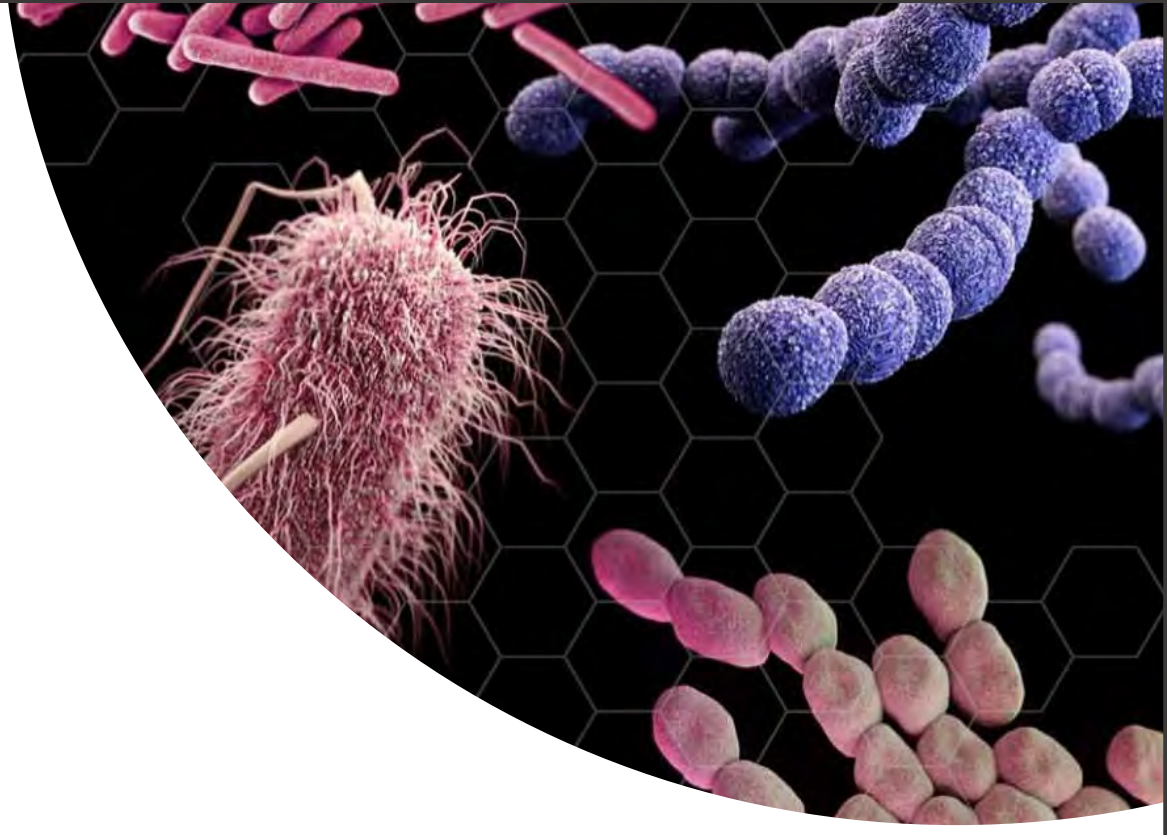

6th Annual Texas Medical Center Antimicrobial Resistance and Stewardship Conference

January 18-20, 2023

Houston, Texas

Gulf Coast Consortia
QUANTITATIVE BIOMEDICAL SCIENCES

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 research consortia gather interested faculty around research foci within the quantitative biomedical sciences, and currently include: Antimicrobial Resistance, Cellular and Molecular Biophysics, Innovative Drug Discovery and Development, Immunology, Mental Health Research, Regenerative Medicine, Single Cell Omics, Theoretical and Computational Neuroscience, and Translational Pain Research. GCC training programs currently focus on Biomedical Informatics, Cancer Therapeutics, Computational Cancer Biology, Molecular Biophysics, Pharmacological Sciences, Precision Environmental Health Sciences, and Antimicrobial Resistance. 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, The Institute of Biosciences and Technology of Texas A&M Health Science Center and Houston Methodist Research Institute.

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Gulf Coast Consortia - Research

Day 1 - Wednesday, January 18, 2023
Mechanisms of Resistance and Drug Discovery

7:30-8:30 *Career Mentoring: Women in Microbiology and Infectious Diseases* (Event Hall)
Helen Boucher, MD
Tufts University, Boston, MA
Sara Cosgrove, MD, PhD
Johns Hopkins University, Baltimore, MD
Robin Patel, MD
Mayo Clinic, Rochester, MN

8:30-8:35 *Welcome*
Cesar A. Arias, MD, PhD
Houston Methodist Research Institute and Weill Cornell Medical College, Houston, TX
Suzanne Tomlinson, PhD, MBA
Gulf Coast Consortia

8:35-9:00 *Antimicrobial Resistance in the 21st Century: Trials and Tribulations*
Helen Boucher, MD
Tufts University, Boston, MA

Session 1
Conveners: **Julian Hurdle, PhD**, Texas A&M Health Science Center

9:00-9:25 *Mechanisms of Cell Envelope Defense Against Antibiotics in Gram-positive Bacteria*
William Miller, MD
Houston Methodist Research Institute and Weill Cornell Medical College, Houston, TX

9:25-9:50 *Tracking Emerging Mechanisms of Resistance with Genomics*
Francois Lebreton, PhD
Walter Reed Army Institute of Research, Washington, DC

9:50-10:15 *Heteroresistance in Gram-negative Bacteria*
David Weiss, PhD
Emory University, Atlanta, GA

10:15-10:45 Break and Vendor Show (pre-function and event hall)

Session 2 *T32 Trainee Symposium: Texas Medical Center Training Program on Antimicrobial Resistance (TP-AMR), Emory Training Program on Antimicrobial Resistance, University of Pittsburgh Training Program on Antimicrobial Resistance*

Conveners: **Taryn Eubank, PharmD,** University of Houston (GCC-TPAMR), Houston, TX
Madison Stellfox, MD, PhD, University of Pittsburgh, Pittsburgh, PA

10:45-11:00 *Dissecting the Mechanism of Cell Membrane Adaptation Against Antimicrobials*
Kara Hood, **PhD**
Houston Methodist Research Institute (GCC-TP-AMR), Houston, TX

11:00-11:15 *Kip Proteins Promote Clostridoides difficile Growth in Bile Salts*
Cheyenne Lee
Emory University, Atlanta, GA

11:15-11:30 *Pathogenesis, Localization, and Host Response During Influenza and Streptococcus Pneumoniae Co-infection in Ferrets*
Janie French
University of Pittsburgh, Pittsburgh, PA

11:30-11:45 *Prospective Assessment of TonB Receptor Mutants and Cefiderocol Susceptibility Across Clinical Isolates of Pseudomonas Aeruginosa*
Stephanie Egge, MD
Houston Methodist Research Institute (GCC-TP-AMR), Houston, TX

11:45-11:50 *Introduction to Keynote*
Natasha Kirienko, PhD
Rice Univ.

11:50-12:20 **Keynote Lecture**
Drug Efflux in Gram-negative Bacteria
Helen I. Zgurskaya, PhD
University of Oklahoma, Norman, OK

12:20-2:00 Lunch/Rapid Fire/Poster Session (Event Hall)
12:20 pick up lunch

12:35-1:05 Rapid Fire presentations:

Investigation of Fecal pH in Healthy Volunteers Receiving Oral Omadacycline or

Vancomycin

Samantha Agyapong, Univ. of Houston

Real-world Clinical Outcomes of Cefiderocol Therapy in the Veterans Health Administration
Eva Amenta, Baylor College of Medicine

High Throughput Screen of Group A Streptococcus Clinical Isolates to Identify Conserved Strain-Specific Polymorphisms in Two-Component Systems Associated with Susceptibility to Membrane-Targeting Antimicrobials
Dalton Bui, McGovern Medical School

Machine Learning Text Mining for Carbapenemase-Producing Organisms and Susceptibility Testing Results for Ceftazidime/avibactam & Ceftolozane/tazobactam
Andrew Chou, Baylor College of Medicine

Vancomycin-Resistant vanB- and vanA/vanB-type Enterococcus faecium Causing Invasive Infections in Adult Patients in Chile (2018-2022)
Lorena Diaz, Clínica Alemana - Universidad del Desarrollo

Simulated Human Dosing of Ceftazidime in a Murine Pneumonia Model
Brianna Eales, University of Houston

1:05-2:00 Poster Session, Posters 1-26

Session 3
Conveners: **Tim Palzkill, PhD,** Baylor College of Medicine, Houston, TX

Cecilia Tran, PharmD, Houston Methodist Research Institute, Houston, TX

2:00-2:25 *Mechanisms of Resistance to Novel B-lactam/B-lactam Inhibitors*
Laurent Poirel, PhD
University of Fribourg, Switzerland

2:25-2:50 *Environmental Contamination and the Evolution of MRSA in Latin America*
Jose M. Munita, MD
Clinica Alemana and Universidad del Desarrollo, Santiago, Chile

2:50-3:15 *Novel Insights into Daptomycin Resistance in Staphylococcus aureus*
Adriana Rosato, **PhD**
Maine Health Institute for Research

3:15-3:30 Break

Session 4 *NIH Antimicrobial Resistance Leadership Group (ARLG)*
Early Stage Investigators

Conveners: **Vance Fowler, MD MPH,** Duke University, Durham, NC
Anthony Harris, **MD**., University of Maryland, Baltimore, MA

3:30-3:45 *Complicated Intra-abdominal Infection Trials: FDA Geographic Variation*
Tori Kinamon, MD
Duke University, Durham, NC

3:45-4:00 *A ZEPHYR in the DOOR: Reanalysis of a Controversial Trial*
Jess Howard-Anderson, MD
Emory University, Atlanta, GA

4:00-4:15 *Making the SCENE: Interim Results from the SCENE Study*
Michael Satlin, MD
Weill Cornell Medical College, New York, NY

4:15-4:30 *Carbapenem-Resistant E. coli from CRACKLE*
Angelique Boutzoukas, MD
Duke University, Durham, NC

Session 5 Selected Abstracts

Convener: **Sam Shelburne, MD, PhD**, UT MD Anderson Cancer Center, Houston, TX
Natasha Kirienko, PhD, Rice University, Houston, TX

4:30-4:45 *GENO-STELLAR: A Clinically Actionable Tool for Identifying Anti-Microbial Resistant Klebsiella pneumoniae Species*
Hossaena Ayele, UT Health Science Center Houston

4:45-5:00 *Clonal Dynamics of Methicillin-Resistant Staphylococcus aureus in a Tertiary Healthcare Center Between 2000-2016 in Chile*
Jose RW Martinez, Universidad del Desarrollo

5:00-5:15 *Phosphorodiamidate Morpholino Oligomers Targeting acpP Reduce the Biofilm Burden in Burkholderia cepacia Complex*

Antonio Mendez, UT Southwestern

Day 2 - Thursday, January 19, 2023
Translational and Clinical Aspects of Antibiotic Resistance

7:30-8:30 *Career Mentoring: Careers in Computational Genomics Applied to Infectious Diseases* (Event Hall)
Todd Treangen, PhD
Rice University, Houston, TX
Blake Hanson, PhD
University of Texas Health Science Center, Houston, TX
Nadim Ajami, PhD
MD Anderson Cancer Center, Houston, TX
Lee Harrison, MD
University of Pittsburgh

Session 6

Conveners: **Tor Savidge, PhD**, Baylor College of Medicine, Houston, TX
Blake Hanson, PhD, University of Texas Health Science Center at Houston

8:30-8:55 *Cell Envelope in Gram-negative Bacteria*
Anna Konovalova, PhD
University of Texas Health Science Center, Houston, TX

8:55-9:20 *Shoving the Envelope: Towards Point-of-care Characterization of Antimicrobial Resistance and Emerging Pathogens with SeqScreen*
Todd Treangen, PhD
Rice University, Houston, TX

9:20-9:45 G*enomic Insights into Local Persistence and Global Spread of Antibiotic Resistance*
Ashlee Earl, PhD
Broad Institute, Boston, MA

9:45-10:15 Vendor Show and Networking (pre-function and event hall)

Session 7 *T32 Trainee Symposium: Texas Medical Center Training Program on Antimicrobial Resistance (TP-AMR), Emory Training Program on Antimicrobial Resistance, University of Pittsburgh Training Program on Antimicrobial Resistance*

Conveners: **Cheyenne Lee,** Emory University, Atlanta, GA
Kara Hood PhD, Houston Methodist Research Institute (GCC-TPAMR), Houston, TX

10:15-10:30 *Elucidation of Molecular Mechanisms Underlying Successful Adaptation to Carbapenem Antimicrobials in High Risk Carbapenem Resistant Escherichia coli Lineages*
William Shropshire, PhD
MD Anderson Cancer Center (GCC-TPAMR)

10:30-10:45 *Transcriptional Thermoregulation of the Protease PrpL in Pseudomonas aeruginosa*
Rachel Done

Emory University, Atlanta, GA

10:45-11:00 *A Molecular Epidemiological Exploration of Reduced Vancomycin Susceptibility in Clostridioides difficile*
Taryn Eubank, PharmD
University of Houston (GCC-TPAMR)

11:00-11:15 *Within-host Evolution of Staphylococcus aureus Stringent Response Impart Growth Advantage Under Nutrient Stress*
Edwin Chen, PhD
University of Pittsburgh, Pittsburgh, PA

11:15-11:30 *Bacteriophage Therapy in Recurrent vancomycin-resistant E. faecium bacteremia*
Madison Stellfox, MD, PhD
University of Pittsburgh, Pittsburgh, PA

11:30-11:35 *Introduction to Keynote*
Julian Hurdle, PhD
Texas A&M University

11:35-12:05 **Keynote Lecture**
Discovering New Antibiotics from Unlikely Sources
Kim Lewis, PhD
Northeastern University, Boston, MA

12:05-2:00 Lunch/Rapid Fire/Poster session (Event Hall)
12:05 pick up lunch

12:20-12:50 Rapid Fire Presentations:

Understanding the Effects of Staphylococcus aureus Urease on Biofilm Production and Antibiotic Recalcitrance in Clinical Isolates
Jana Gomez, Univ. of Texas Health Science Center at Houston

Identifying LiaFSR Residues Contributing to ExPortal Integrity and Response to Antimicrobials in Group A Streptococcus (GAS)
Madeline Guy, McGovern Medical School at University of Texas Health Science Center at Houston

The Effects of Oral Omadacycline and Vancomycin on the Gut Microbiome in Healthy Subjects
JinheeJo, University of Houston

Mapping the Determinants of Catalysis and Substrate Specificity of the Antibiotic Resistance Enzyme CTX-M β-lactamase
Allison Judge, Baylor College of Medicine

Activity of Newer Antibiotics Against Carbapenem-Resistant Enterobacterales Isolates - Emory Healthcare, 2016-2021
Christina Lin, Emory School of Medicine

A Retrospective, Observational Study of 12 Cases of Expanded Access Phage Therapy
Austen Terwilliger, Baylor College of Medicine

12:50-2:00 Poster Session, Posters 30-53

Session 8

Conveners: **Cesar A. Arias MD, PhD**, Houston Methodist Research Institute and Weill Cornell Medical College, Houston, TX

2:00-3:00 *Challenging Clinical Cases in Antimicrobial Resistance*
Andrew Chou, MD, PhD
Baylor College of Medicine, Houston, TX
Sara Cosgrove, MD
Johns Hopkins University, Baltimore, MD
Saima Aslam, MD
University of California, San Diego, CA

Session 9 **ARLG Session 2**
Clinical Research in Antimicrobial Resistance

Conveners: **Henry Chambers, MD,** University of California San Francisco, San Francisco, CA
Vance Fowler, MD MPH, Duke University, Durham, NC

3:00-3:15 *DEI in MRSA Clinical Trials*
Melinda Pettigrew, PhD
Yale University, New Haven, CT

3:15-3:30 *Carbapenemases in XDR Pseudomonas*
Michael Satlin, MD
Weill Cornell Medical College, New York, NY

3:30-3:45 "*You Don't Know How It Feels" QOL Assessments by Patients with Complicated Urinary Tract Infections and Their Treating Physicians*
Heather King, PhD
Duke University, Durham, NC

3:45-4:00 *The FAST Study*
Ritu Banerjee, MD, PhD
Vanderbilt University, Nashville, TN

4:00-4:30 Vendor Show and Networking

Session 10

Conveners: **Rodrigo Baptista, PhD**, Houston Methodist Research Institute, Houston, TX.
Vincent Tam, PharmD, University of Houston, Houston, TX

4:30-4:55 *Deploying new B-lactam/B-lactamase Inhibitors in Clinical Practice*
Erin McCreary, PharmD
University of Pittsburgh, Pittsburgh, NC

4:55-5:20 *Phage Therapy for Multidrug-resistant Organisms*

Saima Aslam, MD
University of California, San Diego, CA

5:20-5:45 *Combating Antimicrobial Resistance in Orthopedic Infections*
Robin Patel, MD
Mayo Clinic, Rochester, MN

Day 3 – Friday, January 20, 2023

Antibiotic Stewardship

7:30-8:30 *Careers in Antibiotic Stewardship* (Event Hall)
Ed Septimus, MD
Harvard Medical School
Shivani Patel, PharmD
Memorial Hermann Southwest Hospital, Houston, TX
Michael L. Chang, MD
University of Texas Health Science Center, Houston, TX

Session 11
Conveners: **Kevin Garey PhD University** of Houston College of Pharmacy
Ed Septimus, MD Harvard Medical School

8:30-8:35 *Welcome*
Ed Septimus, MD
Harvard Medical School and Texas A&M College of Medicine, Houston, TX

8:35-8:55 *Notable Collaborative Accomplishment Highlight: Houston Wastewater Surveillance Program*
Kathy Ensor, **PhD**, Rice Univ.
Loren Hopkins, Phd, Houston Health Dept.
David Persse, **MD,** Houston Fire Dept.
Lauren Stadler, PhD, Rice Univ.

8:55-9:35 **Keynote:**
Antimicrobial Stewardship in the ICU
Marin Kollef, MD
Washington University School of Medicine, St Louis MO

9:35-10:05 *Epidemiology and Management of Carbapenem-Resistant Acinetobacter baumannii (CRAB)*
Keith Kaye, MD
Rutgers Robert Wood Johnson Medical School, New Brunswick, NJ

10:05-10:35 *Evolving Clinical Resistance to Novel Agents in Pseudomonas aeruginosa*
Ryan Shields, PharmD, MS
University of Pittsburgh, Pittsburgh, PA

10:35-11:05 Vendor show and networking (pre-function and event hall)

Session 12

Conveners: **Taryn Eubank**, **PharmD Houston** Methodist Research Institute
Robert Atmar, MD Baylor College of Medicine Houston TX

11:05-11:35 *Treating Serious Gram-Positive Infections: Resistance, Biofilm, and High Inoculum*
Kerry L. LaPlante, PharmD
Brown University, Providence, RI

11:35-12:05 *A Statewide Registry for MDROs: Illinois' Experience*
William Trick, MD
Rush University Medical Center, Chicago, IL

12:05-12:35 *Looking Ahead: β-Lactam Agents on the Horizon Targeting Carbapenem-Resistant Gram-Negative Infections*
Pranita Tamma, MD, MHS
John Hopkins University School of Medicine, Baltimore, MD

12:35-2:05 Lunch/Rapid Fire/Poster session (Event Hall)
12:35 pick up lunch

12:50-1:20 Rapid Fire Presentations:

Perspectives on Non-prescription Antibiotic Use Among Hispanic Patients in the Houston Metroplex
Lindsey Laytner, Baylor College of Medicine, Family and Community Medicine

"Evaluation of Cefazolin High Inoculum Effect in Methicillin-Susceptible Staphylococcus aureus (MSSA) Using Gold standard MICs and Rapid Colorimetric Test (RCT)"
Husna Malikzad, Houston Methodist Hospital

Virulence Factors of Multi-drug Resistant Aeromonas Isolates Elucidated Using RNA Sequencing
Blake Neil, University of Texas Medical Branch

CL Synthases Play Redundant Roles and Are Required for Membrane Remodeling in Daptomycin Resistance Enterococcus faecalis
April Nguyen, McGovern Medical School

Simplified Microbial Communities as Antibiotic Alternative in Treatment of Clostridioides difficile Infection
Eva Preisner, Baylor College of Medicine

A Novel Type of Cytotoxic Membrane Vesicles Produced by Pseudomonas aeruginosa
Qi Xu, Rice University

1:20-2:05 Poster Session, Posters 60-85

2:05-2:35 *CLSI updates: New Year and New Breakpoints*
James Lewis, PharmD
Oregon Health & Science University, Portland OR

Session 13

Conveners: **Yasser Alsafadi, MD** Houston Methodist Research Institute
Jinhee Jo, PharmD University of Houston College of Pharmacy

2:35-3:05 *The Long and Short of it: Assessing Antibiotic Durations for Common Pediatric Infections*
Michelle Mitchell, MD
Children's Wisconsin

3:05-3:35 *Candida auris*
Thomas Patterson, MD
University of Texas Health Science Center San Antonio TX

3:35-4:05 *Microbiome Inroads Toward MDRO Decolonization*
Michael Woodworth, MD
Emory University School of Medicine, Atlanta GA

4:05 Introduction to Keynote
Ed Septimus, MD Harvard Medical School

4:10-4:40 **Closing Keynote**
Preparedness for Emerging Pathogens: Are We Ready?
Susan LF McLellan, MD
University of Texas Medical Branch Galveston, TX

4:40 Closing Remarks

Presenters in alphabetical order

Saima Aslam, MD, MS
Professor of Medicine
Medical Director, Solid Organ Transplant Infectious Diseases
Division of Infectious Diseases and Global Public Health
University of California, San Diego

Phage Therapy for Multidrug-resistant Organisms

Dr. Aslam is a Professor of Medicine, Director of the Solid Organ Transplant Infectious Diseases service, and Clinical Lead for the Center of Innovative Phage Applications and Therapeutics at UCSD. She is engaged in providing exceptional clinical care as well as clinical/translational research in the field of transplantation and phage therapy. Dr Aslam graduated with honors from the Aga Khan University in Pakistan in 1999 and then trained at Baylor College of Medicine (BCM), Texas in Internal Medicine and Infectious Diseases. Dr Aslam also received a Masters of Science in Clinical Investigation from BCM in 2008 and a certificate from the Health Leadership Academy at UCSD in 2020.

Hossaena Ayele, MSc
Graduate Research Assistant
School of Public Health, Center for Infectious Diseases
University of Texas at Houston

GENO-STELLAR: A Clinically Actionable Tool for Identifying Anti-Microbial Resistant Klebsiella pneumoniae Species

Hossaena Ayele is a Graduate Research Assistant (GRA) in Dr. Blake Hanson's lab in the School of Public Health and Center for Infectious Diseases at the University of Texas at Houston. Hossaena received her Bachelor of Science in Microbiology and Master of Science in Medical Microbiology from the University of Manitoba in Winnipeg, Manitoba, Canada. Hossaena's past research experience has consisted of examining host and microbial proteomic changes with contraceptive use in a population at high risk of HIV infection. She is currently at UTHealth studying to receive her PhD in Epidemiology. As a GRA in Dr. Hanson's lab, Hossaena has worked on multiple projects assisting in bioinformatic analyses. Her interests lie in the human microbiome, specifically the vaginal and gut microbiome. She is also interested in method development for the analysis of microbial omics data to aid in the surveillance and understanding of the molecular epidemiology of anti-microbial resistant bacterial strains.

Ritu Banerjee, MD, PhD
Professor
Division of Pediatric Infectious Diseases
Vanderbilt University Medical Center
The FAST Study

Dr. Ritu Banerjee is Professor in the Division of Pediatric Infectious Diseases at Vanderbilt University Medical Center. She is the Director of the Pediatric Antimicrobial Stewardship Program and Interim Director of Pediatric Infectious Diseases at Vanderbilt. She received her MD and Ph.D. degrees from Washington University in St. Louis and then completed Pediatrics residency and Pediatric Infectious Disease fellowship at the University of California, San Francisco. She is a member of many national committees through the Pediatric Infectious Diseases Society, the American Academy of Pediatrics, the Infectious Diseases Society of America, and the Antibacterial Resistance Leadership Group. Dr. Banerjee conducts clinical research about antibiotic stewardship, implementation and outcomes of rapid blood culture diagnostics, and enhanced detection of carbapenem-resistant organisms.

Helen W. Boucher, MD, FACP, FIDSA
Dean and Professor of Medicine
Tufts University School of Medicine
Chief Academic Officer, Tufts Medicine
Antimicrobial Resistance in the 21st Century: Trials and Tribulations

Helen Boucher, MD, is the Dean and Professor of Medicine at Tufts University School of Medicine and Chief Academic Officer of the Tufts Medicine Health System. An active Infectious Diseases physician, she was previously Chief of the Division of Geographic Medicine and Infectious Diseases at Tufts Medical Center, and Director of the Stuart B. Levy Center for Integrated Management of Antimicrobial Resistance (Levy CIMAR).

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 Chair of the National Institutes of Health (NIH) Antibacterial Resistance Leadership Group (ARLG) Innovations Working Group, and serves on the Executive and Steering Committees. Dr. Boucher 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, Editor of the Sanford Guide to Antimicrobial Therapy, and Infectious Diseases Clinics of North America.

In 2015, Dr. Boucher was appointed a voting member of the Presidential Advisory Council on Combating Antibiotic Resistant Bacteria (PACCARB), and elected Treasurer of the Infectious Diseases Society of America (IDSA). She was awarded the IDSA Society Citation Award in October 2015. Dr. Boucher serves as Chair of 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.

Angelique Boutzoukas, MD
Pediatric Infectious Diseases
Duke University
Carbapenem-Resistant E. coli from CRACKLE

Angelique Boutzoukas, MD is in her final year of Pediatric Infectious Diseases fellowship at Duke University. She is co-chief of the Clinical Research Fellowship at Duke Clinical Research Institute and in her final year of an Applied Epidemiology MPH at UNC Gillings School of Public Health. Her primary research interests are in determining the optimal duration and dosing of antimicrobial therapies in children, and the epidemiology and prevention of emergence of antimicrobial resistance in pediatrics. She has collaborated with ARLG through a secondary analysis of CRACKLE-2 isolates, focusing on the molecular and clinical epidemiology of carbapenemase-producing E. coli, under the mentorship of Dr. David van Duin.

Edwin Chen, MD, PhD
Infectious Diseases Fellow
Univ. of Pittsburgh

Within-host Evolution of Staphylococcus aureus Stringent Response Impart Growth Advantage Under Nutrient Stress

Edwin Chen obtained his MD and PhD at Washington University in St. Louis where he completed his PhD thesis in the laboratory of Dr. Niraj Tolia characterizing inhibitory antibodies targeting P. falciparum and P. vivax invasion proteins. He then completed both an Internal Medicine residency and an Adult Infectious Diseases fellowship at the University of Pittsburgh Medical Center. He is currently at T32 post-doctoral scholar at the University of Pittsburgh in the laboratory of Dr. Matthew Culyba investigating mechanisms of antibiotic tolerance in persistent methicillin-resistant S. aureus bacteremia.

Andrew Chou, MD, PhD
Physician and Researcher
Michael E. DeBakey VA Medical Center
and Baylor College of Medicine
Challenging Clinical Cases in Antimicrobial Resistance

Andrew Chou is an infectious diseases physician and researcher at the Michael E. DeBakey VA Medical Center and Baylor College of Medicine. Research interests include developing and applying novel predictive models and machine learning to identify antimicrobial resistance using the collection of clinical databases in the VHA Corporate Data Warehouse.

Sara Cosgrove, MD, MS
Professor of Medicine
Infectious Disease
Johns Hopkins University School of Medicine
Challenging Clinical Cases in Antimicrobial Resistance

Dr. Sara Cosgrove is a Professor of Medicine in the Division of Infectious Disease (ID) 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 is the Director of Research for the ID Fellowship Program and PI of the T32 training grant that supports ID fellow training. 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. Early in her career, she recognized the critical need to study antimicrobial stewardship strategies and has led a series of outcomes studies over the past 15 years that have defined the practice of antimicrobial stewardship in the United States. Her recent research focuses on strategies for implementation of antimicrobial stewardship activities across all healthcare settings via a large, multi-center project including hospitals, long-term care facilities and ambulatory practices as well as assessing and quantifying harm associated with antibiotic therapy. She is a past Voting Member of 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, her medical degree from Baylor College of Medicine, and her master of science degree in epidemiology from Harvard School of Public Health. She completed her postgraduate training in internal medicine at The Johns Hopkins Hospital and underwent subsequent training in ID at Beth Israel Deaconess Medical Center.

