraXT DNA kit and whole-genome sequenced on Illumina HiSeq or MiSeq. An allotype was defined as a unique amino acid sequence of the BlaZ enzyme deduced from the DNA sequence, taking the BlaZ of ATCC29213 as reference. For the *blaZ in trans* expression, the gene with its native promoter was amplified from the prototypical CzIE+ strain (TX0117, High Inoculum MIC of 64 µg/ml) and from the prototypical CzIE – strain (ATCC29213, High Inoculum MIC of 2 µg/ml) using primers that inserted EcoRI restriction sites. Later on, the PCR product was cloned into the shuttle vector pWM401 and electroporated into RN4220, a *blaZ* (-) restriction deficient *S. aureus*.

Results: All of the 690 isolates were susceptible to Cz at standard Inoculum, yet 40% of them displayed a High Inoculum MIC ≥ than 16 µg/ml. The analysis of the *blaZ* gene and its deduced BlaZ amino acid sequence revealed 29 allotypes: 11 of BlaZ type A, 7 of type C, one of type D and 9 of type B. 5 allotypes accounted for almost the 80% of the isolates. Allotype 2 (type A) was clearly associated with the CzIE, as 96% of the strains showed CzIE+ and most of the type A CzIE+ Isolates belonged to this allotype. Yet, other allotypes such as allotype 1 (type C) were as likely as not to be associated with this phenomenon. Furthermore, *in trans* expression of the BlaZ of TX0117 (allotype 1) and ATCC29213 (allotype 0) with their native promoter lead in both cases to a High Inoculum MIC ≥64 µg/ml.

Conclusion: A classification of the *S. aureus* beta-lactamase based on allotypes better predicts the display of the CzIE in MSSA isolates when compared to the serotype classification. Yet, the role of specific types of BlaZ is still controversial as *in trans* expression of the *blaZ* gene from a CzIE + and a CzIE – strain in a *blaZ* (-) strain led in both cases to the display of the CzIE.

Poster #46

Founding sources: Universidad El Bosque, Colciencias Grant 130880764150 and University of Texas McGovern Medical School, NIH NIAID grants K24 AI121296

Creating an Outpatient-Specific Antibiogram to Guide Treatment for Urinary Tract Infections

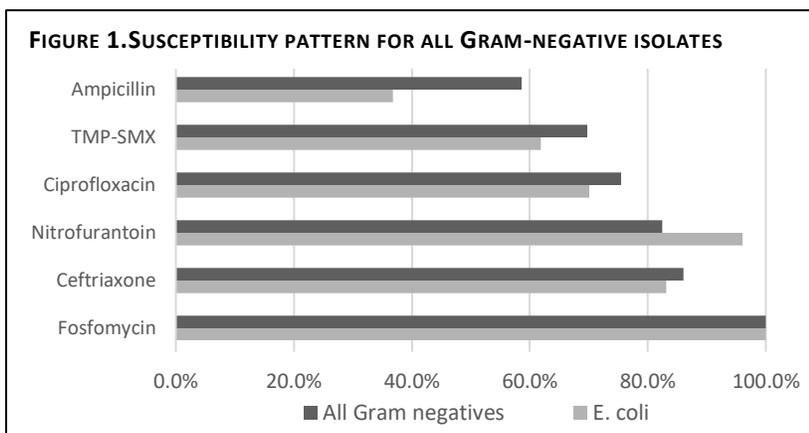
Larissa Grigoryan,*¹ Melanie Goebel,² Samuel E. Willis,^{1,3} Lisa C.K. Danek,^{1,3} Jennifer Matas,¹ Neal Kachalia,³ Anna Katta,³ Kenneth Muldrew,^{3,4} Mohammad Zare,^{3,5} Forrest Hudson,³ Robert L. Atmar,^{2,3} and Barbara W. Trautner,^{6,7}

1. Department of Family and Community Medicine, Baylor College of Medicine, Houston, TX
2. Section of Infectious Diseases, Departments of Medicine, Baylor College of Medicine, Houston, TX
3. Harris Health System, Houston, TX
4. Department of Pathology and Immunology, Baylor College of Medicine, Houston, TX
5. Department of Family and Community Medicine, University of Texas McGovern Medical School, Houston, TX
6. Center for Innovations in Quality, Effectiveness and Safety, Michael E. De Bakey VA Medical Center, Houston, TX,
7. Section of Health Services Research, Departments of Medicine and Surgery, Baylor College of Medicine, Houston, TX

* Corresponding author: L. Grigoryan, Baylor College of Medicine, 3701 Kirby Dr. Houston, grigorya@bcm.edu

Objectives: Outpatients with uncomplicated urinary tract infection (UTI) are often treated empirically without culture, while urine cultures are typically collected from patients with complicated UTI. Susceptibilities for fosfomycin (a first-line agent) are not routinely performed in the antibiogram. Estimating the prevalence of resistance in UTI is critical for empiric treatment and stewardship.

Methods: We are developing a UTI-focused antibiogram from outpatients in two public clinics in an urban area (November 2018 to present). During the study, providers order a urine culture for any adult presenting with UTI symptoms. We estimated the prevalence of resistance to UTI-relevant antibiotics in the overall study population and compared it between U.S. and non-U.S. born patients.



Results: We collected 678 urine cultures from 644 unique patients (79% female). Of all cultures, 23% had no growth, 49% grew mixed flora, and 28% were positive (>10,000 CFU/mL). Patients with positive cultures were mostly female (88%), with mean age of 47 ± 15 yrs. Susceptibility results for *E. coli* and all gram-negative organisms combined are presented

in **Figure 1**. Susceptibility of uropathogens to TMP-SMX was higher in U.S. born patients than patients from Mexico or Central America (82% vs. 61%, P value=0.03). Susceptibility to ciprofloxacin was similar in U.S. and non-U.S. born patients (79% vs. 72%, P value=0.5). Of 77 *E. coli* isolates, 11 (14%) were positive for extended-spectrum beta-lactamase production, including 8 isolates from patients born in Mexico or Central America.

Conclusions: Among outpatients with uncomplicated and complicated UTI, uropathogens had a high prevalence of resistance to ciprofloxacin and TMP-SMX, but susceptibility to fosfomycin was 100%. Resistance rates for TMP-SMX were higher in patients from Mexico or Central America. Our findings question whether TMP-SMX remains a first-line agent in U.S. primary care.

Poster #56

Funding sources: This study was supported by the National Institute of Allergy And Infectious Diseases of the National Institutes of Health under Award Number UM1AI104681. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Effectiveness of Antibiotic Stewardship Intervention for Urinary Tract Infections in Primary Care: a Difference in Differences Study

Larissa Grigoryan MD, PhD^{1*}, George Germanos, MD, MPH¹, Roger Zoorob MD, MPH,¹ Mohamad Sidani MD, MS,¹ Haijun Wang PhD,¹ Mohammad Zare, MD,² Melanie Goebel,³ MD, Barbara W. Trautner MD, PhD^{4,5}

1. Department of Family and Community Medicine, Baylor College of Medicine, 3701 Kirby, Suite 600, Houston, TX 77098 (*address for corresponding author)

2. Department of Family and Community Medicine, University of Texas McGovern Medical School, Houston, TX

3. Division of Infectious Diseases, Department of Medicine, Baylor College of Medicine, Houston, TX

4. Center for Innovations in Quality, Effectiveness, and Safety (IQuEST), Michael E. DeBakey Veterans Affairs Medical Center, Houston, TX

5. Section of Health Services Research, Department of Medicine, Baylor College of Medicine, Houston, TX

*Corresponding author: Larissa Grigoryan, Email: grigorya@bcm.edu

Objectives: Fluoroquinolones are commonly prescribed to treat uncomplicated cystitis, and most antibiotic prescriptions have durations that exceed current recommendations. We performed a difference-in-differences study to assess the effectiveness of a stewardship intervention in a family medicine clinic at an academic outpatient center from August 2016 to March 2019. During our intervention period, the FDA released two additional warnings about side effects of fluoroquinolones.

Methods: The study had two sites (intervention and comparison) and three time periods: baseline, pre-intervention, and intervention. During the first two years, we obtained baseline data and performed interviews exploring provider prescribing decisions for cystitis at both sites. During the intervention period at the intervention site only, we presented an educational lecture including an overview of the IDSA guidelines, definitions for various UTI syndromes and actual clinical examples, and instruction on use of a decision aid. During the audit and feedback phase, providers were contacted monthly in person or by phone to provide follow-up on whether their treatment decision was in adherence with the guidelines. We performed a log-binomial regression analysis of the primary outcome, adherence to the guidelines for treatment of uncomplicated cystitis, both to antibiotic choice and treatment duration.

Results: We performed 156 audit and feedback sessions with 13 providers during the intervention period (March 2018-2019). Patients in both sites were similar in terms of age and Charlson comorbidity index. Adherence to the guidelines increased in the intervention period at both sites. The treatment of cystitis in the intervention period of the intervention site was 11.5 times (95% confidence interval 6.1-21.6) as likely to be guideline-adherent as the treatment in the baseline period of the comparison site.

Conclusions: Adherence to IDSA guidelines increased in both intervention and comparison sites, but improvement was greater in the intervention site. FDA warnings about side effects of fluoroquinolones released during the intervention period may have contributed to avoidance of fluoroquinolones at both sites. Since our intervention was effective at improving antibiotic choice and duration, future plans include incorporating our decision-support algorithm into the electronic medical record.

Funding sources: This research was funded by Zambon Pharmaceuticals. The work was supported by the Veterans' Affairs Health Services Research and Development Service (grant no. IIR 16-025) and by the

Poster #10

Center for Innovations in Quality, Effectiveness and Safety (grant no. CIN 13-413) at the Michael E. DeBakey VA Medical Center, Houston, Texas.

Ceftaroline Combination Therapy with Daptomycin or Vancomycin for Methicillin-Resistant *Staphylococcus aureus* Bacteremia after Monotherapy Failure: A Single-Center Experience

Hornak JP¹, Anjum S², Reynoso DA^{1,3}

1. Department of Internal Medicine, University of Texas Medical Branch, Galveston, TX, USA
2. National Institute of Allergy & Infectious Diseases, Bethesda, MD, USA
3. Division of Infectious Diseases, University of Texas Medical Branch, Galveston, TX, USA

Corresponding author: Dr. David A. Reynoso, Assistant Professor of Medicine, Division of Infectious Diseases, University of Texas Medical Branch, 301 University Boulevard, Rte. 0435, Galveston, TX 77555
Email: dareynos@utmb.edu

Background:

Methicillin-resistant *Staphylococcus aureus* bacteremia (MRSA-B) may fail to improve with standard monotherapy, particularly in patients with metastatic foci, incomplete source control, or persistent infection. Synergy observed *in vitro* between ceftaroline (CPT) and either daptomycin (DAP) or vancomycin (VAN) may translate into clinical benefit. Here, we describe our experience with DAP/CPT and VAN/CPT for complicated MRSA-B after monotherapy failure.

Methods:

Single-center, retrospective review of patients treated with DAP/CPT or VAN/CPT for complicated MRSA-B since January 1, 2016. Descriptive statistics were calculated with Microsoft Excel.

Results:

We identified 11 instances of combination therapy in 10 patients (DAP/CPT = 6, VAN/CPT = 5) with one patient receiving VAN/CPT followed by DAP/CPT. Rates of metastatic infection, incomplete source control, persistent bacteremia, and infective endocarditis were high (100%, 80%, 60%, and 60%). Combination therapy was initiated most commonly for persistent bacteremia (60%). When patients were bacteremic, the median preceding duration was 8 days and the median time to clearance was 3 days. Total microbiologic cure rate was 100%. At 30 days from infection onset, all-cause mortality was 11.1% and there were zero bacteremia relapses.

Discussion:

Ceftaroline combination therapy demonstrated success in diverse cases of refractory MRSA-B. When persistent bacteremia was paired with incomplete source control, combination therapy remained effective. We propose this to be a clinical niche particularly worthy of further study. The ideal timing for initiating combination therapy remains unanswered. In closing, our findings suggest that daptomycin/ceftaroline and vancomycin/ceftaroline combination therapy can be considered for complicated MRSA bacteremia when other treatment options fail or are unavailable.

Funding:

No funding sources were used for this research project.

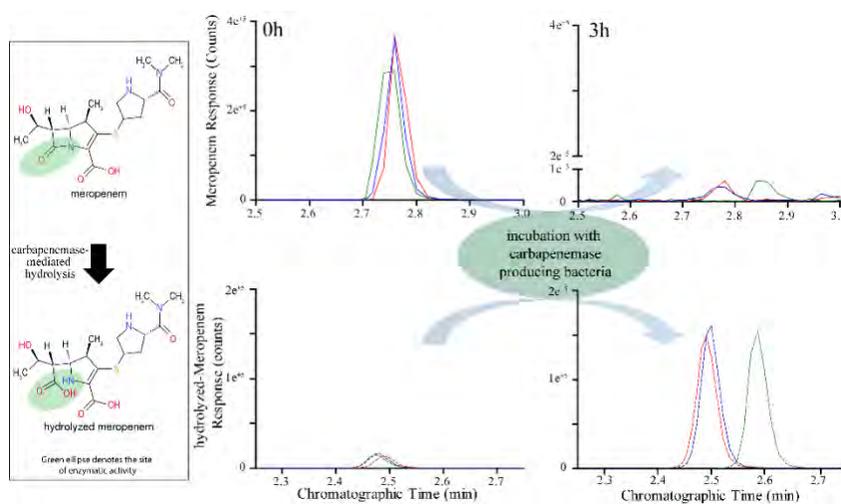
Bioanalytical Capabilities of the Texas Children's Microbiome Center – Mass Spectrometry Laboratory (TCMC-MSL).

Horvath, T.D.^{1,2}, Haidacher, S.J.^{1,2}, Hoch, K.^{1,2}, Haag, A.M.^{1,2}

1. Department of Pathology and Immunology, Baylor College of Medicine, Houston, TX
2. Texas Children's Microbiome Center, Department of Pathology, Texas Children's Hospital, Houston, TX

Abstract

The Texas Children's Microbiome Center – Mass Spectrometry Laboratory (TCMC-MSL) is an expertly staffed and fully equipped bioanalytical research laboratory that specializes in high-performance liquid chromatography-tandem mass spectrometry (LC-MS/MS)-based analysis of the molecular content of microbiologically-relevant sample matrices (*e.g.*, filter-sterilized media, bacterial cells, and stool). This poster showcases a handful of bioanalytical capabilities offered by the TCMC-MSL.



For example, the lab uses a low-resolution LC-MS/MS system consisting of a Shimadzu Nexera X2 MP UHPLC coupled to a Sciex 6500 QTRAP triple-quadrupole mass spectrometer (TQMS) to perform Antimicrobial Resistance (AMR) screening of pathogenic bacterial. In the illustration on the far end of the figure on the left, the green ellipses highlight the location of carbapenemase-mediated enzymatic hydrolysis of

meropenem. The chromatograms ($n=3$ biological replicates) in the middle of the figure are for meropenem (top) and hydrolyzed meropenem (bottom) with 0h of exposure to carbapenemase producing bacteria. The chromatograms on the right-hand side of the figure are meropenem (top) and hydrolyzed meropenem (bottom) after 3h of exposure to suspended carbapenemase producing bacteria. The TCMC-MSL has developed TQMS methods for a whole host of antibiotic/hydrolyzed antibiotic pairs for a small subset of AMR-bacteria.

Generally, the TCMC-MSL lab uses the TQMS system to perform the following targeted analyses: i) quantitative analysis of metabolites, quorum sensing compounds, and short-chain fatty acids (SCFAs); ii) measurement of antibiotic (substrate) and hydrolyzed antibiotic (product) pairs after exposure to beta-lactamase-producing bacteria; iii) screening of novel bacteria-derived antibiotic metabolites; iv) drug metabolism (and potentially pharmacokinetic and pharmacodynamics); and, v) for targeted proteomics analysis. The lab uses an ultra-high resolution LC-MS/MS system consisting of a Thermo Fisher Scientific Orbitrap Fusion mass spectrometer (OTMS) that can be connected to either a standard-LC flow Shimadzu Nexera UHPLC system for non-biased metabolomics, or to a Dionex Ultimate 3000 RSLCnano system for shotgun proteomics applications.

Poster #12

The Texas Children's Hospital Department of Pathology and Immunology has purchased the scientific instrumentation described, and provides salary support to TCMC-MSL staff.

Repurposing Bioactive Compounds for Treatment of Multidrug-Resistant Pathogens

Hummell N¹, Kirienko N¹

1. Department of Biosciences, Rice University

Corresponding author: Natasha Kirienko, Department of Biosciences, Rice University, 6100 Main St, Houston, TX, kirienko@rice.edu

Infection by multidrug-resistant pathogens is a growing problem worldwide. Unfortunately, antimicrobial development has diminished due to a range of reasons including regulatory difficulties and non-profitability. An effective alternative is drug repositioning/repurposing, wherein known molecular entities are used for treatment of bacterial infections. In our study we sought to characterize the antimicrobial properties of five known bioactives (DMAQ-B1, carboplatin, oxaliplatin, CD437, and PSB-069) discovered in a high-throughput phenotypic screen for small molecules that extended *Caenorhabditis elegans* survival during exposure to the multidrug-resistant pathogen *Pseudomonas aeruginosa* PA14. We used CFU assays, crystal violet staining, and fluorescence microscopy to assay the effect of the molecules on bacterial growth, biofilm production, and production of virulence factors. Additionally, we assessed synergy between our molecules and standard of care drugs and the ability of the molecules to rescue from additional pathogens *Staphylococcus aureus*, and *Enterococcus faecalis*. Lastly, we determined the toxicity of our compounds in both mammalian cell culture and *C. elegans*.

We observed that several of these molecules rescued infections with common Gram-positive pathogens *E. faecalis* and *S. aureus*. Interestingly, the platinum complexes displayed increased antimicrobial activity against *P. aeruginosa* compared to *S. aureus* or *E. faecalis*. Most notably, the naturally occurring insulin mimetic DMAQ-B1 exhibited low micromolar MICs against multiple pathogens and was capable of rescuing *C. elegans* against all pathogens. CD437 showed slight synergy with ampicillin. Although CD437 and DMAQ-B1 showed significant toxicity in mammalian cell culture, it is unclear whether this can be separated from their strong antimicrobial activity and low rescuing concentrations, making them compelling candidates for future studies aimed at determining their potential for drug repositioning.

A Single-Center Surveillance Study of Cystic Fibrosis Microbiological Culture

Jo J, Gonzales-Luna AJ, Garey KW

Department of Pharmacy Practice and Translational Research, University of Houston

Corresponding author: Jinhee Jo, Department of Pharmacy Practice and Translational Research, University of Houston, 4849 Calhoun Rd, Houston, TX, E-mail: jjj3@central.uh.edu

Objectives: Patients with cystic fibrosis (CF) are known to suffer from chronic pulmonary infections, often with gram-negative organisms such as *Pseudomonas aeruginosa*. As the disease progresses, these organisms are rarely eradicated and known to chronically colonize patients. Overtime, they grow to be multidrug resistant (MDR); however, the patterns and mechanisms of resistance are now well known. The objective of this study was to examine the pathogen diversity of respiratory cultures from CF patients, with a focus on the microbiological characteristics of MDR *Pseudomonas aeruginosa*.

Methods: This is a descriptive analysis of CF patients with respiratory cultures positive for *Pseudomonas aeruginosa* from February 2017 through October 2019 at Baylor St. Luke's Medical Center (BSLMC). A retrospective chart review was performed to collect patient demographics, organism identification and susceptibility, and intravenous antibiotic use.

Results: A total of 62 *P. aeruginosa* isolates were identified from CF patients at BSLMC. Thirty-six (58%) isolates were obtained from outpatient settings and 26 (42%) from inpatient settings. The majority of the patients were female (n=34, 55%) and Caucasian (n=49, 78%) and the average age was 32.2 ± 11.2 years. The last known predicted FEV₁ average was 45.8 ± 19.4 %. Of 62 patients, 43 (69%) grew either mucoid *P. aeruginosa* or both mucoid and non-mucoid phenotypes. Susceptibility of *P. aeruginosa* most commonly demonstrated resistance to meropenem (88%), gentamicin (79%), and tobramycin (62%). Common organisms that co-existed with *P. aeruginosa* were *Staphylococcus aureus* (n=30, 48%) and *Candida* species (n=21, 34%). Analysis of a cohort of patients with pulmonary exacerbation (n=27) showed that intravenous tobramycin (74%) was the most commonly used agent to treat *P. aeruginosa*, followed by meropenem (41%), colistin (22%), 3rd/4th generation beta-lactams (19%), and piperacillin-tazobactam (19%). Lastly, 17 patients (65%) of this cohort study were re-admitted to the hospital within a year time-frame since discharge.

Conclusions: Cystic fibrosis remains a challenging disease state for many clinicians. This study emphasizes the lack of consensus for managing pulmonary exacerbation as well as highlights the gap between organism *in vitro* susceptibility and choice of intravenous antibiotics during pulmonary exacerbation. Additional investigation will be beneficial to identify risk factors and to explore combinations of antibiotics against CF pathogens to improve clinical outcomes.

Funding sources: No funding sources to disclose.

Mapping the Determinants of Antibiotic Catalysis and Substrate Specificity of CTX-M β -lactamases

Judge A¹, Soeung V¹, Huang W², Palzkill T^{1,2}

1. Department of Biochemistry and Molecular Biology, Baylor College of Medicine

2. Department of Pharmacology and Chemical Biology, Baylor College of Medicine

Corresponding author: Dr. Timothy Palzkill, Department of Pharmacology and Chemical Biology, Baylor College of Medicine, 1 Baylor Plaza, Houston, TX, E-mail: timothyp@bcm.edu

β -lactamases are the most commonly found source of antibiotic resistance and a pressing public health threat. Initially identified by their ability to hydrolyze penicillins, β -lactamases have evolved to hydrolyze more recently developed cephalosporins and carbapenems. Of these extended spectrum β -lactamases (ESBLs), the CTX-M family is the most commonly found in the clinic. CTX-M enzymes are characterized by their efficient hydrolysis of cefotaxime, in addition to penicillins. We have chosen CTX-M-14 as a representative enzyme for this study with the goal of identifying essential and non-essential residues for antibiotic catalysis in CTX-M β -lactamases. To this end, we selected 17 amino acids in and around the CTX-M-14 active site. Using site-directed mutagenesis, we randomized the codon for each position to create libraries with all possible substitutions at each of the 17 sites. The libraries were introduced into *E. coli* for growth in media containing ampicillin or cefotaxime to select functional mutants. Subsequently, deep sequencing of the surviving clones provided the frequency of each amino acid variant, which allowed us to determine the fitness level of each mutant compared to wild type. This revealed which residues are essential for hydrolysis of ampicillin or cefotaxime, many of which are substrate-specific. Additionally, among the non-essential residues, we have identified previously unknown substitutions that are more functional or as functional as the wild-type amino acid. These results elucidate the role of active site residues in CTX-M family β -lactamases, which is a crucial tool for understanding the mechanism and evolution of these clinically relevant antibiotic resistance enzymes.

Research reported in this publication was supported by **R01-032956** from the National Institute of Allergy and Infectious Disease and by **T32-059285** through the University of Texas Health Science Center and the Gulf Coast Consortia.

Pyoverdine Production Drives Gallium Nitrate Persistence in *Pseudomonas aeruginosa*

Kang, D, Kirienko, NV

Department of BioSciences, Rice University, Houston, TX

Correspondence: Natasha Kirienko, Department of BioSciences Rice University, 6100 Main St., Houston, TX, E-mail: kirienko@rice.edu

Pseudomonas aeruginosa is a gram-negative, multidrug-resistant pathogen that causes life-threatening infections in immunocompromised patients particularly those with cystic fibrosis. The emergence of multi and pan-drug resistant *P. aeruginosa*, especially strains resistant to carbapenems, necessitates the development of new therapeutic avenues. Gallium nitrate has been proposed as a promising antimicrobial for this purpose. Cationic gallium (Ga^{3+}) disrupts bacterial iron homeostasis and inhibits essential metabolic enzymes, killing drug-resistant strains and dispersing established biofilms. However, we demonstrate that pyoverdine, primary virulence factor and major siderophore produced by the bacterium, functions as a key defense mechanism against gallium. When compared to wild-type *P. aeruginosa*, an isogenic pyoverdine biosynthetic mutant exhibits increased susceptibility to gallium treatment with an approximately two-fold decrease in the minimum inhibitory concentration (MIC). Furthermore, at concentrations far above the MIC, gallium persistence is observed for wild-type *P. aeruginosa*, but not the pyoverdine mutant. Some of these persistent cells exhibit increased pyoverdine production, which suggests that during infection, repopulation by gallium-persistent cells may exacerbate the disease. We currently postulate that pyoverdine binds and sequesters gallium in the periplasm of the bacterium, preventing the metal from exerting antimicrobial properties in the cytoplasm. While this work cautions the use of gallium as an antipseudomonal therapeutic, it also demonstrates that gallium is a highly effective drug against pyoverdine-negative strains of *P. aeruginosa*, which are frequently observed in chronic cystic fibrosis lung infections.

This work was supported by the National Institutes of Health grants NIAID K22AI110552 and NIGMS R35GM129294 and the Welch Foundation grant C-1930 awarded to NVK.

Mathematical Modeling of Bacterial Population Size Measurements Produced by an Optical Instrument

Iordanis Kesisoglou^a, Vincent H Tam^{a,b}, and Michael Nikolaou^a

a) Department of Chemical & Biomolecular Engineering, University of Houston, Houston, TX 77204-4004

b) Department of Pharmacy Practice and Translational Research, University of Houston, Houston, TX 77204-5039

Corresponding author: Dr. Michael Nikolaou, Department of Chemical & Biomolecular Engineering, 4800 Calhoun Rd, Houston, TX 77004, E-mail: nikolaou@uh.edu

Background: Aids in guiding the selection and dosing of effective antibiotic treatments (including combinations of antibiotics) are useful both for therapeutic purposes and for mitigating the emergence of resistant bacterial strains. Our research group is currently developing an integrated approach towards rapidly and reliably making decisions on personalized combinations of antibiotics to combat resistance. The basic idea of the proposed approach is that efficient numerical processing of purposefully collected time-kill data can greatly improve decision making on effective antibiotics and dosing regimens against a bacterial population

Material/methods: The approach under development relies on (a) use of optical methods (optical density and forward light scatter intensity) for efficient continuous measurements of the size of a bacterial population exposed to antibiotics at various concentrations fixed over a period of time, and (b) analysis of collected data using a mathematical model, to determine optimal antibiotics and dosing regimens against that bacterial population. As measurements of a bacterial population size by optical methods cannot distinguish between live and dead bacterial cells in a suspension, careful quantitative analysis of collected data is needed. The purpose of this presentation is (a) to show the development and application of the mathematical equations relevant to modeling the signals produced by an instrument of this nature for heterogeneous populations of susceptible and resistant bacteria, and (b) to explain how such equations can be used in related decision making. An experimental case study on an instrument under joint development with an industrial partner is used to demonstrate the proposed approach

Three experimental trials and one with the optical density device were performed. The bacteria used was ATCC *Acinetobacter baumannii* BAA747 (AB) and was treated with levofloxacin (LEVO) during the time kill experiments. The medium used was cation adjusted Mueller- Hinton broth. The concentrations tested: placebo, 0.5, 2, 8 MIC where MIC has a value of 0.25mcg/ml. The lab experiment was performed for 24 hours and in the optical density (OD) device operated for 48 hours. Bacteria burden was quantified via quantitative culture and optically accordingly. The two approaches were compared to verify the mathematical model

Results: The mathematical models N_{total} and N_{live} were able to represent with reasonable accuracy the optical device results and the actual lab results.

Conclusion: The impact of the paper is that it establishes a linkage between the experimental results and the optical device results allowing for future utilization of the researched technology. The experimental confirmation of the model opens the doors to future study of multidrug resistant bacteria that can solve current occurring matters and save lives.

Poster #48

Funding source: This study is supported by the National Institutes of Health (R01AI140287-01)

Resensitization to β -lactams in Daptomycin (DAP) Resistant Enterococci is Caused by Multifaceted Penicillin-Binding Protein (PBP) Alterations and Cell Membrane (CM) Remodeling, Mediated by a Single Protein

Ayesha Khan^{1,2}, A. Nguyen^{1,2}, O. Pemberton³, H. Vitrac⁵, D. Panesso^{1,5,6}, T. T. Tran^{1,3}, M. Arthur⁷, Y. Shamoo³, W.R Miller^{1,3}, C.A. Arias^{1,2,3,4,8}

¹Center for Antimicrobial Resistance and Microbial Genomics, UTHealth, ²MD Anderson Cancer Center, UT Health, Graduate School, ³Rice Univ, ⁴Department of Biochemistry, McGovern Med School, ⁵Division of Infectious Diseases, McGovern Med School, ⁶U. El. Bosque, ⁷INSERM E0004-LRMA, Université Paris VI, ⁸Center for Infectious Diseases, School of Public Health, UTHealth.

Background: DAP disrupts the bacterial CM by binding to septal anionic phospholipids (APLs). LiaX, an effector of the LiaFSR stress system, modulates DAP-R by diverting APLs away from the septum. Enterococci are intrinsically resistant to β -lactams due to the presence of PBPs (e.g., PBP5) with low affinity to these drugs. However, emergence of DAP-R leads to increased susceptibility to β -lactams, a phenomenon designated as the see-saw effect. Here, we dissect the molecular mechanism of this phenomenon.

Methods: We studied a clinical strain pair of DAP-S (S613) and DAP-R (R712) *E. faecalis* strains recovered from a patient before and after DAP therapy. We generated deletions of *liaX* and *pbp* genes in DAP-susceptible (DAP-S) *E. faecalis* OG1RF using a CRISPR Cas9 system and in JH2-2 using a P-CI-Phe counter selection system. APLs and membrane structures were visualized with NAO and/or FM4-64. PBPs and LiaX localization was evaluated with bocillin-FL or immunofluorescence. *PBP* transcripts and PBP5 protein levels were measured by qRT-PCR or immunoblotting, respectively. β -lactam binding affinity of PBPs was assessed by SDS-PAGE of bocillin-FL stained membranes. The LiaX-PBP5 interaction was evaluated by the bacterial two-hybrid (BACTH) system, an *in vivo* pull down assay and microscale thermophoresis. MICs were determined via E-test.

Results: Deletion of *liaX* led to DAP-R and redistribution of APL microdomains away from the division septum in all strains, with a ~250 fold decrease in ceftriaxone (CRO) MICs. PBP5 was essential for β -lactam resistance but not for DAP-R. PBPs were mislocalized to sites of nonseptal CM deformities in DAP-R strains. LiaX and PBP5 were confirmed to strongly interact and colocalized to the septum in DAP-S strains but were redistributed away from the septum upon emergence of DAP-R. PonA, *pbp5* and *pbpA/B* had increased bocillin binding affinity in all DAP-R strains. This increased β -lactam affinity was not due to increased *pbp* transcription or PBP5 protein levels. Notably, the class A *pbpF* was upregulated in all DAP-R strains relative to DAP-S strains and was the only cell wall synthesis protein directly regulated by the LiaFSR system. Previous studies show that the class A *pbpZ* is highly susceptible to cephalosporins. Deletion of *pbpZ* abolished the seesaw effect in a DAP-R strain making it resistant to both DAP and CRO.

Conclusion: LiaX regulates CM adaptation and cell wall synthesis via CM remodeling and direct interactions with key PBPs. DAP-R results in mislocalization of PBPs to sites of non-septal CM deformities—a consequence of CM remodeling, and this likely increases access of β -lactams to the active site of some PBPs. *PbpF* is upregulated when the LiaFSR system mediates DAP-R in order to likely compensate for mislocalized and functionally compromised PBPs. *PbpZ* is essential for the seesaw effect. Thus, the likely mechanism of the seesaw effect is that DAP-R causes mislocalization of key low-affinity PBPs like *pbp5*

Poster #16

which compromises their function and leaves pbpF and pbpZ, the pbp that is hypersusceptible to cephalosporins, to compensate for cell wall synthesis.

Funding: R01AI093749 and R21/R33 AI121519 to C.A.A, R01AI080714 to Y.S, K08AI135093 to W.R.M, K08AI113317 to T.T.T.

Epidemiologic Surveillance of Carbapenem-resistant Enterobacteriaceae in a Large Academic Teaching Hospital in Houston, Texas Update 2020

Kuo J¹, Carlson T^{1§}, Begum K¹, Jo J¹, Lancaster C¹, Alam MJ¹, Gonzales-Luna AJ¹, Garey K¹

1. Pharmacy Practice and Translational Research, University of Houston College of Pharmacy

[§] Current Affiliation: Fred Wilson School of Pharmacy, High Point University

Background: Carbapenem-resistant Enterobacteriaceae (CRE) have been classified as an urgent threat by the Centers for Disease Control and Prevention (CDC) since 2013. This study sought to understand the current epidemiological trends and characteristics of CRE at our institution.

Methods: Clinical CRE isolates were collected from a single hospital in the Texas Medical Center (TMC) between February 2017 to October 2019. CRE were identified daily by TheraDoc (Premier Inc., Charlotte, NC) and defined using the CDC definition found in the 2012 CRE Toolkit. Organism identification. MIC determinations were performed using the Vitek 2 system (bioMérieux, Marcy l'Étoile, France), and minimum inhibitory concentrations (MICs) were interpreted using the 29th edition of the Clinical Laboratory Standards Institute M100 document or product package insert. The STRECK ARM-D kits (Omaha, NE) was used to differentiate *bla*_{KPC}, *bla*_{NDM}, *bla*_{VIM}, *bla*_{OXA-48}, and *bla*_{IMP} gene sequences from pure colonies.

Results: A total of 142 CRE isolates were identified during the study period. The most common culture sites were urine (42.2%), lung (17.6%), wound (14.1%), and blood (13.4%). Twelve species were identified, the most prevalent of which were *Klebsiella pneumoniae* (49.3%), *Escherichia coli* (17.4%), and *Enterobacter cloacae* complex (10.9%). Polymerase chain reaction identified only *bla*_{KPC}, which was present in 30.1% of tested isolates. The gene *bla*_{KPC} was most commonly prevalent in *Klebsiella pneumoniae* (50.0%) and *Escherichia coli* (28.6 %). Overall, the MIC₅₀/MIC₉₀ values for meropenem and ertapenem were 16 µg/mL (range 0.25-128 µg/mL) and 8 µg/mL (range 0.5-16 µg/mL), respectively.

Conclusions: Carbapenemase production was limited to *bla*_{KPC} and was present in 30.1% of clinical CRE isolates, which is similar to previous epidemiological observations in the United States.