Rachel Done
Graduate Student
Emory University

Transcriptional Thermoregulation of the Protease PrpL in Pseudomonas aeruginosa

Rachel Done is a PhD candidate in the Microbiology and Molecular Genetics program in the laboratory of Dr. Joanna Goldberg at Emory University. As trainee under the Antimicrobial Resistance and Therapeutic Discovery Training Program (ARTDTP), she studies how the opportunistic pathogen Pseudomonas aeruginosa senses and responds to temperature changes as it transitions from living in the environment to infecting the human body. Rachel earned a B.S. in Ecology and Evolutionary Biology from Yale University, where she conducted research in Dr. Paul Turner's lab on the application of bacteriophages for phage therapy.

Ashlee Earl, MD, PhD
Research Scientist, Senior Group Leader, Institute Scientist
Broad Institute of MIT and Harvard
Microbiome Analyses and AMR

Ashlee Earl founded and directs the Bacterial Genomics Group at the Broad Institute of MIT and Harvard, where she is an Institute Scientist. Within the Broad's Genomic Center for Infectious Diseases and Infectious Disease and Microbiome Program, she's working to understand the relationship between microbes and human health, including how multidrug-resistant pathogens emerge and spread. Earl coordinated much of the Broad's research in the Human Microbiome Project and now leads a team of computational scientists to develop and deploy "omics" analytical approaches to dissect bacterial and host contributions to infectious diseases. She has organized and led collaborations with world-leading experts to bring these approaches to the study of tuberculosis, urinary tract infections, and hospital-acquired infections.

Stephanie Egge, MD
Post-doctoral Research Fellow
Internal Medicine
Houston Methodist Research Institute

Prospective Assessment of TonB Receptor Mutants and Cefiderocol Susceptibility Across Clinical Isolates of Pseudomonas Aeruginosa

Stephanie Egge is a current T32 post-doctoral research fellow at the Houston Methodist Research Institute, Department of Internal Medicine, Division of Infectious Diseases under the mentorship of Dr. William Miller. She completed her clinical fellowship in infectious disease at the University of Texas Houston/MD Anderson Cancer Center 2020-2022 and is board certified to practice medicine in both internal medicine and infectious diseases. Her research focuses on mechanisms of Gram-negative antibiotic resistance, particularly as it pertains to multi-drug resistant Pseudomonas aeruginosa and the last-line siderophore cephalosporin cefiderocol. Recent studies have demonstrated discrepancies between microbiologic susceptibility testing and clinical treatment success. Stephanie's work aims to define parameters for predicting treatment success and/or failure of cefiderocol as monotherapy to optimize multi-drug resistant Pseudomonas aeruginosa treatment algorithms. Her work is currently funded by the Texas Medical Center Training Program in Antimicrobial Resistance (TPAMR) (NIAID), T32 AI141349.

Katherine Ensor, PhD
Noah G. Harding Professor
Statistics, Rice University
Notable Collaborative Accomplishment Highlight: Houston Wastewater Surveillance Program

Noah G. Harding Professor of Statistics, Rice University; Center for Computational Finance and Economic Systems, Rice University; In 2022 served as President, American Statistical Association Board of Directors

Houston Wastewater Epidemiology: A CDC National Wastewater Surveillance System (NWSS) Center of Excellence

Katherine Ensor is a leading expert in applying computational and statistical analysis to track and forecast issues in public health, community informatics, environmental statistics, and computational finance.

In May 2020, she began establishing and implementing the statistical system for assessing the pertinent health assessment information from wastewater samples for SARS-CoV-2. Through Houston Wastewater Epidemiology, this scope has been expanded.

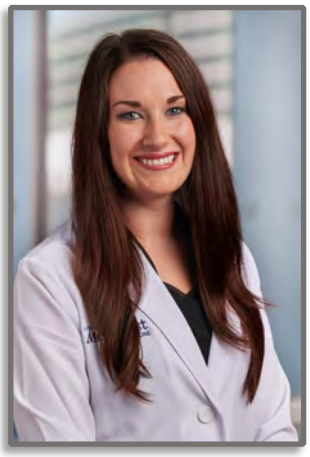
Ensor also led the creation and development of the Kinder Institute Urban Data Platform (UDP), a secure data repository and an analytical computing environment that provides research-ready urban data for the Greater Houston Area. The platform facilitates cross-disciplinary research and community studies to advance knowledge and information about Houston's people, government, and built environment. UDP studies have provided information on COVID-19, evictions, flooding impacts and more.

Ensor has been a faculty member of Rice’s Department of Statistics for 35 years. Her research is highly cited and published in over 40 journal publications. In addition to developing statistical techniques to answer large-dimension problems in public health and environmental science, she specializes in the application of time-series data to analyze problems in finance. She is director of Rice’s Center for Computational Finance and Economic Systems (CoFES).

Ensor is the 117th president of the American Statistical Association, a fellow of the American Statistical Association and a fellow of the American Association for the Advancement of Science. She served as chair of Rice’s Department of Statistics from

1999 to 2013. She led the development of a joint Ph.D. program between Rice and MD Anderson Cancer Center, and the first professional master's program in statistics in the Houston area.

More information can be found at: https://hou-wastewater-epi.org/about/kathy-ensor



Taryn A. Eubank, PharmD
Postdoctoral Fellow
University of Houston

A Molecular Epidemiological Exploration of Reduced Vancomycin Susceptibility in Clostridioides difficile

Dr. Taryn A. Eubank received her PharmD from Harding University College of Pharmacy and went on to complete a PGY1 residency at Houston Methodist Hospital as well as a PGY2 in Infectious Diseases also at Houston Methodist. During her PGY2, she became involved with many of the COVID-19 clinical trials at Houston Methodist including co-site investigator for the ACTT-4 international clinical trial. Following residency, she received a fellowship position through the Gulf Coast Consortia Training Program in Antimicrobial Resistance funded by the National Institute of Allergy and Infectious Diseases under Dr. Kevin W. Garey at University of Houston of which she is currently completing her second year. Dr. Eubank has also acquired Board Certification in Infectious Diseases and works part time at Houston Methodist as a pharmacy clinical specialist. Her career interests include antimicrobial resistance and the human gut resistome.

Janie French, BS
Graduate Student
Univ. of Pittsburgh

Pathogenesis, Localization and Host Response During Influenza and Streptococcus Pneumoniae Co-infection in Ferrets

Janie French, BS in Biochemistry and Spanish, University of Wisconsin – Madison, is a 4th year graduate student in the Program in Microbiology and Immunology at the University of Pittsburgh. Her work examines viral/bacterial co-infection with Streptococcus pneumoniae and other factors influencing transmission of influenza virus. She is interested in public health and hopes that her work may be useful in future policy decisions.

Kara Schoenemann Hood, PhD
Postdoctoral Trainee
Houston Methodist Research Institute
Dissecting the Mechanism of Cell Membrane Adaptation Against Antimicrobials

Dr. Kara Schoenemann Hood is a postdoctoral trainee in Texas Medical Center Gulf Coast Consortia Training Program in Antimicrobial Resistance, working under her primary mentor Dr. Cesar A. Arias at the Houston Methodist Research Institute in Houston, Texas. Dr. Hood earned her bachelor's degree in Biology from Trinity University in San Antonio, Texas before earning her Ph.D. in Microbiology and Molecular Genetics from The University of Texas MD Anderson Cancer Center UTHealth Houston Graduate School of Biomedical Sciences.

Loren Hopkins, PhD
Chief Environmental Science Officer, Houston Health Department; Bureau Chief, Data Science Division, Houston Health Department; Professor in the Practice of Statistics, Rice University; National Environmental Justice Advisory Council
Notable Collaborative Accomplishment Highlight: Houston Wastewater Surveillance Program

Chief Environmental Science Officer, Houston Health Department; Bureau Chief, Data Science Division, Houston Health Department; Professor in the Practice of Statistics, Rice University; National Environmental Justice Advisory Council

Houston Wastewater Epidemiology: A CDC National Wastewater Surveillance System (NWSS) Center of Excellence

Loren Hopkins is a nationally recognized expert in environmental science and engineering. Her unique affiliation with Rice University's Department of Statistics and the Houston Health Department has played a central role in applied research and the translation of advances in science, engineering, and higher education to inform city policymakers and improve public health. In March 2022, she was named to the National Academies' Committee on Community Wastewater-based Disease Surveillance.

Since 2001, Hopkins has served as a lecturer, faculty fellow, and professor in the practice of statistics at Rice University. She teaches courses in her areas of expertise, including: environmental statistics and decision making; the association between human health and air pollution exposure; and human health risk assessment.

Hopkins has been involved in all aspects of human health risk assessment, including as a practitioner in the private sector, regulatory reviewer, policy developer, and instructor. She is currently the Chief Environmental Science Officer for the Houston Health Department. In this role, Hopkins leads the Data Services, Data Science, and Wastewater Sampling and Surveillance programs for the City of Houston. In 2014 she served as a visiting scientist on the Centers for Disease Control and Prevention (CDC) Air Pollution and Respiratory Health Branch in Atlanta, Georgia. Hopkins has served as the chair for the Regional Air Quality Planning Advisory Committee Executive Board, and as the chair for the Houston Wilderness Executive Board. Currently, she serves on the National Environmental Justice Advisory Council.

For the City of Houston and its Department of Health, Hopkins has provided local, state, and national leadership on environmental studies and has reviewed proposed

state, federal and local environmental policy impacting the Greater Houston Area. In May 2020, Hopkins began leading efforts between Rice and the City of Houston to establish and implement a city-wide wastewater epidemiology surveillance program to serve as an early-warning system to inform a planned response to viral outbreaks.

Hopkins' research has been published in 24 peer-reviewed journal papers and has been presented at many local, state, and national conferences. She has been involved in all aspects of human health risk assessment, including as a practitioner in the private sector, regulatory reviewer, policy developer, and continuing education instructor at various locations across the U.S.

More information can be found at: https://hou-wastewater-epi.org/about/loren-hopkins

Jessica Howard-Anderson, PhD
Assistant Professor
Medicine
Emory University

A ZEPHYR in the DOOR: Reanalysis of a Controversial Trial

Dr. Howard-Anderson is an Assistant Professor of Medicine at Emory University School of Medicine and the Associate Hospital Epidemiologist and Co-Director of Antimicrobial Stewardship at Emory University Hospital Midtown. She completed her medical school, residency and chief residency at University of California Los Angeles. Dr. Howard-Anderson completed fellowship training in infectious diseases at Emory University in 2021 and during her fellowship obtained a Master of Science in Clinical Research and was selected for a research fellowship with the NIH-funded Antibacterial Resistance Leadership Group. Dr. Howard-Anderson's research focuses on: 1) the epidemiology of multidrug-resistant Gram-negative organisms, 2) using novel methodologies such as DOOR (desirability of outcome ranking) to better understand clinical outcomes of patients infected with multidrug-resistant organisms, and 3) employing diagnostic stewardship to improve antimicrobial prescribing and decrease healthcare associated infections. She is an active member of Society of Healthcare Epidemiology of America (SHEA) and the Infectious Diseases Society of America (IDSA).

Keith S. Kaye, MD, MPH
Chief, Division of Allergy, Immunology and Infectious Diseases
Professor of Medicine
Robert Wood Johnson Medical School
Epidemiology and Management of CRE/CRAB

Dr. Kaye is the Chief, Division of Allergy, Immunology and Infectious Diseases, and is Professor of Medicine in the Department of Medicine at Rutgers Robert Wood Johnson Medical School.

He has devoted his career to the prevention and effective management of healthcare-associated infections. In addition to serving in a variety of quality improvement and administrative roles in infection prevention, antimicrobial stewardship, and quality and patient safety, he has served on national and international clinical guidelines committees.

Dr. Kaye's research interests include prevention and treatment of antimicrobial resistant organisms, prevention of healthcare associated infections, and innovative approaches to antimicrobial stewardship. He has a long and productive track record of federal funding for research pertaining to management of healthcare associated infections (HAIs) and multi-drug resistant organisms (MDROs) including Acinetobacter baumannii, carbapenem-resistant Enterobacterales (CRE), and Pseudomonas aeruginosa. He has conducted innovative, groundbreaking clinical trials on HAIs and MDROs.

Dr. Kaye received his medical degree from the University of Pennsylvania and completed his Internal Medicine residency and Infectious Diseases fellowship at Beth Israel Deaconess Medical Center in Boston, MA. During fellowship, Dr. Kaye earned a Masters in Public Health from the Harvard School of Public Health. Dr. Kaye has authored over 350 peer-reviewed articles and 20 book chapters and has frequently presented original research at national and international conferences. Dr. Kaye is a past President of the Society for Health Epidemiology of America (SHEA). He is an internationally recognized expert in healthcare epidemiology and antimicrobial resistance and has been invited to speak on these topics at venues throughout the world.

Tori Kinamon
MD Candidate
Duke Univ.

Complicated Intra-abdominal Infection Trials: FDA Geographic Variation

Air Force 2nd Lt. Tori Kinamon is an MD Candidate at Duke University School of Medicine and the recipient of the FDA Antibacterial Drug Resistance (DOOR) Fellowship. Her research focuses on evaluating and developing ordinal endpoints using the Desirability of Outcome Ranking (DOOR) approach for anti-infective clinical trials with the aim of assessing global benefits and risks of antibacterial intervention. She is a member of the Antibacterial Resistance Leadership Group DOOR Exploratory Task Force. Her clinical and research interests include antibacterial resistance and staphylococcal infections.

Heather King, PhD
Research Health Scientist, Durham VA Health Care System
"You Don't Know How It Feels" QOL Assessments by Patients with Complicated Urinary Tract Infections and Their Treating Physicians

Dr. Heather A. King is an investigator at the Durham VA Health Care System, Health Services Research and Development (HSR&D), Center of Innovation to Accelerate Discovery and Practice Transformation (ADAPT) and part of the Center's Implementation and Improvement Science Lab (Assistant Director, faculty leader of the Rapid Response Review) and Qualitative Core, among others. She is also an Assistant Professor in the Department of Population Health Sciences (member of the Implementation Science Research Collaborative [INTERACT, leader of education and outreach initiatives] and Center for Health Measurement) and Division of General Internal Medicine at Duke University School of Medicine. She is a health services researcher and methodologist with an interest in implementation science and patient and family health-related quality of life, particularly in bacterial infections. She has significant expertise in qualitative and mixed methods, partner engagement, and measurement at a large scale, across multiple sites and health systems, including in rural areas.

Marin Kollef, MD
Professor
Medicine
Washington University
Antimicrobial Stewardship in the ICU

Dr. Marin Kollef is a Professor of Medicine at Washington University School of Medicine, holds the Virginia E. and Sam J. Golman Chair in Respiratory Intensive Care Medicine, and is Director of Respiratory Care Services and Director of Critical Care Research at Barnes-Jewish Hospital in St. Louis, Missouri. Dr. Kollef attended the U.S. Military Academy at West Point for his undergraduate training and the University of Rochester for his M.D. degree. Dr. Kollef completed his residency in Internal Medicine and his fellowship in Pulmonary and Critical Care Medicine at Madigan Army Medical Center in Tacoma, Washington. He served as the director for the medical ICU at Fitzsimons Army Medical Center from 1988 to 1992. During that time he also served as a general medical officer in support of the 1st Infantry Division during Operation Desert Storm. He joined Washington University School of Medicine and Barnes-Jewish Hospital in 1992.

Dr. Kollef is the recipient of numerous honors and awards including selection to “Best Doctors in America,” Central Region and Barnes-Jewish Hospital Team Awards for Quality Improvement for programs directed to VAP prevention, bloodstream infection prevention, and the “Surviving Sepsis Initiative.” His awards for military service with the First Infantry Division (Mechanized) during Operation Desert Storm include the Bronze Star, Meritorious Service Medal, and Combat Medical Badge in Support of Combat Operations. He is also a member of the American Thoracic Society, Society of Critical Care Medicine, American Association for Respiratory Care, and American Society of Clinical Investigation. He is a member of the CDC/OID/NPC DCID Defining Surveillance Definitions for VAP and the Chair for Global Anti-Infectives Leadership Academy.

Dr. Kollef currently serves on the editorial boards of *Respiratory Care, Critical Care*-the Official Journal of the Critical Care Forum, *Critical Care Medicine, Informed Decisions/Clinical Strategies*, and the *Journal of Surgical Infections*. He is a fellow of the American College of Physicians and the American College of Chest Physicians.

Anna Konovalova, PhD
Assistant Professor
Microbiology and Molecular Genetics
McGovern Medical School
Univ. of Texas Health Science Center
Houston

Targeting Cell Envelope in Gram-negative Bacteria

Dr. Konovalova is an Assistant Professor in the Department of Microbiology and Molecular Genetics at UTHealth Houston's McGovern Medical School. Dr. Konovalova joined the department in 2017. Dr. Konovalova received her Ph.D. in 2011 for her graduate thesis work in the laboratory of Prof. Lotte Søgaard-Andersen at the Max-Plank Institute for Terrestrial Microbiology in Marburg, Germany. She completed her postdoctoral training with Professor Thomas J. Silhavy at Princeton University in Princeton, USA. Dr. Konovalova is a recipient of the Texas Rising STAR Award (2017). Dr. Konovalova's research program is focused on how Gram-negative bacteria build and maintain the integrity of the outer membrane (OM). The OM is an essential structure and a major factor of intrinsic antibiotic resistance. Her lab aims to provide a deep functional understanding of the OM assembly and homeostasis pathways and their interconnectivity as the first step in the scientific roadmap to antibiotic discovery.

Kerry LaPlante, PharmD
Department Chairperson, University of Rhode Island College of Pharmacy
Adjunct Professor, Medicine, Brown University

Challenging Cases: Gram-positive Infections / Biofilm Medical Device

Dr. Kerry LaPlante is an internationally recognized expert on antimicrobial use and resistance. She is a licensed clinical pharmacist, researcher and policy adviser. She serves as department chairperson at the University of Rhode Island College of Pharmacy. She is also an adjunct professor of medicine at Brown University, a fellowship director at the Veterans Affairs Medical Center in Providence, RI and leads the Rhode Island Department of Health Antimicrobial Stewardship Task Force.

Dr. LaPlante earned her BS degree in biology, with a psychology minor at Canisius College in Buffalo, NY, a BS in biopharmaceutical sciences, and a PharmD from Wayne State University in Detroit, Michigan. She completed a post-doctoral fellowship in infectious diseases pharmacotherapy at the Anti-Infective Research Laboratory at Wayne State University.

Dr. LaPlante is known for her expertise in antibiotic therapy where she has extensively researched biofilm-associated infections, use of combination therapy, and how antimicrobial stewardship programs prevent resistance and improve patient outcomes. Dr. LaPlante has given over 100 invited lectures and published over 130 peer-reviewed articles throughout her career. Her contributions also include authorship on the 2021 American College of Gastroenterology C. difficile treatment guidelines. She has also published a book titled "Antimicrobial Stewardship Principles and Practices”

She is a past president of the Society of Infectious Diseases Pharmacists (SIDP), current vice-president for Making a Difference in Infectious Diseases (MAD-ID), and an elected Fellow of the Infectious Diseases Society of America, American College of Clinical Pharmacy and SIDP. She serves as an editor for Pharmacotherapy, and Clinical Infectious Diseases.

Francois Lebreton, PhD
Head of Bioinformatics
Walter Reed Army Institute of Research
U.S. Department of Defense

Tracking Emerging Mechanisms of Resistance with Genomics

Dr. Francois Lebreton is the head of bioinformatics within the Multidrug-resistant organism Repository & Surveillance Network (MRSN) at the Walter Reed Army Institute of Research. His team uses next generation sequencing and comparative genomics to provide real-time surveillance and detection of MDR bacterial outbreaks in a large network of military treatment facilities, in continental USA and overseas. His research focuses on conducting retrospective and prospective outbreak analyses to identify the factors that influence the emergence of MDR populations, their distinguishing characteristics, and the evolutionary drivers that shape them.

Cheyenne Lee
Graduate Student
Emory University

Kip Proteins Promote Clostridoides difficile Growth in Bile Salts

Cheyenne Lee graduated with a BS in biotechnology from The University of North Carolina at Pembroke in May 2019. At UNCP, she worked with Dr. Conner Sandefur on characterizing the antimicrobial properties of Lumbee Tribe herbal teas under the NSF-COMPASS and NIH-RISE programs. Currently, she is a 4th year Ph. D. candidate in the Microbiology and Molecular Genetics (MMG) program and has been an ARTDTP fellow at Emory University since 2021. Under the mentorship of Dr. Shonna McBride, Cheyenne's project focuses on characterizing Clostridioides difficile sporulation initiation and growth specifically through the activities of the KipOTIA proteins. Without the ability to form spores, C. difficile cannot be transmitted as efficiently through the environment to infect new hosts. Knowing this, Cheyenne's project focuses on understanding how C. difficile forms the spores that make it easily transmissible so that new targets for novel therapeutics to inhibit sporulation initiation may be uncovered.

James S. Lewis II, PharmD, FIDSA
Clinical Supervisor for Infectious Disease
Oregon Health & Science University
CLSI Breakpoints Update

James S. Lewis II, PharmD, FIDSA, received his PharmD from Washington State University and completed his infectious diseases pharmacy residency training at UT Health San Antonio. He is currently the infectious diseases pharmacy supervisor and co-director of antibiotic stewardship at Oregon Health and Science University (OHSU). Dr. Lewis is also an associate professor in the division of infectious diseases at OHSU. Dr. Lewis currently serves as the chairholder of the antimicrobial susceptibility testing subcommittee of the Clinical and Laboratory Standards and served as co-chair of the CLSI breakpoint working group for 8 years previous to chairing the AST subcommittee.

Kim Lewis, PhD
University Distinguished Professor and Director
Antimicrobial Discovery Center
Northeastern University in Boston

Discovering New Antibiotics from Unlikely Sources

Kim Lewis is a University Distinguished Professor and Director, Antimicrobial Discovery Center at Northeastern University in Boston. He is a Fellow of the American Society of Microbiology, and a Fellow of the American Association for the Advancement of Science. He is a Highly Cited Researcher (Clarivate Analytics) and an Expertscape World Expert in Microbial Drug Resistance (top 0.1% of scholars in the field).

He obtained his Ph.D. in Biochemistry from Moscow University in 1980, and has been on the Faculty of MIT, University of Maryland, and Tufts University prior to coming to Northeastern.

Dr. Lewis has authored over 100 papers and is an inventor on several patents.

Dr. Lewis has served as a panelist and contributor to reports on antimicrobial resistance (AMR) by National Academies Institute of Medicine, the Pew Charitable Trust, and the European Academies of Science. Dr. Lewis is a member of Faculty 1000, a world-wide panel of experts evaluating research advancements. He is a recipient of the MIT C.E. Reed Faculty Initiative Award and is a recipient of the NIH Director's Transformative Award and the ASM Applied Biology and Biotechnology Research Award.

Jose RW Martinez
Graduate Student
Universidad del Desarrollo

Clonal Dynamics of Methicillin-Resistant Staphylococcus aureus in a Tertiary Healthcare Center Between 2000-2016 in Chile

Rodrigo earned a degree in Biological Sciences in 2008 at the Universidad Austral de Chile, in the rainy city of Valdivia. He then worked for seven years as a research assistant at the Pontificia Universidad Católica de Chile developing molecular tests for the diagnosis and prognosis of thyroid cancer. In recent years, he has switched gears, migrating from oncology to microbiology, where during his Ph.D. program at Universidad del Desarrollo is trying to understand the genomic evolution and clonal dynamics of methicillin-resistant Staphylococcus aureus. Currently, he is finishing his Ph.D. and working as an associate researcher in the Genomics and Resistant Microbes (GeRM) group at the Universidad del Desarrollo, Chile.

Erin McCreary, PharmD, BCPS, BCIDP
Clinical Assistant Professor
Department of Medicine
Univ. of Pittsburgh

Deploying new B-lactam/B-lactamase Inhibitors in Clinical Practice

Erin McCreary, PharmD, BCPS, BCIDP is a Clinical Assistant Professor within the University of Pittsburgh Department of Medicine, Division of Infectious Diseases (ID) and the Director of Infectious Diseases Improvement and Clinical Research Innovation for UPMC. She received her PharmD from the Auburn University Harrison School of Pharmacy and completed her PGY1 Pharmacy and PGY2 Infectious Diseases residencies at the University of Wisconsin Health.

Dr. McCreary co-chairs the UPMC COVID-19 Therapeutics Committee and served as a co-investigator for the REMAP-CAP trial, a global, adaptive, clinical trial evaluating multiple therapies for COVID-19. She has also led system-wide implementation of multiple infectious diseases and antimicrobial stewardship initiatives. She has published numerous peer-reviewed manuscripts in the areas of antimicrobial stewardship and infectious diseases. She also served on the Society of Infectious Diseases Pharmacists Executive Board and is currently a host of Breakpoints—The SIDP Podcast.

Her practice and research interests include infectious diseases and antimicrobial stewardship in immunocompromised hosts, gram-negative resistance, and antimicrobial pharmacokinetic/pharmacodynamic optimization. She is also passionate about professional leadership, mentorship, and preceptorship.

Susan McLellan, MD
Professor
Infectious Diseases Division
Univ. of Texas Medical Branch

Preparedness for Emerging Pathogens: Are We Ready?

Dr. McLellan is Professor in the Infectious Diseases Division at UTMB, Medical Director of the Biocontainment Treatment Unit, Director of Biosafety for Research-related Infectious Pathogens, and Director of the Special Pathogens Excellence in Clinical Treatment, Readiness, and Education (SPECTRE) program. After training in internal medicine, pediatrics, and infectious diseases, she returned to Tulane where she held joint appointments in the School of Medicine and in the School of Public Health and Tropical Medicine before being recruited to UTMB in 2018. She has over 25 years of experience in medical and public health education and in the clinical care of and public health response to emerging infectious diseases. She has participated in outbreak and disaster response in various resource-poor settings, including as a clinical consultant for WHO during the West Africa and DRC Ebola outbreaks, providing direct care as well as assessment of treatment units and support of clinical trials of medical therapies. In her position at UTMB her focus is on improving the clinical care of individuals infected with high containment pathogens in both high and low resource settings and in developing programs for integrated response to pandemic threats, including the rapid scale up of research during outbreaks.

Antonio Mendez
Medical Student
University of Texas Southwestern Medical Center

Phosphorodiamidate Morpholino Oligomers Targeting acpP Reduce the Biofilm Burden in Burkholderia cepacia Complex

Antonio Mendez is a third-year medical student at the University of Texas Southwestern Medical Center. He is currently completing a year-long research fellowship at his home institution in the lab of Dr. David Greenberg. His work focuses on using antisense technology to eradicate biofilms formed by Burkholderia cepacia complex.

William R. Miller, MD
Assistant Professor, Medicine, Division of Infectious Diseases
Houston Methodist Hospital, Houston Methodist Academic Institute, and Weill Cornell Medical College

Mechanisms of Cell Envelope Defense Against Antibiotics in Gram-positive Bacteria

William R. Miller, M.D. is an Assistant Professor of Medicine with the Division of Infectious Diseases at Houston Methodist Hospital, Houston Methodist Academic Institute, and Weill Cornell Medical College. Dr. Miller is a member of the Center for Infectious Diseases at the Houston Methodist Research Institute, where his current research interests involve the clinical impact and mechanistic bases of antimicrobial resistance. Active projects include studying the multilayered cell membrane defense networks of Gram-positive pathogens using enterococci as model organisms, understanding the inoculum effect in severe methicillin-sensitive Staphylococcus aureus infections, and characterizing the molecular mechanisms of resistance of multidrug resistant Pseudomonas aeruginosa.

Michelle Mitchell, MD
Associate Program, Pediatric Infectious Diseases Fellowship Program, Medical College of Wisconsin and Medical Director of the Antimicrobial Stewardship Program at Children's Wisconsin

The Long and Short of it: Assessing Antibiotic Durations for Common Pediatric Infections

Michelle Mitchell MD is an Associate Professor of Pediatric Infectious Diseases at the Medical College of Wisconsin in Milwaukee, Wisconsin. She received her MD and completed a pediatric residency at Saint Louis University followed by a fellowship in pediatric infectious diseases at the University of Colorado/Children's Hospital Colorado. She is currently the Associate Program Director of the Pediatric Infectious Diseases fellowship program at the Medical College of Wisconsin and Medical Director of the Antimicrobial Stewardship Program at Children's Wisconsin.

Jose M. Munita, MD
Associate Professor
Clinica Alemana – Universidad del Desarrollo

Environmental Contamination and the Evolution of MRSA in Latin America

Jose M. Munita is a physician scientist currently working at Clinica Alemana – Universidad del Desarrollo in Santiago, Chile, where he holds a position as an Associate Professor and serves as the Director of the Institute for Science and Innovation in Medicine (https://medicina.udd.cl/icim). Dr. Munita received his medical degree from Universidad de los Andes, Santiago, Chile in 2004 and trained as an Internal Medicine specialist in Clinica Alemana, also in Santiago, Chile. Jose then moved to the US where he completed his Infectious Diseases fellowship at the University of Texas McGovern Medical School and the MD Anderson Cancer Center, Houston, TX. After his training, he moved back to Chile where he is currently working. In 2018, Jose received the Young Investigator award by the International Society for Infectious Diseases and is a member of the Editorial Board for Antimicrobial Agents and Chemotherapy. His group is studying AMR from different perspectives. One of the main projects focuses in the study of the genomic evolution of the Chilean-Cordobes clone of methicillin-resistant S. aureus and he is currently leading a country wide effort to improve the knowledge about antimicrobial resistant organisms in Chile (https://microb-r.org).

Robin Patel, MD

Elizabeth P. and Robert E. Allen Professor of Individualized Medicine; Director, Infectious Diseases Research Laboratory, Co-Director, Clinical Bacteriology Laboratory; Vice Chair, Education in the Department of Laboratory Medicine and Pathology
Mayo Clinic

Combating Antimicrobial Resistance in Orthopedic Infections

Robin Patel is the Elizabeth P. and Robert E. Allen Professor of Individualized Medicine and the Director of the Infectious Diseases Research Laboratory, Co-Director of the Clinical Bacteriology Laboratory, Vice Chair of Education in the Department of Laboratory Medicine and Pathology, and former Chair of the Division of Clinical Microbiology, at the Mayo Clinic.

Since the beginning of her tenure at the Mayo Clinic, Dr. Patel has focused her research on bacterial infections. Her work focuses on three major areas: (1) improvement of next-generation diagnostic techniques, (2) understanding the inherent biology of periprosthetic infection, and (3) understanding antibiotic resistance through a clinical lens. She has published over 540 peer-reviewed publications and is supported by the National Institutes of Health and the Centers for Disease Control and Prevention. She is the Director of the Laboratory Center of the Antibacterial Resistance Leadership Group of the National Institutes of Health.

Dr. Patel received an undergraduate degree in Chemistry from Princeton University, where she graduated magna cum laude. From there, she obtained a medical degree from McGill University. Afterwards, Dr. Patel completed Internal Medicine Residency and Fellowships in Medical Microbiology and Infectious Diseases at the Mayo Clinic. Since then, she has been involved in setting standards for diagnostic and clinical care of bacterial infections, as evidenced by the (select) positions she has held or holds within the American Society for Microbiology (President), American Board of Pathology (Microbiology Test Writing Committee Member), Clinical and Laboratory Standards Institute (Subcommittee on Antimicrobial Susceptibility Testing Voting Member), National Institutes of Allergy and Infectious Diseases (Council Member), National Board of Medical Examiners (Microbiology/Immunology Test Material Development Committee Chair), Journal of Clinical Microbiology (Associate Editor), and Clinical Infectious Diseases (Associate Editor).

In addition, Dr. Patel's continued commitment to mentorship can be translated into a long list of trainees from around the world; she had dedicated hours of teaching to train the next generation of clinical and research laboratory scientists.

More information can be found at: https://journals.asm.org/doi/full/10.1128/JCM.01259-20.

Thomas F. Patterson, MD, FACP, FIDSA
Chief, Division of Infectious Diseases
Vice-Chair for Clinical Research
Professor of Medicine
Director, San Antonio Center for Medical Mycology
UT Health San Antonio
Candida auris

Dr. Patterson's clinical and research interests focus on the diagnosis and treatment of fungal diseases. He has been involved in developing new antifungal drugs and in clinical trials of new antifungal compounds and is funded by the NIH and industry for grants and contracts on drug and diagnostic development. He has conducted pre-clinical studies and clinical trials for invasive mycoses. During the COVID-19 pandemic he has led the UTHSA Infectious Diseases efforts in COVID-19 care and clinical research and received the UTHSA Presidential Distinguished Research Scholar award.

Dr. Patterson has published and lectured extensively with over 350 peer reviewed publications, chapters, books and reviews. He has served as member of the American Board of Internal Medicine, Subspecialty Committee for Infectious Diseases and is a Fellow of the American College of Physicians and the Infectious Diseases Society of America, past-President of the Texas Infectious Disease Society, and past-President, International Immunocompromised Host Society.

David Persse, MD

Professor of Medicine and Surgery, at the Baylor College of Medicine; Professor, Department Of Emergency Medicine, Univ. of Texas Health Science Center; EMS Physician Director, Houston Fire Department; Public Health Authority, City Of Houston; Tactical Physician, Houston Police Department SWAT Team

Notable Collaborative Accomplishment Highlight: Houston Wastewater Surveillance Program

Dr. Persse's career in medicine started with ten years experience as a field paramedic and paramedic instructor in upstate New York and New Jersey. After receiving his pre-med training at Columbia University in New York, he then attended Georgetown University School of Medicine. Graduating with honors in emergency medicine from Georgetown, Dr. Persse then completed residency training in emergency medicine at Harbor-UCLA Medical Center in Torrance, California. After residency, Dr. Persse completed a resuscitation research fellowship at the Ohio State University. Dr. Persse was then awarded a grant from the Society for Academic Emergency Medicine and completed fellowship training in emergency medical services and resuscitation at the Baylor College of Medicine and the City of Houston Emergency Medical Services program. In 1996 Dr. Persse became Director of Emergency Medical Services for the City of Houston. In May of 2004 he was appointed by City Council as Houston's Public Health Authority. He is also a Tactical Physician with the Houston Police S.W.A.T. team. During the COVID-19 Pandemic, Dr. Persse was named the Chief Medical Officer for the City of Houston. Dr. Persse is responsible for the medical aspects of clinical care quality management, disease control and public health preparedness.

Dr. Persse is a Professor of Medicine and Surgery at the Baylor College of Medicine and Professor of Emergency Medicine at the University of Texas Medical School – Houston.

Melinda Pettigrew, PhD
Anna M. R. Lauder Professor of Epidemiology
Interim Dean
Yale School of Public Health
DEI in MRSA Clinical Trials

Melinda M. Pettigrew is the Anna M. R. Lauder Professor of Epidemiology in the Department of Epidemiology of Microbial Diseases and the Interim Dean at the Yale School of Public Health. Dr. Pettigrew is an infectious disease epidemiologist whose research focuses on the microbiome and the global health threat of antibiotic resistance. She uses laboratory, population-based, and One Health approaches to identify factors that lead to the selection, emergence, and transmission of antimicrobial resistant bacteria. Dr. Pettigrew's research has been supported by organizations that include the NIAID, NIDCD, the CDC, and private foundations. She serves on the Steering and Executive Committees for the Antibiotic Resistance Leadership Group (ARLG). As the Associate Director of the Scientific Leadership Core, focusing on Diversity, Dr. Pettigrew leads efforts implement and integrate principles of diversity, access, equity, and inclusion throughout the ARLG. She completed a fellowship from the Hedwig van Ameringen Executive Leadership in Academic Medicine (ELAM) Program for Women and was a Public Voices Thought Leaders Fellow. Dr. Pettigrew serves on the editorial board of mBio. She earned her BA in biology from Grinnell College and her Ph.D. in epidemiology from Yale University.

Laurent Poirel, PhD
Associate Professor
University of Fribourg

Mechanisms of Resistance to Novel B-lactam/B-lactam Inhibitors

Laurent Poirel is Associate Professor at the Emerging Resistance to Antibiotics Research Unit and Swiss National Reference Center for Emerging Antibiotic Resistance at the University of Fribourg. His research interests emerging mechanisms of resistance to ß-lactams, polymyxins, and quinolones in Gram-negative rods, either in human and veterinary medicine. He is specialized on the genetics of acquisition of resistance genes in Enterobacteriaceae, Pseudomonas aeruginosa and Acinetobacter baumannii, plasmid-mediated quinolone resistance, and polymyxin resistance determinants in Enterobacteriaceae. He has co-invented a series of rapid diagnostic tests for detection of emerging resistance traits. He is the author of ca. 600 publications in international journals, his Google Scholar H-index being 140. He is the Editor-in-Chief of the European Journal of Clinical Microbiology and Infectious Diseases and Associate Editor of two highly-ranked journals, i.e. Antimicrobial Agents and Chemotherapy and Journal of Antimicrobial Agents. He has co-invented a series of rapid diagnostic tests for detection of emerging resistance traits, including the Carba NP test. In addition he is co-inventor of a series of 15 patents mainly corresponding to rapid diagnostic tests or antibiotic selective media.

Adriana Rosato, PhD
Director of the Center for Molecular Medicine
Maine Medical Institute for Research

Novel Insights into Daptomycin Resistance in Staphylococcus aureus

Dr. Adriana Rosato is the Director of the Center for Molecular Medicine at Maine Medical Institute for Research visitor Professor at Tufts University and Professor at University of California, Riverside, CA. Dr. Rosato is an experienced, national and international clinical, basic microbiologist/molecular biologist scientist with special interests in the area of infectious diseases/antimicrobial development and antimicrobial resistance. Her works in Infectious Diseases have extended for more than 25 years covering both aspects clinical, basic the translational aspects of related diseases and their- interactions with the host. She is contributing and advising the field of antimicrobial resistance by participating in revision of scientific advances and discoveries at the NIH and European Agencies, having had the opportunity of contributing her input to important decisions of funding and studies in the area of Antimicrobial Resistance. More important, over the years she has strongly committed to mentoring young investigators and served as a primary mentor for several individuals including minorities as part of her education mission. She serves on several editorial boards, has received many national and international honors and awards, and has published more than 60 research articles.

Michael Satlin, MD
Infectious Diseases Ohysician and
Associate Professor of Medicine and of
Pathology and Laboratory Medicine
Weill Cornell Medicine
Carbapenemases in XDR Pseudomonas

Dr. Michael Satlin an infectious diseases physician and Associate Professor of Medicine and of Pathology and Laboratory Medicine at Weill Cornell Medicine. He is the Clinical Director of the Transplantation-Oncology Infectious Diseases Program at Weill Cornell. He completed medical school at the University of Virginia School of Medicine and internal medicine residency and infectious diseases fellowship training at NewYork-Presbyterian Hospital/Weill Cornell. His research focuses on the epidemiology, prevention, and treatment of multidrug-resistant Gram-negative infections, with a focus on immunocompromised hosts. He has authored or co-authored over 100 peer-reviewed manuscripts. He is Associate Editor of Journal of Antimicrobial Chemotherapy-Antimicrobial Resistance, serves on the Editorial (Advisory) Boards of Journal of Clinical Microbiology, Clinical Infectious Diseases and Open Forum Infectious Diseases. He is a Member of the Clinical and Laboratory Standards Institute's (CLSI) Subcommittee on Antimicrobial Susceptibility Testing and Co-Chair of its Breakpoint Working Group. He also serves on multiple committees for NIAID's Antibacterial Resistance Leadership Group.

Ryan Shields, PhD
Associate Professor
Medicine and Clinical and Translation Research
University of Pittsburgh

Evolving Clinical Resistance to Novel Agents in Pseudomonas aeruginosa

Ryan Shields is an Associate Professor in the Departments of Medicine and Clinical and Translation Research at the University of Pittsburgh. He serves as the Director of UPMC Presbyterian Hospital Antibiotic Management Program and Co-Director of the Center for Innovative Antimicrobial Therapeutics. He is actively engaged in the diagnosis and management of patients infected by multi-drug resistant bacteria, including CRE and XDR Pseudomonas. 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 new antimicrobial agents and innovative stewardship approaches to implement new diagnostic tests.

William Shropshire, PhD
Postdoctoral Fellow
Training Program in Antimicrobial Resistance

Elucidation of Molecular Mechanisms Underlying Successful Adaptation to Carbapenem Antimicrobials in High Risk Carbapenem Resistant Escherichia coli Lineages

William Shropshire earned his B.A. in Biochemistry from the University of Texas at Austin in 2010, completed a postbaccalaureate fellowship at the NIH in 2013, and obtained his PhD in Epidemiology from the UTHealth School of Public Health in 2020. His PhD training focused on investigating the molecular epidemiology of carbapenem resistant Enterobacterales and their antimicrobial resistance mechanisms within the Houston, TX region. Currently, Dr. Shropshire is a second-year postdoctoral research fellow at the University of Texas MD Anderson Cancer in the Department of Infectious Diseases and Infection Control under the guidance of Dr. Samuel Shelburne. As part of his T32 training program, his work has shifted towards experimental investigation of clinical Enterobacterales isolates to understand the evolutionary pathways that underlie the successive adaptation to carbapenem selective pressures.

Lauren Stadler, PhD
Assistant Professor, Civil & Environmental Engineering, Rice University; Research Faculty, NEWT Nanosystems Engineering Research Center for Nanotechnolgy-Enabled Water Treatment
Notable Collaborative Accomplishment Highlight: Houston Wastewater Surveillance Program

Lauren Stadler brings 13 years of leadership experience in civil and environmental engineering and a vision to reimagine wastewater systems as a valuable source of information for the protection of public health. Stadler is an environmental engineer whose research focuses on wastewater-based epidemiology, environmental antibiotic resistance, wastewater treatment and resource recovery, and environmental synthetic biology.

In May 2020, Stadler began working with the Houston Health Department and Houston Water to establish and implement protocols for Houston's wastewater initiatives to track community COVID-19 infection dynamics. Her laboratory has developed a highly sensitive assay to reliably detect low concentrations of viral load in wastewater. Additionally, Stadler has worked extensively with collaborators to develop and implement methods for the detection of viral variants and antibiotic resistance genes and bacteria in wastewater.

Stadler joined the faculty in the Civil and Environmental Engineering Department at Rice University in 2016 as an assistant professor after completing her doctoral degree in environmental engineering at the University of Michigan. She was named a "New Engineer to Watch" by the Water Environment Federation, a Gulf Research Program Early Career Fellow by the National Academies of Science, Engineering, and Medicine, and a Johnson & Johnson WiSTEM2D Engineering Scholar. Results of her work have been published in over 30 peer-reviewed journal publications and disseminated at numerous conferences and workshops.

More information can be found at: https://hou-wastewater-epi.org/about/lauren-stadler

Madison Stellfox, MD, PhD
Infectious Disease Fellow and Postdoctoral Scholar
University of Pittsburgh Medical Center

Bacteriophage Therapy In Recurrent vancomycin-resistant E. faecium bacteremia

Dr. Madison Stellfox is currently an infectious disease fellow and postdoctoral scholar the University of Pittsburgh Medical Center (UPMC). She obtained her PhD in Biochemistry and Molecular Genetics from the University of Virginia, studying human centromere epigenetics with Dr. Daniel Foltz. Afterwards, she obtained her MD from New York Medical College, where she developed a clinical and research interest in infectious diseases. She then completed her internal medicine residency at UPMC and continued at Pittsburgh for her fellowship and postdoctoral studies in infectious diseases. She is currently working in the laboratory of Daria Van Tyne, where she studies the adaptations of vancomycin-resistant enterococci during recurrent and persistent infections as well as VRE-targeting bacteriophages.

Pranita Tamma, MD, PhD
Associate Professor, Pediatrics; Director, Antimicrobial Stewardship Program, The Johns Hopkins University School of Medicine

Drugs on the Horizon for Multidrug-Resistant Gram-negative Infections

Dr. Tamma is an Associate Professor of Pediatrics and the Director of the Pediatric Antimicrobial Stewardship Program at The Johns Hopkins University School of Medicine. She is also an Associate Professor in the Department of Epidemiology at The Johns Hopkins Bloomberg School of Public Health. Her research focuses on: (a) elucidating the mechanisms of resistance in gram-negative organisms, (b) developing and enhancing rapid phenotypic and genotypic methods to identify gram-negative resistance to enable critically-ill patients to be placed on appropriate antibiotic therapy as early as possible, and (c) identifying optimal treatment strategies for patients infected with multidrug-resistant gram-negative infections. She currently has funding from the NIH, FDA, CDC, PCORI, and AHRQ to investigate these areas. She had the opportunity to work in the national and international arena to advance including: serving as an Editor at Antimicrobial Agents and Chemotherapy and The Journal of the Pediatric Infectious Diseases Society; serving as 1 of 12 international voting members of the Clinical Laboratory and Standards Institute that provides international guidance on phenotypic and genotypic methods for identifying antimicrobial resistance; serving as a voting member of the NIH-funded Antibacterial Resistance Leadership Group Gram-Negative Resistance Committee; and serving as the lead author of the Infectious Diseases Society of America Antimicrobial Resistance Guidance.

Todd Treangen, PhD
Assistant Professor
Computer Science
Rice Univ.

Shoving the Envelope: Towards Point-of-care Characterization of Antimicrobial Resistance and Emerging Pathogens with SeqScreen

Dr. Todd Treangen completed his Ph.D. in Computer Science in 2008 at the Polytechnic University of Catalonia (Barcelona, Spain), receiving a European Ph.D. with Distinction (highest honor). After completing his Ph.D., he was a postdoctoral research scientist at the Pasteur Institute (Paris, France), Center for Bioinformatics and Computational Biology (CBCB) at the University of Maryland College Park (College Park, Maryland), and Johns Hopkins University (Baltimore, Maryland). After completing his postdoctoral research, he spent several years at the National Biodefense Analysis and Countermeasures Center (Frederick, Maryland) as a principal investigator leading the bioinformatics research group. In 2018, Dr. Treangen joined the Computer Science department at Rice University as an Assistant Professor. He is also a faculty member in the Systems, Synthetic, and Physical Biology (SSPB) graduate program. The primary research focus of his research group at Rice is on designing, developing, and implementing open-source software tools capable of tackling emerging computational research questions specific to biosecurity, infectious disease, and microbiome analysis.

William Trick, MD
Director of Health Research & Solutions,
Cook County Health and
Professor of Medicine, Rush University Medical Center

A Statewide Registry for MDROs: Illinois' Experience

Dr. Trick is the Director of Health Research & Solutions for Cook County Health and Professor of Medicine at Rush University Medical Center. He directs an informatics team that develops and administers a research data warehouse, which is foundational to development of their customized software solutions. These solutions are designed to meet the needs of Cook County Health patients and public health partners. For many years, he has been a close collaborator with local, state, and federal public health agencies to advance surveillance solutions.

David S. Weiss, PhD
Professor, Medicine/Div. of Infectious Diseases
Director, Emory Antibiotic Resistance Center Emory University School of Medicine and Emory Vaccine Center

Heteroresistance in Gram-negative Bacteria

Dr. Weiss received his PhD in Microbiology from New York University in 2004. Working under Dr. Arturo Zychlinsky, he studied how Toll-like Receptors work together to fight bacterial infections. He completed his postdoctoral training at Stanford University under Drs. Stanley Falkow and Denise Monack, studying virulence mechanisms of Francisella and the role of the inflammasome in host defense, where he was the recipient of a three-year postdoctoral fellowship from the Giannini Family Foundation. He is a Professor of Medicine/Infectious Diseases at Emory University and director of the Emory Antibiotic Resistance Center. His research is now focused on mechanisms of antibiotic resistance and in particular, heteroresistance. He is currently a Burroughs Wellcome Fund Investigator in the Pathogenesis of Infectious Disease and was recently named a Kavli Fellow.

Mike Woodworth, MD, MSc
Assistant Professor, Infectious Disease
Emory University School of Medicine

Microbiome Inroads Toward MDRO Decolonization

Dr. Woodworth is an infectious disease physician whose research is focused on the translational investigation of microbial therapeutics. He conducts clinical trials of fecal microbiota transplantation (FMT) to treat multidrug resistant organism (MDRO) colonization for which there are no FDA approved therapies and uses metagenomic approaches to identify potential mechanisms of action of FMT. His work has been funded by the ARLG, NIAID, and the CDC.

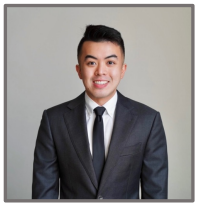
Helen I. Zgurskaya, PhD
George Lynn Cross Research Professor
University of Oklahoma
Drug Efflux in Gram-negative Bacteria

Dr. Helen I. Zgurskaya is the George Lynn Cross Professor of the Department of Chemistry and Biochemistry at the University of Oklahoma and the founding member of the Center for Antibiotic Discovery and Resistance. Dr. Zgurskaya is a graduate of Dnipropetrovsk State University, Ukraine (B. Sc. And M. S.) and Russian Academy of Sciences, Russian Federation (Ph.D.) and completed postdoctoral work at the Department of Microbiology and Immunology at Stanford University School of Medicine and the Department of Molecular and Cell Biology at University of California, Berkeley. In 2000-2010 she rose from Assistant Professor to full Professor in the Department of Chemistry and Biochemistry at the University of Oklahoma where she developed an interdisciplinary program on the mechanisms of antibiotic resistance, permeation and efflux and the discovery of new therapeutics for multidrug resistant bacterial infections.

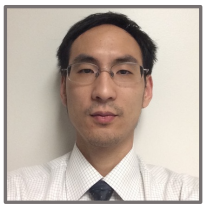
Rapid Fire Presenters Day 1

Samantha Agyapong, Univ. of Houston
*Investigation of Fecal pH in Healthy Volunteers Receiving Oral Omadacycline or Vancomycin*Poster 2

Eva Amenta, Baylor College of Medicine
Real-world Clinical Outcomes of Cefiderocol Therapy in the Veterans Health Administration
Poster 4



Dalton Bui, Univ. of Texas Health Science Center Houston
High Throughput Screen of Group A Streptococcus Clinical Isolates to Identify Conserved Strain-Specific Polymorphisms in Two-Component Systems Associated with Susceptibility to Membrane-Targeting Antimicrobials
Poster 15



Andrew Chou, Michael E. DeBakey VA Medical Center
Machine Learning Text Mining for Carbapenemase-Producing Organisms and Susceptibility Testing Results for Ceftazidime/avibactam & Ceftolozane/tazobactam.
Poster 17

Lorena Diaz, Clínica Alemana - Universidad del Desarrollo
Vancomycin-Resistant vanB- and vanA/vanB-type Enterococcus faecium Causing Invasive Infections in Adult Patients in Chile (2018-2022)
Poster 23

Brianna Eales, Univ. of Houston
Simulated Human Dosing of Ceftazidime in a Murine Pneumonia Model
Poster 25

Rapid Fire Presenters

Day 2

Jana Gomez, Univ. of Texas Health Science Center Houston
Understanding the Effects of Staphylococcus aureus Urease on Biofilm Production and Antibiotic Recalcitrance in Clinical Isolates
Poster 32

Madeline Guy, Univ. of Texas Health Science Center Houston
Identifying LiaFSR Residues Contributing to ExPortal Integrity and Response to Antimicrobials in Group A Streptococcus (GAS)
Poster 33

Jinhee Jo, Univ. of Houston
The Effects of Oral Omadacycline and Vancomycin on the Gut Microbiome in Healthy Subjects
Poster 41

Allison Judge, Baylor College of Medicine
Mapping the Determinants of Catalysis and Substrate Specificity of the Antibiotic Resistance Enzyme CTX-M β-lactamase
Poster 43

Christina Lin, Emory School of Medicine
Activity of Newer Antibiotics Against Carbapenem-Resistant Enterobacterales Isolates - Emory Healthcare, 2016-2021
Poster 51

Austen Terwilliger, Baylor College of Medicine
A Retrospective, Observational Study of 12 Cases of Expanded Access Phage Therapy
Poster 49

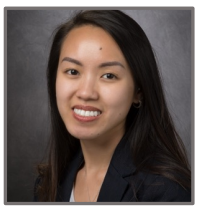
Rapid Fire Presenters

Day 3

Lindsey Laytner, Baylor College of Medicine
Perspectives on Non-prescription Antibiotic Use Among Hispanic Patients in the Houston Metroplex
Poster 78

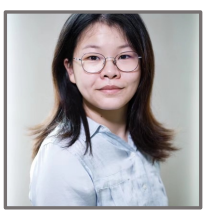
Husna Malikzad, Houston Methodist Research Institute
Evaluation of Cefazolin High Inoculum Effect in Methicillin-Susceptible Staphylococcus aureus (MSSA)
Using Gold standard MICs and Rapid Colorimetric Test (RCT)
Poster 60

Blake Neil, Univ. of Texas Medical Branch Galveston
Virulence Factors of Multi-drug Resistant Aeromonas Isolates Elucidated Using RNA Sequencing
Poster 61



April Nguyen, Univ. of Texas Health Science Center Houston
CL Synthases Play Redundant Roles And Are Required for Membrane Remodeling in Daptomycin Resistance Enterococcus faecalis
Poster 62

Eva Preisner, Baylor College of Medicine
Simplified Microbial Communities as Antibiotic Alternative in Treatment of Clostridioides difficile Infection
Poster 65



Qi Xu, Rice Univ.
A Novel Type of Cytotoxic Membrane Vesicles Produced by Pseudomonas aeruginosa
Poster 82

Poster Presenters
In alphabetical order

Presenter First Name	Presenter Last Name	Presenter Institution	Title of Submission	Poster #	Day of Presentation
Max	Adelman	Houston Methodist Hospital	Antimicrobial-resistant bloodstream infections after solid organ transplantation	1	1
Francesca	Agobe	Texas A&M School of Medicine	Novel Drug Combination for Treatment of Rhodococcus equi Infection	85	3
Samantha	Agyapong	Univ. of Houston	Investigation of Fecal pH in Healthy Volunteers Receiving Oral Omadacycline or Vancomycin	3	1
Eva	Amenta	Baylor College of Medicine	Real-world Clinical Outcomes of Cefiderocol Therapy in the Veterans Health Administration	4	1
Ikechuwku	Anyakee	University of Texas Medical Branch at Galveston	The Fight Against Antimicrobial Resistance: Synergy of Phage-antibiotic Combinations Against ESKAPE Pathogens	5	1
Rachel	Atterstrom	Houston Methodist Research Institute	Association Between Definitive Therapy and Duration of E. faecalis Bloodstream Infections	69	3
Dierdre	Axell-House	Houston Methodist	Non-E. faecium Non-E. faecalis enterococcal bloodstream infections in patients with cancer	7	1

Poster Presenters
In alphabetical order

Presenter First Name	Presenter Last Name	Presenter Institution	Title of Submission	Poster #	Day of Presentation
Advait	Balaji	Rice University	SeqScreen-Nano: Metagenomic Pathogen Characterization through Long Read Sequencing and Screening for Antimicrobial Resistance (AMR) and other Functions of Sequences of Concern (FunSoCs).	8	1
Eugénie	Bassères	University of Houston	Ibezapolstat Initial Clinical Response: in vitro Efficacy and Effect on Motility of Clostridioides difficile	9	1
Kirsten	Bevan Rydell	Houston Methodist Hospital	Gut Colonization and Infection by Multidrug-Resistant Organisms in Liver Transplant Patients Admitted to an Intensive Care Unit	10	1
Caroline	Black	Texas Tech University	Polymicrobial Communities Alter Antibiotic Susceptibilities Via Potentially Targetable Mechanisms	11	1
Megan	Bradley	University of Texas Medical Branch at Galveston, John Sealy School of Medicine	Exploring the Current and Future Applications of Antimicrobial Carbon Dots	12	1