Corresponding author: Julie Kim Kuo, PharmD, Pharmacy Practice and Translational Research, University of Houston College of Pharmacy, 4849 Calhoun Road, Houston, Texas, E-mail: kgarey@uh.edu

Rcs Envelope Stress Response Detects and Counteracts Cationic Antimicrobial Peptides

Lach SR¹, Konovalova A¹

Department of Microbiology and Molecular Genetics, McGovern Medical School, The University of Texas Health Science Center at Houston (UTHealth)

Corresponding author: Anna Konovalova, Department of Microbiology and Molecular Genetics, McGovern Medical School, The University of Texas Health Science Center at Houston (UTHealth), 6431 Fannin St, Houston, TX. Email: Anna.Konovalova@uth.tmc.edu

Gram-negative bacteria have a multi-layer cell envelope which is an important protective barrier against toxic molecules, including antibiotics. Bacteria have several envelope stress response pathways to monitor the integrity of the cell envelope. One of the pathways that bacteria use to cope with outer membrane (OM) stress is the Regulator of Capsule Synthesis (Rcs) pathway. Rcs is a complex phosphorelay; it is conserved in *Enterobacteriaceae* and is an important factor of intrinsic antibiotic resistance. The phosphorelay consists of two inner membrane components, RcsC – the hybrid histidine kinase, and RcsD – a phosphotransmitter, as well as a cytoplasmically localized transcriptional response regulator – RcsB. The phosphorelay is regulated by IgaA, an inner membrane protein which acts as an inhibitor of the system, and by the surface-exposed lipoprotein sensor, RcsF, which assumes a transmembrane topology by spanning the lumen of OM proteins (OMPs). Cationic antimicrobial peptides (CAMPs) activate Rcs by binding and disrupting packing of lipopolysaccharides (LPS). RcsF monitors LPS and when it detects disruption, it transduces the stress signal across the OM to its downstream partner IgaA, relieving inhibition of the phosphorelay. Interaction between IgaA and RcsF has been observed but the molecular mechanism of signal transduction is not understood. Our hypothesis is that in response to LPS stress, the RcsF/OMP complex undergoes a conformational change allowing the interaction between the periplasmic domain of RcsF with IgaA. To elucidate the interaction interface between RcsF and IgaA, I use a combination of genetic and biochemical approaches. We have generated a site-saturated mutant library of *rscF* and used it in combination with next generation sequencing to isolate *rscF* mutants defective in signal transduction to IgaA. I also use *in vivo* crosslinking to monitor how RcsF/IgaA interaction changes under stressed conditions. These findings will help elucidate the molecular mechanism involved in Rcs signal transduction. As the Rcs stress response is an important factor of intrinsic antibiotic resistance, the knowledge gained from the proposed studies will improve our understanding of how bacteria remodel their envelopes to promote survival during antibiotic challenges.

Funding: Welch Foundation Research Grant

Development And Evaluation Of A Novel Protein-based Assay For Specific Detection Of KPC β -lactamases From *Klebsiella pneumoniae* Clinical Isolates

Shuo Lu¹, Victoria Soeung¹, Hoang A.T. Nguyen², S. Wesley Long²,

James M. Musser^{2,3} and Timothy Palzkill^{1,4*}

1.Department of Pharmacology and Chemical Biology, Baylor College of Medicine,

2.Department of Pathology and Genomic Medicine, Houston Methodist Hospital Research Institute,

3.Department of Pathology and Laboratory Medicine, Weill Cornell Medical College

4.Department of Biochemistry and Molecular Biology, Baylor College of Medicine

Corresponding author: Timothy Palzkill, Department of Pharmacology and Chemical Biology, Department of Biochemistry and Molecular Biology, Baylor College of Medicine, One Baylor Plaza, Houston, Texas, Email: timothyp@bcm.edu

Abstract:

Carbapenemases confer resistance to nearly all β -lactam antibiotics. The extensive spread of carbapenemase-producing multidrug-resistant bacteria contributes significantly to hospital-acquired infections. We have developed a novel protein-based binding assay that identifies KPC β -lactamases from clinical isolates. We used the protein-protein interaction between KPCs and a soluble β -lactamase inhibitory protein (BLIP) variant, BLIP^{K74T/W112D}, which specifically inhibits KPCs but not other β -lactamases. In this assay, BLIP^{K74T/W112D} was allowed to form complexes with KPC-2 in bacterial cell lysates and then extracted using His-tag binding resins. We demonstrated the presence of KPC-2 by monitoring the hydrolysis of a colorimetric β -lactam substrate. Also, to further increase the accuracy of the method, a BLIP^{K74T/W112D} mediated inhibition assay was developed. The binding and inhibition assays were validated by testing 127 *K. pneumoniae* clinical isolates with known genome sequences for the presence of KPC. Our assays identified a total of 32 strains as KPC-2 producers, a result in 100% concordance with genome sequencing predictions. To further simplify the assay and decrease the time to obtain results, the BLIP^{K74T/W112D} protein was tested in combination with the widely used Carba-NP assay. For this purpose, the genome-sequenced *K. pneumoniae* strains were tested for the presence of carbapenemases with the Carba-NP test with and without the addition of BLIP^{K74T/W112D}. The test accurately identified carbapenemase-producing strains and the addition of BLIP^{K74T/W112D} allowed a further determination that the strains contain KPC carbapenemase. Thus, the BLIP^{K74T/W112D} protein is an effective sensor to specifically detect KPC β -lactamases produced by clinical isolates.

Antimicrobial Mode of Action of Ebselen Against *Clostridium difficile*

Ravi K. R. Marreddy¹, Min Dong² and Julian G. Hurdle¹

¹Centre for Inflammatory and Infectious Diseases, Institute for Bioscience and Technology, Texas A&M, Houston, TX, USA

²Department of Microbiology and Immunology, Harvard Medical School, Boston, MA USA

Corresponding author: [Julian G. Hurdle](mailto:jhurdle@ibt.tamhsc.edu), Center for Infectious and Inflammatory Diseases, Institute of Biosciences and Technology, Texas A&M Health Science Center, 2121 West Holcombe Blvd., Houston, Texas 77030, USA, E-mail: jhurdle@ibt.tamhsc.edu

Abstract:

Clostridium difficile, an anaerobic Gram-positive spore forming pathogen, is the leading cause of nosocomial diarrhoea. High recurrence rates and emergence of more virulent strains necessitate the development of alternative approaches to combat *C. difficile* infections (CDIs). Most CDI anti-virulent approaches focus on inactivating TcdA and TcdB, the organism's main virulence toxins. Ebselen, an organoselenium compound, was identified as an anti-toxin that forms covalent adducts with the cysteine protease domains of TcdA and TcdB. From animal efficacy studies, it was suggested ebselen lacked anti-microbial activity against *C. difficile*, suggesting its anti-toxin action as the main explained why ebselen attenuated CDI pathogenesis. We therefore investigated the *in vitro* anti-*C. difficile* action of ebselen, because of reports of its antimicrobial activity against various bacteria, and because anaerobic *C. difficile* carry cysteine-containing redox enzymes that could react with ebselen. Ebselen (from Sigma) was found to inhibit growth of various *C. difficile* strains with MICs 2-8 µg/ml. Only strains of *C. difficile* PCR-ribotype 078 were resistant to ebselen with MIC ≥64 µg/ml. Growth of other clostridial species like *C. perfringens* and *C. sporogenes* were inhibited at higher concentrations (MICs >32 µg/ml). Similarly, growth of *P. neonis* and *B. fragilis* were not affected until 32 µg/ml. However, *L. reuteri* and *B. ovatus* were inhibited by 8 and 2 µg/ml of ebselen, respectively. In terms of effects of *C. difficile* pathogenesis, ebselen at ~8 x MIC (64 µg/ml) inhibited cellular production of toxins. It inhibited toxin activity at IC₅₀ ~3.5 µg/ml against toxin B from List Biologicals. Mechanistic studies of ebselen's target action against *C. difficile* is ongoing and these updates of will be presented. These studies suggest ebselen exhibits dual action against *C. difficile* and that its anti-toxin activity might not be the only reason for *in vivo* efficacy of this compound.

Acknowledgement:

We are grateful to the National Institutes of Health for funding R01AI132387.

Evolution of Resistance to Doxycycline and Ciprofloxacin in the Category A Bioterrorism Agent, *Francisella tularensis*

Heer H. Mehta¹ and Yousif Shamoo¹

¹ Department of Biosciences, Rice University, Houston, TX, USA.

Corresponding author: Yousif Shamoo, Department of Biosciences, Rice University, 6100 Main St., Houston, TX, USA: shamoo@rice.edu

One of the prerequisites to combat the global rise in antimicrobial resistance is to identify mechanisms causing resistance which will in turn enable the design and development of novel strategies to tackle this phenomenon. In addition to being a threat in the healthcare industry, antimicrobial resistant pathogens are also a potential bioterrorism risk. *Francisella tularensis*, one of the most infectious pathogenic bacteria, is a potential bioterrorism agent that has been weaponized by various countries in the past. As few as 10 organisms are sufficient to cause serious illness and death. For mass casualty settings and postexposure prophylaxis, the Centers for Disease Control and Prevention (CDC) recommends administration of doxycycline and ciprofloxacin, and maintains stockpiles of the same. With the rise in antimicrobial resistance around the globe, resistance to antimicrobial agents among *Francisella* isolates is a concern, especially if a resistant strain is deployed as a WMD. In this work, we have systematically evolved a susceptible, live vaccine strain of *Francisella tularensis* subsp. holarctica (LVS) to different regimens of doxycycline and ciprofloxacin to uncover the mechanisms by which resistance can be achieved. The different regimens include: (a) adaptation to ciprofloxacin and doxycycline individually (monotherapy), (b) sequential evolution of doxycycline adapted populations to ciprofloxacin (sequential monotherapy) and (c) adaptation to a combination of ciprofloxacin and doxycycline (combinatorial therapy). Following serial passaging of 5 replicate populations for each adaptation regime, individual colonies (end point isolates) were isolated from the final resistant populations and screened for their antimicrobial susceptibilities to doxycycline, ciprofloxacin as well as chloramphenicol, gentamicin and streptomycin that are routinely used for the treatment of tularemia. Adaptation to doxycycline led to an increase in tolerance, but not resistance, to ciprofloxacin, which in turn allowed the cells to adapt more rapidly to sequential treatment with ciprofloxacin. Surprisingly, the time taken for the susceptible cells to adapt to the combinatorial regime was no greater than the time taken for them to adapt to each drug individually. This finding was counterintuitive since ciprofloxacin (inhibits replication) and doxycycline (inhibits translation) have two distinct mechanisms of action and adaptation to the two drugs simultaneously would imply that the cells would have to evolve different mutations affecting two major aspects of cellular metabolism simultaneously. We are currently in the process of using whole genome deep sequencing to identify potential mutations in each of the evolved populations and their associated end point isolates which will shed some light on the mechanisms of resistance. We hypothesize that in the case of the combinatorial treatment, the cells could have mutations within an efflux pump that can export both, doxycycline and ciprofloxacin, thus allowing them to acquire resistance to both drugs in one step. Findings from this study will provide the basis for designing novel strategies to combat antimicrobial resistant *F. tularensis* which will in turn impact the health of civilians as well as warfighters in the event of bioterrorism.

The project is sponsored by the Department of the Defense, Defense Threat Reduction Agency (HDTRA1-15-1-0069) to Y.S.

Population Structure of CTX-M-Producing Extraintestinal Pathogenic *E. coli* (ExPEC) from Patients with Urinary Tract Infections (UTI) and Bloodstream Infections from Colombia

De La Cadena E^{1,2}, Mojica MF^{1,3,4}, Castillo N¹, Correa A^{2,5}, Appel T¹, Pallares CJ¹, and Villegas MV^{1,2}

¹ Grupo de Investigación en Resistencia Antimicrobiana y Epidemiología Hospitalaria, Universidad El Bosque, Bogotá, Colombia.

² Centro Internacional de Entrenamiento e Investigaciones Médicas, Cali, Colombia

³ Department of Infectious Diseases, Case Western Reserve University, Cleveland, OH

⁴ Research Service, Louis Stokes Veterans Affairs Medical Center, Cleveland, OH

⁵ Universidad Santiago de Cali, Cali, Colombia.

Corresponding author: Maria Virginia Villegas, Grupo de Investigación en Resistencia Antimicrobiana y Epidemiología Hospitalaria, Universidad El Bosque, Bogotá, Colombia. mariavirginia.villegas@gmail.com

Objectives: Local surveillance studies in Colombia have shown high rates of cephalosporin resistance and more than 20% of ESBL-producing *E. coli* (*Eco*). This caused an increased use of carbapenems, leading to the emergence of carbapenemase-producing bacteria. However, phylogenetic group, ST, virulence factors and antibiotic susceptibility profile of ExPEC remains unexplored. The aim of the present study was to determine the molecular characteristics of CTX-M group 1 producing-*Eco* causing urinary tract and bloodstream infections community-acquired in Colombia.

Methods: 26 *Eco* non-duplicate isolates, CTX-M group 1 positive from urinary tract and bloodstream infections acquired in hospital and community in Colombia were selected from our repository. Isolates were whole-genome sequenced (WGS), and virulence factors (VF), acquired resistance genes (AR), plasmid replicon (PR), quinolone resistance–determining region (QRDR) mutations and phylogenetic group were identified.

Results: 22/26 isolates produced CTX-M-15 (84.6%), 3/26 produced CTX-M-55 (11.6%) and 1/26 produced CTX-M-3 (3.8%). 11 STs were identified among CTX-M *Eco*, being ST131 the most frequent. WGS revealed that isolates in this clone were from phylogenetic group B1, O25b:H4 and most of them belonged to the H30-Rx pandemic subclone. Other AR identified among these isolates included *bla*_{OXA-1}, *aac(6′)Ib-cr*, *mdfA*, *tetA* and *catB3*. These isolates were significantly associated with the VF *gat*, *iss*, *iha* and *sat*. Resistance to ciprofloxacin was associated with mutations in the QRDR of *gyrA* (S83L, D87N) and *parC* (S80I); only *Eco* ST131 harbored a mutation in *parC* (E84V). Fluoroquinolone-resistant H30-Rx subclone isolates harbored the *gyrA1AB/parC1aAB* combination. IncF plasmids were the most common type found among CTX-M *Eco*. We detected two carbapenem resistant *Eco*, none of them belonging to ST131, one of them co-producing CTX-M 15, KPC-2 and NDM-1; and one isolate harboring *mcr-1*.

Conclusions: Our results shows circulation of *Eco* ST131 clone, B2, O25b:H4 and H30-Rx subclone, with spread of CTX-M-15, QRDR mutations and other resistance genes. Although association of this lineage with carbapenemase genes has been reported elsewhere, our study did not reveal that this is yet happening in Colombia. However active surveillance and antimicrobial stewardship programs along with infection control strategies are warranted.

Funding sources: This work was supported by the Universidad El Bosque grant PCI-2017-9453.

Evaluating the Unnecessary Use of Intravenous Broad-Spectrum Antibiotics in Presumed Sepsis and Septic Shock Patients in the Emergency Department

Esther Y. Bae¹, Tiffeny T. Smith¹, [Marguerite L. Monogue¹](#)

1. Department of Pharmacy, University of Texas Southwestern Medical Center, Dallas, Texas, United States of America

Corresponding author: Marguerite Monogue, Department of Pharmacy, University of Texas Southwestern Medical Center, 6201 Harry Hines Blvd., Dallas, Texas, E-mail: marguerite.monogue@utsouthwestern.edu

Objectives: Recognition of sepsis frequently occurs in emergency departments. To demonstrate the need to optimize antibiotic use in the setting of suspected sepsis, the frequency of unnecessary use of intravenous broad-spectrum antibiotics as well as the percentages of antibiotic-related adverse drug effects were quantified in the emergency department at an academic medical center.

Methods: Electronic medical records of adult patients who were admitted to the emergency department between January 2018 and June 2018 with suspected sepsis (as defined as having two or more systemic inflammatory response syndrome [SIRS] criteria) and received at least one dose of intravenous broad-spectrum antibiotic were reviewed retrospectively.

Results: A total of 218 patients were included in the final cohort. The percentages of confirmed, suspected, and absence of bacterial infections were 19.3%, 44.5%, and 35.9%, respectively. Elevated SIRS (≥ 2) and Quick Sequential Organ Failure Assessment (qSOFA; ≥ 2) scores were not significantly associated with the presence of bacterial infections. Ninety-day *Clostridioides difficile* infections and drug-resistant organism infections were identified in 7 and 6 patients, respectively, regardless of the presence of bacterial infections.

Conclusions: A high number of patients received intravenous broad-spectrum antibiotics in the emergency department without objective evidence of bacterial diseases supported by microbiologic cultures, radiographic images, or other symptoms of infections. The majority of patients who were initially admitted to the emergency department for suspected sepsis were discharged home after only a single dose of intravenous antibiotic. Our findings suggest that identification of sepsis using SIRS may lack specificity and can lead to the overuse of unnecessary antibiotic use in the emergency departments.

No funding sources to disclose.

Cardiolipin Synthase Mediates Daptomycin Resistance in *Enterococcus faecalis*

Nguyen AH¹, Tran TT¹, Panesso D¹, Khan A¹, Shamoo Y⁶, Mileykovskaya E⁵, Vitrac H⁵, Arias CA¹⁻⁴

¹Department of Internal Medicine, Division of Infectious Diseases, ²Center for Antimicrobial Resistance and Microbial Genomics, McGovern Medical School, Houston, Texas ³Center for Infectious Disease, UTHSC School of Public Health, Houston, Texas, USA ⁴Universidad El Bosque, Bogota, Colombia, ⁵Department of Biochemistry and Molecular Biology, McGovern School of Medicine at Houston, Houston, Texas, USA ⁶BioSciences Department, Rice University, Houston, TX, USA

Background. Daptomycin (DAP) is a lipopeptide antibiotic targeting the cell membrane (CM) at the division septum. DAP resistance (DAP-R) in *E. faecalis* (*Efs*) is partly mediated through redistribution of CM anionic phospholipid (APL) microdomains away from their native location at the bacterial division septum. DAP-R has been linked to mutations in genes encoding *i*) the LiaFSR stress response system, and *ii*) lipid biosynthetic proteins, including cardiolipin synthase (*cls*). *Efs* contains two *cls* genes (*cls1* and *cls2*), and only mutations in *cls1* are associated with DAP-R. However, there have been few studies differentiating the roles of the two enzymes in *Efs* and in the development of DAP-R.