Poster Presenters
In alphabetical order

Presenter First Name	Presenter Last Name	Presenter Institution	Title of Submission	Poster #	Day of Presentation
Jordan	Bremer	The University of Texas MD Anderson Cancer Center	Extended-Spectrum β-Lactamase Positive Escherichia coli Bloodstream Infection Periodicity Is Dominated by Sporadic Introductions of Multiclonal Strains	13	1
Catherine	Bryan	Texas Department of State Health Services	Development and Evaluation of Antibiotic Susceptibility Trends and Clinical Implications in Long-Term Acute Care Hospitals in Texas between 2019-2020.	14	1
Dalton	Bui	McGovern Medical School	High Throughput Screen of Group A Streptococcus Clinical Isolates to Identify Conserved Strain-Specific Polymorphisms in Two-Component Systems Associated with Susceptibility to Membrane-Targeting Antimicrobials	15	1
Andrea	Carlo Angleró	UTHealth Houston McGovern Medical School	A Retrospective Review of Endotracheal Aspirate Cultures in a Neonatal Intensive Care Unit	16	1

Poster Presenters
In alphabetical order

Presenter First Name	Presenter Last Name	Presenter Institution	Title of Submission	Poster #	Day of Presentation
Andrew	Chou	Michael E. DeBakey VA Medical Center	Machine Learning Text Mining for Carbapenemase-Producing Organisms and Susceptibility Testing Results for Ceftazidime/avibactam & Ceftolozane/tazobactam.	17	1
Hubert	Chua	University of Houston College of Pharmacy	Comparison Between Enrichment and Direct Plating Culturing Methods for Growth and Recovery of Clostridioides difficile from Clinical Stool Samples	18	1
Shane	Cristy	University of Texas Health Science Center at Houston	Interactions Between Candida and Staphylococcus Species in Polymicrobial Catheter-associated Urinary Tract Infections	19	1
Brittany	Dang	University of Texas Medical Branch	Sharkskin-Inspired Antimicrobial Surfaces and Their Potential Use in Healthcare Settings	20	1
Andrea	deTranaltes	Houston Methodist Research Institute	Colonization by Multidrug Resistant Pathogens in Immunocompromised and Critically Ill Patients	21	1
Alex	Deyanov	Houston Methodist Research Institute	An Integrated 'Omics Framework for the DYNAMITE Project	22	1

Poster Presenters
In alphabetical order

Presenter First Name	Presenter Last Name	Presenter Institution	Title of Submission	Poster #	Day of Presentation
Lorena	Diaz	Clínica Alemana - Universidad del Desarrollo	Vancomycin-Resistant vanB- and vanA/vanB-type Enterococcus faecium Causing Invasive Infections in Adult Patients in Chile (2018-2022)	23	1
Jesus	Duran Ramirez	UTHealth Houston	Staphylococcus aureus Breast Implant Infection Isolates Display Recalcitrance to Antibiotic Pocket Irrigants in vivo Despite Exhibiting Susceptibility in vitro	24	1
Brianna	Eales	University of Houston	Simulated Human Dosing of Ceftazidime in a Murine Pneumonia Model	25	1
Stephanie	Egge	Houston Methodist Research Institute	Cefiderocol Heteroresistance in Clinical Isolates of Pseudomonas aeruginosa with Mutations in TonB-dependent Receptor Pathways is Detectable in Iron-depleted Media	26	1
Taryn	Eubank	University of Houston	Evidence of Systemic Vancomycin Bowel Penetration by High Performance Liquid Chromatography	30	2

Poster Presenters
In alphabetical order

Presenter First Name	Presenter Last Name	Presenter Institution	Title of Submission	Poster #	Day of Presentation
Jiayi	Fan	Baylor college of medicine	Discovery of Novel Broad-spectrum Antibiotics and Inhibitors for β-lactamases using Combinatorial Approaches	31	2
Jana	Gomez	University of Texas Health Science Center at Houston	Understanding the Effects of Staphylococcus aureus Urease on Biofilm Production and Antibiotic Recalcitrance in Clinical Isolates	32	2
Madeline	Guy	McGovern Medical School at University of Texas Health Science Center at Houston	Identifying LiaFSR Residues Contributing to ExPortal Integrity and Response to Antimicrobials in Group A Streptococcus (GAS)	33	2
Basel	Hamwi	John Sealy School of Medicine	The Beneficial Utility and Future Direction of Silver Nanoparticles against Multidrug-Resistant Bacteria	34	2
Nora	Harmouch	University of Texas Medical Branch	Public Health and Economic Challenges of Increased Antimicrobial Resistance In The COVID-19 Pandemic Era	35	2

Poster Presenters
In alphabetical order

Presenter First Name	Presenter Last Name	Presenter Institution	Title of Submission	Poster #	Day of Presentation
Mark	Herrington	MD Anderson Cancer Center	Comparison of Ceftazidime-Avibactam and Ceftolozane-Tazobactam Activity Against Multidrug Resistant Pseudomonas aeruginosa at a Large Academic Cancer Center	36	2
Samantha	Hitt	UT Health Houston	Elucidation Of The Molecular Signal for the Regulator Of Capsule Synthesis Stress Response	37	2
Holly	Hoffman	Paratek Pharmaceuticals, Inc.	Comparison of 30-Day Healthcare Resource Utilization (HRU) Among Adult Patients with Approved or Unapproved Omadacycline Prescriptions for Nontuberculous Mycobacterial Infections (NTM)	38	2
Kara	Hood	Houston Methodist Research Institute	Topology of Enterococcus faecalis LiaF Suggests Complex Interaction with Enterococcal-specific Regulator LiaX	39	2
Cole	Hudson	University of Houston College of Pharmacy	In Vitro Model to Simulate Multiple Drugs with Distinct Elimination Half-Lives	40	2

Poster Presenters
In alphabetical order

Presenter First Name	Presenter Last Name	Presenter Institution	Title of Submission	Poster #	Day of Presentation
Jinhee	Jo	University of Houston College of Pharmacy	The Effects of Oral Omadacycline and Vancomycin on the Gut Microbiome in Healthy Subjects	41	2
Bishnu	Joshi	Baylor college of Medicine	Investigating The Potential of Bacteriophage and Vaginal Bacterial Communities to Limit Uropathogenic E. coli Colonization	42	2
Allison	Judge	Baylor College of Medicine	Mapping the Determinants of Catalysis and Substrate Specificity of the Antibiotic Resistance Enzyme CTX-M β-lactamase	43	2
Donghoon (Alex)	Kang	Rice University	Utilizing in vitro Pathosystems to Identify Novel Antivirulence Therapeutics against Pseudomonas aeruginosa	44	2
Tori	Kinamon	Duke/ FDA	Participant, Geographic, and Surgical Factors Are Associated with Clinical Failure in Registrational Trials for Complicated Intraabdominal Infection	45	2

Poster Presenters
In alphabetical order

Presenter First Name	Presenter Last Name	Presenter Institution	Title of Submission	Poster #	Day of Presentation
Rachelle	Koch	University of Texas Southwestern Medical Center	Genotype, Phenotype, and Clinical Outcomes in Hospitalized Patients with Gram-Negative Infections: A Retrospective Review	46	2
Santosh	Kumar	UTHealth Houston	Elucidation of Molecular Function of BamE in the Essential Bam Complex	47	2
Sarah	Lach	UTHealth	Conformational Rearrangements in the Sensory RcsF/OMP Complex Mediate Signal Transduction Across the Bacterial Cell Envelope	48	2
Lindsey	Laytner	Baylor College of Medicine, Family and Community Medicine	Perspectives on Non-prescription Antibiotic Use Among Hispanic Patients in the Houston Metroplex	49	2
ThanhPhuong	Le	University of Houston College of Pharmacy	An Epidemiologic Exploration of Fidaxomicin Reduced Susceptibility in Clostridioides difficile	50	2
Christina	Lin	Emory School of Medicine	Activity of Newer Antibiotics Against Carbapenem-Resistant Enterobacterales Isolates - Emory Healthcare, 2016-2021	51	2

Poster Presenters
In alphabetical order

Presenter First Name	Presenter Last Name	Presenter Institution	Title of Submission	Poster #	Day of Presentation
Monica	Lou	Baylor College of Medicine	Reliability of Gram Stain with Culture in Samples Obtained by Cotton Swab with Agar Gel Medium	52	2
Husna	Malikzad	Houston Methodist Hospital	Evaluation of Cefazolin High Inoculum Effect in Methicillin-Susceptible Staphylococcus aureus (MSSA) Using Gold standard MICs and Rapid Colorimetric Test (RCT)	60	3
Alexandra	Martynova Van Kley	SFA SU	The microbiota-gut-brain axis as a risk factors for the development of depressive disorders after bariatric surgery	54	2
Jonathon	McNeil	Baylor College of Medicine, Department of Pediatrics, Division of Infectious Diseases	Penicillin-Susceptibility among Staphylococcus aureus Skin and Soft-Tissue Infections in Children: Prevalence and Clinical Impact	55	2
Jacob	McPherson	University of Houston College of Pharmacy	Intra-Phylum Differences of the Firmicute polC Gene	56	2
Blake	Neil	University of Texas Medical Branch	Virulence Factors of Multi-drug Resistant Aeromonas Isolates Elucidated Using RNA Sequencing	61	3

Poster Presenters
In alphabetical order

Presenter First Name	Presenter Last Name	Presenter Institution	Title of Submission	Poster #	Day of Presentation
April	Nguyen	McGovern Medical School	CL Synthases Play Redundant Roles And Are Required for Membrane Remodeling in Daptomycin Resistance Enterococcus faecalis	62	3
Kiara	Olmeda	Baylor College of Medicine	Prevalence of Using Antibiotics Without a Prescription in a Pediatric Population	53	2
Diana	Panesso-Botero	Houston Methodist Research Institute	LiaF is necessary for LiaX-mediated resistance against daptomycin and antimicrobial peptides in Enterococcus faecalis	63	3
Jason	Pizzini	Baylor College of Medicine	Microbial Therapeutics to Prevent ExPEC Colonization and Disease	64	3
Eva	Preisner	Baylor College of Medicine	Simplified Microbial Communities as Antibiotic Alternative in Treatment of Clostridioides difficile Infection	65	3

Poster Presenters
In alphabetical order

Presenter First Name	Presenter Last Name	Presenter Institution	Title of Submission	Poster #	Day of Presentation
Andrew	Purssell	University of Ottawa	A Novel Model For Rapid Prediction of Antibiotic Susceptibility In Blood Stream Infections Using Direct Sequencing From Blood Cultures Coupled With Neighbour-Typing Prediction Algorithms.	66	3
Jinnethe Cristina	Reyes Manrique	Universidad El Bosque	Regulation of Bla Operon is Associated with the Cefazolin Inoculum Effect in Methicillin Susceptible Staphylococcus aureus	67	3
Jinnethe Cristina	Reyes Manrique	Universidad El Bosque	Validation of a Rapid Nitrocefin-Based Test for The Detection of the Cefazolin Inoculum Effect (CzIE) in Methicillin-Susceptible Staphylococcus aureus In a Colombian Clinical Laboratory	68	3
Samie	Rizvi	Houston Methodist Research Institute	Daptomycin Induced Expression of the MadR Regulon in E. faecalis OG1RF is Independent of the MadS Histidine Kinase	6	1

Poster Presenters
In alphabetical order

Presenter First Name	Presenter Last Name	Presenter Institution	Title of Submission	Poster #	Day of Presentation
Viviann	Robles	Texas Tech University	Polymicrobial Communities Contribute to Increased Recalcitrance Towards Hydrogen Peroxide	70	3
Susana	Rodriguez	University of Texas Health Science Center at Houston	Finding Additional Surface-Exposed Lipoprotein Substrates of the Bam Complex	71	3
Marissa	Schettino	Houston Methodist Research Institute	Clinical Epidemiology of Bacterial Infections in Critically Ill Patients: A Prospective Cohort Analysis 2020-2022	72	3
Selvalakshmi	Selvaraj Anand	University of Texas MD Anderson Cancer Center	Genomic Characterization of Extended-Spectrum β-lactamase producing Klebsiella pneumoniae Bacteremia at MD Anderson Cancer Center	73	3
William	Shropshire	MD Anderson Cancer Center	Using Whole Genome Sequencing to Genetically Profile and Analyze Escherichia coli Isolates with Varying Resistance to β-Lactam/β-lactamase Inhibitor Combinations	74	3

Poster Presenters
In alphabetical order

Presenter First Name	Presenter Last Name	Presenter Institution	Title of Submission	Poster #	Day of Presentation
William	Shropshire	The University of Texas MD Anderson Cancer Center	Elucidation of Molecular Mechanisms Underlying Successful Adaptation to Carbapenem Antimicrobials in High Risk Carbapenem Resistant Escherichia coli Lineages	75	3
Shelby	Simar	UTHealth School of Public Health	Clinical and Genomic Characterization of Persistent Enterococcal Bacteremia in the VENOUS Cohort	76	3
Filemon	Tan	Rice University	Genetic Screen Suggests Pyocins Contribute to Pseudomonas aeruginosa Strain Dominance in Blood Stream Infections	77	3
Austen	Terwilliger	Baylor College of Medicine	A Retrospective, Observational Study of 12 Cases of Expanded Access Phage Therapy	78	3
Bunnarin	Theng	University of Texas Medical Branch at Galveston	The Future Direction Of Multidrug-Resistant Tuberculosis With The Latest Treatment Guidelines	57	2

Poster Presenters
In alphabetical order

Presenter First Name	Presenter Last Name	Presenter Institution	Title of Submission	Poster #	Day of Presentation
Marissa	Valentine-King	Baylor College of Medicine	Qualitative Analysis of a Twitter-Disseminated Survey Reveals New Patient Perspectives on the Impact of Urinary Tract Infection	80	3
Ender	Volkan	Cyprus International University & UT Health	Antimicrobial and Antibiofilm Activities of Endemic Plant Species of Cyprus on Drug Resistant Clinical Staphylococcus aureus Isolates	81	3
Qi	Xu	Rice University	A Novel Type of Cytotoxic Membrane Vesicles Produced by Pseudomonas aeruginosa	82	3
Liyang	Zhang	Rice University	The Mechanisms of the Long-term Dominance of Pseudomonas aeruginosa Isolates in Patients	83	3
Duolong	Zhu	Baylor College of Medicine	Flagellin modulates regulation of Clostridiodes difficile pathogenesis in the absence of motility	84	3

Poster 1

Antimicrobial-Resistant Bloodstream Infections after Solid Organ Transplantation

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Background: Solid organ transplant (SOT) recipients are at high risk of bloodstream infections (BSI) and infections with antibiotic-resistant organisms. Knowledge of pathogens and antibiotic resistance associated with different organ transplants is crucial for management.

Hypothesis/goals: We conducted this study to assess the characteristics, prevalence, organisms, and antibiotic resistance profiles associated with BSIs across several SOT types.

Methods: We conducted a single-institution retrospective cohort study of patients ≥18 years who had liver, kidney, heart, or multi-organ (within the same hospitalization) transplantation from 06/01/16-10/01/21. We excluded patients with dual-organ (during different hospitalizations) or repeat transplantation. The primary outcome was first BSI ≤1 year from SOT; commensal bacteria isolated from 1 blood culture were excluded. Antibiotic resistance profiles for different organism types were determined per CDC criteria. Demographic, clinical, and microbiologic data were compared between the four SOT groups with $\chi 2$ or ANOVA.

Results: Overall 2403 patients were included, of whom 1250 (52%) were kidney, 662 (28%) liver, 274 (11%) multi-organ, and 217 (9%) heart transplant recipients. Kidney transplant recipients were most likely to be female (43%, $p<0.001$) and Black (28%, $p<0.001$; Table 1). Multi-organ and liver transplant recipients had the highest Charlson Comorbidity Indices at transplantation (7, IQR 5-9 and 5-10, respectively). Overall, 210 patients (9%) had a BSI within one year of SOT. BSI prevalence varied significantly by SOT type: 17% for multi-organ, 12% for liver, 8% for heart, and 5% for kidney transplant recipients ($p<0.001$). The most common organisms were Enterobacterales (eg, *Escherichia coli* and *Klebsiella* spp.), which accounted for 47% of BSIs. Kidney transplant recipients had the highest proportion caused by Enterobacterales (62%, $p<0.001$); heart (41%) and liver (32%) transplant recipients had the highest proportion of BSIs caused by *Enterococcus* spp. ($p<0.01$). A smaller proportion of BSIs were caused by coagulase-negative staphylococci (9%), *Pseudomonas aeruginosa* (8%), *Staphylococcus aureus* (7%), and *Candida* spp. (5%). Regarding antibiotic resistance, 39% of all Enterobacterales isolates had an extended-spectrum β-lactamase phenotype and 8% were carbapenem-resistant (CRE). Liver transplant recipients were most likely to have CRE (20% of Enterobacterales isolates although not statistically significant $p=0.71$); multi-organ transplant recipients were most likely to have vancomycin-resistant *Enterococcus* (VRE; 89% of all *Enterococcus* isolates, $p<0.01$). Further, 24% of all *P. aeruginosa* isolates in this cohort were carbapenem non-susceptible and 60% of all *Candida* isolates were resistant to azoles, driven by the predominance of *C. glabrata.*

Conclusions: Multi-organ and liver transplant recipients were at highest risk of developing BSI. These patients had a high proportion of antibiotic-resistant isolates, including with VRE and CRE, respectively. Urgent strategies are needed to combat antibiotic resistance in this vulnerable population.

Poster 85

Novel Drug Combination for Treatment of Rhodococcus equi Infection

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Background. *Rhodococcus equi* is a Gram-positive intracellular pathogen known to infect alveolar macrophages causing pneumonia in foals. It is considered an opportunistic pathogen in humans with a life cycle similar to that of *Mycobacterium tuberculosis. R. equi* is endemic to many horse breeding farms and infects neonatal foals with immature immune systems. Although prophylaxis is thought to be the best course of action, the current standard of care (SoC), combination treatment with a macrolide and rifampin, is becoming ineffective due to the rise of multi-drug resistant isolates.

Goal. To address the growing need for a novel approach to therapy, we evaluated the efficacy of a novel compound, C58, in combination with gallium maltolate (GaM). Previously, GaM has shown activity against *R. equi* both *in vitro* and in a clinical trial that demonstrated GaM to be non-inferior to SoC in *R. equi* infected foals.

Methods. The antimicrobial efficacy of C58 and GaM was assessed against *R. equi* strains 701+, 701-, 703, and 05331, using the standard CSLI broth microdilution method to determine minimum inhibitory and bactericidal concentrations (MIC and MBC). Synergistic ratios were determined against *R. equi* 703. Cellular toxicity of C58 and GaM both alone and in combination was evaluated against J774.A1 murine macrophages. To improve solubility and promote uptake by macrophages, C58 was encapsulated within nanoparticles fabricated from poly(lactide-co-glycolide) (PLGA) and PLGA-polyethylene glycol (PLGA-PEG) (PLGA-PEG; C58-NP) via nanoprecipitation. C58-NPs were characterized for size, zeta potential, and percent C58 encapsulation. The uptake of rhodamine-loaded NPs was assessed by flow cytometry. C58-NPs and GaM were simultaneously administered at a synergistic ratio to *R. equi* 703 infected J774.A1 murine macrophages to assess the potential intracellular synergistic antimicrobial effects of this combination therapy.

Results. We found an MIC of C58 of 1 μg/mL and an MBC of 4-8 μg/mL demonstrating the antimicrobial efficacy of C58. Further, C58 and GaM were synergistic in combination, as indicated by a fractional inhibitory concentration of 0.5 at a C58/GaM ratio of 0.25/32 μg/mL against *R. equi*. An LD_{50} of C58-treated J774.A1 murine macrophages of 40 μg/mL highlighted the low toxicity. Studies revealed that the NPs had a loading of 4.2%. Further, studies confirmed macrophage uptake of NPs. We also observed a greater than 3-log reduction of intracellular *R. equi* 703 treated with C58-NPs/GaM confirming synergistic activity.

Conclusions. Combination treatment of intracellular *R. equi* with C58-NPs and GaM demonstrated synergistic antimicrobial efficacy. These data demonstrate the potential for C58 and GaM to replace the current SoC treatment for *R. equi* pneumonia. Nanoparticle encapsulation of C58 expands the therapeutic applications of this novel antimicrobial by facilitating nebulized, local delivery to the lungs that may be investigated in future clinical trials in *R. equi* infected foals.

Acknowledgments. Graduate research was supported by Texas A&M University College of Medicine. This work was also made possible in part by the Morris Animal Foundation (D16EQ-810).

Poster 3

Investigation of Fecal pH in Healthy Volunteers Receiving Oral Omadacycline or Vancomycin

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Background: Antibiotics have profound disrupting effects on the gut microbiome including pH. An easy method to measure gut dysbiosis is not currently available. This study aims to investigate the fecal pH in healthy volunteers receiving antibiotics and to assess the utility of fecal pH as a potential gut dysbiosis marker.

Hypothesis/Goal: To analyze and compare the fecal pH in healthy volunteers receiving oral omadacycline or vancomycin

Methods: Healthy subjects aged 18 and 40 years were recruited and randomized to receive either oral omadacycline or vancomycin for 10 days. Fecal samples were collected at baseline, during therapy, and follow-ups. All samples were stored at -80°C and thawed to reach room temperature prior to pH measurements. The fecal pH was measured using the Compact pH Meter (Horiba Advanced Techno, Japan) and the device was calibrated for each batch of samples using pH 4.01, 7 and 10 solutions. Approximately 100 mg of solid fecal sample was treated with 50 uL of NaCl for the pH measurement. For the liquid fecal samples, 200 uL was pipetted onto the pH meter. The daily pH changes were assessed in respect to the baseline and were compared between omadacycline and vancomycin groups.

Results: From October 2020 to December 2021, a total of 16 healthy volunteers aged 26 ± 5 years (male: 69%; Caucasian: 31%; mean body mass index: 23.6 ± 3.8 kg/m^2) were enrolled in this study. Subjects were randomized to receive either oral omadacycline (450 mg on the first 2 days followed by 300 mg daily for the remaining days) or vancomycin (125 mg four times daily) for 10 days. A total of 276 fecal samples were tested and analyzed in this study. The average fecal pH at baseline in subjects given oral omadacycline or vancomycin were similar (6.05 ± 0.39 versus 6.27 ± 0.16, respectively). A major shift from the baseline pH was observed on day 9 in the vancomycin group (7.12 ± 0.74; mean ± SD) while on day 5 in the omadacycline group (6.86 ± 0.8; mean ± SD). Overall, there was an increase in the fecal pH during therapy for both antibiotic groups and a decreasing trend was observed by the follow-up days.

Conclusions: While antibiotics are known to disrupt the symbiotic environment within the host, their impact on fecal pH and its relation to gut dysbiosis has not been thoroughly assessed. The findings of our study suggest that both omadacycline and vancomycin modify the pH of the gastrointestinal tract of otherwise healthy adults to be more alkaline. Future studies are needed to better understand the impact of fecal pH changes on gut-resident microbes and its potential role as a biomarker for gut dysbiosis.

Real-world Clinical Outcomes of Cefiderocol Therapy in the Veterans Health Administration

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Introduction: Cefiderocol is a novel siderophore cephalosporin that provides broad spectrum activity. In the CREDIBLE-CR phase 3 clinical trial examining treatment of carbapenem-resistant gram-negative infections, cefiderocol had similar clinical and microbiological efficacy compared to best available therapy but the mortality rate was unexpectedly higher in the cefiderocol group. Post-approval, real-world use of cefiderocol has mainly been reported for therapy of infections by *Acinetobacter baumannii*.

Hypothesis/Aims: We sought to report the post-approval, real-world clinical outcomes of cefiderocol therapy in the Veterans Health Administration (VHA).

Methods: We conducted a prospective, observational study of patients who received cefiderocol for at least 2 days within the VHA between the date of approval by the U.S. Food and Drug Administration (FDA), November 14, 2019, and August 31, 2022. Types of infections were defined by National Healthcare Safety Network (NHSN) criteria. Clinical failure was a compositive outcome based on type of infection and included survival (30- and 90-day mortality) and resolution of signs and symptoms of infection. Structured data was sourced from the VHA Corporate Data Warehouse, including data from 132 VA Medical Centers. Only the first eligible episode was included in the outcomes analysis. All eligible episodes underwent manual chart review to validate extracted structured data and to extract unstructured data, including clinical notes.

Results: We found 41 unique individuals had received cefiderocol, with a total of 48 cefiderocol courses prescribed from 132 VA medical centers. Patients had a median age of 70.5 (61-75), and a median Charlson comorbidity score, age-unadjusted of 6 (3-9), and age-adjusted of 8 (6-11). RRT was present in 17% (7) of cases and augmented renal clearance was present in 21% (9) of cases. 30-day all -cause mortality was 27% (11/41) and 90-day all-cause mortality was 44% (18/41). Infection sites included pulmonary in 50% (24/41) of cases, urinary in 33% (16/41) of cases, endovascular in 19% (9/41) of cases, and osteomyelitis in 8% (4/41) of cases. *Pseudomonas aeruginosa* was the causative agent in the majority of infections (71%), followed by *Acinetobacter baumanii* complex (19%), *Stenotrophamonas maltophilia* (10%), and Enterobacterales organisms (40%). No growth was reported in 4% of cases. 30-day microbiologic failure occurred in 39% of cases and 90-day microbiologic failure occurred in 54% of cases.

Conclusions: Our study cohort included older individuals with multiple co-morbid conditions who were treated with cefiderocol for infections including lower respiratory tract and urinary tract infections, with *Pseudomonas aeruginosa* as the main causative pathogen. These data contribute to the growing body of literature on the real-world use of cefiderocol and provide multiple measured outcomes including clinical, microbiologic failure and mortality.

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Poster 5

The Fight Against Antimicrobial Resistance: Synergy of Phage-antibiotic Combinations Against ESKAPE Pathogens

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Background: A staggering 35,000 fatalities in the United States have been attributed to multidrug-resistant organisms (MDROs), thereby highlighting the alarming proliferation of antimicrobial resistance (AMR) and the imminent risk of antibiotics becoming ineffective as a sole treatment option for MDROs. The World Health Organization (WHO) has reported that only twelve new antibiotics have been approved since 2017, with the majority of them being in the same classes associated with antimicrobial resistance. As research and development of new antibiotics has been decreasing, attention has shifted to alternative therapies such as phage therapy, which is being increasingly viewed as a viable supplemental treatment for antimicrobial resistance.

Hypothesis/Goals: This report aims to review the literature on the possible synergistic effects of bacteriophage therapy in combination with antibiotic treatment against ESKAPE pathogens (*Enterococcus faecium, Staphylococcus aureus, Klebsiella pneumoniae, Acinetobacter baumannii, Pseudomonas aeruginosa, and Enterobacter* species), which the WHO has identified as the most critical MDROs and a major contributor to the growing global issue of AMR.

Methods: A keyword search of medical literature was executed using PubMed with search the terms "phage therapy", "phage", "antibiotic", and in addition to the genus and species of the specified MDRO in question. Eight articles and six studies were selected for inclusion in this report.

Results: The results of our literature review indicated that the combination of an isolated bacteriophage and sub-minimum inhibitory concentration (MIC) antibiotics resulted in a significantly greater reduction of bacterial populations (in CFU/mL) than the antibiotic agent alone in all six studies of critical MDROs. In a study utilizing a checkerboard assay to analyze the synergy of phage-antibiotic combination (PAC) against multidrug-resistant (Ceftriaxone, Cefazolin, Ceftazidime, Ampicillin, and Imipenem) Klebsiella pneumoniae (K. pneumoniae), it was demonstrated that despite its resistance to ceftriaxone, the application of the antibiotic in combination with phage vB_1086 led to a significant decrease in the effective concentration of ceftriaxone, ranging from 5-7 gradients, suggesting a strong synergistic effect. Given the high mortality rate associated with Klebsiella pneumoniae, one of the most common MDROs, it is plausible that synergistic PACs may provide a more effective treatment than the current standard of care for bacterial infections caused by MDROs.

Conclusions: It is evident that AMR constitutes a major impending medical crisis that has yet to be comprehensively addressed. The mechanism of resistance displayed by phage therapy is distinct from that of antibiotics, and thus the use of PACs does not confer antibiotic resistance, a major advantage of phage therapy. Studies of the literature suggest that PAC therapy can not only slow down the development of antimicrobial resistance but also has synergistic effects against even the most resistant MDROs, namely the ESKAPE pathogens.

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Poster 69

Association Between Definitive Therapy and Duration of E. faecalis Bloodstream Infections

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Background *Enterococcus faecalis* is an important causative pathogen for both community-acquired and nosocomial infections and ranks in the top three most common organisms causing bloodstream infections in the United States and Europe. Currently, the double beta-lactam therapy using ampicillin and ceftriaxone is the preferred treatment regimen for *E. faecalis* bacteremia, due to its clinical efficacy and safety profiles. Alternatives, including a combination therapy of ampicillin plus an aminoglycoside as well as vancomycin, are also efficacious, though they are associated with a higher risk of adverse events.

Goal The goal of this study is to investigate any potential association between type of definitive therapy administered for treatment of *E. faecalis* bacteremia and duration of bacteremia.

Methods A sub-cohort of patients (n=142) previously enrolled in VENOUS, a multicenter international prospective cohort studying enterococcal bloodstream infections, was used for this study. Patients were enrolled between 2016-2021 and represent three U.S. recruitment sites. Definitive therapy was defined as antibiotics which started on, or within 24 hours after, the day finalized results for a positive *E. faecalis* blood culture were available. Duration of bacteremia was calculated as the number of days between the first positive and the first negative culture, and was categorized into short (lasting less than four days) and prolonged (lasting four or more days) bacteremia. A Fisher's exact test was selected for analysis.

Results The median age for the studied cohort was 66 years, and 62.68% of patients were male. The median duration of bacteremia was three days (IQR 2-4), and 30.99% of patients had bloodstream infections lasting over four days. Five therapy categories were assessed: ampicillin monotherapy (n=23), ampicillin and ceftriaxone combination therapy (n=6), ampicillin and aminoglycoside (n=5) and vancomycin (n=11), with all other therapies grouped into an "other" category (n=97). The Fisher's exact test did not yield statistically significant results ($p = 0.444$).

Conclusions Our study did not find a statistically significant association between definitive therapy and duration of *E. faecalis* bacteremia, likely due to the limited sample size of the sub-cohort. Recruitment to expand the VENOUS cohort is currently underway, and additional analyses to incorporate other known clinically relevant variables such as antibiotic profiles, comorbidities, microbiologic outcome, and toxicity are ongoing.

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Poster 7

Non-E. faecium Non-E. faecalis Enterococcal Bloodstream Infections in Patients with Cancer

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Background: Non-*E. faecium* non-*E. faecalis* (NFF) enterococci are a heterogeneous group of organisms consisting of enterococci with intrinsic low-level vancomycin resistance as well as several other species known to infect humans. Patients with cancer are at increased risk for bloodstream infections (BSIs) with NFF enterococci, but their optimal treatment and outcomes have not been extensively described.

Methods: We conducted a retrospective review of patients (pts) with blood cultures positive for all NFF by searching the microbiology database at a major cancer center in Houston, TX from 2016 to 2021. Patients were included if they were ≥ 18 years old, had ≥ 1 blood culture with NFF enterococci, and had a repeat blood culture within 7 days (d) of the index culture, to permit outcome analysis. Outcomes were a) in-hospital mortality, b) microbiological failure (blood culture clearance >4 d after index culture), and c) recurrence of bacteremia (new positive blood culture <14 d after eradication).

Results: Sixty-two unique pts had NFF enterococcal BSI. Patients with hematological malignancy made up 53.2% of the cohort (78% had leukemia). The majority (83%) of solid malignancies were pancreatic, biliary, or intestinal in origin. In the 30 d preceding NFF enterococcal BSI, 79% of pts had exposure to antibiotics. The NFF species isolated were *E. gallinarum* (50%), *E. casseliflavus* (30.6%), *E. avium* (11.3%), *E. raffinosus* (3.2%), *E. hirae* (3.2%), and *E. durans* (1.6%). Only 23.3% of NFF enterococci were susceptible to vancomycin, and 53.8% were susceptible to linezolid. Most (62.9%) pts received combination therapy; the most frequent was daptomycin plus a beta-lactam (33.9%). Bacteremia recurred in 8.1% of pts, 27.4% had in-hospital mortality, and 4.8% had microbiological failure.

Conclusions: This retrospective review provides preliminary insight into the treatments, and outcomes of cancer pts with NFF enterococcal BSIs. The NFF enterococci isolates in this study had a higher rate of linezolid non-susceptibility than previously reported. Molecular investigation of these NFF enterococcal isolates is needed to elucidate the mechanisms and transmission of antibiotic resistance. Comparison of BSIs caused by NFF enterococci to *E. faecium*/*E. faecalis* will provide insight to physicians caring for these pts.

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Poster 8

SeqScreen-Nano: Metagenomic Pathogen Characterization through Long Read Sequencing and Screening for Antimicrobial Resistance (AMR) and other Functions of Sequences of Concern (FunSoCs).

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Background: Affordable and accessible long read sequencing has opened the door to incorporating long read data into a wide variety of metagenomic analysis tasks. Though long reads from sequencing platforms like Oxford Nanopore Technology (ONT) offer better resolution than short-reads, assigning accurate functional and taxonomic labels to sequences is challenging due to: (i) individual reads spanning multiple genes, (ii) presence of truncated genes, and (iii) the error rate of the ONT platform that may introduce frameshifts and missense errors. Taken together, these challenges create a need for novel computational approaches that can both identify and annotate genes on individual ONT reads. Here, we build upon our short-read functional characterization tool, SeqScreen, and adapt it to create the first ever Functions of Sequences of Concern (FunSoCs) based approach tailored to long read data.

Hypothesis: We hypothesize that accurate identification of all possible Open Reading Frames (ORFs) in a long read can lead to sensitive characterization of pathogenic markers. This includes AMR genes and other toxins and virulence factors that might have been missed due to frameshifts. We also reason that in addition to taxonomic information obtained from ORFs, calculating breadth of coverage of specific genomes using read mapping coordinate information can allow for detection of low-abundance pathogens in the sample.

Methods: SeqScreen relies on carefully optimized parameters in DIAMOND for accurate and sensitive ORF calling in bacterial and viral genomes. This represents the first attempt at ORF calling in long reads. The taxonomic assignment over the entire read is carried out using a greedy weighted minimum-set cover approach. Taxonomic assignments from individual ORF refined using a reference-based recruitment approach that uses breadth of coverage and average nucleotide identity (ANI) to predict sample wide taxonomic profiles. The reference-inference step uses Minimap2 to map reads to genomes from candidate taxa in two steps. The second stage simulates "read stealing" to ascertain the most probable source of a given read. Observed and Expected (Probabilistic) coverage are calculated at each step to assign the read to the correct genome.

Results: We show that on simulated and synthetic metagenomic data, SeqScreen-Nano using DIAMOND, can identify Open Reading Frames (ORFs) across the length of raw ONT reads and use this information to accurately assign functional and taxonomic labels. SeqScreen-Nano can achieve higher precision and comparable recall at sample-wide species and genus level classification. Also, we show that the FunSoC

based framework in SeqScreen-Nano is better suited for the analysis of low abundance pathogens in metagenomes and annotating them with AMR genes. Further, we optimized SeqScreen-Nano to run efficiently in a memory constrained environment (less than 32GB of RAM), allowing it to be utilized in resource limited settings. Lastly, SeqScreen-Nano is also capable of processing batches of sequencing runs directly from the ONT MinION sequencing device.

Conclusion: SeqScreen-Nano's capability of streaming profiling of metagenomic samples for anti-microbial resistance and other pathogenic markers in a resource-efficient way makes it viable for on-field microbiome analysis using a portable sequencer ushering in a new era for microbial surveillance.

Poster 9

Ibezapolstat Initial Clinical Response: in vitro Efficacy and Effect on Motility of **Clostridioides difficile**

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Background: Ibezapolstat (IBZ) is a Gram-positive selective spectrum antibiotic in phase 2 clinical trials for the treatment of C. difficile infection (CDI). With a unique mechanism of action that targets the DNA pol IIIC enzyme, preferentially upregulating genes near the origin of replication, IBZ should maintain activity against C. difficile with reduced susceptibility to other CDI-directed antibiotics and may demonstrate unique pharmacologic properties. The goal of this study was to assess the activity of IBZ against strains with reduced susceptibility to current CDI antibiotics as well as motility inhibition.

Methods: Agar dilution MIC and MBC studies were performed against C. difficile strains with reduced susceptibility to metronidazole, vancomycin, and fidaxomicin following CLSI document M11-A7 for anaerobic bacteria. C. difficile motility was assessed using a phenotypic motility assay and quantitative RT-PCR vs. relevant flagellar genes (flgA, flgb, flgC-VIP) using C. difficile strain CD630 pre-treated with sub-MIC of IBZ adapted from the methodology of Doan et al. (Antibiotics 2022).

Results: Twelve isolates with reduced susceptibility to metronidazole (MIC range: 0.25-8 µg/mL), vancomycin (MIC range: 1-16 µg/mL) or fidaxomicin (<0.03125-2 µg/mL) were tested. IBZ MIC50 and MIC90 did not differ between susceptible and reduced susceptibility isolates. MBC values did not differ between wild-type and reduced susceptibility isolates with values similar to results with vancomycin using wild-type strains. Motility assay demonstrated reduced C. difficile movement in agar with pre-treatment with sub-MIC IBZ and reduction in flagellar gene expression with sub-MIC IBZ exposure.

Conclusion: IBZ maintains activity against C. difficile strains with reduced susceptibility to other commonly used antibiotics. A novel pharmacologic property of IBZ was identified likely due to its unique mechanism of action. These findings support the continued clinical development of IBZ.

Poster 10

Gut Colonization and Infection by Multidrug-Resistant Organisms in Liver Transplant Patients Admitted to an Intensive Care Unit

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Background Post-transplant infections are a leading cause of mortality in patients who receive liver transplants. Vancomycin-resistant enterococci (VRE), extended spectrum β-lactamase producing/carbapenem resistant Enterobacterales (ESBL-E/CRE), and *Clostridioides difficile* often infect immunocompromised patients and are of particular interest as they colonize the gastrointestinal tract. Under the selective pressure of antimicrobial use, these bacteria can dominate the gut. This "domination" has been associated with an increased risk of developing a clinical infection.

Hypothesis/Goals The goal of this study is to characterize a cohort of liver transplant recipients who were admitted to the intensive care unit (ICU) by assessing comorbidities, clinical cultures, outcomes, and the results of gut colonization by VRE, ESBL-E/CRE, and *C. difficle*. We postulate that patients with a gastrointestinal tract dominated by pathogenic bacteria are at an increased risk of clinical infection.

Methods Included patients received a liver transplant prior to ICU admission or were transplanted during their hospitalization. Patients were enrolled in the DYNAMITE study within 24 hours of ICU admission and participated for up to 4 weeks. Up to two stool samples, one blood sample and one oral swab were collected weekly. Any clinical culture during hospitalization was collected and the organisms underwent whole genome sequencing. Stool samples were plated on selective media to detect *C. difficile*, VRE, and ESBL-E/CRE; positive results were confirmed with MALDI-TOF (excluding *C. difficile*).

Results Of 17 patients, 10 (59%) had gut colonization with any of the target organisms (*C. difficile* (n=4), VRE (n=4), or ESBL-E/CRE (n=5)). Three patients had samples with more than one target organism: co-colonization occurred twice with VRE and ESBL-E and once with VRE and *C. difficile.* Half of the colonized patients had a positive initial stool sample. In patients with an initial colonized sample, 2 patients did not have a positive subsequent sample, while the other 3 had multiple instances of colonization. At any point during hospitalization, 59% (n=10) of patients had a positive fungal or bacterial clinical culture. Among patients with gut colonization, 60% also had a positive culture (n=6). The most commonly isolated organisms were *Pseudomonas aeruginosa* (n=6), *Candida dublinesis* (n=4), and *Enterococcus faecium* (n=2). There was no difference in proportion of patients with a positive culture, 90-day readmission, or length of hospital stay when comparing the colonized and non-colonized subcohorts.

Conclusions Liver transplant patients in this cohort commonly exhibited gut colonization by pathogenic bacteria and a majority of patients had a positive clinical culture during hospitalization, emphasizing the prevalence of gut dysbiosis and infection in this population.

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Table 1. Colonization and infection status of 17 liver transplant patients included in this study

Patient	**Clinical culture**	**Colonization**	**Sample number where colonization is detected**	**Outcome 90-days after discharge**
1	No	*C. difficile*	First sample colonized	No readmission
2	No	No		No readmission
3	*P. melanogenica* VR *E. faecium* *Acinetobacter* Other	**ESBL-E:** *E. coli*, *C. freundii* complex **VRE:** *E. faecium*	First sample colonized	Readmission
4	*P. aeruginosa*	**ESBL-E:** *E. coli*	First sample not colonized	Readmission
5	No	*C. difficile*	First sample colonized	No readmission
6	*Candida* species	No		Readmission
7	No	*C. difficile*	First sample not colonized	No readmission
8	*P. aeruginosa* *Candida* species	No		Death
9	No	No		No readmission
10	No	**ESBL-E:** *P. mirabilis*	First sample not colonized	No readmission
11	VR *E. faecium*	**ESBL-E:** *E. cloacae* complex **VRE:** *E. faecium*	First sample not colonized	Readmission
12	*Candida species*	**ESBL-E:** *E. coli*	First sample not colonized	Readmission
13	*S. aureus*	**VRE:** *E. faecium* *C. difficile*	First sample colonized	Readmission
14	*P. aeruginosa*	No		Readmission
15	*P. aeruginosa*	No		No readmission
16	*S. maltophilia*	**VRE:** *E. faecium*	First sample colonized	No readmission
17	No	No		Readmission

VR = vancomycin-resistant
ESBL-E = β-lactamase producing/carbapenem resistant Enterobacterales
VRE = vancomycin resistant enterococci

Poster 11

Polymicrobial Communities Alter Antibiotic Susceptibilities Via Potentially Targetable Mechanisms

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Background: Recent advances in sequencing technologies have demonstrated that many chronic wounds are polymicrobial in nature. Species interactions within a polymicrobial community can lead to decreases in antibiotic efficacy through polymicrobial cooperation or increases through polymicrobial competition. Despite the knowledge that polymicrobial communities are common occurrences in persistent infections, current antimicrobial susceptibility testing (AST) is performed on monomicrobial suspensions.

Hypothesis/Goals: Polymicrobial interactions within communities will alter antimicrobial susceptibilities of individual species via defined mechanisms. These mechanisms could potentially be targetable and exploited in the prescription of better therapeutics.

Methods: Four relevant chronic wound pathogens (*Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, and *Enterococcus faecalis*) were grown in both monomicrobial and polymicrobial conditions. Changes in individual organism's susceptibilities was compared for both conditions.

Results: When *E. faecalis* was grown in a polymicrobial community, it demonstrated increased susceptibility to gentamicin. It was determined this phenomenon is due to *E. faecalis* acquiring heme from the community, which activates cellular respiration, and also allows more gentamicin to enter the cell via proton motive force. When *E. faecalis* was grown in community with *A. baumannii*, it exhibited decreased susceptibility to cephalexin. Further investigation determined that *A. baumannii* likely produces a beta-lactamase in the presence of cephalexin, allowing for the neutralization of the antibiotic and protection for susceptible *E. faecalis*.

Conclusions: These mechanisms demonstrate that the community plays a role in determining an individual bacterium's antibiotic susceptibility, meaning that current AST testing, which focuses on the monomicrobial agent of disease, may not be truly reflective of the infection environment. However, by acknowledging the role of community interactions within infections in determining antibiotic susceptibilities, we can more effectively treat persistent infections, leading to improved patient outcomes.

Acknowledgements: I would like to thank Dr. Catherine Wakeman for her guidance, as well as the rest of the Wakeman lab for their support. I would also like to thank our funding sources: NIH/NIGMS (R15GM128072) as well as TTU Mid-career grant.

Poster 12

Exploring the Current and Future Applications of Antimicrobial Carbon Dots

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Background
Infectious diseases caused by bacteria, viruses, and other microorganisms are a leading cause of hospitalizations and death. Immerging infectious diseases, in addition to the development of multi-drug resistant bacteria, are becoming an increasing health concern due to both cost and mortality, fueling the need to research innovative antimicrobial agents. Carbon dots have attracted attention and corresponding research into their effectiveness as antimicrobial agents due to their various properties such as good biocompatibility, low-cost, high stability, abundance of functional groups, and photoluminescence attributes. These unique qualities provide the capability for widespread application of carbon dots in combating advancing infectious microbes.

Hypothesis/Goals
The goal of this report is to review current literature on the applications of carbon dots as antimicrobial agents.

Methods
A keyword search of the terms “carbon dots” and “antimicrobial” was performed. Medical literature articles that further discussed the current applications and future directions of the role of carbon dots as antimicrobial agents were selected for this review.

Results
The results of this literature review show that carbon dots are effective in both the wound healing process and as antiviral, antifungal, and antibacterial agents, including activity against multi-drug resistant species. The broad-spectrum antimicrobial activity is likely a result of the generation of reactive oxygen species from a photoexcited state since carbon dots are activated by visible light. Additionally, because of their strong photoluminescent effects, they have shown promise in cancer therapy. Finally, there is evidence that the unique properties of carbon dots can be further manipulated to create specifically targeted, multifunctional antimicrobial agents, providing the potential for diverse applications in the future.

As with any antimicrobial agent, there are limitations to carbon dots. One limitation is due to their diverse properties, no uniform method for their synthesis has been developed, prompting the need for continued research. However, one study further elaborates on several limitations of carbon dots in addition to practical procedures to combat these limitations.

Conclusions
Utilization of carbon dots provides an innovative and cost-effective approach against immerging infectious diseases, including multi-drug resistant agents. While continued research is necessary, the antimicrobial action shown in several studies in addition to the broad application potential of carbon dots provides strong evidence for an additional agent in the fight against infectious microorganisms.

Acknowledgements
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Poster 13

Extended-Spectrum β-Lactamase Positive Escherichia coli *Bloodstream Infection Periodicity Is Dominated by Sporadic Introductions of Multiclonal Strains*

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Background: Rates of extended-spectrum β-lactamase (ESBL) producing *Escherichia coli* (ESBL-*Ec*) infections have recently been increasing in the United States. Impactfully, ESBL-*Ec* infections are highly prevalent and difficult to treat within immunocompromised populations.

Hypothesis/Goals: The goal of our study was to determine the epidemiological trends of ESBL-*Ec* bloodstream infections (BSIs) within the University of Texas MD Anderson Cancer Center (MDACC) which serves a high percentage of immunocompromised persons. We sought to characterize the high-risk lineages driving infections at our institution to test the hypothesis that a small number of lineages carrying a limited repertoire of ESBL enzymes are responsible for driving ESBL-*Ec* infections.

Methods: ESBL positivity was defined as either testing positive for ESBL production in the clinical microbiology laboratory and/or being ceftriaxone resistant. Epidemiologic trends of *E. coli* BSIs, including rates of ESBL and non-ESBL infections, were abstracted from EPIC with data normalized per 1,000 hospital admissions between March 2016 (start of our use of EPIC) and December 2020. ESBL-*Ec* bacteremia isolates available in our Microbe Bank were selected for sequencing with even representation over the study period. Isolates meeting selection criterion for first occurrence, index ESBL-*Ec* or recurrent 14-day ESBL-*Ec* BSIs were included in our sampling frame. Whole genome sequencing was performed using short- and long-read platforms. Genomic data was analyzed using the high-performance computing cluster Seadragon.

Results: ESBL-*Ec* accounted for 33.7% (389/1154) of all *E. coli* index BSI cases. The percentage of *E. coli* that were ESBL positive increased from 2016 (32.2%) to 2019 (36.8%) before declining in 2020 (31.4%). Importantly, time series data showed that ESBL rather than non-EBSL strains drove peaks of total *E. coli* BSIs within certain infection windows (e.g., windows 2,4, and 6) documented in **Figure 1**. We identified 48 distinct sequence types (ST) with ST131 being by far the most common ST

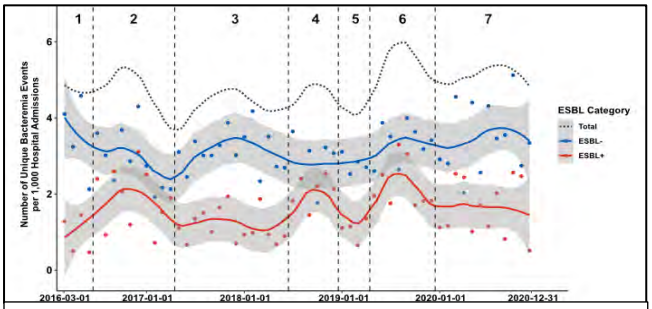

Figure 1: Epidemiological Trends of *E. coli* BSIs based on ESBL status.

(41.1%) among index ESBL-*Ec* isolates. Whereas the relative prevalence of ST131 remained stable over the study period, peaks of ESBL E. coli infections were driven by expansions of less common STs such ST405, ST1193, and ST648 which were found only during limited time periods. There was limited evidence of highly related (i.e., SNPs <20) *E. coli* strains in our population. CTX-M encoding genes were the most common ESBL detected (89.0%; 220/247) with the three most common variants being $bla_{\text{CTX-M-15}}$ (n=136), $bla_{\text{CTX-M-27}}$ (n=31), and $bla_{\text{CTX-M-55}}$ (n=28) and were widely distributed throughout the population. Complete genomes provide evidence of both IS*26* and IS*Ecp1* mediated dissemination of CTX-M encoding genes within our cohort.

Conclusions: We identified periodicity in both total and ESBL-*Ec* BSIs that was driven by peaks of relatively rare and diverse CTX-M containing STs which were non-clonal in nature. Our results suggest that spikes in ESBL-*Ec* within our population are not due to nosocomial transmission but rather likely reflective of community acquisition. Further analyses of community trends of E. coli isolates, such as intensive wastewater sampling, could assist in understanding and perhaps mitigating serious ESBL infections.

Poster 14

Development and Evaluation of Antibiotic Susceptibility Trends and Clinical Implications in Long-Term Acute Care Hospitals in Texas between 2019-2020.

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Background: Antimicrobial resistance is an ongoing public health problem around the world. Antimicrobial resistance may be caused by using antimicrobials incorrectly, lack of a standard treatment, and poor infection prevention and control practices. Long Term Acute Care Hospital (LTACH) patients have been shown to have high rates of healthcare-associated infections (HAIs) and LTACHs have been implicated in various regional outbreaks of AR organisms.

Hypothesis/Goals: The goals for this study are to define antibiotic susceptibility trends and suggest clinical management of antibiotic resistant organisms in Texas LTACHs.

Methods: First-line antibiotic treatment along with alternative drug classes were researched utilizing the UpToDate Clinical Management Database. An antibiogram for Texas LTACHs was created using data from isolates that were reported in 2019-2020 via the National Healthcare Safety Network (NHSN) as part of their HAI reporting requirements. Antimicrobials with fewer than 30 isolates reported per pathogen were excluded from this antibiogram. Treatment recommendations and antibiotic susceptibility patterns were compared for *Escherichia coli, Klebsiella pneumoniae* and *Pseudomonas aeruginosa*.

Results: The first-line treatment for *E. coli* consists of Macrolides and Fluoroquinolones drug classes. However, the Texas LTACH antibiogram shows that only 49-54% of *E. coli* isolates were susceptible to Fluoroquinolones. *E. coli* isolates showed the highest susceptibility to Meropenem (94%) and Gentamicin (76%).

The first-line treatment for *K. pneumoniae* consists of 3rd, 4th generation Cephalosporins, Fluroquinolones, and Carbapenems. The antibiogram shows that 47-63% of *K. pneumoniae* isolates were susceptible to Cephalosporins, 57-62% to Fluroquinolones, and 88-97% to Carbapenems. Additionally, *K. pneumoniae* isolates showed high susceptibility to Amikacin (92%) and very low susceptibility to Ampicillin (9%).

The first-line treatment for *P. aeruginosa* consists of the beta-lactam antibiotic Piperacillin/Tazobactam, Cephalosporins, Monobactam, and Fluroquinolones. The antibiogram shows that 76% of *P. aeruginosa* isolates were susceptible to Piperacillin/Tazobactam, 60-64% to Cephalosporins, and 67-73% to Fluroquinolones. *P. aeruginosa* isolates showed the highest susceptibility to Aminoglycosides (84-94%).

Conclusions: *E. coli, K. pneumoniae, and P. aeruginosa* isolates tested in Texas LTACH have low susceptibility to their recommended first-line treatments. These results support that antibiograms should be considered when selecting appropriate clinical treatment options to improve patient outcomes and decreases further development of AR in healthcare facilities.

Poster 15

High Throughput Screen of Group A **Streptococcus** *Clinical Isolates to Identify Conserved Strain-Specific Polymorphisms in Two-Component Systems Associated with Susceptibility to Membrane-Targeting Antimicrobials*

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Background: Group A *Streptococcus* (GAS) is a common human pathogen that causes various diseases including pharyngitis, impetigo, and rheumatic fever. Although penicillin remains an effective first-line treatment for GAS infections, GAS strains are becoming increasingly resistant to second-line treatments used when patients have beta-lactam allergies. Two-component systems (TCS) in bacteria sense and respond to environmental cues like cell envelope stresses, such as oxidative and antibiotic stress. The TCS known as LiaFSR is specific to Gram-positive bacteria and associated with daptomycin resistance in *Enterococcus* spp. A major target of LiaFSR regulation is SpxA2, a known regulator of GAS virulence associated with tolerance to oxidative stress. LiaFSR single nucleotide polymorphisms (SNPs) that potentially influence GAS cell envelope stress response are present in a strain-specific pattern. We sought to define SNPs in LiaFSR that affect the ability of GAS to resist and respond to cell envelope stress.

Hypothesis: We hypothesized that conserved strain-specific polymorphisms in the LiaFSR two-component system influence GAS response to cell envelope stress.

Methods: We identified conserved strain-specific polymorphisms in LiaFSR in a collection of pediatric GAS isolates from Texas Children's Hospital and Children's Memorial Hermann Hospital in Houston, TX. 55 clinical isolates were chosen from eight *emm* (M protein gene) types for testing. Isolates were screened for susceptibility to oxidative stress on plates containing diamide, a thiol oxidizing agent. Survival of serially diluted isolate cultures was assessed relative to an *emm3* wild-type strain. Representative isolates from *emm* types showing differences in diamide tolerance were subjected to varying concentrations of bacitracin, polymyxin B, LL-37, nisin, or daptomycin and compared to the *emm3* wild-type strain. Survival in the presence of antimicrobials was measured on a 96-well plate reader and compared to calibration growth curves to obtain virtual colony counts (CFU_V). Differences in isolate CFU_V following antimicrobial exposure relative to the *emm3* wild-type strain were validated by colony counts (CFU) on blood agar plates of selected isolate cultures following exposure to inhibitory concentrations of antimicrobials.

Results: A P170S mutation in LiaF (*emm25* and *emm81*) appeared to increase susceptibility to diamide-induced oxidative stress independent of genomic background. In the *emm75* background, an H210N mutation in LiaS showed decreased diamide susceptibility relative to wild-type LiaS *emm75* isolates. The *emm75* isolate analyzed showed reduced susceptibility to nisin relative to an *emm3* wild-type strain.

Conclusion: Strain-specific polymorphisms in LiaF and LiaS are worth pursuing to further our understanding of the influence LiaFSR has on cell envelope stress phenotypes. The findings of this screen provide a starting point for future research that will enable the production of targeted therapies against LiaFSR to optimize clinical outcomes and reduce the burden of multidrug resistance in GAS.

Acknowledgements: I would like to express my appreciation for Dr. Anthony Flores for providing me the opportunity and funding to conduct this research. I am grateful for Dr. Luis Vega for his mentorship

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Poster 16

A Retrospective Review of Endotracheal Aspirate Cultures in a Neonatal Intensive Care Unit

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BACKGROUND: Endotracheal aspirate cultures (EACs) are frequently used for the diagnosis of lower respiratory tract infections in mechanically ventilated patients. However, a positive EAC may represent colonization rather than symptomatic infection. There is great variability of EAC utilization across U.S. pediatric hospitals, with higher rates of EACs correlated with increased antibiotic use[1]. Here, we describe the current EAC practices in a single institution's neonatal intensive care unit (NICU).

HYPOTHESIS/GOALS: The goal of this study was to describe EAC practices and trends in the 118-bed NICU at Children's Memorial Hermann Hospital (CMHH) in Houston, TX, identifying reasoning for obtaining EACs and describing impact on antibiotic utilization for these patients.