We have identified a transmembrane protein, LiaY, as one of the effectors of the LiaFSR system. Deletion of *liaY* abolished redistribution of APL microdomains. Thus, LiaY appears to be involved in the CM response to DAP through an unclear mechanism. Preliminary data using the bacterial two-hybrid system has identified a potential interaction between LiaY and Cls1. We hypothesize that CM adaptation in *Efs* occurs through LiaY-mediated re-localization of Cls1 away from the septum.

Methods To study the roles of Cls1 and Cls2 in *Efs*, deletion mutants of both *cls* genes (individually or together) were generated using the CRISPR/Cas9 system in DAP-S *Efs* OG117 and *Efs* OG117 Δ *liaX* (a DAP-R derivative of OG117). These strains were characterized by measuring *i*) DAP minimum inhibitory concentration (MIC) using E-test on Mueller-Hinton II agar, and *ii*) localization of APL microdomains with 1 μ M 10-N-nonyl-acridine orange staining of exponential phase cells. Quantitative PCR was used to study differential gene expression of *cls1* and *cls2* in *Efs* OG117 Δ *liaX* relative to *Efs* OG117 using the Pfaffl method normalized to the gene for *Efs* OG117 16S rRNA.

Results Single and double gene deletion of *cls1* or *cls2* in DAP-sensitive (DAP-S) *Efs* OG117 showed no changes in DAP MIC nor APL microdomain localization. When *cls1* was deleted in the DAP-R derivative of OG117 (individually or in combination with *cls2*), there was a decrease in the DAP MIC, and double deletion of both *cls* genes in the DAP-R background restored septal localization of anionic phospholipid microdomains. In contrast, no changes in DAP MIC nor anionic phospholipid microdomains were seen when *cls2* alone was deleted in DAP_R OG117 Δ *liaX*. Gene expression studies reveal differential expression of *cls1* and *cls2* in DAP-R *Efs* OG117 Δ *liaX* relative to DAP-S *Efs* OG117, with *cls1* being highly upregulated during late stationary phase in addition to a significant decrease in *cls2* expression.

Conclusions. Our results suggest a major role for Cls1 in the CM adaptive response and subsequent development of DAP-R. We propose a model in which, upon activation of the LiaFSR response, LiaY interacts with and relocalizes Cls1 away from the septum. The resulting mislocalized production of APL diverts DAP from the septum, preventing the antibiotic from reaching critical septal targets.

Funding: R01AI134637 to CAA.

A General In Vitro Model for Simultaneous Simulation of the Dynamics of an Arbitrary Number of Drugs with Different Half-Lives

Iordanis Kesisoglou^a, Vincent H Tam^{a,b}, and Michael Nikolaou^a

a) Department of Chemical & Biomolecular Engineering, University of Houston, Houston, TX 77204-4004

b) Department of Pharmacy Practice and Translational Research, University of Houston, Houston, TX 77204-5039

Corresponding author: Dr. Michael Nikolaou, Department of Chemical & Biomolecular Engineering, 4800 Calhoun Rd, Houston, TX 77004, E-mail: nikolaou@uh.edu

Background: Bacterial resistance to antibiotics has rendered the combined use of antibiotics for therapeutic purposes increasingly important. Laboratory testing of antibiotic combinations often relies on a hollow fiber (HF) system, which allows for patient-relevant antibiotic concentration profiles that vary over time. While the design of such a system is fairly simple for a single antibiotic, it is more elaborate for a combination of two or more antibiotics with different half-lives, as documented in literature, where a specific solution for only two antibiotics has appeared.

Material/methods: The contribution of this work is to propose a general methodology for integrated design of a HF system to be used for testing the bactericidal effectiveness of an arbitrary number, N , of antibiotics with different half-lives. The resulting mathematical formulas are derived based on an experimentally validated dynamic model of a HF system, are simple to apply, and produce designs that are easy to implement in one of two basic configurations (in series or in parallel).

Results: Applied to the case of one antibiotic only, the proposed approach successfully reproduced known designs and confirmed experimental data for four different antibiotics (cefepime, meropenem, piperacillin, and tazobactam). In addition, computer simulations confirmed the validity of proposed designs for combinations of two, three, or four antibiotics with different half-lives.

Conclusion: A general methodology was developed for systematic design of an experimental HF system capable of producing time-varying concentrations for a combination of an arbitrary number, N , of antibiotics with different half-lives. The methodology reproduces known results for a single antibiotic, and has been validated for two, three, and four antibiotics on computer simulations. Experimental verification is currently underway. The proposed methodology will be a useful tool for experimental study of combination therapy in vitro.

Funding source: This study is supported by the National Institutes of Health (R01AI140287-01)

Evaluation of Updated Antimicrobial Susceptibility Testing Assays for *P. aeruginosa* and Aztreonam, Cefotaxime, Cefepime, Meropenem, and Piperacillin/Tazobactam Directly from Positive Blood Culture on the Accelerate Pheno™ System

Oppermann N¹, Shamsheyeva A¹, Sikorski A¹, Taku A¹, Gamage D¹, Chantell C¹, Humphries R¹

1. Accelerate Diagnostics, Inc.

Corresponding author: Niels Oppermann, Accelerate Diagnostics Inc., 3950 S. Country Club Rd., Suite 470, Tucson, AZ 85714, E-mail: noppermann@axdx.com

Objectives: Bacterial bloodstream infections with *Pseudomonas aeruginosa* are associated with significant healthcare costs and mortality, but are clinically indistinguishable from other forms of Gram-negative bacterial infections. For this reason, patients with *P. aeruginosa* infections might receive empiric antimicrobial therapy that is inactive against *P. aeruginosa*, especially before antimicrobial susceptibility results are available, typically 1-2 days later by traditional standard of care methods. Inappropriate therapy has been associated with adverse patient outcomes. In contrast to traditional methods, the Accelerate Pheno™ system delivers phenotypic antimicrobial susceptibility testing (AST) results approximately 7 hours from positive blood culture; the time frame in which therapy changes can positively impact outcomes. This study evaluates the performance of updated AST assays for the following beta-lactam drugs with *P. aeruginosa*: aztreonam (ATM), cefepime (FEP), ceftazidime (CAZ), piperacillin-tazobactam (TZP) and meropenem (MEM). These assays are currently CE-marked and in use in Europe and the Middle East, and have been submitted for FDA-clearance in the U.S.

Methods: One hundred blood culture bottles containing healthy donor blood were inoculated with challenge strains of *P. aeruginosa* and incubated until positivity. Aliquots of the positive blood cultures were tested on the Accelerate Pheno™ system according to the manufacturer's instructions for use. The MIC results were compared to reference broth microdilution. Only samples with valid results from both methods were included in the analysis. Essential agreement (EA), categorical agreement (CA), very major (VME), major (ME), and minor error (mE) rates were calculated using FDA-recommended breakpoints.

Results: EA and CA for all five drugs ranged from 94.0-99.0%. No VMEs were observed. The ME rates were below 2% for all drugs except FEP. For FEP, a ME rate of 6% was observed. However, FDA-recommended breakpoints for FEP do not include an intermediate range and 4 of the 5 MEs were in EA.

Conclusions: This study demonstrates excellent performance of the updated assays for ATM, CAZ, FEP, MEM, and TZP with *P. aeruginosa* on the Accelerate Pheno™ system. Availability of these results in hours rather than days has the potential to improve patient outcomes.

Table 1. Performance results based on 100 challenge strains of *P. aeruginosa*.

Antimicrobial	N	EA	CA	VME	ME	mE
ATM	100	94 (94.0%)	98 (98.0%)	0	0	2 (2.0%)
CAZ	97	94 (96.9%)	96 (99.0%)	0	1 (1.2%)	0
FEP	99	96 (97.0%)	94 (94.9%)	0	5 (6.0%)*	0
MEM	100	97 (97.0%)	94 (94.0%)	0	1 (1.3%)	5 (5.0%)

Poster #22

TZP	94	90 (95.7%)	89 (94.7%)	0	0	5 (5.3%)
------------	----	------------	------------	---	---	----------

*4 of 5 MEs in EA

Evaluation of an Updated Antimicrobial Susceptibility Testing Assay for Enterobacterales and Meropenem Directly from Positive Blood Culture on the Accelerate Pheno™ System

Oppermann N¹, Shamsheyeva A¹, Sikorski A¹, Taku A¹, Gamage D¹, Chantell C¹, Humphries R¹

1. Accelerate Diagnostics, Inc.

Corresponding author: Niels Oppermann, Accelerate Diagnostics Inc., 3950 S. Country Club Rd., Suite 470, Tucson, AZ 85714, E-mail: noppermann@axdx.com

Objectives: Meropenem (MEM) is an important antimicrobial with broad coverage of organisms, including ESBL- and Amp-C-producing Enterobacterales species. Due to the emergence of carbapenem resistance in several geographies, confirmation of a pathogen’s susceptibility to the drug is essential for choosing the correct treatment. The Accelerate Pheno™ system produces phenotypic AST results directly from positive blood cultures in about 7 hours. Meropenem suppression rules were developed and implemented on the system in response to an elevated very major discrepancy rate observed in infrequently occurring challenge isolates at two external study sites. Subsequent updates to the meropenem assay were developed for all Enterobacterales except for *Proteus* spp., that provide MIC results in the majority of cases and a categorical “resistant” result in rare cases, in place of suppression rules, resulting in improved meropenem reportability. The new assay has been CE-marked recently, is in use in Europe and the Middle East, and will be submitted to the FDA for clearance in the U.S.

Methods: 275 Enterobacterales challenge strains (119 *E. coli*, 87 *Klebsiella* spp., 39 *Enterobacter* spp., 25 *Citrobacter* spp., and 5 *S. marcescens*) were seeded into blood culture bottles containing healthy donor blood and incubated until positivity. Aliquots of the positive blood cultures were tested using the Accelerate PhenoTest™ BC kit on the Accelerate Pheno™ system according to the manufacturer’s instructions for use. The rate of non-reports with the new assay was assessed and the MIC and categorical results according to FDA/CLSI breakpoints were compared to reference broth microdilution (BMD). Only samples with valid results from both methods were included in the categorical comparison.

Results: Only 2 of the 275 challenge strains (0.7%) resulted in suppressed MEM susceptibility results. All 75 resistant (by reference) strains were correctly identified as resistant by the Accelerate Pheno™ system; 57 of these produced an MIC result, whereas 18 gave the newly introduced categorical “resistant” result. Only a single isolate was wrongly identified as resistant by the Accelerate Pheno™ system.

Conclusions: This study demonstrates close-to-total reportability and high accuracy of the updated assay for meropenem and Enterobacterales on the Accelerate Pheno™ system.

Table 1. Categorical comparison of results obtained from the Accelerate Pheno™ system and BMD.

		Broth microdilution reference result		
		S	I	R
ate Phe no™ syst em	MIC (S)	197	0	0
	MIC (I)	0	0	2

Poster #54

	MIC (R)	0	0	55
	Categorical R	1	0	18

LiaF might have a an Activator role of the LiaR-Mediated Response Against daptomycin and Antimicrobial Peptides in Multidrug-Resistant *Enterococcus faecalis* (*Efs*)

Diana Panesso¹⁻³, Sandra L. Rincon S^{2,3}, Truc T. Tran¹⁻³, Laura C. Ortiz-Velez¹, Ayesha Khan¹, April Nguyen¹, Rafael Rios³, Lorena Diaz^{2,3}, Yousif Shamoo⁴, Cesar A. Arias, ¹⁻³

¹UTHealth McGovern Med School, Houston, TX, Div. of Infect. Dis., Dept. of Internal Medicine ²CARMiG,

³UGRA, Universidad El Bosque, Bogota, Colombia, UTHealth McGovern Med School Houston, TX,

⁴Department of Biosciences, Rice University, Houston, Texas.

Corresponding author: Cesar A. Arias. Department of Internal Medicine, UTHealth, 6431 Fannin st, Houston, TX, Cesar.arias@uth.tmc.edu

Background: Daptomycin (DAP) is a first-line agent for the treatment of vancomycin-resistant enterococcal infections. Resistance to DAP in enterococci is controlled by the *liaFSR* three-component regulatory system that consists of a histidine kinase sensor (LiaS), a response regulator (LiaR) and a transmembrane protein of unknown function (LiaF). Our previous studies have indicated that deletion of isoleucine in position 177 of LiaF results in DAP tolerance and is sufficient to change membrane architecture. Here, we study the role of LiaF in DAP resistance.

Methods: We obtained two *liaF* mutants in OG1RF, a DAP-susceptible laboratory strain of *Efs* (DAP MIC = 2 µg/ml), **a**) a null *liaF* mutant with a premature stop-codon (OG1RF/*liaF**₁₁), and **b**) an isoleucine deletion at position 177 (OG1RF/*liaF*Δ₁₇₇). Mutants were confirmed by whole genome sequencing. In addition, we complemented *in trans* using the pMSMP3535 nisin inducible vector with the *liaF* wild type and the *liaF*Δ₁₇₇ alleles. DAP MIC was performed by Etest and the characterization of the anionic phospholipids microdomains was done using 10-*N*-nonyl-acridine-orange (NAO). The expression of the *liaXYZ* (the main target of LiaR) and *liaFSR* clusters were evaluated by qRT-PCR and relative expression ratios (log₂-fold change) were calculated by normalizing to *gyrB* expression. We assessed activation of LiaFSR by evaluating surface exposure of LiaX by ELISA. We used the bacterial adenylate cyclase two-hybrid system (BACTH) to evaluate the protein-protein interaction between LiaF-LiaS and LiaF-LiaX

Results: Inactivation of *liaF* did not have any effect on DAP MICs, membrane architecture or a significant increase in LiaX surface exposure compared to parental strain OG1RF. In contrast, deletion of the codon encoding isoleucine in position 177 of LiaF caused a major increase in LiaX exposure (8-fold) and redistribution of anionic phospholipid microdomains away from the septum without changes in the DAP MIC. The complementation *in trans* of the null mutant with the *liaF*Δ₁₇₇ allele, OG1RF/*liaF**₁₁ (pMSP3535::*liaF*Δ₁₇₇) showed redistribution of the anionic phospholipid microdomains away from septum and septal localization for the OG1RF/*liaF*Δ₁₇₇ mutant complemented with the *liaF* wild type allele, OG1RF/*liaF*Δ₁₇₇ (pMSP3535::*liaF*). Transcriptional analyses indicated upregulation (> 2 log₂-fold) in the *liaXYZ* gene cluster indicating activation of the stress response in the (OG1RF/*liaF*Δ₁₇₇).mutant. We also observed a positive interaction between LiaF and LiaS but no interaction was observed between LiaF and LiaX.

Conclusions: LiaF is likely a key activator of the LiaFSR stress response and the critical regulatory domain appears to be located in a stretch of four isoleucines towards the C-terminal of the protein.

Funding: NIH/NIAID R01AI134637, K08 AI113317

Deciphering The Role of *Enterococcus faecium* PBP5 In The See-saw Effect

Pemberton O¹, Singh K^{2,3}, Khan A^{3,4}, Murray B^{2,3}, Arias C^{3,4}, Shamoo Y¹

1. Department of BioSciences, Rice University, Houston, TX, USA
2. Division of Infectious Diseases, Department of Internal Medicine, McGovern Medical School, University of Texas Health Science Center at Houston, Houston, TX, USA.
3. Center for Antimicrobial Resistance and Microbial Genomics and Division of Infectious Diseases, University of Texas Health Science Center, McGovern Medical School, Houston, TX, USA
4. Department of Microbiology and Molecular Genetics, University of Texas Health Science Center, McGovern Medical School, Houston, TX, USA

Corresponding author: Orville Pemberton, Department of BioSciences, Rice University, 6100 Main St., Houston, TX, USA, Email: oap1@rice.edu

Multi-drug resistant strains of enterococci are emerging and are quickly becoming a public health threat. Currently, our supply of effective antibiotics used to treat these pathogens is declining. This project aims to decipher a phenomenon seen in enterococci known as the see-saw effect, where β -lactam sensitivity is correlated with daptomycin resistance and vice versa. In enterococci, the see-saw effect is mediated by penicillin-binding proteins (PBPs) and the extracellular protein, LiaX. The intrinsic resistance of enterococci to β -lactams can be attributed to their low affinity for PBP5.

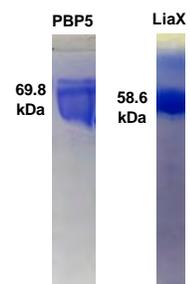


Figure 1. SDS-PAGE of PBP5 and LiaX.

To understand the role of PBP5 in the see-saw effect, the following methods have been used: X-ray crystallography to characterize the three-dimensional structure of PBP5 in complex with β -lactam antibiotics and LiaX; and microscale thermophoresis (MST), a novel and versatile method of measuring biomolecular interactions such as those between PBP5/LiaX.

Investigation into PBP5's role in the see-saw effect involved purification of PBP5 from a clinical isolate of *E. faecium*. PBP5 was expressed in BL21 (DE3) *E. coli* cells and purified to homogeneity. Purity was assessed by SDS-PAGE (Fig. 1). The protein was concentrated and screened with sparse matrix kits. *E. faecium* LiaX was purified in a similar manner to PBP5 and purity was assessed by SDS-



Figure 2. Crystal of apo PBP5.

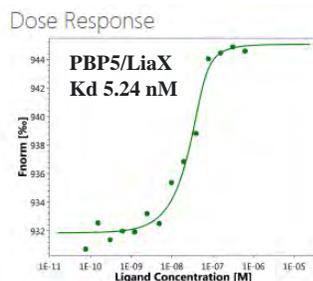


Figure 3. MST of PBP5/LiaX interaction.