METHODS: We performed a single-center retrospective observational study of NICU patients with positive EACs obtained from January 2021 through December 2021 at CMHH. Positive EACs during this period were identified with TheraDoc surveillance software. Gestational age at birth, birthdate, age at time of sample collection, organism identification and susceptibility, reason for obtaining EAC, antibiotic choice, antibiotic length of therapy were abstracted from the electronic medical records by a pediatric infectious diseases fellow. Conflicts were adjudicated with a pediatric infectious diseases faculty member.

RESULTS: A total of 2,381 EACs were obtained in the NICU in the 12-month period. All EACs were obtained more than 24 hours after birth. There were 141 positive EACs (5.92%) from 42 NICU patients. One EAC was excluded as no organism was identified. Gestational ages ranged from 22w4d to 39w3d, with peaks at 25 weeks and 35 weeks. No correlation between the number of EACs obtained per patient and gestational age at birth was found. The top 3 organisms identified were *Stenotrophomonas*, *Pseudomonas* and *Staphylococcus* spp. Reasons for obtaining EAC included: respiratory decompensation (43, 30.7%), change in tracheal secretions (31, 22%), repeat EAC while on therapy or upon completion of therapy (29, 20.7%), sepsis workup (28, 20%), and repeat EAC while off therapy without documented clinical change (15, 10.7%). While the majority of positive EACs were obtained in the setting of clinical change, 30% (44) of EACs were not associated with clinical deterioration. Review of antibiotic use for these 44 EACs demonstrated 102 days of antibiotic administration solely based on EAC findings. Of 19 patients with multiple (2+) positive EACs, each had at least 1 organism identified in a prior culture, with a total of 98 repeat positive EACs. Of these, 84 EACs had been obtained after the patient had received an antibiotic course to which the organisms were susceptible, suggesting colonization rather than clinically significant isolates.

CONCLUSIONS: At least 30% of EACs obtained in our NICU were unnecessary, leading to 102 excess days of antimicrobial exposure. Moreover, a significant amount of EACs remained positive despite appropriate treatment, consistent with colonization. Given lack of supporting data and risk of unnecessary antimicrobial exposure, obtaining EACs for therapy response assessment and surveillance should be avoided. Investigating EAC use remains an important opportunity for furthering diagnostic and antimicrobial stewardship.

References

Poster 16

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Poster 17

Machine Learning Text Mining for Carbapenemase-Producing Organisms and Susceptibility Testing Results for Ceftazidime/avibactam & Ceftolozane/tazobactam.

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Background: Antimicrobial resistance is an important health threat that needs to be closely monitored, ideally in real-time. Healthcare informatics tools for real-time monitoring have at least two major challenges: (1) tools are institution-specific and not inter-operable between networks; this hinders availability of regional/national real-time monitoring tools; (2) important portions of microbiology reports are stored in EMR databases as semi-structured data types (*e.g.* free text boxes) and require additional steps before the data are suitable for secondary uses.

Hypothesis/Goals: The goal of this project was to automate data extraction of microbiology free-text boxes to identify carbapenemase testing, and last-line antibiotic susceptibility testing results.

Methods: Data source was the VHA Corporate Data Warehouse. All microbiology records were queried with keyword search using wildcards, and the free-text fields were extracted. Each entry was reviewed and labelled for each last-line antibiotic (ceftazidime/avibactam, ceftolozane/tazobactam) and carbapenemase production, and the result of the test. The entire dataset was split into 80% as training set and 20% as test set; the test set data were only used for final analysis. The models were developed with training set data with hyperparameter tuning using 5-fold cross-validation to optimizing model hyperparameters and reduce model overfitting.

Results:

	Ceftazidime /avibactam		Ceftolozane/tazobactam		Carbapenemase Producer	
	PPV	Sensitivity	PPV	Sensitivity	PPV	Sensitivity
Gradient Boost	98.0%	86.0%	92.2%	90.4%	90.9%	95.2%
Naïve Bayes	100.0%	5.3%	46.4%	25.0%	83.1%	88.1%
SGD	90.2%	80.7%	91.8%	86.5%	89.0%	96.4%
Random Forest	---	0.0%	---	0.0%	100.0%	69.0%
Ada Boost	100.0%	73.7%	90.5%	73.1%	90.5%	90.5%
Bagging	100.0%	80.7%	88.0%	84.6%	92.0%	96.4%
K Nearest Neighbor	79.4%	47.4%	83.3%	38.5%	91.9%	81.0%
Decision Tree	90.4%	82.5%	84.0%	80.8%	89.5%	91.7%
Logistic Regression	92.6%	87.7%	88.5%	88.5%	85.7%	92.9%
SVC	92.6%	87.7%	88.5%	88.5%	85.7%	92.9%

Gradient boost and Bagging classifier machine learning models performed well when tested on previously unseen data across each of the three microbiology text-mining tasks.

Conclusions: Machine learning can accurately mine semi-structured microbiology text fields and is promising for automation. Further work with transformer-based models may further increase performance.

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Poster 18

Comparison Between Enrichment and Direct Plating Culturing Methods for Growth and Recovery of* Clostridioides difficile *from Clinical Stool Samples

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Background: Current methods to grow *Clostridioides difficile* involves a multi-step process involving an enrichment step with brain heart infusion (BHI) medium incubated anaerobically for 48-72 hours prior to plating onto cefoxitin-cycloserine-fructose agar (CCFA) for identification of the organism. However, whether direct plating without enrichment would provide similar results is unknown.

Hypothesis/Goals: To compare *C. difficile* growth from clinical stool samples results using the direct stool culturing method vs. the enrichment culturing method

Methods: From Jan 2022 to Sept 2022, stool samples being tested for *C. difficile* infection (CDI) using the C. diff Quik Chek Complete assay from hospitalized patients were collected. Stool samples were either cultured directly from stool or enriched with a mixture of BHI, bile salts, and oxyrase. All samples were incubated anaerobically for 48 hours. Enriched samples (10 µL) were streaked onto CCFA plates in quadrants to isolate *C. difficile* colonies and incubated for an additional 48 hours.

Results: A total of 50 stool samples including 20 with GDH+/toxin+ results were tested. Overall, 24/50 enriched cultures grew compared to 8/50 direct cultures. From the 20 *C. difficile* positive samples (GDH+/toxin+), 19 of 20 enriched cultures grew compared to 7 of 20 direct cultures. All positive direct cultures were also positive by enrichment.

Conclusions: Enrichment cultures are needed for the detection of *C. difficile*. Direct culture and enrichment may allow for a crude quantitative measurement.

Poster 19

Interactions Between Candida and Staphylococcus Species in Polymicrobial Catheter-associated Urinary Tract Infections

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Background: Catheter-associated urinary tract infections (CAUTIs) are the most common healthcare associated infections. CAUTIs begin when microbes colonize and form biofilm within the bladder and the walls of catheters. These biofilms typically consist of multiple species and are capable of growth so prolific as to occlude the catheter and seed bladder and kidney infections, thus impacting patient quality of life. *Candida*, a genus of fungi that includes many opportunistic pathogens, is the second most common cause of CAUTIs. Little is known about *Candida* polymicrobial interactions during CAUTI; however, in other environments, *Candida albicans* forms cooperative biofilms with *Staphylococcus aureus*, which is also commonly isolated from CAUTI biofilms. *S. aureus* and *Staphylococcus epidermidis* encode the enzyme urease, which converts urea to ammonium, thus increasing the pH of the urine and causing salt precipitation, catheter encrustation, and biofilm formation. The regulation of this enzyme is not fully understood, but its transcription is influenced by quorum sensing systems. Notably, the presence of *Candida* alters the transcription of quorum sensing regulated genes in *Staphylococcus* in other infection contexts. Thus, coculture of *Candida* and *Staphylococcus* species may alter urease activity and therefore biofilm formation compared to monoculture biofilms.

Goals: Our goal is to understand how polymicrobial biofilms consisting of *Candida* and *Staphylococcus* species influence biofilm ultrastructure, resistance to antimicrobial treatment, and urease activity.

Methods: Biofilm assays and antimicrobial susceptibility testing using historical lab strains and clinical isolates of *Candida albicans, Candida glabrata, Staphylococcus aureus,* and *Staphylococcus epidermidis* were performed. Minimum inhibitory concentration and urease activity assays against monocultures and cocultures of the microbes growing as biofilms and planktonic cells are being characterized.

Results: We report that many of our clinical isolates of *Candida albicans* are resistant to fluconazole, a frontline antifungal, despite the fact that the individuals enrolled in the study did not receive antifungal treatment in the previous 12 months. Preliminary data indicate that *C. albicans* and *S. aureus* are capable of forming cooperative biofilms in conditions that simulate the CAUTI environment, and the presence of urease greatly improves the biomass of these biofilms. The completion of this study will characterize the antimicrobial resistance patterns of polymicrobial biofilms in the CAUTI environment and the effect the presence of *Candida* has on *Staphylococcus* urease activity.

Conclusions: As we and others have shown in other infections, understanding polymicrobial interactions may inform clinical practice and uncover novel approaches for controlling CAUTIs.

Acknowledgements: Hultgren lab at Washington University, St. Louis for providing clinical isolates.

Poster 20

Sharkskin-Inspired Antimicrobial Surfaces and Their Potential Use in Healthcare Settings

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Background: Healthcare-associated infections (HAIs) have increased by 36% in the past 20 years, affecting approximately 2 million patients. Central-line-associated bloodstream infections, ventilator-associated pneumonia, and catheter-associated urinary tract infections are among the leading causes of these increased HAIs. Additionally, fomite transmission has been attributed to 20-40% of all HAIs. The antimicrobial effect of micropatterned surfaces has long been studied as a potential application in the healthcare setting to reduce and prevent HAIs. Microtopography is an attractive antimicrobial option for indwelling medical devices and "high-touch" areas in healthcare settings because of its ability to continuously inhibit bacterial and viral adhesion.

Goals: The aim of this study was to review current literature regarding the efficacy of using sharkskin-micropattern as an antimicrobial surface and assess the practicality of its use in healthcare settings.

Methods: A keyword search of medical literature using the search terms "micropattern" and "antimicrobial surface" was performed. Relevant articles were reviewed and studies that reported quantitative data on the efficacy of using Sharklet surfaces, from Sharklet Technologies Inc., to decrease the transmission of pathogenic microbes to environmental surfaces or indwelling medical devices.

Results: We found considerable clinical evidence for the efficacy of micropatterned antimicrobial surfaces to decrease surface contamination and spread. The included studies from the literature search demonstrated a significant reduction in the adherence and biofilm formation of several common nosocomial microbes (E. *coli*, MSSA, MRSA, P. *aeruginosa*, A. *baumannii*) on environmental surfaces and several indwelling medical devices. Most studies observed this reduction after inoculation in a lab and one was able to achieve similar findings in a simulated in-patient setting. Notably, one study in the search also showed a reduction in percent transmission for two viruses (Influenza B, Human Coronavirus) and T4 bacteriophage, though more moderate than the reduction seen in bacterial transmission.

Conclusion: The integration of altered topography into hospital surfaces and indwelling medical devices would help reduce the number of HAIs and need for subsequent antibiotic treatment. Additionally, it would allow for less human error and provide continuous disinfection of surfaces by reducing the dependency placed on providers/staff to frequently monitor medical devices and disinfect. It was estimated that a 20% reduction in HAIs would save up to $6.8 billion, and a 70% reduction would save up to $31.5 billion in medical costs. Incorporation of such antimicrobial surfaces into healthcare not only has the potential to reduce the suffering and expenses caused by HAIs, but also slow the overuse of antibiotics and antibiotic resistance long-term. Technology has been made by Sharklet Technologies Inc. that allows for the production of large sheets of this flexible surface, making manufacturing of such medical devices and surfaces cost-effective. However, further studies on the logistics of manufacturing and implementation of these micropatterned surfaces is needed to fully assess its utilization in the fight against HAIs and antimicrobial resistance.

Acknowledgements: This research has no funding or training grants to report.

Poster 21

Colonization by Multidrug Resistant Pathogens in Immunocompromised and Critically Ill Patients

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Background Antimicrobial resistance is a rapidly emerging global health threat with vancomycin-resistant enterococci (VRE) and extended spectrum β-lactamase producing/carbapenem resistant Enterobacterales (ESBL-E/CRE) classified by the CDC as major public health threats. Risk of acquiring such an infection increases significantly with prolonged hospitalization, previous antibiotics exposure, as well as immunosuppression.

Hypothesis/Goals The objective of this study is to examine the rates of colonization by antimicrobial resistant pathogens in the gastrointestinal tract of critically ill and immunocompromised individuals hospitalized in intensive care units (ICU).

Methods A total of 78 patients were enrolled within the first 24 hours of ICU admission and followed for up to four weeks, or until discharge from the ICU. A maximum of two stool samples were collected weekly, at least two days apart. To test for organisms of interest, samples were plated on three selective medias for CRE, ESBL-E, and VRE respectively, then sub-plated on antibiotic media to confirm resistance. Speciation was completed via MALDI-TOF.

Results Colonization was observed in 36% of individuals in at least one stool sample by a minimum of one of the target organisms. Of the colonized patients, 57% were colonized with VRE alone, 36% with ESBL, and 18% were colonized by multiple organisms (11% VRE/ESBL-E, 3.5% CRE/ESBL-E, 3.5% VRE/CRE/ESBL-E). Indeed, 33% of patients colonized by ESBL-E showed simultaneous co-colonization with VRE.

Conclusions The high rates of gastrointestinal colonization by multidrug resistant pathogens exhibited by patients hospitalized in the ICU emphasize the pressing need to better understand the complex dynamics of pathogenic acquisition in order to actively mediate risks and prevent future infection.

Acknowledgements
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Figure 1. Colonization by species of intensive care patients

Patient #	VRE	ESBL	CRE
1	*E. faecium*	-------	-------
2	*E. faecium + P. acidilactici*	-------	-------
3	*E. gallinarum + E. faecium*	-------	-------
4	*E. faecium*	-------	-------
5	-------	*K. pneumoniae*	-------
6	*E. faecium*	-------	-------
7	*E. faecium*	-------	-------
8	*E. gallinarum*	-------	-------
9	*E. faecium*	-------	-------
10	*E. faecium*	*Enterobacter cloacae complex*	-------
11	*E. faecium + E. gallinarum*	-------	-------
12	*E. gallinarum*	-------	-------
13	*E. casseliflavus*	-------	-------
14	*E. faecium*	-------	-------
15	-------	*E. coli*	*E. coli*
16	*E. faecalis*	-------	-------
17	-------	*Enterobacter cloacae complex*	-------
18	*E. faecium*	*K. pneumoniae*	*K. pneumoniae*
19	*E. faecium*	*E. coli + Citrobacter freundii complex*	-------
20	-------	*E. coli + K. oxytoca*	-------
21	*E. gallinarum*	-------	-------
22	-------	*Enterobacter cloacae complex*	-------
23	-------	*E. coli*	-------
24	-------	*Proteus mirabilis*	-------
25	*E. faecium*	*Enterobacter cloacae complex*	-------
26	-------	*E. coli*	-------
27	*E. faecium*	-------	-------
28	*E. faecium*	-------	-------

Poster 22

An Integrated 'Omics Framework for the DYNAMITE Project

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Background
The rise of antimicrobial resistance is a critical concern in healthcare. Notably, carbapenem-resistant Enterobacterales, extended-spectrum beta-lactamase (ESBL) producing Enterobacterales, vancomycin-resistant Enterococci, and *Clostridioides difficile* are all classified as urgent or serious threats by the CDC (2019 AR Threats Report) and caused an estimated 480,400 infections and 28,400 deaths in 2017. We have initiated the Dynamics of Colonization and Infection by Multidrug-Resistant Pathogens in Immunocompromised and Critically Ill Patients (DYNAMITE) project to understand how changes in the microbiome for these patients increases their susceptibility these pathogens. As a part of DYNAMITE, we are generating targeted 16S microbiome sequencing and shotgun metagenomics sequencing from stool, culturing and sequencing the pathogens listed above from stool, and sequencing infection and colonization isolates collected as a part of routine clinical care.

Goals
We describe a systematic framework for characterizing pathogens in the gut microbiome using a multiomic approach to generate complete assemblies of isolated and collected single bacteria, and how we are utilizing that data to interrogate changes in the microbiome during the course of stay in the intensive care unit (ICU).

Methods
Longitudinal stool samples were collected from a cohort of seventeen liver-transplant ICU patients. Shotgun metagenomics as well as 16S rRNA short- and long-read sequencing was performed on stool samples, and short and long-read sequencing of single bacterial cultures and clinically collected bacteria were performed to characterize the content of the microbiome.

Results
Here we demonstrate our genomic workflow and how that facilitates our integrated 'omics approach to interrogating microbiome changes during a patient's stay in the ICU. We present a vignette of a single patient with clinical cultures, bacterial cultures from collected stool, and metagenomic data detailing the consortia of their microbiome during their ICU stay, demonstrating the utility of our framework.

Conclusions
This framework provides the foundations for the metagenomic approaches of the DYNAMITE project as demonstrated by our vignette.

Acknowledgements
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Poster 23

Vancomycin-Resistant vanB- *and* vanA/vanB-*type* Enterococcus faecium *Causing Invasive Infections in Adult Patients in Chile (2018-2022)*

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Background: Vancomycin-resistant *Enterococcus faecium* (VR*Efm*) represents a health threat due to the antibiotic resistance and the ability to spread and cause outbreaks. Thus, VREfm is a particular challenge for clinical management. Rising proportions of vancomycin resistance in enterococcal infections have been reported worldwide and the vancomycin resistance genes display genetic variability and a continued evolution. This study aims to characterize the vancomycin resistance genotypes and lineages of the VREfm isolates causing infections in Chilean hospitals.

Methods: A total of 535 VR*Efm* clinical isolates were collected from adult patients in 11 Chilean hospitals from 2018 to 2022. All isolates were recovered from sterile sites (49% from blood). *E. faecium* species was confirmed by MALDI-TOF, susceptibility profiles were determined by Kirby Bauer (CLSI,2022). The detection of *vanA* and *vanB* genes was performed by PCR. In order to confirm vancomycin resistance genotypes, eleven representative isolates were subjected to short-read whole genome sequencing (WGS) on an Illumina platform.

Results: All isolates were resistant to vancomycin, ampicillin and ciprofloxacin. We also detected resistance to teicoplanin (23%), linezolid (2%) and high-level resistance to gentamycin (53%) and streptomycin (30%). A total of 68% of VR*Efm* were harbored *vanB* and 9% *vanA.* Surprisingly, 20% of the isolates simultaneously carried *vanA* and *vanB* (*vanA/vanB*). The WGS analyses showed that *vanB*-VR*Efm* isolates belonged to ST656, meanwhile the *vanA/vanB*-VR*Efm* isolates belonged to an ST233. Although WGS confirmed the concomitant presence of the *vanA* and *vanB* genes, they were located in different contigs. While *vanB* genes were always found on a single contig of ~43500bp, the *vanA* genes were

consistently found in three small contigs (Fig1) that covered almost the whole structure of the Tn1546 transposon.

Conclusions: We report the presence of two lineages of VR*Efm* causing invasive infections in Chile: *vanB*-ST656 and *vanAB*-ST233, which had not been previously reported in the country. Further, we confirmed the simultaneous presence of *vanA* and *vanB* clusters in VR*Efm* that exhibited resistance to both vancomycin and teicoplanin. An in depth genomic characterization of VR*Efm* is essential to monitor the epidemiology of this critical pathogen in South America.

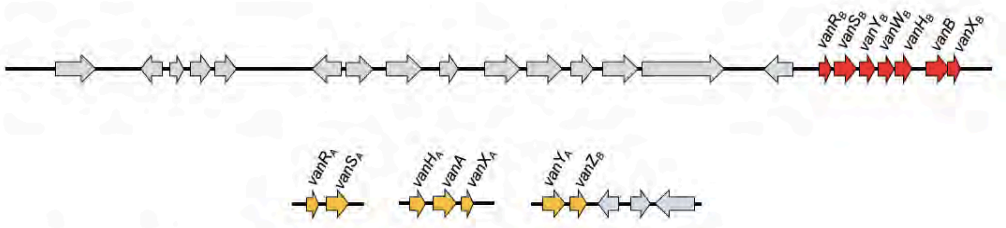

Figure 1. Schematic representation of *vanA* and *vanB* gene clusters in *vanA/vanB*-VREfm SCL9300

Poster 24

Staphylococcus aureus Breast Implant Infection Isolates Display Recalcitrance to Antibiotic Pocket Irrigants *in vivo* Despite Exhibiting Susceptibility *in vitro*

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Background: Breast implant associated infection (BIAI) following reconstructive surgery post-mastectomy is common, with a prevalence of up to 35%. For these patients, BIAI results in increased patient morbidity, including swelling, pain, and tissue necrosis, as well as escalated healthcare costs. Furthermore, these infections can result in the delay of critical oncologic treatments, such as radiation and chemotherapy. Additionally, BIAIs require explantation of the infected protheses and additional broad spectrum antibiotic treatment for complete resolution of the infection. To reduce infection rates, surgeons have implemented additional prevention strategies, including flushing the surgical pocket with a triple antibiotic pocket irrigant (TAPI) before implant placement. TAPI usually consists of 50,000 U bacitracin, 1 g cefazolin, and 80 mg gentamicin diluted in 500 mL of saline. Despite these additional strategies, infections rates remain high.

Goals: This study examines the efficacy of TAPI against *Staphylococcus aureus*, one of the most common causes of BIAIs, both *in vitro* and *in vivo*.

Methods: The antimicrobial resistance pattern of *S. aureus* BIAI isolates (117 and 158) and a reference strain (JE2) were assessed via Minimal inhibitory concentration (MIC) assays using TAPI, as well as the individual antibiotics that make up the solution. Additionally, the recalcitrance of the biofilm formed by these strains to TAPI was assessed. Furthermore, one BIAI isolate (117) and JE2 were further characterized in a mouse BIAI model. Finally, whole genome sequencing was performed on the BIAI isolates to identify potential virulence and antimicrobial resistance mechanisms that may contribute to recalcitrance to TAPI.

Results: MIC assays revealed *S. aureus* BIAI isolates were susceptible to gentamicin, cefazolin, and TAPI, and resistant to bacitracin. JE2 was the only strain that was also resistant to gentamicin. All strains formed biofilm under standard *in vitro* conditions and these biofilms resisted TAPI treatment. Notably, in the mouse BIAI model, TAPI significantly reduced JE2 infection on the implant and in the surrounding tissue at 1- and 7- day post infection (dpi). In contrast, infection with the BIAI isolate (117) persisted out to 14-dpi, despite TAPI treatment. To gain insights into how the BIAI isolates were resisting TAPI we sequenced the strains. These data revealed that the sequence types differed among the *S. aureus* strains, JE2 is a ST 8, 117 is a ST 39, and 158 is a ST 45. Additionally, JE2 was the only strain to encode the *mecA* gene, which provides resistance to β-lactams, while the BIAI isolates carry *tet-38* and *mepA/R* and encodes resistance to tetracyclines. Furthermore, while all three strains carried 57 known virulence genes, the BIAI isolates share 6 factors not found in JE2, including cap8H-K, sec, selL. While these factors are known virulence determinants, it is unclear how they affect biofilm formation or recalcitrance to antimicrobials.

Conclusions: This study indicates that *S. aureus* BIAI isolates encode unique mechanisms that allow them to persist despite the use of prophylactic antibiotic treatment, such as TAPI, and promote chronic infection.

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Poster 25

Simulated Human Dosing of Ceftazidime in a Murine Pneumonia Model

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Background: As antimicrobial resistance continues to grow as a global healthcare crisis, novel therapeutic solutions are needed to combat the drug-resistant pathogens. To be able to evaluate new approaches, *in vivo* models are developed to not only understand pathogenesis but mimic the standard dosing regimen of antibiotics a patient would receive during treatment. The difficulty comes with the difference in renal clearance in rodents. To accommodate rapid drug clearance in rodents, serial supplemental doses are given to upkeep serum concentration around the target human pharmacokinetic profile.

Hypothesis/Goals: We expect to derive a dosing regimen in a murine pneumonia model that closely mimics the pharmacokinetic exposures of 2g every 8 hours of ceftazidime in humans.

Methods: Female Swiss Webster mice (20-25g) were rendered neutropenic by two doses of intraperitoneal cyclophosphamide prior to infection; first dose of 150mg/kg was given four days prior, and the second dose 100mg/kg was given one day prior. To slow renal clearance 5mg/kg of uranyl nitrate was given two days prior to infection. On infection day, anesthetized mice were inoculated with approximately 10^7 CFU of *A. baumannii* under laryngoscopic guidance. An iterative approach was taken to determine the appropriate doses and timing of dosing. Two hours after infection, different ceftazidime doses were given intraperitoneally. Serial blood samples were obtained over 8 hours and were clotted at room temperature. The serum samples were frozen prior to assaying for ceftazidime concentration using LCMS/MS. Observed concentration-time profiles of different doses were characterized using a one-compartment pharmacokinetic model with a bolus absorption input. The best-fit parameters were used to alter the dose if needed and guide the timing for the subsequent dose. The finalized dosing regimen was validated to mimic the dosing exposure in humans.

Results: The intraperitoneal doses of 100mg/kg, 60mg/kg, and 20mg/kg given at 0, 2.5, and 5 hours, respectively, achieved the desired simulated human profile. The exposure of the drug was within 20% of the AUC of the human pharmacokinetic profile.

Conclusions: The validated dosing regimen can be used in a murine pneumonia model to simulate the clinical dosing exposure of 2g every 8 hours of ceftazidime in humans. This will be used as the reference for comparing other treatment options in future studies.

Acknowledgements: This research was funded by the National Institutes of Health, grant number R01AI140287-05.

Poster 26

Cefiderocol Heteroresistance in Clinical Isolates of **Pseudomonas aeruginosa** *with Mutations in TonB-dependent Receptor Pathways is Detectable in Iron-depleted Media*

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Background: The siderophore cephalosporin cefiderocol (FDC) is a last line treatment option for multi-drug resistant (MDR) *Pseudomonas aeruginosa* (PA). However, the emergence of resistance with therapy has been increasingly reported. Heteroresistance (hR) to FDC is a phenomenon where a minority of the bacterial population possesses a decreased susceptibility to the antibiotic and is a possible explanation for the discrepancy between laboratory reported susceptibilities and clinical outcomes. The phenotype of hR in clinical PA isolates has been associated with the presence of mutations in genes encoding the TonB-dependent receptor (TBDR) pathways responsible for FDC import. The gold standard for detecting hR is the population analysis profile (PAP). However, traditional PAP methods have not fully addressed the role of iron and inoculum size on the identification of the hR phenotype.

Hypothesis/Goals: We sought to evaluate the impact of iron-limited media and a controlled inoculum on the detection of hR in clinical PA isolates.

Methods: Four clinical strains with a defined hR phenotype as determined by agar dilution were used in this study: C1408 (FDC MIC 32 µg/mL, resistant), C1814 (FDC MIC 1 µg/mL, hR), C4593 (FDC MIC 1 µg/mL, hR), C1273 (FDC MIC $\leq$ 0.5 µg/mL, susceptible), and the laboratory strain PAO1 (FDC MIC $\leq$ 0.5 µg/mL, susceptible). All strains were tested per CLSI-defined Kirby Bauer (KB) disk diffusion testing, broth microdilution (BMD) in iron depleted Mueller-Hinton (ID-MH), and standard agar dilution (PAP). A modified PAP was performed with inoculation of $1x10^7$ CFU/mL into ascending concentrations of FDC (0, 2, 4, 8, 16 µg/mL) in ID-MH broth. After 24 hours, serial 10-fold dilutions were plated for colony counts. Heteroresistance was defined as less than 50% isolate survival at 4 µg/mL with greater than .0001% survival at 8 and/or 16 µg/mL FDC. Colonies were selected randomly from the 0, 4, and 16 µg/mL plates to assess for the emergence of resistance.

Results: The susceptible clinical strain C1273 and laboratory isolate PAO1 showed no evidence of hR on PAP, while the FDC resistant isolate C1408 was also resistant by PAP. Both C1814 and C4593 met criteria for hR by ID-MH broth PAP, and these results mirrored those seen with the agar dilution method (**Figure 1a**). While both strains were classified as hR by PAP, only C1814 showed a statistically significant difference in colony counts as compared to the susceptible C1273 (P-value $\leq$ 0.05 at 4 and 8 µg/mL). Interestingly, an analysis of the subpopulations collected from the 4 and 16 ug/mL FDC plates for C1814 displayed a statistically significant increase in MICs (**Figure 1b**), while C4593 did not. Further, C1814 was noted as hR per KB, while C4593 did not have a clear hR pattern on KB.

Conclusion: We demonstrate FDC hR is detectable in iron-depleted conditions at a defined inoculum of 10^7 CFU/mL. The strain C1814 demonstrated a statistically significant survival on iron-depleted PAP, with the emergence of resistant isolates on subculture MIC assessments. Our data suggests that KB may be a viable option for identifying consequential hR in MDR *P. aeruginosa* strains.

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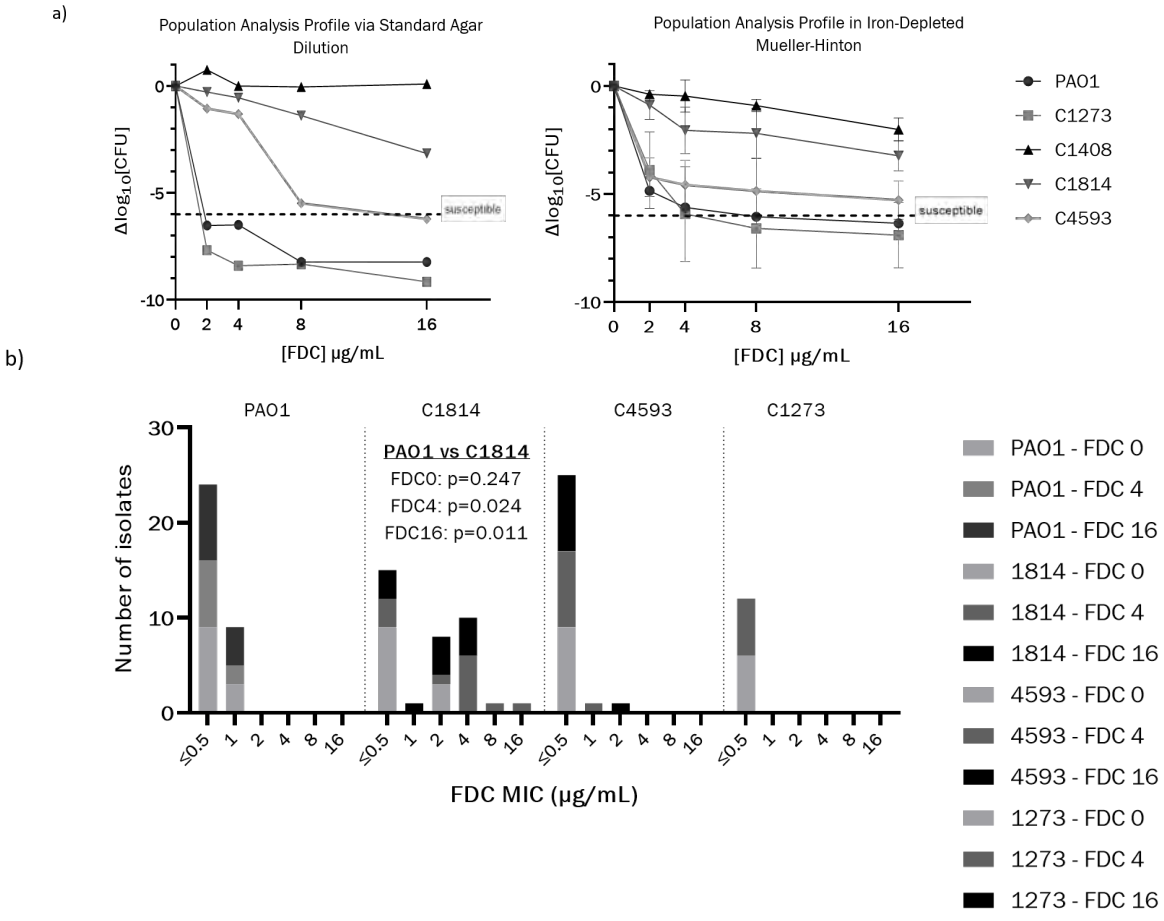

Figure 1. Population analysis profile for MDR PA TBDR mutants via traditional MH PAP technique versus grown in iron depleted broth (a) with subculture MIC population distribution (b). Statistically significant difference in C1814 versus susceptible clinical strain C1273 defined as * (P-value ≤0.05), ** (P-value ≤0.005).

Poster 30

Evidence of Systemic Vancomycin Bowel Penetration by High Performance Liquid Chromatography

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Background Vancomycin is a glycopeptide antibiotic widely used in clinical practice. Available formulations include an intravenous (IV) solution for systemic infections and oral forms exclusively used for gastrointestinal (GI) tract infections. As vancomycin is a water-soluble, tricyclic glycosylated peptide, it is not able to penetrate the gut barrier; the oral formulation is minimally absorbed from the human GI tract and is largely excreted into the stool. However, several case reports/series have described systemic vancomycin levels following oral vancomycin receipt. Penetration of IV vancomycin into the GI tract has not been reported but would carry large implications on the development of gut dysbiosis and antimicrobial resistance.

Hypothesis/Goals Our study aims to determine the frequency of detectable vancomycin concentrations in the stool of patients with antibiotic-associated diarrhea receiving IV vancomycin through utilizing a high-performance liquid chromatography (HPLC) array detector method.

Methods This was a multicenter, retrospective study utilizing stool samples obtained from two hospital systems in the Texas Medical Center in Houston, Texas. Stool samples from patients tested for *Clostridioides difficile* infection (CDI) as part of routine clinical care were collected and brought to a centralized research laboratory at the University of Houston. Patients' electronic health records were screened for: 1) IV vancomycin receipt for ≥48 hours prior to stool collection, 2) ≥1 dose of IV vancomycin administered <24 hours prior to stool collection (exception for hemodialysis patients with documented serum level), and 3) no oral vancomycin administration prior to stool collection. Fecal vancomycin was quantified based on the standard calibration curve with vancomycin standard concentrations plotted against the corresponding HPLC peak areas.

Results The study cohort included 33 samples from unique patients. The majority were female (54.5%) and the mean age was 59.6 (range 23-84) years. Active infection was present in 84.8% (28/33) of the population with 54.5% (18/33) patients being diagnosed with CDI. The average duration of systemic vancomycin administration prior to stool collection was 3.5 (range 2 – 15) days. Approximately 9% (3/33) of samples had a detectable vancomycin level (range 1.2-13.2 mcg/mL). All patients with detectable levels were male sex.

Conclusion IV vancomycin penetrates the GI barrier and achieves detectable fecal concentrations, as presented here in nearly one-tenth of our cohort. This theoretically may promote the development of vancomycin-resistant enterococcus, *Clostridioides difficile* infection, and/or *van* mutations in *C. difficile* leading to vancomycin resistance. Further studies on implications as well as stewardship initiatives to protect the microbiome/resistome are warranted.

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Poster 31

Discovery of Novel Broad-spectrum Antibiotics and Inhibitors for β-lactamases using Combinatorial Approaches

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Background: Antibiotic resistance due to the emergence, spread, and persistence of multidrug-resistant bacteria has become a rising threat to the public health. Currently, β-lactams are the most widely used class of antibiotics. Resistance to β-lactams is primarily caused by the bacterial production of β-lactamase enzymes, which hydrolyze and inactivate the drugs. Prevalent β-lactamases such as OXA-48 and NDM-1 are able to hydrolyze a broad set of substrates including carbapenems, the last resort β-lactam antibiotics. Discovery of β-lactamase inhibitors is one avenue to address the antibiotic resistance problem. Alternatively, finding a new drug target to screen for novel antibiotics is another strategy to combat drug resistance. The targets of β-lactams are penicillin-binding proteins (PBPs), which are involved in bacterial cell wall formation. Gram-negative bacteria have an outer membrane that can decrease antibiotic penetration, making Gram-negatives less susceptible to many β-lactams. In the outer membrane of Gram-negative bacteria, a β-barrel assembly machine (BAM) catalyzes the integration of β-barrel proteins into the outer membrane. The BAM subunit A (BamA) is conserved in all Gram-negative species and is essential for cell viability. Since BamA is exposed at the surface of the outer membrane, potential inhibitors do not need to permeate the outer membrane. Therefore, BamA is an excellent target for the development of new antibiotics.

Goals: Use combinatorial approaches including established DNA-encoded small molecule libraries (DELs) and a focused combinatorial peptide library to discover, produce, and validate new inhibitors against β-lactamases and novel antibiotics that act on BamA.

Methods: Target protein specific binders were selected from combinatorial libraries using affinity-based selections. The inhibition potency of selected binders was tested by determining inhibition constant (K_i) and minimum inhibitory concentration assay (MIC).

Results: Several potent NDM-1 and OXA-48 inhibitors were selected from DELs. The most potent of these have K_i values of 0.04 ± 0.01 μM (NDM-1 inhibitor CDD2998) and 0.20 ± 0.03 μM (OXA-48 inhibitor CDD2801). MIC results showed that the NDM-1 inhibitor CDD2522 achieved a 16-fold reduction of ampicillin MIC at a concentration of 128 μg/mL in *E.coli* expressing NDM-1. BamA specific binders were selected from both DEls and the peptide library.

Conclusions: Combinatorial approaches were used to select potent inhibitors for target proteins to provide potential drug leads to combat the antibiotic-resistant problem.

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Poster 32

Understanding the Effects of **Staphylococcus aureus** *Urease on Biofilm Production and Antibiotic Recalcitrance in Clinical Isolates*

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Background: Catheter-associated urinary tract infections (CAUTIs) are one of the most common hospital-associated infections in the United States. CAUTI are caused by a wide range of uropathogens, including *Staphylococcus aureus. S. aureus* CAUTI are particularly problematic, as these infections often disseminate to bacteremia and are commonly resistant to antibiotics, making them difficult to treat. Furthermore, *S. aureus* produces the enzyme urease, which promotes crystal formation on the catheter surface that subsequently results in encrustations, further antibiotic recalcitrance, and chronic biofilm-related CAUTI. Notably, previous studies have also shown that the urease operon is upregulated during biofilm formation, which suggests that this enzyme is important in biofilm formation during CAUTI.

Hypothesis/ Goals: We seek to determine the role of urease in biofilm production and antibiotic recalcitrance in well-characterized strains and clinical *S. aureus* CAUTI isolates. We anticipate that urease activity promotes both biofilm formation and antibiotic recalcitrance.

Methods: To test this, I have determined the urease activity among well-characterized *S. aureus* strains and clinical CAUTI isolates. I am also conducting MIC assays on four antibiotics commonly used to treat *S. aureus* (gentamicin, cefazolin, ciprofloxacin, and nitrofurantoin) on our clinical isolates. To further characterize the role of urease in biofilm formation I have generated mutations in the gene that encodes the active site of urease, *ureC,* in JE2 and UTI MRSA. Biofilm formation was assessed following growth in BHI and artificial urine media using the standard crystal violet assay. Furthermore, I have also performed these biofilm assays in clinical *S. aureus* CAUTI isolates. Mutations in *ureC* are also being developed in these clinical isolate backgrounds.

Results: Urease activity is variable across clinical isolates and can even vary across isolates obtained from the same patient. Furthermore, there does not seem to be a correlation between urease activity and antibiotic resistance in planktonic cultures. However, our biofilm assays have shown that while there is no significant difference between our wild type strains and mutants of *ureC* in BHI, there is a significant decrease in biofilm production in the *ureC* mutants when the biofilms are grown in our artificial urine media. Furthermore, clinical isolates that have little to no urease activity also have significantly lower biofilms compared to a UTI MRSA control.

Conclusions: While urease activity and MICs are variable between clinical *S. aureus* isolates of CAUTI, urease is an important virulence factor in biofilm production in an environment rich in urea. Since urease is important in *S. aureus* biofilm production, it may provide recalcitrance to antibiotics during CAUTI.

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Poster 33

***Identifying LiaFSR Residues Contributing to ExPortal Integrity and Response to Antimicrobials in Group A* Streptococcus**

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Background: Group A *Streptococcus* (GAS), or *Streptococcus pyogenes*, is responsible for a myriad of diseases (pharyngitis, scarlet fever, impetigo, toxic shock syndrome) of which several are prevalent in the pediatric population. The LiaFSR two-component regulatory system (TCS) and the ExPortal functional membrane microdomain (FMM) of GAS have been shown to coordinate the response to cell membrane stress when the bacterium is exposed to antimicrobials or antimicrobial peptides (AMPs). The ExPortal coordinates translocation and processing of secreted GAS proteins and contributes to sensing membrane. In an unstressed state, LiaF acts as an inhibitor of LiaS activity, both residing within the ExPortal. In a stressed state, such as exposure to antimicrobial agents, LiaF and S dissociate, allowing LiaS to phosphorylate LiaR, resulting in subsequent activation and expression of downstream target genes. Genomic analysis indicates a strict conservation of specific protein domains and certain amino acid residues in LiaF, S, and R, which suggests their critical involvement in the LiaFSR mechanism of action.

Hypothesis/Goals: We hypothesize that conserved amino acid residues in LiaFSR, such as the LiaF C-terminal domain (CTD) and a 3xK residue motif, are essential to ExPortal formation and maintenance and may contribute to differences in antimicrobial susceptibility and virulence.

Methods: Two different mutant strains were analyzed and compared to (wild-type) WT: one lacking the LiaF CTD (LiaF_ΔCTD) and one mutagenized in the 3xK motif (LiaF_K91-93A). Five different assays were used to examine phenotypes associated with LiaFSR activity: SpeB protease activity through bacterial growth on milk plates, ExPortal integrity via fluorescence microscopy, diamide-induced oxidative stress tolerance, antimicrobial/antimicrobial peptide (AM/AMP) susceptibility, and a direct bactericidal assay in human blood (Lancefield). For the AM/AMP susceptibility, we tested 6 different antimicrobial agents with varying mechanisms of action: bacitracin, polymyxin B, LL-37, nisin, daptomycin, and HNP-1.

Results: Milk plate analysis revealed a significant decrease in SpeB production in the LiaF-ΔCTD vs. WT, but no difference in LiaF-K91-93A relative to WT. During fluorescence microscopy, no significant differences were detected between foci of fluorescence of either mutant strain relative to WT. When exposed to diamide-induced oxidative stress, both mutants exhibited increased tolerance relative to WT. AM/AMP susceptibility assays did not reveal any significant differences for any antimicrobial agent between either mutant strain vs. WT. Finally, the Lancefield assay revealed a significant decrease in survival in human blood between both mutant strains and WT. Mutant strains also had significantly decreased survival relative to a strain lacking LiaF (ΔLiaF).

Conclusions: The results of the Lancefield assay indicate that these residues are physiologically relevant in GAS infection. However, their mechanism underlying this contribution remains unclear. Future research will examine downstream gene regulation to elucidate the LiaFSR-associated mechanism of decreased survival in human blood, with the aim of defining determinants of GAS bacteremia.

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Poster 34

The Beneficial Utility and Future Direction of Silver Nanoparticles against Multidrug-Resistant Bacteria

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Background/intro: Multi-drug resistance (MDR) in pathogenic bacteria is consistently one of the biggest challenges of pharmaceutical and clinical medicine. Individuals infected with MDR bacteria have increased hospital stay time (56.67%) and treatment costs (67.8%) ($P<0.0001$). MDR microbe emergence is continually facilitated by traditional antibiotic treatments igniting a shift in research towards more innovative bactericidal agents such as silver nanoparticles. Nanotechnology has provided a new and exciting platform for modifying silver, a long-known antimicrobial agent, in terms of size, shape, concentration, and dosage, with promising implications for their use in combating multi-drug resistant bacteria.

Hypothesis/Goals: This report aims to review the current literature on the practical utility and challenges of silver nanoparticles as agents against multidrug-resistant bacteria (E. *Coli*, P. *aeruginosa*, S. *pyogenes*, and S. *aureus*).

Methods: A keyword search of medical literature with search items "silver nanoparticles" and "antimicrobial" was performed. Relevant articles discussing the current impact, challenges, and future direction of silver nanoparticles as antimicrobial agents were reviewed and selected for inclusion in this report.

Results: We found substantial evidence of silver nanoparticles' effectiveness against multi-drug resistant bacteria. Silver nanoparticles show antibacterial activity against a myriad of drug-resistant bacteria, including E. *Coli*, P. *aeruginosa*, S. *pyogenes*, and S. *aureus*, among many others. Across the multiple studies referenced for this report, silver nanoparticles' range of effectiveness against MDR bacteria was found due to their many mechanisms of action, including inhibition of cell wall formation, intercalation between DNA bases, formation of free radicals, and prevention of biofilm formation.

Although effective, silver nanoparticles have some limitations, such as discoloration of the skin and eyes, toxicity to local and distant organs, and high manufacturing cost, limiting their large-scale production. However, studies are researching the manipulation in size, shape, concentration, and dosage of silver nanoparticles influencing the presence/absence of harmful effects on human health.

Conclusions: As pathogenic bacteria continue to mutate and find resistance to multiple drugs/antibiotics, the emergence of MDR pathogens will also continue. The current infectious disease society of America (IDSA) guidelines list a wide range of treatments for these pathogens, including broad-spectrum antibiotics that are not associated with improved outcomes and have a 10.3% increase in adverse effects. Silver nanoparticles have shown significant effectiveness against MDR bacteria with their ability to be modified at the nano level, facilitating a variety of effective mechanisms of action. Although promising, further investigation into the safe and cost-effective production of silver nanoparticles will allow their use as a new antimicrobial agent to be potentially groundbreaking.

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Poster 35

Public Health and Economic Challenges of Increased Antimicrobial Resistance In The COVID-19 Pandemic Era

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Background: Certain practices to alleviate the COVID-19 pandemic may have unwittingly exacerbated antimicrobial resistance, which has developed into a public health threat and economic burden in recent years[1,4]. These include higher rates of multidrug-resistant organism transmissions from increased hospital admissions leading to co-infection and increased administration of antibiotics[3]. The Organization has reported for Economic Co-operation and Development (OECD) that 2.4 million people in Europe, North America, and Australia will die from resistant microorganism infections in the next 30 years, with significant economic implications[3]. A separate study showed that bacteria resistant to "last-line antibiotics" was found to cause 39% of resistant infections in Europe[3]. Over the pandemic, an increase in multidrug-resistant organisms has been reported, including a retrospective study showing an increase of specific organisms from 6.7% to 50% between 2019 to 2020[4].

Hypothesis: We aimed to review the literature concerning the economic implications and public health threats of the COVID-19 pandemic on antimicrobial resistance.

Methods: A keyword search was performed for the terms "antimicrobial resistance" and "COVID-19 Pandemic"; relevant articles were reviewed and included in this report.

Results: We found evidence of an increase in antimicrobial resistance over the pandemic, which stems from multiple factors, including increased hospital admission leading to co-transmission and increased administration of antibiotics[2]. A study performed in 88 intensive care units (ICU) showed that 70% of patients were administered antibiotics, and only 54% of those patients had symptoms of bacterial infections[3]. Multiple studies have shown an increased number of COVID-19 patients in the ICU considered to be co-infected with a pathogenic bacterium[4]. Additionally, antimicrobial resistance is estimated to cost $55 billion every year in the United States and $20 billion for healthcare, according to the CDC[1].

Conclusions: Combating antimicrobial resistance has become more of a priority than ever in the wake of the pandemic. Various public health organizations continue to look to implement changes in the healthcare system to decrease adverse health outcomes and the economic burden of antimicrobial resistance[4]. As it becomes a financial burden, more attention has been paid to contributory practices, including the overuse of antibiotics and increased hospital admissions[2]. However, we can alleviate this issue by educating and training healthcare workers to recognize and differentiate symptoms of COVID-19 and that of a "superimposed bacterial or fungal" disease, decreasing unnecessary use of antibiotics and improving measures of control of co-transmission in healthcare facilities[2,4].

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Poster 36

Comparison of Ceftazidime-Avibactam and Ceftolozane-Tazobactam Activity Against Multidrug Resistant* Pseudomonas aeruginosa *at a Large Academic Cancer Center

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Goals: To determine the utility of routinely testing ceftazidime/avibactam susceptibility on multidrug-resistant (MDR) *Pseudomonas aeruginosa* isolates.

Background: Multidrug-resistant bacterial infections lead to increased morbidity and mortality. Subsequent use of broad-spectrum antibiotics has led to widespread resistance resulting in diminished therapeutic options. Antibiotic shortages further complicate this issue by limiting those alternatives. In early 2021, a manufacturer recall was issued for ceftolozane-tazobactam (C/T), a potent beta-lactam/beta-lactamase inhibitor used for the treatment of MDR *Pseudomonas aeruginosa*. The recall resulted in a year-long absence of C/T for clinical use, necessitating the use of alternative antimicrobials. Ceftazidime-avibactam (CZA) is also considered a potent antipseudomonal beta-lactam/beta-lactamase inhibitor with initial *in vitro* data indicating activity comparable to C/T against MDR *P. aeruginosa*. Antimicrobial susceptibility testing (AST) via gradient strip is routinely performed for both CZA and C/T on MDR *P. aeruginosa* and was necessary during the C/T shortage. However, recent data show that CZA may be an inferior agent compared to C/T in treating MDR *P. aeruginosa* infections, with CZA having a higher $MIC_{50/90}$ profile. In addition, the availability of more favorable alternative agents makes the utility of performing routine AST for CZA in these cases unclear. This observational study attempts to determine the usefulness of CZA susceptibility testing on all MDR *P. aeruginosa* isolates.

Methods: This is a retrospective, observational study of ceftazidime-avibactam and ceftolozane-tazobactam activity via gradient strip against MDR *P. aeruginosa* isolates reported at MDACC in 2021.

Results: We found 105 MDR *P. aeruginosa* isolates from 64 patients with the primary medical conditions documented as solid tumor (42%), leukemia (27%), lymphoma (20%), and stem cell transplantation (11%). Of the 64 patients, 52% had a documented history of *P. aeruginosa* infection. Of those, 79% (26/33) had a history documented within 90 days of the MDR *P. aeruginosa*. Isolates were mostly derived from respiratory cultures (29%), followed by wound (25%), blood (22%), and urine (19%). Non-susceptibility to cefepime, carbapenems, piperacillin/tazobactam, and levofloxacin was reported in 95%, 88%, 93%, and 92% of isolates, respectively. Carbapenamases were detected in 4 isolates (3.8%), including one metallo-beta-lactamase. Among 64 unique MDR *P. aeruginosa* isolates tested, 67% (n=64; $MIC_{50/90}$, 8/24 µg/ml) were susceptible to CZA, while 85% (n=60; $MIC_{50/90}$, 2/8 µg/ml) were susceptible to C/T. Of the 20 isolates reported as non-susceptible to CZA, 60% (12/20) remained susceptible to C/T. All isolates (n=9) reported as non-susceptible to C/T, were also non-susceptible to CZA. Additional AST to other alternatives included cefiderocol (8 isolates from 4 unique patients) which were all susceptible.

Conclusion: During the ceftolozane-tazobactam shortage, susceptibility testing and utilization of alternatives such as ceftazidime-avibactam was necessary in the treatment of MDR *P. aeruginosa* infections. In our study, CZA was not as active as C/T which highlights the importance of C/T as a treatment option for MDR *P. aeruginosa*. Isolates non-susceptible to C/T are highly unlikely to be susceptible to CZA. The data presented indicates routine testing of CZA in all MDR *P. aeruginosa* is unnecessary as it will unlikely impact clinical decision making while C/T is an option.

Poster 37

Elucidation Of The Molecular Signal for the Regulator Of Capsule Synthesis Stress Response

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Background: The Regulator of Capsule Synthesis (Rcs) envelope stress response is highly conserved in Enterobacteriaceae. Rcs is activated by multiple host immune factors and antibiotics, which target the bacterial cell envelope. These include *1)* cationic antimicrobial peptides (CAMPs), both innate immune CAMPs and polymyxin antibiotics, that disrupt the outer membrane by targeting polyanionic lipopolysaccharide (LPS), and *2)* lysozyme and β-lactam antibiotics that target the peptidoglycan (PG) cell wall. Rcs regulates expression of many genes to prevent or mitigate cell envelope damage, and as such, Rcs is essential for survival in the host, virulence, and intrinsic antibiotic resistance. Despite its importance, how Rcs detects envelope damage remains unknown. Rcs is a phosphorelay-based signal transduction pathway consisting of six components, including the sensor protein RcsF. RcsF forms a complex with several outer membrane proteins (OMP), which allows RcsF to co-localize with LPS at the cell surface. Assembly of RcsF/OMP complex is required for RcsF signaling, but the underlying reasons have not been resolved.

Hypothesis/goals: The overall goal of my project is to identify a molecular signal and the mechanism of RcsF activation. Our hypothesis is that RcsF monitors perturbations in LPS packing through direct interaction with LPS.

Methods: We use in vivo transcriptional reporter fusions to monitor Rcs activity in response to genetic perturbations of the cell envelope as well as antibiotics, such as the β -lactam mecillinam, A22, polymyxin B, and globomycin. We use cation-dependent and cation-independent ways to stabilize LPS interactions, and study how it impacts the Rcs response to antibiotics.

Results: Mutations that alter LPS charge and structure induce Rcs in a Mg^{2+}-dependent manner. I showed that increased expression of *eptA,* which modifies LPS and strengthens lateral interactions in a cation-independent manner, also causes a reduction in Rcs signaling in an LPS biosynthesis mutant, providing strong evidence for LPS lateral interactions as a potential Rcs signal. Moreover, the addition of divalent cations during PG synthesis inhibition by antibiotics such as A22 and mecillinam also leads to a significant reduction in Rcs activity.

Conclusions: My result support two initial conclusions. First, RcsF seems to monitor LPS packing at the outer membrane and not the LPS structure itself. Second, stabilizing LPS packing alleviates Rcs signaling, not only when LPS is targeted but also when peptidoglycan biosynthesis is inhibited, for example, by β -lactams. Together, these findings suggest that disruptions to LPS packing, not cell wall, may be a direct and universal signal for Rc induction.

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Poster 38

Comparison of 30-Day Healthcare Resource Utilization (HRU) Among Adult Patients with Approved or Unapproved Omadacycline Prescriptions for Nontuberculous Mycobacterial Infections (NTM)

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Background: Omadacycline is a tetracycline antibiotic indicated for the treatment of adults with acute bacterial skin and skin structure infections and community-acquired bacterial pneumonia. Preliminary clinical studies suggest that omadacycline may be effective among patients with NTM. There is a need to understand the outcomes of patients with NTM who are treated with omadacycline to understand real-world effectiveness. Consistent with other new agents for NTM, there is a high potential that an omadacycline prescription faces reimbursement challenges (i.e., potential claim rejection by the payer or reversed due to patient abandonment based on high copayment) and it is not known whether patients who have an unapproved omadacycline claim are at higher risk for 30-day inpatient (IP) and Emergency Department (ED) visits relative to those with filled omadacycline prescriptions.

Hypothesis/Goals: This retrospective study sought to characterize the real-world outcomes of adult outpatients who were prescribed omadacycline for NTM, determine the incidence of unapproved omadacycline among adult NTM patients, and compare outcomes before and after patients' index omadacycline claim among those who had an unapproved and those with an approved omadacycline claim. Thirty-day outcomes were evaluated in this study as it is an important quality metric for both private and public payers.

Methods: The study population included patients who received ≥1 omadacycline prescription from a large US claims database (10/2018-9/2020) and had an NTM diagnosis within -90 d to +30 d of omadacycline prescription. Patients were classified in the approved or unapproved cohorts based on the approval status of their index omadacycline prescription claim. Risks of 30-day IP and ED visits were compared.

Results: During study period, 172 NTM patients met the inclusion criteria: 117 (68%) had an approved and 55 (32%) were unapproved omadacycline prescription. Comparison of baseline characteristics and 30-day HRU outcomes between the approved and unapproved omadacycline groups are shown in Table 1. HRU significantly decreased after index omadacycline for those with an approved claim, driven by a reduction of IP, and no significant reduction in HRU was seen in the unapproved claim group. The proportion of 30-day post-index IP visits for those with an approved vs unapproved claim was 8% vs 25%, respectively. The overall 30-day IP visits incidence difference was 17%, corresponding to an unadjusted number needed to treat (NNT) of 6.

Conclusions: This study provided the first real world characterization of NTM patients with approved and unapproved claims for omadacycline. A high incidence of unapproved omadacycline claims was observed in this study. The findings suggested that 1 out of 6 patients with unapproved omadacycline claims had a 30-day IP visit that could have been potentially avoided if omadacycline was approved.