PAGE (Fig. 1). A single crystal of PBP5 was observed in a condition containing 0.2 M Calcium chloride, 0.1 M HEPES pH 6.5, and 35% (v/v) Pentaerythritol ethoxylate (Fig. 2). MST was performed on the PBP5/LiaX interaction. Briefly, 50 nM LiaX was labeled with a fluorescent dye and increasing concentrations of PBP5 were titrated (up to 2.5 μ M). The binding affinity of the PBP5/LiaX interaction was calculated to be 5.24 nM (Fig. 3). In conclusion, apo PBP5 crystals will be used to obtain complex crystal structures with β -lactam antibiotics and further screening will be performed to obtain a PBP5/LiaX complex. In addition, MST has

Poster #23

demonstrated that PBP5 and LiaX interact with high affinity, further underscoring their important role in the see-saw effect.

Funding sources: R01AI080714, R01AI134637, R21AI133289

Cefiderocol Retains Anti-Biofilm Activity in Gram-Negative Pathogens

Pybus C¹, Obuekwe V¹, Greenberg DE¹

1. Department of Internal Medicine, Infectious Diseases and Global Medicine, University of Texas Southwestern Medical Center

Corresponding author: David E. Greenberg, Internal Medicine, Infectious Diseases and Global Medicine, University of Texas Southwestern Medical Center, 5323 Harry Hines Blvd, Dallas, Texas, E-mail:

David.Greenberg@utsouthwestern.edu

Cefiderocol is a siderophore cephalosporin with potent antibacterial activity against a broad range of Gram-negative pathogens, including multi-drug resistant strains. Siderophore antibiotics bind ferrous iron and utilize iron transporters to cross the cell membrane. In the biofilm setting (eg complicated urinary tract infection), where antibiotic resistance is high, but iron acquisition is important, Cefiderocol may have advantageous antimicrobial properties. In this study, we compared the antimicrobial activity of Cefiderocol to seven commonly used antibiotics in well-characterized multi-drug resistant pathogens and then determined their efficacy in the biofilm setting.

We first determined minimum inhibitory concentrations (MICs) in Mueller-Hinton II broth (MHII) and iron-depleted cation-adjusted MHII (ID-CAMHB) for Cefiderocol and seven comparator antibiotics in isolates of *Pseudomonas aeruginosa*, *Burkholderia cepacia* complex (Bcc), *Klebsiella pneumoniae*, *Escherichia coli*, *Acinetobacter baumannii*, and *Stenotrophomonas maltophilia*. The MIC₉₀ of Cefiderocol ranged from 0.125 µg/ml (Bcc) to 1 µg/ml (*P. aeruginosa*) in ID-CAMHB. MIC₉₀ values were consistently lower for Cefiderocol in all strains tested compared to other agents (ceftolozane-tazobactam, ceftazidime-avibactam, ceftazidime, piperacillin-tazobactam, imipenem, tobramycin, clarithromycin). This result was recapitulated in MHII, although the MIC₉₀ for Cefiderocol was typically two-fold higher.

We then used MBEC (minimum biofilm eradication concentration) inoculators to test antibiotic activity in biofilms formed on pegs. Established biofilms were challenged with 4 µg/ml Cefiderocol and comparator antibiotics every 12 h for 24 h, then quantified for viable bacteria. In *P. aeruginosa*, Cefiderocol treatment displayed a superior reduction in biofilm (>90% reduction compared to untreated control) as opposed to comparator drugs (15 to 82% reduction). Cefiderocol also reduced biofilm in *K. pneumoniae*, *S. maltophilia*, and *B. cepacia* complex, by 83-91%. Cefiderocol was as generally as effective at eradication as imipenem in *K. pneumoniae* or ceftolozane-tazobactam in *B. cepacia* complex. For *S. maltophilia*, tobramycin (97% reduction) and Cefiderocol (91% reduction) were exceptional in comparison to other antibiotics (12-63% reduction). In contrast, the most potent antibiotic for *A. baumannii* and *E. coli* biofilm reduction was imipenem (>90% reduction vs. Cefiderocol 67-80% reduction). We conclude that Cefiderocol effectively reduces biofilm and is a potent inhibitor of planktonic growth across a range of Gram-negative medically important pathogens.

Disclosures: Funding by Shionogi & Co., Ltd.

A User-Friendly QlikSense® Application To Track & Report Essential Stewardship Metrics

Reynoso D¹, Ferren RS², Britt RS², Nguyen D³, Mitrache I⁴, Trevino R⁴, Palmberg K⁴, McClure M⁴, Williams-Bouyer N⁵, Ren P⁵, Thwe P⁵, Patel J⁶, Bellister S⁷, Williams S⁷, Sharma G¹, Keiser P¹

1. Department of Internal Medicine, University of Texas Medical Branch (UTMB) at Galveston
2. Department of Pharmacy, University of Texas Medical Branch at Galveston
3. Department of Pediatrics, University of Texas Medical Branch at Galveston
4. Department of Clinical Data Management, University of Texas Medical Branch at Galveston
5. Department of Pathology, University of Texas Medical Branch at Galveston
6. Department of Healthcare Epidemiology, University of Texas Medical Branch at Galveston
7. Department of Surgery, University of Texas Medical Branch at Galveston

Corresponding author: David Reynoso MD, PhD, Department of Internal Medicine, University of Texas Medical Branch at Galveston, 301 University Blvd, Galveston, TX 77555. Email: dareynos@utmb.edu

Objectives: Our antimicrobial stewardship program (ASP) consists of clinicians, pharmacists, infection preventionists, microbiologists, nurses, and data scientists. Since January 1, 2017, our ASP has implemented over 15 evidence-based interventions across four campuses (five hospitals), including prospective audit and feedback (“handshake stewardship”), formulary restriction and pre-authorization for select antimicrobials, pharmacy-driven intravenous-oral switching, “nudging” appropriate antibiotic decisions by optimizing the EMR, and development of institutional guidelines for empiric antibiotics, among others. Beyond actions to improve the quality of antimicrobial use, the core elements of ASP include longitudinal tracking and reporting of essential ASP metrics, such as antimicrobial utilization, antimicrobial resistance, *Clostridioides difficile* infections, and cost of care. Real-time tracking and reporting of these metrics, and taking timely and relevant actions in response, is often limited by the functionality of electronic medical record (EMR), the complexity of health systems that span multiple campuses, cross-talk across software platforms, and accessibility to administrative silos of data. Herein, we report the implementation of a successful multidisciplinary ASP, and establishment of a user-friendly internal QlikSense® application for tracking and reporting.

Methods: To track and report on our progress and process prospectively, we adapted a QlikSense® application to function as a real-time dashboard for antimicrobial resistance rates, *Clostridioides difficile* infections, cost of care, IV-PO conversions, and antimicrobial utilization. Its functionality allows data to be analyzed by anti-infective class and spectrum, time period, campus, unit, specialty, service, provider, billing diagnosis-related group (DRG), and many other filters and categories. Antimicrobial utilization is tracked as days of therapy per 1000 patient days (DOTs), point prevalence, or proportion of all discharges who received an antimicrobial, and real-time resistance rates can be analyzed by culture type and setting.

Results: At our Galveston campus, monthly utilization of systemic antimicrobials decreased significantly from 553 DOTs pre-ASP to 527 post-ASP ($p=0.0224$), a 5% decrease from baseline. This was driven by improved use of levofloxacin (69 monthly DOTs pre-ASP vs 47 post-ASP; $p<0.0001$) and de-escalation from empiric vancomycin and piperacillin-tazobactam combination (230 DOTs pre-ASP vs 192 DOTs post-ASP; $p=0.0002$). Conversely, use of narrow-spectrum agents increased without impacting costs, resistance, treatment failure or mortality. Testing for, and diagnosis of, *C. difficile* infections declined

Poster #25

significantly after “nudging” interventions. There is significant variability in antimicrobial utilization across service lines and campuses, which corresponds to variability in acceptance of ASP interventions.

Conclusions: The interventions of a multidisciplinary ASP are facilitated and guided by a user-friendly internal QlikSense® application for tracking and reporting essential ASP metrics.

An Academic-Information Technology Partnership to Create an Infectious Diseases Translational Science Database

Rutter N¹, Neptune R¹, Webster B¹, Killen J², Dugas C², Lancaster C³, Gonzales-Luna A³, Garey K³

1. Populus Global Solutions
2. Momentum Canada
3. Department of Pharmacy, University of Houston

Corresponding author: Joanna Killen, Momentum Canada, Fundy Drive, Saint John, New Brunswick, Canada Email: joanna@momentumcanada.co

Background: Translational science is the process of turning observations in the laboratory, clinic, and community into interventions that improve human health. The coordinated effort to maintain integrated laboratory and clinical data is often a rate-limiting step for research laboratories, especially for multi-laboratory or multi-site studies. The purpose of this project was to create a translational science database prototype that would be responsive to the unmet needs of the translational research community.

Materials/methods: Planning groups of translational scientists, IT experts, and lab technicians mapped the workflow of a high-throughput translational research laboratory. Workflows were created for clinical or laboratory data. Database goals were to develop processes that would minimize data entry time, avoid redundancies, and prevent errors in a data secure environment (HIPAA-compliant). Unique to this platform was the ability to map creation of new samples (for example, PCR products) from parent samples (example, biologic samples). The platform was developed through an iterative process utilizing interviews, workflow study, analysis of supporting artifacts, and mock-ups.

Results: The current prototype allows for electronic upload or manual data entry of clinical data. Pre-populated data entry screens map laboratory work-flow with customized data entry fields produced based on laboratory results earlier in the work flow. Work-flow mapping includes microbiology (growth characteristics), phenotypic descriptions (MIC), molecular biology (PCR), strain typing, and customized experiments. Sequence data is housed separately with data linkers stored in the database. Database launch screen and data entry forms are populated based on specific criteria entered for each user. Data is downloadable using a customized query form to be used for statistical and sequence analysis.

Conclusions: The Translational Science Database allows for efficient capture of high-quality data enabling seamless linking of translational data for single or multi-site laboratories. Future development work will expand the number of experiments and also incorporate stored biobank information into the database.

Countermeasures to Viral Infection Reveal Therapeutically Exploitable Bacterial Compromises

Salazar K^{1,2}, Ma L³, Green S², Clark J², Terwilliger A², Ramig R², and Maresso A²

1. Department of Integrative Molecular and Biomedical Science, Baylor College of Medicine
2. Department of Molecular Virology and Microbiology, Baylor College of Medicine
3. Department of Microbiology, Northwestern State University

Extraintestinal pathogenic *E. coli* (ExPEC) is a leading cause of infections and is difficult to treat conventionally; due to the alarmingly rapid increase in multidrug resistant (MDR) pathogens. Bacteriophage (phage), viruses with kill bacteria, are shown to be host-specific and therapeutically effective in humans and animals. Though an appealing answer to MDR infections, bacterial resistance to phage is a pressing concern. “Preferred” phage-resistance mechanisms, and paired fitness or virulence costs are currently underexplored; our goal is to understand these factors in MDR pathogens.

Using a murine model of ExPEC sepsis, we’ve shown phage HP3 is an effective therapeutic. Using this model and *in vitro* methods, we isolated HP3-resistant ExPEC isolates. “Resisters” are defined by lack of phage expansion, and bacterial killing when challenged with HP3. Whole genome sequencing revealed two prevailing deletions, likely causing resistance in the majority of these isolates, resulting in truncation at the inner core of lipopolysaccharide (LPS). Further, HP3’s tail spike shows significant homology with the LPS-binding tail fiber of phage T4. These implicate LPS as the receptor of HP3, and prevention of adsorption as the mechanism of resistance in these isolates.

Resisters show variable decreases in growth within human blood and urine, suggesting decreased fitness in more biologically-relevant conditions. Further, tested resisters show significantly decreased virulence in our murine sepsis model, showing a 100% survival rate and significantly lower organ titers post-infection relative to the parental strain. This suggests these ExPEC isolates lack an evolutionary trajectory which allows for concomitant phage-resistance and complete fitness in their host.

To counter phage-resisters, we used one isolate as a target for directed evolution of HP3. We found the resulting phage isolate not only kills the target and parental strains, but each of the other HP3-resistant isolates. Together, these findings suggest that while phage-resisters will develop, resistance can be costly and readily subverted by counter-evolution of phage.

This work was supported by: U19AI116497, R21 AI125778, R21 AI133001, R01 NS102594, R01 AI097167, R01 AG058463, R56 AI105135, U19AI144297, R21AI146481, VA MERIT AWARD, McDonald Foundation, Mike Hogg Foundation, and Research Contracts from Anizome Biosciences

Plasmidome in Co-Circulating, Carbapenem Resistant *Klebsiella pneumoniae* ST258 and ST307 Strains in Houston, TX

William C. Shropshire MPH^{1,2}, An Q. Dinh BS¹, , Truc T. Tran PharmD¹, William R. Miller MD¹, Luis Ostrosky MD¹, Audrey Wanger PhD¹, Cesar A. Arias MD, PhD^{1,2,3}, Blake Hanson PhD^{1,2}

¹UTHealth McGovern Medical School, ²UTHealth School of Public Health, TX, USA, ³Molecular Genetics and Antimicrobial Resistance Unit –International Center for Microbial Genomics, Universidad El Bosque, Bogota, Colombia.

Corresponding author: Cesar A. Arias, Center for Antimicrobial Resistance and Microbial Genomics (CARMiG), University of Texas McGovern Medical School, 6431 Fannin St. MSB 2.112, Houston, TX 77030, E-mail: Cesar.Arias@uth.tmc.edu

Background: Carbapenem-resistant *Klebsiella pneumoniae* (CR-Kpn) cause a wide range of hospital-associated infections worldwide that result in significant morbidity and mortality. The class A β -lactamases known as *Klebsiella pneumoniae* carbapenemases (KPCs) are a significant mediator of CR-Kpn development. The transmission of *bla*_{KPC} and other antimicrobial resistance (AMR) genes is driven largely by the exchange of mobile genetic elements (MGEs) with intercellular transmission largely dictated by plasmids. The purpose of our study is to characterize the CR-Kpn ‘plasmidome’, i.e. the plasmid genomic content, from a convenience sampling at a large hospital system in Houston, TX.

Methods: Long-read sequencing technologies allow us to fully resolve plasmid sequences and their associated AMR genes as well as characterize a comprehensive range of MGEs enabling transmission of these clinically important resistance mechanisms. CR-Kpn isolates were collected as part of a study to describe CRE burden within a large Houston metropolitan hospital system. The Oxford Nanopore Technology (ONT) GridION X5 was used for long-read sequencing with Illumina short-read data used to polish and generate high quality, consensus assemblies. A custom bioinformatic pipeline was used to resolve plasmid structures and identify genomic context of plasmids carrying *bla*_{KPC} variants.

Results: 95 CR-Kpn isolates were collected from May to December 2017. Phylogenetic analyses and *in silico* MLST revealed diverse plasmid-harboring sequence types (STs) with two predominant clades, the pandemic strain ST258 (38/95; 40.0%) and the globally emerging strain ST307 (35/95; 36.8%), co-circulating in Houston, TX. All of the ST258 isolates harbored *bla*_{KPC-2} (n = 36) or the *bla*_{KPC-3} (n = 2) variant with the majority of ST258 *bla*_{KPC-2} carriage identified on the FIB type plasmid pKpQIL (27/31; 71.1%). 31/35 (88.6%) ST307 isolates were *bla*_{KPC-2} carriers with no single plasmid type dominating carriage. There were 30/35 (85.7%) ST307 isolates carrying a plasmid with a unique *repA* gene that was almost exclusively found in this clade with the exception of one other ST834 isolate. 10/30 (33.3%) of these plasmids were *bla*_{KPC-2} carriers of which 8/10 (80%) were multi-replicon plasmids.

Conclusion: While ST258 predominantly carries *bla*_{KPC} on one particular plasmid type, pKpQIL, the ST307 clade has a much more diverse vector pool of plasmids that are disseminating *bla*_{KPC-2} within this cohort. Furthermore, a unique plasmid replication initiation protein gene was found predominantly in the ST307 clade with the ability to harbor *bla*_{KPC-2}. These observations suggest there are plasmid signatures that may be potentially associated with particular sequence types, which may differentiate how *bla*_{KPC} transmission occurs within each clade.

The Role of the Accessory Genome in Enterococcal Bacteremia: Results from the Vancomycin-Resistant Enterococcal Bacteremia Outcomes Study (VENOUS)

Shelby Simar, MPH^{1,2}, German Contreras, MD, MSc¹, An Q. Dinh¹, Maria de los Angeles Spencer, MSc³, Pranoti Sahasrabhojane, MS⁴, Rafael Rios, MSc⁵, Lorena Diaz, PhD^{5,7}, Katherine C. Reyes, MD, MPH⁶, Marcus Zervos, MD⁶, Samuel L. Aitken, PharmD^{1,4}, Samuel A. Shelburne, MD, PhD^{1,4}, Truc T. Tran, PharmD¹, Jose M. Munita, MD^{1,3,7}, Cesar A. Arias, MD, PhD, FIDSA^{1,2,3,7}, Blake Hanson, PhD^{1,2} for the VENOUS Working Group.

¹Center for Antimicrobial Resistance and Microbial Genomics (CARMiG), University of Texas McGovern Medical School, Houston, Texas, ²UTHealth School of Public Health, Houston, Texas, ³Genomics & Resistant Microbes (GeRM), Instituto de Ciencias e Innovación en Medicina, Facultad de Medicina Clínica Alemana, ⁴The University of Texas MD Anderson Cancer Center, Houston, Texas, ⁵Molecular Genetics and Antimicrobial Resistance Unit – International Center for Microbial Genomics, Universidad El Bosque, Bogota, Colombia ⁶Department of Internal Medicine, Division of Infectious Diseases, Henry Ford Hospital, Detroit, Michigan, ⁷Millenium Initiative for Collaborative Research On Bacterial Resistance (MICROB-R), Universidad del Desarrollo, Chile

Corresponding author: Cesar A. Arias, Center for Antimicrobial Resistance and Microbial Genomics (CARMiG), University of Texas McGovern Medical School, 6431 Fannin St. MSB 2.112, Houston, TX 77030, E-mail: Cesar.Arias@uth.tmc.edu

Background: Vancomycin-resistant enterococci (VRE) are a major cause of nosocomial bloodstream infections. Enterococci exhibit remarkable genomic plasticity and can recombine through the acquisition of genetic material, including antimicrobial resistance (AMR) genes, via mobile genetic elements (MGEs). The accessory genome plays a major role in the evolution of enterococci within the human host. Thus, examining the entire genome (pan-genome) is of vital importance to characterize the population structure of enterococci causing disease.

Methods: VENOUS is an ongoing prospective, observational study of adults with enterococcal bacteremia. From September 2016-March 2018, *E. faecalis* (*Efs*) and *E. faecium* (*Efm*) were collected in 11 hospitals that included a major cancer center in Houston, TX, and 10 general hospitals in both Houston and in Detroit, MI. Short-read whole genome sequencing was performed with Illumina MiSeq and HiSeq 4000 platforms, and long-read sequencing utilized the Oxford Nanopore Technologies GridION X5. A custom bioinformatics pipeline was utilized for genome assembly and further analyses.

Results: Short-read sequencing of 156 *Efs* and 96 *Efm* isolates was performed. The average proportion of core (shared) genes in each genome was 64.6% (53.0-74.1) and 49.1% (45.2-51.0) for *Efs* and *Efm*, respectively. The *vanA* operon was identified in 5.1% (8/156) of *Efs* and 57.3% (55/96) of *Efm*. Of note, all *vanA*-harboring *Efs* possessed *aac(6')*-*le-aph(2'')*-*la* conferring high-level aminoglycoside resistance, and the majority belonged to ST6. Long-read sequencing of *vanA*-harboring plasmids from a subset of VRE revealed that the *vanA* cluster was carried by a variety of plasmid types, with sizes ranging from 20.7-132.3 kb. Although the *vanA* cluster was fairly conserved in both *Efm* and *Efs*, insertions of MGEs and sets of other AMR genes were identified in the intergenic regions of *vanS/vanH* and *vanX/vanY*. Furthermore, a variety of MGE insertions mediated integration of the *vanA* operon, including IS1216.

Poster #57

Conclusions: Accessory genes, including AMR genes, comprise a significant proportion of the enterococcal pan-genome, indicating major genetic malleability in these organisms that is not captured with traditional, core gene-focused surveillance methods. Acquired resistance genes appear to have a high degree of recombination, and they play a substantial role in the expansion of the genomic repertoire in clinical isolates.

Bacteria-Specific Drug Delivery: Hetero-multivalent Targeted Liposomes for Treatment of *Pseudomonas aeruginosa*

Simbassa SB,¹ Singla A,² Shah KN,¹ Chen Q,¹ Chirra B,¹ Dangol N,¹ Raina R,¹

Wu HJ,² Cannon CL¹

1. Department of Microbial Pathogenesis and Immunology, Texas A&M University Health Science Center, Bryan, TX, USA.
2. Department of Chemical Engineering, Texas A&M University, College Station, TX, USA.

Corresponding author: Carolyn L. Cannon, M.D., Ph.D., Department of Microbial Pathogenesis and Immunology, Texas A&M University Health Science Center, 8447 Riverside Parkway, TX 77807, E-mail: carolyn.cannon@tamu.edu

Background: Persistent lung infection with *Pseudomonas aeruginosa* is a hallmark of cystic fibrosis (CF) and contributes to the morbidity and mortality of the disease. A novel delivery vehicle capable of specifically targeting *P. aeruginosa*, and encapsulating antimicrobials may aid in the preservation of lung function. Consequently, we have developed hetero-multivalent, ligand-targeted liposomes to deliver antimicrobial agents directly to the site of infection. We have shown that these hetero-multivalent targeted liposomes functionalized with host cell glycans bind in vitro with higher affinity to *P. aeruginosa* in biofilm growth mode than mono-valent targeted liposomes (Worstell NC et al., Sci. Rep. 2018; 8:8419). We next tested the hypothesis that targeted liposomes would accumulate at the site of *P. aeruginosa* infection in vivo resulting in improved survival.

Methods: In order to assess dye-tagged liposome biodistribution in vivo, CD-1 mice were inoculated with PAO1-GFP, injected with targeted and untargeted liposomes, euthanized, and tissue homogenate fluorescence analyzed. We then encapsulated ciprofloxacin and characterized the size of the drug-loaded liposomes, and loading and release of the drug. To evaluate the antimicrobial efficacy of ciprofloxacin-loaded liposomes, broth microdilution was performed in accordance with CLSI guidelines. Liposome internalization by J774A.1 macrophages was determined by pre-incubating with dye-tagged liposomes and analyzing with flow cytometry. We then demonstrated the efficacy of ciprofloxacin-loaded, targeted liposomes, as compared to sham, free drug and control liposomes, in mice inoculated with PAO1.

Results: The biodistribution study in CD1 mice demonstrated that hetero-multivalent targeted liposomes accumulate at the site of infection; 2-hours post treatment, we found greater amounts of targeted liposomes at site of infection, as well as in the circulation, compared with non-targeted liposomes. However, in vitro, flow cytometry demonstrated similar liposomal uptake of targeted and non-targeted liposomes by macrophages, as compared to PEGylated liposomal controls. We successfully formulated stable liposomes that encapsulate ciprofloxacin at a therapeutic concentration, and demonstrated their antimicrobial efficacy in vitro. Lastly, PAO1-inoculated mice treated with the ciprofloxacin-loaded, hetero-multivalent targeted liposomes survived longer than mice treated with either ciprofloxacin-loaded, non-targeted liposomes or free ciprofloxacin.

Conclusions: We have demonstrated that liposomes functionalized with host cell glycans target *P. aeruginosa* in vivo resulting in increased retention of the liposomes in the circulation, accumulation at the site of infection, and increased survival in an infection model. Thus, this formulation strategy may improve outcomes in CF patients infected with *P. aeruginosa*.

Acknowledgement: Supported by Men of Distinction Foundation.

Engineering Protease-Stable DARPins Inhibitors of *Clostridium Difficile* Toxin B

Simeon R¹, Chonira V¹, Martinez Aguirre A², Sorg J², Chen Z¹

1. Department of Microbial Pathogenesis and Immunology, Texas A&M University, College Station, Texas 77843, USA

2. Department of Biology, Texas A&M University, College Station, Texas 77843, USA

Corresponding author: Zhilei Chen, Department of Microbial Pathogenesis and Immunology, Texas A&M University, College Station, Texas 77843, USA. Email: zchen4@tamu.edu

Abstract:

Clostridium difficile is a gram positive, spore-forming gastrointestinal pathogen that causes bloody diarrhea and even pseudomembranous colitis. The pathology of *C. difficile* infection (CDI) is primarily caused by the toxins (TcdA and TcdB) secreted by the bacteria. Each year in North America, 1-3% of hospitalized patients receiving antibiotics acquire CDI, causing ~30,000 deaths and over \$4.8 billion in treatment-associated costs.

CDI is treatable with antibiotics, but recurrence rates can be as high as 35% after cessation of treatment. In 2016 the FDA approved bezlotoxumab (Zinplava), an antibody inhibitor of *C. difficile* toxin B (TcdB), for treating recurrent CDI when used in combination with antibiotics. The potential market value of bezlotoxumab was estimated to be over US\$212 million. However, the potency of bezlotoxumab is limited as 15-17% of the treated patients still suffer from recurrent CDI.

Our overall goal is to engineer an oral, anti-toxin protein therapeutic for treating CDI. We selected the designed ankyrin repeat protein (DARPin) as our protein scaffold because of its small size, very high thermostability, very low immunogenicity and ease of expression in microbial organism (15 g soluble protein per liter of *E. coli* culture in a fermenter). We previously engineered a dimeric DARPin, DLD-4, composed of two monomeric DARPins U3 and 1.4E, that inhibits TcdB with an EC₅₀ of 4 pM *in vitro*, which is ~330-fold more potent than bezlotoxumab.

Although DARPins have been shown to be stable against some proteases, DLD-4 was rapidly degraded by intestinal proteases (i.e. trypsin, chymotrypsin). Sequence analysis revealed the presence of several protease-labile residues in the solvent-exposed regions. In this work we improved the trypsin and chymotrypsin stability of DARPin 1.4E by rational designed coupled with directed evolution. All protease-sensitive residues were mutagenized and the resulting library underwent phage panning and high throughput screening. The two best mutants, T10-2 and C3, showed significantly improved trypsin and chymotrypsin stability while preserving their anti-TcdB activity. T10-2 and C3 also retained significant activity after incubation in both mouse and hamster small intestinal fluid. Furthermore, T10-2 was found to be active in mouse cecum fluid *ex vivo*, and survived transit through the mouse gastrointestinal tract after oral gavage, highly supportive of its application as oral anti-toxin therapeutics.

Funding:

Funding was provided by NIH grants R21AI126025, DP2OD024146, and R21AI137803 to RS, VC and ZC

Using Synthetic Ecology to Explore the Evolution of Social Interactions among Streptomyces

Song X¹, Prabhakar R¹, Shamoo Y¹

1. Department of Biosciences, Rice University

Corresponding author: Yousif Shamoo, Department of Biosciences, Rice University, 6100 Main St, Houston, TX, E-mail: shamoo@rice.edu

Streptomyces are Gram positive, high GC content actinobacteria typically found in soils. They have contributed more than two-thirds of all current antibiotics and have remarkable potential for secondary metabolite biosynthesis, as indicated by a huge reservoir of cryptic biosynthetic pathways in their genomes. Moreover, in their natural soil habitat, neighboring streptomyces have evolved to form complex interspecies interaction networks mediated mostly by a rich collection of signaling molecules and other unique secondary metabolites. Within this interaction network, various biological activities are regulated by both cooperative (promotion) and non-cooperative (inhibition) interactions. However, it remains unclear how these complex networks evolve and what are the crucial factors contributing to social network dynamics.

Our study uses a microfluidics-based experimental evolution platform that allows the introduction of streptomyces strains to each other under conditions that can be used to study the evolution of new biochemical relationships. The pair-wise interaction assays in this study typically involve an engineered reporter strain and a wild streptomyces isolate serving as the interaction partner. Reporter strains have been constructed by introducing fluorescence (green and red fluorescent protein) and gas (methyl halide transferase) reporter systems into *S. roseosporus* and *S. venezuelae*. Further, we have used a wild streptomyces library isolated from soil to identify several inhibitive partner strains as well as a cooperative one. Efficient droplet generation and streptomyces encapsulation followed by selection for interspecies interactions via monitoring cell growth and imaging have also been achieved. More importantly, the inhibition interaction identified by batch assays has been qualitatively recapitulated in a conditioned media assay conducted in pico-liter droplets, demonstrating the feasibility of utilizing the emulsion droplet system as a high-throughput platform for social interaction screening and evolution.

Funding source: National Institutes of Health R01 A1080714 to Dr. Yousif Shamoo

Deep Sequencing of Combinatorial Libraries Reveals the Active Site Requirements for the Function of the Colistin Resistance Enzyme MCR-1

Sun Z¹, Palzkill T¹

¹Department of Pharmacology and Chemical Biology, Baylor College of Medicine.

Corresponding author: Timothy Palzkill, Department of Pharmacology and Chemical Biology, Baylor College of Medicine. One Baylor Plaza, Houston, TX 77030. E-mail: timothy@bcm.tmc.edu.

Abstract

Colistin (polymyxin E) and polymyxin B are the two clinically relevant members of the polymyxin class of cationic polypeptide antibiotics that have been used as the last resort for treating infections caused by multidrug resistant bacteria. These drugs exhibit bactericidal activity by permeabilizing the outer membrane of Gram-negative bacteria. However, their efficacy has been compromised by the occurrence of a transferable colistin resistance gene *mcr-1*, which was first reported in 2016 and has now been identified worldwide in various bacterial pathogens. *mcr-1* encodes a transmembrane phosphoethanolamine transferase enzyme, MCR-1, which functions by modifying the target of polymyxin on the outer membrane of bacteria. MCR-1 consists of a 5-segment transmembrane domain at the N terminus and a catalytic domain at the C terminus. Although our group has solved the crystal structure of the catalytic domain of MCR-1 (cMCR-1), no obvious substrate binding sites were observed on the structure. In addition, phosphoethanolamine transferase activity was not observed with the cMCR-1 protein. This indicates that the transmembrane domain is indispensable for MCR-1 enzyme activity, possibly by contributing to the formation of substrate binding pockets. In order to facilitate understanding of the mechanism of the function of MCR-1 enzyme, 23 active site residues were targeted for randomization by constructing single-codon randomization libraries. The libraries were then individually transformed into *E. coli* bacteria and selected for their function in supporting bacterial growth in the presence of colistin or polymyxin B. Deep sequencing of the functional mutants revealed that wild-type residues predominate among functional clones at 17 active site residue positions after selection by either colistin or polymyxin B, indicating that these residues are essential for the function of MCR-1 enzyme. These residues include an evolutionarily conserved residue Thr285 and Zn²⁺-chelating residues (Asp246, Asp465 and His466). This is consistent with the role of Thr285, which carries out nucleophilic attack on the head group of phosphoethanolamine substrate, and the role of Zn²⁺, which is proposed to stabilize the nucleophilic status of residue Thr285. In addition, essential residues also include positively charged residues (Lys333, His390 and His478) and hydrophobic residues (Phe93, Tyr97, Met105, Leu120, Leu477). They might play an important role in binding negatively charged head group and hydrophobic acyl chains of phosphoethanolamine substrate, respectively. The importance of these essential residues was further validated by the observation that mutations at any of these residues significantly decreased both polymyxin resistance function and phosphoethanolamine transferase activity of the MCR-1 enzyme.

This research was supported by National Institutes of Health grant R01 AI106863 to T.P.

Comparing Mechanisms of *Enterococcus Faecium* and *Enterococcus Faecalis*' Adaptation to Daptomycin-Fosfomycin Combination Therapy

Adeline Supandy¹ and Yousif Shamoo¹

¹Department of Biosciences, Rice University

Corresponding author: Yousif Shamoo, Department of Biosciences, 6100 Main St, Houston, TX, Email: shamoo@rice.edu

The rise of multidrug-resistant (MDR) pathogens is one of the fastest growing medical problems of this century. One of the most significant MDR pathogens is vancomycin-resistant enterococci (VRE). The rising resistance of VRE towards daptomycin (DAP), a last resort or “rescue” drug, further complicates the treatment of VRE infections. Combination therapy has been recommended as a way to improve VRE treatment outcomes. In contrast to monotherapy, combination antimicrobial therapy can slow the development of antibiotic resistance during treatment. An antibiotic that has demonstrated in vitro synergism with DAP is fosfomycin. Fosfomycin (FOS) is a phosphonic acid antibiotic that has substantial antimicrobial activity against both planktonic and biofilm Gram-positive pathogens. The purpose of this study is to compare the mechanisms by which *E. faecium* and *E. faecalis* respond and adapt to DAP-FOS combination therapy. Despite being in the same genus, it has been shown that *E. faecalis* and *E. faecium* evolve different resistance mechanisms. Additionally, resistance will eventually emerge as this combination therapy is used clinically to clear enterococcal infections. Therefore, it is important to know the mechanisms by which enterococci develop resistance to this combination therapy to start preparing alternate treatment strategies.

Funding Sources: National Institute of Allergy and Diseases (R01 A1080714) to Dr. Yousif Shamoo

Use of a DNA-Encoded Chemical Library Approach to Identify Inhibitors For the OXA-48 Carbapenemase

Taylor D¹, Palaniappan M², Faver J², Ucisik M², Campbell J², Simmons N², Anglin J², Zhuang J², Park S, Hu L¹, Prasad B.V.V¹, Huang H², Palzkill T³

1. Department of Biochemistry and Molecular Biology, Baylor College of Medicine
2. Center for Drug Discovery, Baylor College of Medicine
3. Department of Pharmacology and Chemical Biology, Baylor College of Medicine

Corresponding Author: Timothy Palzkill, Department of Pharmacology and Chemical Biology, Baylor College of Medicine, 1 Baylor Plaza, Houston, TX, timothyp@bcm.edu

Resistance to the highly prescribed β -lactam antibiotics is largely mediated by β -lactamases, bacterial enzymes that hydrolyze the pharmacophoric β -lactam ring of these antibiotics. A variety of unique β -lactam antibiotics have been developed to treat bacterial infections, but their extended use leads to the emergence of β -lactamase variants capable of hydrolyzing them. β -lactamase inhibitors have been created to restore effectiveness to β -lactam antibiotics, but most available inhibitors contain a β -lactam ring, making them vulnerable to hydrolysis and rapid resistance. Oxacillinase-48 (OXA-48) is a problematic β -lactamase that hydrolyzes nearly all β -lactam antibiotics including carbapenems, the last resort class of β -lactam antibiotics. Avibactam is the only clinically available non- β -lactam inhibitor and the only effective inhibitor against OXA-48. Due to the prevalence of OXA-48 in the clinics, there is a need for novel inhibitors to combat this public health threat. *We aim to develop a novel non- β -lactam OXA-48 inhibitor, unique from Avibactam, that will ultimately increase the β -lactam antibiotic susceptibility of bacteria expressing OXA-48.*

A DNA-encoded library (DEL) approach was used to rapidly and cost-effectively identify compounds that bind OXA-48. DELs consist of compounds that are tagged with unique DNA barcodes. These compounds can be screened by the millions against a target protein, all at once as binders can later be identified by sequencing the barcodes. With this approach, we screened over a billion non- β -lactam compounds against OXA-48 and discovered our lead compound CDD-97, which exhibits sub-micromolar potency against OXA-48 ($K_i = 0.58 \pm 0.1 \mu\text{M}$). The x-ray crystal structure of CDD-97 in complex with OXA-48 was determined to aid in the design of new versions with increased potency. The most potent inhibitors found were also tested against bacteria expressing OXA-48 to determine whether the inhibitors could make the bacteria more susceptible to ampicillin, a β -lactam antibiotic rapidly hydrolyzed by OXA-48. However, the compounds showed no significant activity, likely due to low membrane permeability or efflux pumps. The combined structural and *in vivo* data is being used to design fragments of CDD-97 that may have increased permeability and can later be modified for increased potency. This process has rapidly provided insights on OXA-48 inhibition and completion of this project will further contribute to knowledge on OXA-48 and general β -lactamase inhibition, which may aid the discovery of a clinically useful OXA-48 inhibitor.

Poster #61

Supported by NIH grants (AI143832 and AI32956), the Gulf Coast Consortia Training Interdisciplinary Pharmacology Scientists program (T32 GM120011), a DOE Office of Science User Facility (contract no. DE-AC02-05CH11231), a Cancer Prevention Research Institute of Texas (RP160805), and the Welch Foundation (Grant H-Q-0042).

Progress on the Development of a Field-To-Practice Phage Therapy Pipeline

Austen Terwilliger¹, Justin Clark¹, Haroldo Santos¹, Sabrina Green¹, Keiko Salazar¹, Barbara Trautner², R. Frank Ramig¹, Anthony Maresso¹

¹Department of Molecular Virology and Microbiology, Baylor College of Medicine

²Michael E. DeBakey Veterans Affairs Medical Center, Houston, TX

Phage therapy occurs when bacteriophages – the viral predators of bacteria and most numerous organism on Earth – are applied medicinally to combat invasive and multi-drug-resistant bacterial infections. The current U.S. pipeline to create novel phage therapies requires months of preparation, with regulatory concerns individually assuaged for each new phage or phage cocktail. This approach is not compatible with bacterial pathogenesis (where a patient's condition can deteriorate rapidly) or phage biology (where host specificity and resistance to phage requires therapeutic formulations to constantly hit a “moving target”).

We are leveraging core resources at the Texas Medical Center while developing technologies that evolve and purify phage to accelerate production and expedite treatment. Wastewater from a local facility yielded lytic phage against several clinical isolates of ESKAPE pathogens (*Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacter* species). While phage purification currently takes several days from a crude lysate, we are improving methods and aim to reduce this time to several hours. Purified phages against an *Enterobacter cloacae* clinical isolate were imaged, sequenced, annotated, and assayed for endotoxin levels on site at the TMC. When lytic phage were not readily available for *P. aeruginosa* and *Escherichia coli* isolates, they could be evolved in hours using a modified co-culture system developed by the lab.

These steps will be improved and challenged with more phage-host combinations to assess their applicability across ESKAPE pathogens. Given a bank of therapeutic-quality phage and clinical isolates, we aim to create a pipeline where lytic phages are discovered, purified, and formulated within a week. Such a system has the potential to reduce production costs, expedite therapeutic formulations, and improve patient outcomes.

Cardiolipin synthase is localized in cell membrane anionic phospholipid microdomains in *Enterococcus faecalis*

Tran TT^{1,2}, Nguyen AH^{1,2}, Panesso D^{1,2}, Mileykovskaya E², Arias CA¹⁻³

¹Center for Antimicrobial Resistance and Microbial Genomics, Houston, TX

²UTHealth McGovern Medical School, Houston, TX

³UTHealth School of Public Health, Houston, TX

Corresponding author: Truc T. Tran, 6431 Fannin St. MSB 2.112, Houston, TX 77030,
truc.t.tran@uth.tmc.edu,

Background: Anionic phospholipid microdomains play a major role in bacterial cell membrane homeostasis. Remodeling of bacterial cell membrane architecture, such as the redistribution of anionic phospholipid microdomains away from the division septum, has been associated with daptomycin resistance in *Enterococcus faecalis*. Whether this phenotype is associated with localization of cardiolipin synthase (Cls), an enzyme that catalyzes the synthesis of the major anionic phospholipid cardiolipin, remains to be elucidated. Of note, *E. faecalis* has 2 predicted Cls. Substitutions associated with daptomycin-resistant strains have been found exclusively in Cls1. In this work, we aim to visualize the localization of Cls in *E. faecalis*.

Methods: *E. faecalis* OG117 and its derivatives (OG117 Δ cls1, OG117 Δ liaX, OG117 Δ liaXcls1, OG117 Δ liaXcls1cls2), were used for genetic experiments as they have different patterns of anionic phospholipid redistribution. The peptide tag CCPGCC was inserted at the N-terminus of Cls1, cloned in pMSP3535, and introduced into recipient strains by electroporation. Bacterial cells were labeled with the biarsenical reagent ReAsH-EDT2 to examine the subcellular localization of Cls1, which becomes fluorescent (excitation 550 nm, emission 580 nm) upon interaction with the tetracysteine motif. Visualization of anionic phospholipid domains was performed using the fluorescent dye 10-N-nonyl acridine orange (NAO) (excitation 495 nm, emission 519 nm).

Results: *E. faecalis* OG117 and OG117 Δ cls1 exhibited clusters of anionic phospholipid microdomains at the poles and septa by NAO staining. DAP-resistant *E. faecalis* OG117 Δ liaX and OG117 Δ liaXcls1 showed redistribution of anionic phospholipid microdomains away from the septum. CCPGCC-Cls1 clustered at distinct foci at the septa and poles of *E. faecalis* OG117 and OG117 Δ cls1 and at non-septal sites in OG117 Δ liaX and OG117 Δ liaXcls1, in a distribution identical to that of phospholipid microdomains. Interestingly, OG117 Δ liaXcls1cls2 showed septal distribution by NAO staining. Upon complementation with CCPGCC-Cls1, the pattern of NAO distribution became non-septal.

Conclusion: Cls1 is localized at sites of anionic phospholipid microdomains of *E. faecalis*. As daptomycin resistance is associated with remodeling of cell membrane architecture, these results suggest that daptomycin resistance is mediated by relocation of Cls1 at sites of membrane damage.

Funding: NIAID K24 AI121296, R01 AI134637 and K08 AI113317

Deposition of Host Proteins on Medical Devices Provide a Bed for MRSA Biofilms

Jennifer N. Walker^{1,2,3}, Michael Caparon⁴, Scott Hultgren⁴

1. Department of Microbiology and Molecular Genetics, McGovern Medical School
2. Department of Internal Medicine, McGovern Medical School, Division of Infectious Diseases
3. Department of Epidemiology, Human Genetics, and Environmental Science, Center for Infectious Disease, School of Public Health, University of Texas Health Science Center
4. Department of Molecular Microbiology, Washington University School of Medicine

Corresponding author: Jennifer N Walker, Depts. of MMG and IM, McGovern Medical School, and Dept. of EHGES, School of Public Health, University of Texas Health Science Center, 6431 Fannin, Houston, Texas, E-mail: Jennifer-N-Walker@uth.tmc.edu

Objectives: Catheter-associated urinary tract infections (CAUTI) are the most common cause of hospital-associated infections in the US and can result in significant morbidity, including bacteremia and death. The ability of uropathogens to form recalcitrant, biofilm-associated infections have made management of CAUTI difficult. Problematically, the presence of a urinary catheter increases the risk of infection, especially to atypical uropathogens, such as *Staphylococcus aureus*. Recent studies show that the strongest predisposing factor for *S. aureus* UTI is urinary catheterization and the majority of isolates are methicillin-resistant *S. aureus* (MRSA). Challengingly, MRSA CAUTI are difficult to treat and frequently result in bacteremia and toxic shock. Thus, this study aimed to elucidate the mechanisms by which urinary catheters facilitate MRSA CAUTI.

Methods: To understand how the presence of a urinary catheter tips the balance in favor of MRSA urinary tract infection, we used established mouse models of UTI and CAUTI, imaging techniques, including fluorescence and scanning electron microscopy, and bacterial genetics.

Results: We discovered that MRSA required a catheter to establish persistent UTI and rapidly disseminated to bacteremia, which replicated what has been reported in the clinical setting. Importantly, previous work indicated that catheterization alone damages the bladder tissue and induces an inflammatory response that results in the release of the host protein fibrinogen (Fg). Fg, which plays a major role in wound healing, accumulates in the bladder and subsequently coats the catheter. We found that MRSA interacted with Fg, via the clumping factor B (ClfB) adhesin, by incorporating the protein into large biofilm structures throughout the bladder and on the catheter. This was surprising as it contrasted with other models of MRSA disease, such as sepsis, where ClfA, a homologous adhesin, exhibits a dominant phenotype. Additionally, analysis of patient infected urinary catheters, suggests our model recapitulates human disease.

Conclusions: These studies indicate that the catheterized bladder facilitates MRSA infection by providing additional binding ligands that MRSA exploits to establish CAUTI. These studies provide important insights into MRSA UTI and other medical device infections. Ultimately, these studies may inform the development of broad-acting strategies that treat these infections.

Poster #62

Funding Sources: R01-DK064540 to Drs. Scott Hultgren and Michael Caparon.

Identification of FDA-approved Drugs That Inhibit Survival of *Mycobacterium Bovis* BCG in Macrophages

Jia Wang, Clint A. Haines, Jourdan A. Andersson, Ashok K. Chopra, Sunhee Lee

Department of Microbiology and Immunology, The University of Texas Medical Branch

Corresponding author: Sunhee Lee, Department of Microbiology and Immunology, The University of Texas Medical Branch, 301 University Boulevard, Galveston, Texas, Email: sunhlee@utmb.edu

Abstract

Tuberculosis (TB) caused by *Mycobacterium tuberculosis* infection ranks the 10th leading cause of death worldwide, which is worsened by spread of multidrug resistance bacteria. New therapeutics are in dire need to drastically improve the response to the current global TB crisis. Previously, 58 drugs were identified by our collaborator as host-directed antimicrobials by a systemic screening of a library of 780 FDA-approved drugs that protect murine macrophages against high virulent *Yersinia pestis* strain induced cytotoxicity (1). Among them, several drugs were shown to be broad-spectrum and were even effective against multidrug resistant pathogens. Here we screened these 58 drugs to identify potential novel drug hits that confer cytoprotecting effects against *Mycobacterium bovis* BCG infection, which was used as a surrogate for *Mycobacterium tuberculosis* in this study. Fixable viability dye staining was used to evaluate the cell viability of murine macrophages RAW264.7 cells, that were infected with BCG, in the absence or presence of post-infection drug treatment. Intracellular bacterial survival in macrophages was determined by colony formation unit assay. Our screening with fixable viability dye staining have identified that post-infection treatment with 5 drugs significantly reduced macrophage cell death induced by BCG infection, when compared to infected but untreated cells. Furthermore, post-infection treatment with several drugs significantly inhibited the growth of intracellular bacteria, when compared to those in untreated and infected cells. Our screening of broad-spectrum nonantibiotic drugs and preliminary findings of potential drug hits against BCG infection demonstrate that drug repurposing is an efficient approach to identify new anti-mycobacterial drugs. Targeting conserved host-directed pathways may present an effective adjunct therapeutic strategy in addition to antibiotics to combat the emergence of multidrug resistant TB.

Funding sources: UTMB startup funds awarded to Dr. Sunhee Lee.

1. Andersson JA, Fitts EC, Kirtley ML, Ponnusamy D, Peniche AG, Dann SM, Motin VL, Chauhan S, Rosenzweig JA, Sha J, Chopra AK. New Role for FDA-Approved Drugs in Combating Antibiotic-Resistant Bacteria. *Antimicrob Agents Chemother.* 2016;60(6):3717-29. doi: 10.1128/AAC.00326-16. PubMed PMID: 27067323; PMCID: PMC4879411.

Development of Antivirulence Compounds Targeting Pyoverdine

Wang X¹, Kleerekoper Q¹, Kirienko NV¹

1. Department of BioSciences, Rice University

Corresponding author: Natasha Kirienko, Department of Biosciences, Rice University, 6100 Main street, Houston, TX, Email: kirienko@rice.edu

Background: *Pseudomonas aeruginosa* exhibits resistance to multiple antibiotics and causes serious infections in people with compromised immune systems. One strategy to treat *P. aeruginosa* infections is to develop inhibitors that directly compromise its virulence factors. A key virulence factor that can be targeted in this way is pyoverdine (PVD), which is important for obtaining iron from the pathogen's environment and is also involved in the regulation of other acute virulence determinants. We carried out a high-throughput biochemical screen to identify compounds that interfere with PVD fluorescence and, by extension, function. We identified a subset of such novel small molecules that may act by directly interacting with PVD.

Results: PQ3, a novel compound identified in a high-throughput screen for such inhibitors, and two of its structural analogs, PQ3a and PQ3c, were shown to reduce the pathogenic effect of PVD and to improve survival of *Caenorhabditis elegans* when challenged with *P. aeruginosa*. Rescue was abolished when a PVD biosynthetic mutant was used in place of wild-type bacteria, indicating that PVD was likely to be the relevant target. This study demonstrated that **1)** the compounds inhibit the innate fluorescence of PVD, normally produced by the chromophore core; **2)** solution NMR studies showed interaction between the compounds and the chromophore and N-terminal amino acids of PVD, particularly D-Ser-1 and the sidechain of Arg-2; PQ3 causes the most structure perturbations on PVD, while PQ3a exhibits the least effect. **3)** a conformational ensemble of apo PVD from 50 ns molecular dynamics simulations was used for molecular docking to predict the structure models; which was **4)** validated by chemical shift perturbations from NMR studies. Structural models reveal that the ligands interact with PVD at the shallow groove between the N-terminal chromophore and the side chain of Arg-2 and the electrostatic interactions are the driving force for the binding.

Conclusions: We discovered a panel of antivirulence compounds which act on PVD by the interaction with the N-terminal chromophore and residues. Molecular modeling provided a hypothetical basis for structural and dynamic binding, which was confirmed using NMR analysis. These findings will be useful for lead optimization.

Funding Sources: This study was supported by National Institute of Health grant R35GM129294, by the Welch Foundation Grant C-1930, and Cancer Prevention and Research Institute of Texas grant RR150044.

Nano-Metal Oxides as a switch-hitter: Killing Antibiotic Resistant Bacteria by Dissolution and Decrease Antibiotic Tolerance by Attachment

Qing-Bin Yuan^{1, 2, #, *}, Ya He^{2, #}, Bu-Yun Mao¹, Pengxiao Zuo², Wen-Bin Wu¹, Ya-Meng Huang¹, Hassan Javed², Nan Hu³

¹ College of Environment Science and Engineering, Nanjing Tech University, Nanjing 211816, China

² Department of Civil and Environmental Engineering, Rice University, Houston, TX, 77005, US

³ College of Biotechnology and Pharmaceutical Engineering, Nanjing Tech University, 211816, Nanjing, Jiangsu, China

These authors contribute equally to this article.

*Corresponding footnote:

¹ College of Environment Science and Engineering, Nanjing Tech University, Nanjing 211816, Jiangsu, China. E-mail: yuangqb@njtech.edu.cn (Qing-Bin Yuan)

Abstract

Increasing discharge of waste nano metal oxides (NMOs) has been an emerging environmental issue. NMOs in wastewater usually co-occur with antibiotic resistant bacteria (ARB), changing their fate and associated risks in manners that are not well understood. In this study, the survival and antibiotic tolerance of ARB in wastewater were examined after exposure to three NMOs retained for different times. Results indicated that NMOs killed 45.0% ~ 62.0% of ARB and decreased their antibiotic tolerance by 11.0% ~ 58.4%. The toxicities of NMOs was in the sequence of nZnO > nCuO > nTiO₂ and were higher with longer retention times. Both direct attachment and ions dissolution of NMOs led to their toxicities in wastewater. Notably, ions dissolution was the main mechanism for ARB death by inducing reactive oxygen species (ROS) and destroying cell membrane. Direct attachment was more responsible for the decrease of antibiotic tolerance, causing antibiotic resistance genes mutation and stress response of transcriptome (mostly upregulation). These novel findings stress the role of NMOs in influencing the potential threats of antibiotic resistance in wastewater and provide insights for its natural attenuation by NMOs.

Structural and Biochemical Studies of MurAA, an Enolpyruvate Transferase that Contributes to Daptomycin Resistance in *Enterococcus faecium*

Zhou Y¹, Prater AG¹, Arias CA^{2,3,4}

1. Department of Biosciences, Rice University

2. Department of Internal Medicine, Division of Infectious Diseases, University of Texas Medical School at Houston

3. Center for Antimicrobial Resistance and Microbial Genomics, University of Texas McGovern Medical School

4. Molecular Genetics and Antimicrobial Resistance Unit, International Center for Microbial Genomics, Universidad El Bosque

Corresponding author: Yousif Shamoo, Department of Biosciences, Rice University, 6100 Main St, Houston, TX, E-mail: shamoo@rice.edu

Objectives

Bacterial infections have re-emerged as a critical crisis in human health due to the evolution of multi-drug resistance. Among these bacterial infections, enterococci infections are becoming a rising concern due to its inherent resistance to many commonly used antibiotics. The CDC estimates that vancomycin-resistant enterococci (VRE) caused 54,500 nosocomial infections in the United States in 2017 and led to 5,400 deaths. VRE is increasingly resistant to other antibiotics, leaving the treatment less effective. Daptomycin (DAP) is an antibiotic of last resort for many patients and is frequently used to treat VRE infections. Prolong the efficacy of DAP is crucial in the absence of other viable treatment options.

Previous studies from our lab using experimental evolution to identify adaptive strategies to DAP resistance in *Enterococcus faecium* revealed that mutations in the gene *murAA*. MurAA is an enolpyruvate transferase that catalyzes the first committed step of peptidoglycan synthesis, transferring enolpyruvate from phosphoenolpyruvate (PEP) to UDP-N-acetylglucosamine (UNAG) to produce UDP-GlcNAc-enolpyruvate. As a cell wall biosynthesis protein, MurAA shows poor homology with mammalian proteins, making it an excellent target for drug discovery. Fosfomycin (FFQ) is a naturally occurring inhibitor that binds to the active site of MurAA. Understanding the structure of MurAA can provide valuable insights into the function of this enzyme and its interactions with the substrate, thereby providing structural basis for the design of novel antibiotics or co-drugs that can be administered with DAP to delay the development of DAP resistance.

Methods

X-ray crystallography was used to solve the structure of MurAA. We have also characterized the steady-state kinetics, thermal stability as well as FFQ binding affinity of MurAA and the adaptive mutant MurAA^{A149E} to understand how this mutation facilitates DAP tolerance. We also tested MurAA expression levels both in DAP susceptible and resistant *E. faecium* strains. Finally the cell wall composition of *E. faecium* is being analyzed to understand the direct effect of this mutation on the composition of the cell wall.

Results and Conclusions

We have solved the structure of MurAA in complex with both inhibitor, FFQ, and substrate, UNAG, in space group P1 with a diffraction limit of ~1.65Å. UNAG binding closes the active site loop (Ala114-Ile125) and the active site Cys119 is occupied by FFQ. MurAA^{A149E} produces similar Km values for PEP compared to MurAA but a 1.7-fold decrease in k_{cat} . In the case of UNAG, k_{cat} and Km are 1.4 and 1.6 folds higher in MurAA. Also, Kd value of FFQ and MurAA^{A149E} is $1.9 \pm 0.7 \mu M$, about 3 folds higher compared to

Poster #64

that of MurAA, which is $0.5 \pm 0.06 \mu\text{M}$. The results suggest that MurAA^{A149E} is slightly less efficient than MurAA and indicate *in vivo* expression level may play a role in regulating the function.

Funding Sources: NIH R01AI080714

Whole Genome Analysis of Antimicrobial Resistance Genotypes of Invasive Group B Streptococci in Cancer Patients

Zuberi Z^{1,2}, Flores A², Shelburne SA¹

1. Department of Infectious Diseases, MD Anderson Cancer Center, Houston, TX
2. Baylor College of Medicine, Houston, TX.
3. Department of Pediatrics, University of Texas Health Science Center at Houston, Houston, TX

Corresponding author: Ayesha Zuberi, MD, Department of Infectious Diseases, MD Anderson Cancer Center, Houston, TX, azuberi8@gmail.com

Objective: Group B *Streptococcus* (GBS), also known as *Streptococcus agalactiae*, has recently been markedly increasing as a cause of invasive disease in adults to the point where it now causes twice the number of invasive infections as the far better studied Group A *Streptococcus* (GAS). Concerningly, GBS is also more adapt compared to GAS in developing antimicrobial resistance (AMR). Patients with cancer have high rates of antimicrobial exposure and are particularly prone to develop invasive GBS infection yet there is limited information available regarding AMR prevalence or mechanisms among invasive GBS strains isolated from cancer patients.

Methods: Illumina based whole genome sequencing was performed on 63 GBS isolates that caused bacteremia at MD Anderson Cancer Center between 2011 and 2019. In silico multi-locus sequence typing (MLST) and identification of AMR determinants were performed using an established computational biology pipeline. Phenotypic determination of AMR was determined using standard microbiologic methods and compared to genotypic derived phenotypic prediction for antimicrobials typically used to treat GBS infection and syndromes.

Results: WGS based sequencing was successful for all isolates with an average genome coverage of 111x. There was high degree of genetic heterogeneity amongst the isolates as evidenced by the detection of thirteen distinct sequence types (ST) with no ST accounting for more than 14% of total infections. Phenotypically, the highest rates of AMR were observed for tetracycline (81%) and erythromycin (52%). Rates of fluoroquinolone (5%) and β -lactam resistance (0%) were low. The concordance between predicted phenotype using WGS and actual phenotype was 100%. The most common tetracycline resistance determinant was *tetM*, which was present in 95% of tetracycline resistant isolates and encodes a ribosomal protection protein. Similarly, the erythromycin ribosomal methylase (*erm*) encoding genes *ermB* and *ermTR* together accounted for 85% of elements conferring macrolide resistance. All fluoroquinolone resistant isolates contained polymorphisms in the target encoding genes *parC* and *gyrA*. Taken together, 90% of invasive GBS isolates were resistant to at least one antimicrobial commonly used in the empiric treatment of infectious syndromes caused by GBS.

Conclusions: Invasive GBS disease in cancer patients is caused by a genetically heterogenous group of organisms rather than particularly clones adapted to the cancer population. Whole genome sequencing accurately identified phenotypic GBS AMR which was extremely prevalent against antimicrobials commonly used empirically in the treatment of GBS infectious syndromes. These data will assist physicians in the selection of antimicrobials in situations where GBS infection is suspected.

Funding: Baylor College of Medicine, T32 Training Program in Infectious Diseases

First Name	Last Name	Institution/Company
Lilian	Abbo	
Tolulope	Adebusuyi	Texas Southern University
Samuel	Aitken	UT MD Anderson Cancer Center
MJ	Alam	University of Houston
zain	Alamarat	UT Health Science Center at Houston
Eddie	Alberado	Accelerate Diagnostics
Ashley	Alexander	Kelsey Foundation
Masaad	Almutairi	University of Houston
Faris	Alnezary	University of Houston
Osvaldo	Alquicira	Baylor College of Medicine
Jourdan	Andersson	Baylor College of Medicine
Cesar	Arias	UT Health Science Center at Houston
Robert	Atmar	
Dierdre	Axell-House	Baylor College of Medicine
Jeff	Babb	Paratek
Jessica	Babic	Memorial Hermann-TMC
Carol	Baker	
Gary	Bannister	T2Biosystems
Arnie	Bayer	LA Biomedical Research Institute - UCLA
Khurshida	Begum	University of Houston
amira	bhalodi	Accelerate Diagnostics, Inc.
Micah	Bhatti	UT MD Anderson Cancer Center
Naomi	Bier	UT Health Science Center at Houston
Gerald	Bills	
Michael	Binkley	Texas Southern University
Kimberly	Blumenthal	
David	Boragine	Baylor College of Medicine
Jovan	Borjan	UT MD Anderson Cancer Center
Helen	Boucher	
Rachel	Britt	UT Medical Branch at Galveston
Cameron	Brown	Baylor College of Medicine Texas Children's Hospital
Eric	Brown	
Paul	Bruegger	Allergan
Karen	Brust	Baylor Scott and White
Amy	Butcher	Baylor College of Medicine Texas Children's Hospital
John	Butler	Memorialhermann
Nicolo	Cabrera	UT Health Science Center at Houston
michelle	cano	Texas Southern University
Lori	Carden	Merck & Co.
Christelle	Chacar	Ferring
Katrina	Chan	University of Houston
Ifrah	Chaudhary	City of Houston
Ashok	Chopra	
Andrew	Chou	Baylor College of Medicine MEDVAMC
Jessica	Clark	T2 Biosystems
Tom	Coleman	Rice University
Peter	Colley	Baylor Scott & White Health
Mandelin	Cooper	
Sara Elizabeth	Cosgrove	
Tony	Cullen	ALK
Heather	Danhof	Baylor College of Medicine

First Name	Last Name	Institution/Company
Arun	Darian	Universidade Municipal de São Caetano do Sul
Rachel	Dawson	Merck
Alejandro	De la Hoz	UT Health Science Center at Houston
Lance	Dible	Allergan
An	Dinh	UT Health Science Center at Houston
Ivan	Dixon	Nabriva Therapeutics
William	Dowhan	UT Health Science Center at Houston
Herbert	Dupont	
Murtala	Ejalonibu	University of KwaZulu-Natal, Durban
Yossi	Eliaz	University of Houston
Kyle	Enriquez	Stanford University
Sam	Erickson	UT Health Science Center at Houston
Selvi	Ersoy	The Lundquist Institute for Biomedical Innovation (formerly LA Bic
GERMAN	ESPARZA	UNIVERSIDAD JAVERIANA
Christopher David	Evans	
Saad	Fallatah	University of Houston
Rong	Fang	UT Medical Branch at Galveston
Natalie	Finch	Ben Taub Hospital
Michael	Fischer	Texas department of state health services
Anthony	Flores	
Vance	Fowler	
Ian	Furey	Baylor College of Medicine
Jessica	Galloway-Pena	UT MD Anderson Cancer Center
Ramya	Ganiga Prabhakar	Rice University
Sheila	Gardner	Paratek
Kevin	Garey	University of Houston
Danielle	Garsin	UT Health Science Center at Houston
Melanie	Goebel	Baylor College of Medicine
Jeremy	Golden	Paratek
sara isabel	Gomez villegas	UT Health Science Center at Houston
Anne	Gonzales-Luna	University of Houston
David	Greenberg	
Larissa	Grigoryan	Baylor College of Medicine
Paul	Grunenwald	Texas Dept of State Health Services
Anthony	Haag	Baylor College of Medicine
Dr. Ray	Hachem	UT MD Anderson Cancer Center
Charlie	Ham	Comprehensive Pharmacy Services
Blake	Hanson	
Blake	Hanson	UT Health Science Center at Houston
Rodrigo	Hasbun	UT Health Science Center at Houston
Joshua	Hendrickson	University of Houston
Jessie	Ho	University of Houston
Holly	Hoffman-Roberts	Nabriva Therapeutics
Troy	Hollar	Accelerate Diagnostics
J. Patrik	Hornak	UT Medical Branch at Galveston
Thomas	Horvath	Baylor College of Medicine
David	Huang	Rutgers of NJ Medical School
Kristina	Hulten	Baylor College of Medicine
Nicholas	Hummell	Rice University
Julian	Hurdle	
Hoang	Huynh	Methodist Hospital Research Institute

First Name	Last Name	Institution/Company
Saki	Ikeda	Baylor College of Medicine Texas Children's Hospital
Kyle	Jackson	Pfizer Inc.
Chase	Janak	
Jinhee	Jo	University of Houston
Christina	Joseph	HCA Houston Medical Center
Allison	Judge	Baylor College of Medicine
Alex	Kang	Rice University
Sheldon	Kaplan	
Laura	Katterhenry	Accelerate Diagnostics
Djene	Keita	Texas Southern University
Iordanis	Kesisoglou	University of Houston
Ayesha	Khan	UT Health Science Center at Houston
Natasha	Kirienko	Rice University
Joshua	Knight	Houston Methodist
Andrew	Koh	
Anna	Konovalova	
Janelle	Korf	UT Health Science Center at Houston
Julie	Kuo	University of Houston
Kristi	Kuper	City of Houston
Kristi	Kuper	
Siphti	Lacey	Allergan
Sarah	Lach	UT Health Science Center at Houston
Al	Lai	Astellas Pharma
Christopher	Lancaster	University of Houston
Lauren Nicole	Laserna	lauren.laserna2@memorialhermann.org
Shonda	Lawson	Astellas Pharma
Jonathan	Le	HCA Houston Healthcare Medical Center
Katherine	Lemon	Baylor College of Medicine
Tameka	Lord	Melinta Therapeutics
Susan	Loughlin	TIRR Memorial Hermann
shuo	lu	Baylor College of Medicine
Ivy	Luong	HCA Houston Healthcare Medical Center
Connie L.	Luthy	Rice University
RaviKanthReddy	Marreddy	Institute of Biosciences & Technology of Texas A&M Health Scie
Alexandra	Martynova-Van K	Stephen F. Austin State University
Jordan	May	Texas A&M
Yaneth	Mclemore	St. Joseph Medical Center
Marlene	McNeese	Houston Health Department
Heer	Mehta	Rice University
Enyinnaya	Merengwa	Texas Department of State Health Services
Firas	Midani	Baylor College of Medicine
Eugenia	Mileykovskaya	UT Health Science Center at Houston
William	Miller	
William	Miller	UT Health Science Center at Houston
Maria	Mojica	Universidad El Bosque
Marguerite	Monogue	University of Texas Southwestern
Shannon	Moritz	T2Biosystems
Lynsie	Morris	Qiagen
Elizabeth	Moulton	Baylor College of Medicine Texas Children's Hospital
Ed	Mundy	Paratek
Jose	Munita	

First Name	Last Name	Institution/Company
Flor	Munoz	
Daniel	Musher	
Amila	Nanayakkara	UT Southwestern Medical Center
Pegah	Nassiri	St Joseph Medical Center - Steward Health
April	Nguyen	UT Health Science Center at Houston
Sean	Nguyen	Shionogi Inc
Michael	Nikolaou	University of Houston
Denver	Niles	Baylor College of Medicine Texas Children's Hospital
Victor	Nizet	
Patrick	Nwachukwu	UT Health Science Center at Houston
Victor	Obuekwe	UT Southwestern
Charlene	Offiong	
Opeyemi	Ojekunle	Texas Southern University
Damola	Olatoregun	Texas Southern University
Tolulope	Olumuyiwa	Houston Health Department
Collins	Onyenaka	Texas Southern University
Niels	Oppermann	Accelerate Diagnostics, Inc.
Luis	Ostrosky-Zeichner	
Timothy	Palzkill	
Suhyeorn	Park	Baylor College of Medicine
Brent	Parker	Merck & Co.
Shivani	Patel	Memorial Hermann
Katy	Patras	Baylor College of Medicine
Orville	Pemberton	Rice University
Norma	Perez	
Trish Marie	Perl-Delisle	
Anh	Pham	
SELENA	PHAM	Michael E. DeBakey VA Medical Center
Reed	Pifer	UT Southwestern Medical Center
Robert	Portinari	Merck
Shea	Posey	Melinta Therapeutics
Christine	Pybus	UT SOUTHWESTERN MEDICAL CENTER
Isaam	Raad	
Paula	Reeves	Accelerate Diagnostics
Alyssa	Reid	Baylor College of Medicine
David	Reynoso	UT Medical Branch at Galveston
Chanu	Rhee	
Edgar	Rios	HCA Healthcare
Mauricio	Rodriguez	Paratek Pharmaceuticals
Adriana	Rosato	
Giuliana	Rosato	Medical School Student , University of Cuyo -Mendoza Argentina
Rachel	Ruehl	ALK
Christie	Rummel	Memorial Hermann
J. Nick	Rutter	Populus Global Solutions
Kirsten	Rydell	Kirsten.N.Bevan@uth.tmc.edu
Keiko	Salazar	Baylor College of Medicine
Belkys	Sanchez	sanchez.belkysc@gmail.com
James	Sanders	UT Southwestern
Amy	Schilling	Memorial Hermann The Woodlands
Cynthia Louise	Sears	
Edward	Septimus	

First Name	Last Name	Institution/Company
Willian Maurice	Shafer	
Yousiff	Shamoo	Rice University
Sam	Shelburne	
Edgar	Sherman	
Ryan Kurtis	Shields	
Kirstin	Short	Houston Health Department
William	Shropshire	UT Health Science Center at Houston
Shelby	Simar	UT Health Science Center at Houston
Sabona	Simbassa	Texas A&M University HSC
Rudo	Simeon	Texas A&M University
Kavindra	Singh	UT Health Science Center at Houston
Anh	Singhania	Summit Therapeutics
Felicia	Skelton-Dudley	Baylor College of Medicine Michael E. DeBakey VA Medical Center
Kristina	Smith	ALK
Tiffany	Smith	GenMark Dx
Xinhao	Song	Rice University
Sarah	Spitznogle	UT MD Anderson Cancer Center
Erica	Stohs	University of Nebraska Medical Center
Ana Paula	Streling	UT Health Science Center at Houston
Christy	Su	
Zhizeng	Sun	Baylor College of Medicine
Adeline	Supandy	Rice University
Vincent	Tam	
Ying	Taur	
Doris	Taylor	Baylor College of Medicine
Margaret	Taylor	Baylor College of Medicine Texas Children's Hospital
Austen	Terwilliger	Baylor College of Medicine
Andrew	Thompson	Medical City Healthcare
Maria	Tort	Pfizer Inc
Mai	Tran	Fannin Innovation Studio
Truc	Tran	UT Health Science Center at Houston
Barbara	Trauner	
Barbara	Trautner	Baylor College of Medicine
Lisa Trinh	Trinh	University of Houston
Kristen	Valencia Deray	Baylor College of Medicine Texas Children's Hospital
John	Valenta	Kelsey Foundation
David	van Duin	
Luis	Vega	
Stephanie	Vega	Fannin Innovation Studio
Diane	Vo	Memorial Hermann Cypress Hospital
Thomas	Voss	Merck Research labs
Nancy	Vuong	UT MD Anderson Cancer Center
Jennifer	Walker	UT Health Science Center at Houston
Jia	Wang	UT Medical Branch at Galveston
Xu	Wang	Rice University
zhao	wang	Baylor College of Medicine
April	Wardenburg	Tetraphase Pharmaceuticals
Angela	Watts	Merck & Co.
Paula	Weaver	Qiagen
Sean	Wells	Allergan
Brian	Werth	

First Name	Last Name	Institution/Company
Kent	Wheeler	Allergan
Kim	Whitener	Merck & Co.
Dona	Wijetunge	Baylor College of Medicine Texas Children's Hospital
Natalie	Williams-Bouyer	UT Medical Branch at Galveston
Laila	Woc-Colburn	Baylor College of Medicine
Linda	Yancey	Memorial Hermann Health System
Pingfeng	Yu	Rice University
Qingbin	Yuan	Rice University
Mara	Zambruni	University of Houston
Dennis	Zavindny	Allergan
Lynn	ZECHIEDRICH	Baylor College of Medicine
Yue	Zhou	Rice University
Andrei	Zidaru	
Karen	Znoj	Merck & Co.