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Table 1. Comparison of baseline characteristics and 30-day HRU outcomes in the approved and unapproved omadacycline NTM groups

	Approved N=117				Unapproved N=55			P value
Age, mean ± SD	54.21 ± 18.31				61.58 ± 16.46			< 0.05 *
Sex, n (%)								
Female	75 (64.1%)				39 (70.9%)			0.5
Male	42 (35.9%)				16 (29.1%)			
Region, n (%)								
South	64 (54.7%)				39 (70.9%)			0.2
Northeast	20 (17.1%)				7 (12.7%)			
Midwest	18 (15.4%)				3 (5.5%)			
West	14 (12.0%)				6 (10.9%)			
Index year, n (%)								
2019	48 (41.0%)				21 (38.2%)			0.9
2020	69 (59.0%)				34 (61.8%)			
Index medical insurance, n (%)								
Commercial	26 (22.2%)				20 (36.4%)			0.1
Medicare	5 (4.3%)				7 (12.7%)			0.1
Medicaid	1 (0.9%)				1 (1.8%)			0.5
Government	1 (0.9%)				0 (0.0%)			> 0.99
Index pharmacy insurance, n (%)								
Commercial	62 (53.0%)				28 (50.9%)			0.9
Medicare	36 (30.8%)				27 (49.1%)			< 0.05 *
Managed Medicaid	8 (6.8%)				6 (10.9%)			0.5
Medicaid	4 (3.4%)				1 (1.8%)			> 0.99
Assistance Program	2 (1.7%)				0 (0.0%)			> 0.99
Cash	1 (0.9%)				2 (3.6%)			0.2
CCI, mean ± SD	1.05 ± 1.23				1.45 ± 1.58			0.07
Outcomes	30-Day Pre-OMC Rx	30-Day Post-OMC Rx	Risk Ratio	P value	30-Day Pre-OMC Rx	30-Day Post-OMC Rx	Risk Ratio	P value
30-Day Inpatient visit	0.15	0.08	0.50	<0.05*	0.31	0.25	0.82	0.37
30-Day ED visit	0.04	0.07	1.60	0.32	0.07	0.02	0.25	0.21

Abbreviations: SD: standard deviation, n: number, CCI: Charlson Comorbidity Index, ED: emergency department, OMC: omadacycline, Rx: prescription

Poster 39

Topology of Enterococcus faecalis *LiaF Suggests Complex Interaction with Enterococcal-specific Regulator LiaX*

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Background and Objective: VRE (Vancomycin Resistant Enterococci)-associated infections are prevalent in healthcare settings and pose a significant therapeutic challenge. The lipopeptide antimicrobial daptomycin (DAP) is a last resort option to treat these organisms. Among VRE, mutations that confer DAP resistance (DAP-R) arise in proteins in the three-component signaling system LiaFSR, which is highly conserved in other Gram-positive pathogens. Similar to *Enterococcus faecalis* (Efs), LiaFSR in *Bacillus subtilis* (Bsu) is specifically activated by DAP and, thus, serves as a proxy for studying mechanisms of DAP-R. In Bsu, LiaF inhibits LiaR phosphorylation; however, the current model for DAP-R in Efs positions LiaF as an activator of LiaFSR directly regulated by the enterococcal-specific protein LiaX.

Hypothesis/Goals: The mechanism of interaction between LiaX and LiaF is still unknown, thus we set out to map Efs LiaF topology in vivo to identify potential interaction sites with LiaX and compare structure predictions of Efs and Bsu LiaF to determine if conformational differences between them could account for its opposing roles in regulation.

Methods: LiaF protein predictions were determined through the RoseTTAFold (RoBetta online web server, David Baker, Univ. of Wash.). Structural comparisons were made using the MatchMaker function in UCSF Chimera. Sequence alignments were performed using EMBOSS Needle Pairwise Alignment (EMBL-EBI). Efs LiaF topology was mapped experimentally in *E. coli* DH5a with 2 assays: first, a LacZ-α complementation assay wherein LacZ- α was fused to truncations of LiaF between its predicted TM domains and analyzed through a blue/white colony screen. Second, a similar blue/white colony screen assay was performed with the same LiaF truncations fused to *E. coli* PhoA.

Results and Conclusions: Predicted structures of LiaF from Efs and Bsu exhibited similar domain organization, with 4 N-terminal transmembrane (TM) helices connected to a C-terminal ß-sheet domain by a flexible linker of variable length. When analyzed for structural similarity, the C-terminal domains were the most like one another. Our analysis of the N-terminal domains revealed distinct differences in the orientation of TM helices 2 and 3 in LiaF from Efs compared to Bsu. In vivo topological mapping of Efs LiaF showed that the N- and C-termini are intracellular, and the 4 predicted transmembrane domains likely thread through the membrane as expected. The absence of an obvious binding region for LiaX suggests that the communication between Efs LiaF and LiaX is much more complex than direct physical interaction. Moreover, the similarity between LiaF from Bsu and Efs suggests that other enterococcal-specific proteins like LiaX may account for the contrasting functions LiaF serves in LiaFSR regulation.

Acknowledgments: This work is supported by a training fellowship awarded to KH from the Gulf Coast Consortia, on the Texas Medical Center Training Program in Antimicrobial Resistance (TPAMR), (NIH Grant No. T32AI141349) and NIH R01-AI134637 awarded to CAA.

Poster 40

In Vitro Model to Simulate Multiple Drugs with Distinct Elimination Half-Lives Hudson CS[1], Smith JE[2], Eales BM[1], Tam VH[1,2]

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Background: The prevalence of multidrug resistance in bacteria has been steadily rising, resulting in an increased need for using multiple antimicrobial agents concurrently. Combination therapy of up to four drugs are often necessary for the treatment of multidrug-resistant tuberculosis. Antimicrobial agents used for these infections may have different elimination half-lives in humans. There is an unmet need for *in vitro* models to evaluate the efficacy of these combination therapies to guide early drug development. In order to realistically reflect *in vivo* conditions, these *in vitro* model systems must be capable of simulating multiple pharmacokinetic profiles with distinct elimination half-lives. Current designs only allow for the simulation of up to three agents with distinct half-lives.

Hypothesis/Goals: To facilitate the transition to *in vivo* preclinical/clinical investigation, the goal of this study was to experimentally simulate four pharmacokinetic profiles with distinct elimination half-lives in an *in vitro* hollow-fiber system.

Methods: The mathematical framework guiding this experimental design was previously reported. Briefly, a parallel experimental setup was used to independently connect four supplemental reservoirs (of different volumes) to a central reservoir, which was connected in series with the hollow-fiber cartridge. The target maximum concentration was achieved by direct drug dosing into the central reservoir. Constant dilution of each supplemental reservoir was used to mimic four distinct rates of elimination from the central reservoir. For illustrative purposes, fluctuating exposures of ceftriaxone (CRO) were simulated with distinct half-lives of 1, 2.5, 8, and 12 hours. All doses were given over 30 minutes. Serial pharmacokinetic samples were obtained over 24 hours and assayed for CRO concentration by LC-MS/MS. The observed concentration-time profiles were characterized using a one-compartment model with zero-order input in ADAPT 5.

Results: The observed elimination half-lives were in agreement with the expected values obtained from the mathematical predictions (**Figure 1**). Additionally, the results were reproducible when the experiment was conducted on a different day.

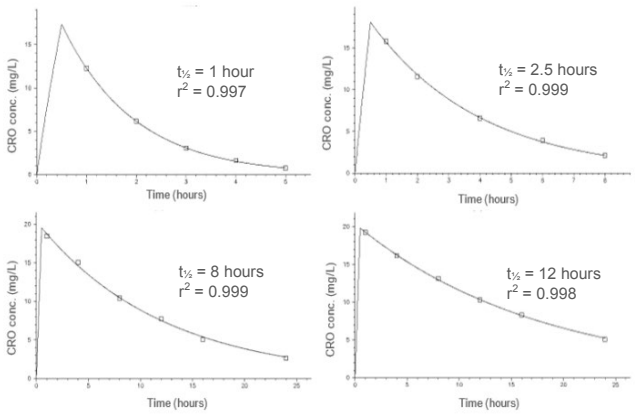

Figure 1: Representative experimentally simulated elimination half-lives using the *in vitro* hollow-fiber model. Half-lives matched the mathematical predictions (n=2): 1, 2.5, 8, and 12 hours. CRO: ceftriaxone.

Conclusions: This *in vitro* experimental design can be used to evaluate the efficacy of up to four-drug combinations against multidrug-resistant bacteria, cancer cell lines, or HIV-infected mammalian cells. The established framework represents an adaptable tool to advance the field of combination therapy.

Acknowledgements: This research was funded by the National Institutes of Health, grant number R01 AI140287-05.

Poster 41

The Effects of Oral Omadacycline and Vancomycin on the Gut Microbiome in Healthy Subjects

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Background: Antibiotic exposure has significant and long-lasting perturbing effects on gut microbiome. Omadacycline is an aminomethylcycline tetracycline with *in vitro* activity against *Clostridioides difficile*. However, the effect of omadacycline on the gut microbiome has not been studied in humans. The purpose of this study was to assess gut microbiome changes in healthy adult volunteers given oral omadacycline and compare to vancomycin which is recommended as one of the first-line treatments for *C. difficile* infection (CDI).

Hypothesis/Goals: To characterize the effects of omadacycline and vancomycin on the gut microbiome of healthy subjects

Methods: This was a single-center, phase 1 microbiome study conducted between 2020-2021. Healthy adults aged between 18 and 40 years were recruited and randomized to receive either oral omadacycline or vancomycin for 10 days. Stool samples were collected at baseline (day 0), during therapy (day 1-10) and follow-up visits (day 13 and 30). Stool DNA extraction was performed using the Qiagen MagAttract Power Microbiome kit. The V4 region of the 16S ribosomal RNA gene was amplified and sequenced using the Miseq platform (Illumina). Six targeted bacterial taxonomic groups were quantified via qPCR. Bacterial abundance and microbiome diversity analysis were performed using CLC Genomics Workbench (Qiagen) and R software.

Results: A total of 16 healthy volunteers aged 26 ± 5 years were enrolled. The majority of subjects were male (63%) and either Caucasian (38%) or Asian (38%). Overall, there was a decrease in alpha-diversity in both vancomycin and omadacycline groups from baseline to antibiotic therapy days. Bacterial abundance and beta-diversity analysis showed different degrees of microbiome changes in subjects who received oral omadacycline and vancomycin. At the phylum level, a proportional increase in Proteobacteria was more pronounced in vancomycin group compared to omadacycline group while Actinobacteria was more preserved in subjects given omadacycline compared to those given vancomycin. At the family level, Enterobacteriaceae was a major driver for the Proteobacteria phylum expansion. A decreased bacterial DNA of *Clostridium coccoides*, *Clostridium leptum*, *Bacteroides thetaiotaomicron*, and Prevotella were observed in vancomycin group.

Conclusions: Overall, both omadacycline and vancomycin resulted in microbiome diversity changes in healthy adult subjects. However, the degree of the changes was distinct in those given omadacycline compared to vancomycin. Further functional microbiome studies are warranted to elucidate these findings.

Acknowledgement: This study was funded by Paratek Pharmaceuticals, Inc as an investigator-initiated grant.

Poster 42

Investigating the Potential of Bacteriophage and Vaginal Bacterial Communities to Limit Uropathogenic* E. coli *Colonization

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Background: Urinary tract infections (UTIs) are the second most frequent bacterial infection affecting ~150 million people worldwide each year. UTIs are common among women and approximately 50% of women will experience at least one UTI during their lifetime. Uropathogenic *Escherichia coli* (UPEC), the main etiological agent for UTIs, gains exposure to the urinary tract from mucosal reservoirs such as vaginal tract where UPEC is a common colonizer. Although FDA-approved antibiotics such as fluoroquinolones, trimethoprim-sulfamethoxazole, nitrofurantoin, and β-lactams are available for the treatment of UTIs, the risk of recurrence and resistance to antibiotics underscores exploration of non-antibiotic approaches to prevent/and or treat UTIs.

Hypotheses: We hypothesize that elimination of UPEC reservoirs such as the vaginal tract will reduce the incidence of UTI and that naturally occurring pathogen-resistant organisms, such as UPEC-targeting (bacterio)phage and/or UPEC-resistant vaginal bacterial communities, can serve as a non-antibiotic method to control UPEC vaginal colonization.

Methods: We test this hypothesis using *in vitro* models of human vaginal epithelial cells (VK2/E6E7) and Humanized MicroBiota mouse (^{HMb}mice) model *in vivo* and UPEC lytic phage and UPEC-resistant vaginal bacterial communities identified using *in vitro* screening. Female ^{HMb}mice were synchronized with 0.5mg β-estradiol administered intraperitoneally 24h prior to vaginal inoculation of 10^7 CFU of UPEC strain UTI89. Beginning 24h post-infection, mice received daily doses of purified UPEC-targeted phage HP3, ES17 (10^8 PFU/mice) and/or UPEC-resistant *Lactobacillus crispatus*-dominant human vaginal communities MVS035 or MVS051 (10^8 CFU/mice) for 5-7 days. The vaginal lumen was swabbed daily to quantify bacterial burdens. After one week, urinary and reproductive organs of mice were harvested to assess UPEC dissemination. We further explored adherence and invasion assays using human epithelial cells VK2/E6E7 to test whether bacteriophage and/or vaginal community cell-free supernatants could prevent cell attachment and invasion by UPEC.

Results: We found that daily dose of phage causes significant reduction in UPEC vaginal burdens after 72h of phage treatment. Similarly, daily dosing of *L. crispatus*-dominant vaginal communities also reduced UPEC CFU compared to the mock-treated group after 72 hours. UPEC dissemination was observed across multiple tissues including vaginal, cervical, uterine, kidney, but burdens were not different between phage or community-treated and mock-treated groups. Additionally, we observed that higher vaginal and cervical UPEC burdens were associated with dissemination to the kidneys. Pretreatment of VK2 cells with the lytic phage also reduces adhesion and intracellular survival of UPEC compared with controls.

Conclusion: Bacteriophage therapy and *Lactobacillus*-dominant vaginal communities could be promising non-antibiotic therapeutic options to reduce UPEC mucosal colonization and limit UTIs.

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Poster 43

Mapping the Determinants of Catalysis and Substrate Specificity of the Antibiotic Resistance Enzyme CTX-M β-lactamase

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Background: Antimicrobial resistance is a growing public health threat, with β-lactamase enzymes causing the largest percentage of resistant clinical infections. β-lactamase enzymes have evolved to hydrolyze even last resort β-lactam antibiotics. This necessitates the rapid design of new antibiotics and β-lactamase inhibitors to provide multiple resources to treat resistant infections. Among β-lactamases, CTX-M enzymes are the most prevalent extended-spectrum enzymes, capable of hydrolyzing a range of β-lactamase antibiotics, including penicillins and the cephalosporin antibiotic, cefotaxime.

Goals: Our goals were to determine the residues within CTX-M enzymes that are responsible for their extended spectrum antibiotic resistance activity and to determine the basis of potential CTX-M resistance against the extended-spectrum cephalosporin, ceftazidime.

Methods: We constructed individual, codon-randomized libraries for 17 residue positions in the CTX-M-14 active site, including amino acids involved in catalysis and those surrounding them. Each library was introduced into *E. coli* and the population was selected, in separate experiments, for wild-type levels of resistance against two antibiotics that CTX-M enzymes readily hydrolyze—ampicillin (a penicillin antibiotic) and cefotaxime (a cephalosporin antibiotic). Additionally, libraries were selected for mutants that hydrolyze the cephalosporin ceftazidime. CTX-M enzymes generally do not efficiently hydrolyze ceftazidime, though some clinical isolates have emerged that contain mutations leading to ceftazidime resistance. Following selection, surviving clones were pooled for each library, DNA was extracted, and Illumina NGS sequencing was used to determine the frequency, and therefore the fitness, of each CTX-M-14 mutant relative to wildtype. To confirm sequencing results and further elucidate the mechanisms of antibiotic hydrolysis by mutant enzymes, we determined functional characteristics for select mutants including steady-state enzyme kinetics, minimum inhibitory concentrations, and X-ray crystal structures.

Results: We have identified residues with stringent sequence requirements that are required for β-lactamase activity versus all substrates tested. We have also identified a residue that can be freely substituted and residues that can adopt a conservative range of mutations while retaining penicillin and cefotaxime activity. Further, we have determined residues responsible for the extended-spectrum β-lactamase activity of the enzyme, defined as those necessary for high levels of cephalosporin, but not penicillin hydrolysis. Finally, we show that omega loop residues (Pro167, Glu166, and Asn170), which are generally essential for ampicillin and cefotaxime activity, do not contribute to ceftazidime hydrolysis.

Conclusions: We have demonstrated that residues considered to be involved in substrate binding are responsible for the extended spectrum activity of CTX-M enzymes against cephalosporins. Additionally, we have shown that these residues contribute to the limited activity of CTX-M against the cephalosporin ceftazidime, but that key omega loop residues are detrimental to hydrolysis of the antibiotic, making mutations to this loop the most likely evolutionary path of ceftazidime resistance by CTX-M β-lactamases.

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Poster 44

Utilizing in vitro *Pathosystems to Identify Novel Antivirulence Therapeutics against Pseudomonas aeruginosa*

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Background: *Pseudomonas aeruginosa* is a multidrug-resistant, nosocomial pathogen that causes acute, life-threatening infections in immunocompromised patients and debilitating chronic infections in those with cystic fibrosis. One key virulence factor is the siderophore pyoverdine, which not only provides the bacterium with iron during infection, but also regulates the production of several secreted toxins. Due to a combination of these functions, pyoverdine production is necessary for *P. aeruginosa* virulence during murine lung infection. We have further developed various *in vivo* and *in vitro* pathosystems using *Caenorhabditis elegans*, murine alveolar macrophages, or human bronchial epithelial cells to model pyoverdine-dependent virulence. We used these models to survey various panels of *P. aeruginosa* clinical isolates and demonstrated that pyoverdine production strongly correlates to pathogen virulence.

Hypothesis/Goals: We aimed to use these model systems to identify several novel classes of antivirulents that target either pyoverdine function or biosynthesis.

Methods: We performed a biochemical screen of ~45,000 compounds from small molecule diversity libraries to identify molecules that directly interact with the siderophore. We also performed a whole-organism, host-pathogen drug screen using *C. elegans*.

Results: Pyoverdine functional inhibitors from the biochemical screen attenuated the production of pyoverdine-regulated virulence factors (exotoxin A and protease PrpL) and rescue *C. elegans* during pathogen exposure. These inhibitors' ability to directly bind pyoverdine was validated by spectral analysis and NMR.

From the *P. aeruginosa* – *C. elegans* drug screen, we identified fluoropyrimidines, most notably 5-fluorocytosine (5-FC) that curtail pyoverdine production without overtly affecting bacterial titer, consistent with an antivirulent mechanism of action. 5-FC was sufficient in rescuing all aforementioned model hosts from *P. aeruginosa*, including murine lung infection. Furthermore, we demonstrated that 5-FC synergizes with the antipseudomonal agent gallium nitrate to inhibit bacterial growth. This is likely due to pyoverdine's ability to sequester the metal, preventing it from reaching cytoplasmic targets. Interestingly, even in the presence of gallium, 5-FC largely functioned as an antivirulent – exerting low selective pressure for resistance. Spontaneous mutants that emerged in the presence of both drugs were resistant to gallium but remained sensitive to 5-FC. We expect these adapted populations to remain less virulent during dual drug treatment due to pyoverdine inhibition.

Conclusions: Overall, these results demonstrate the promise of antivirulence therapeutics against multidrug-resistant pathogens.

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Poster 45

Participant, Geographic, and Surgical Factors Are Associated with Clinical Failure in Registrational Trials for Complicated Intraabdominal Infection

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Background: New antimicrobial drug development for indications including treatment of complicated intra-abdominal infections (cIAIs) is critically important given the spread of antimicrobial resistance. Accurate understanding of geographic variation in participant demographics, clinical characteristics, surgical management and clinical outcomes will better inform clinical trial design for cIAI.

Methods: We reviewed electronic patient-level data (n=5022 participants) from nine Phase 3 noninferiority trials for cIAI submitted to the Division of Anti-Infectives at the US Food and Drug Administration between 2005 and 2019. Geographic region, participant demographics, clinical characteristics, baseline diagnosis, and methods of surgical management were analyzed to identify associations with investigator-assessed outcomes of clinical failure at the test-of-cure visit. We then compared factors associated with clinical failure by geographic region (North America vs non-North America).

Results: Most trial participants were from Eastern Europe (59.3%), followed by South America (13.5%) and North America (13.1%) (Fig. 1). Rates of clinical failure were highest among North American participants (25.6%), and lowest in the Eastern European cohort (5.7%) (Fig. 2A). Participants from North America were significantly more likely to have a BMI $\geq$ 35 kg/m^2 (Fig. 2B), inadequate source control, and percutaneous procedures compared to participants from other geographic regions (*P<0.0001*). In multivariate logistic regression, geographic region, baseline creatinine clearance <60 mL/min, diagnosis of "other cIAI" vs. complicated appendicitis, a body mass index (BMI) of 35.0-39.9 kg/m^2 or $\geq$40 kg/m^2 vs. 18.5-24.9 kg/m^2, inadequate source control, and open or percutaneous procedures vs. laparoscopic procedures were associated with clinical failure (*P<0.05*).

Conclusion: Geographic region, impaired renal function, initial diagnosis other than complicated appendicitis, BMI $\geq$ 35 kg/m^2, inadequate source control and non-laparoscopic procedures were associated with clinical failure in cIAI trial participants. North Americans had significantly higher rates of clinical failure and were more likely to have a BMI $\geq$ 35 kg/m^2, inadequate source control, and percutaneous procedures. These results may help inform trial design and enrollment and underscore the importance of recognizing regional differences in study populations and including populations at risk for poorer outcomes in clinical trials.

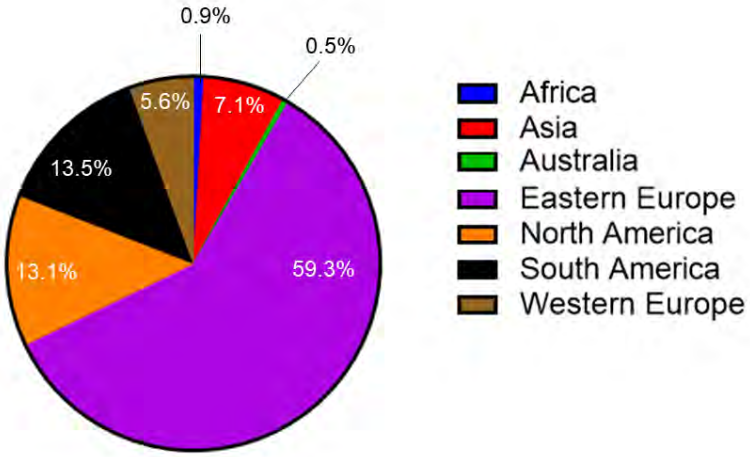

Figure 1. Proportion of participants from each geographic region enrolled in the nine Phase 3 clinical trials with patient-level data for cIAI analyzed in aggregate.

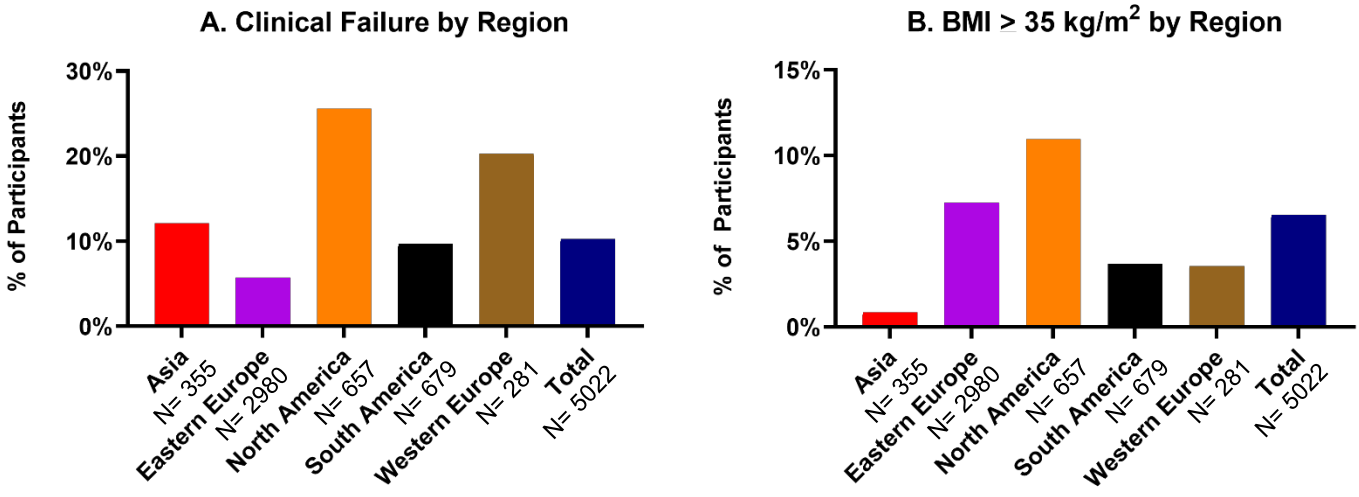

Figure 2. Proportion of participants classified as clinical failure at the TOC visit by geographic region (A). Proportion of participants with a BMI $\geq$ 35 kg/m^2 by geographic region (B). Data from Africa and Australia were not shown due to small sample sizes.

Poster 46

Genotype, Phenotype, and Clinical Outcomes in Hospitalized Patients with Gram-Negative Infections: A Retrospective Review

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Background: Gram-negative bacilli are a major cause of nosocomial infections and are frequently antibiotic resistant. Whole genome sequencing (WGS) allows for correlation of resistance genotype and phenotype with various clinical outcomes. We performed WGS in five medically important pathogens (*Acinetobacter baumannii, Enterobacter cloacae, Escherichia coli, Klebsiella pneumoniae,* and *Pseudomonas aeruginosa*) seen at the Rabin Medical Center to better understand determinants of resistance and impact on outcomes.

Hypothesis/Goals: We hypothesize that specific genotypes are associated with increased mortality.

Methods: 192 blood and respiratory samples were acquired from randomly identified patients with gram-negative infections who were admitted to the Rabin Medical Center from May 2019 to June 2020. Identified isolates were sequenced at the University of Texas Southwestern Medical Center. 168 isolates from 162 patients were included for final analysis. Genomes were analyzed for the presence of resistance determinants, and clinical data was obtained. Fisher's exact test and logistic regression were used to assess for correlations.

Results: Mean age was 70 ± 17 years and 30-day mortality was 21.0% (34/162). Higher levels of albumin corresponded to a decreased risk of 30-day mortality (Odds Ratio=0.162 [0.068, 0.386], p<.0001). Among patients treated with antibiotics in the month preceding their infection (n=47), duration of antibiotic use was associated with a longer hospital stay (p=.0242). 85.2% (n=143) of isolates were obtained from blood, with remaining from sputum or bronchoalveolar lavage (14.8%, n=25). 32/141 (22.7%) of bacteremia patients died within 30 days compared to 2/21 (9.5%) in the pulmonary group. All six patients with multiple isolates survived the initial 30 days. 11 patients were found to have an MDR isolate (11/168 isolates, 6.5%). Commonly encountered beta-lactamase genes included OXA-50 (42/168), TEM-1 (40/168), CTX-M-15 (23/168), OXA-1 (17/168), PDC-3 (14/168), and OXA-23 (10/168). Across all five pathogens, presence of CTX-M-15 and OXA-23 was associated with an increased risk of 30-day mortality (CTX-M-15 OR=2.318; p=.073 and OXA-23 OR=3.28; p=.057).

Conclusions: Certain global resistance markers (CTX-M-15; OXA-23) were present in this population and associated with 30-day mortality. Certain clinical parameters (low albumin) were predictive of mortality in this hospitalized patient population in Israel.

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Poster 47

Elucidation of Molecular Function of BamE in the Essential Bam Complex

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Background: A defining feature of Gram-negative bacteria is the outer membrane (OM). The OM is an essential selective permeability barrier and a major factor of intrinsic antibiotic resistance. OM β-barrel proteins (OMPs) play crucial roles in nutrient transport, signaling, and many serve as adhesion or virulence factors. OMPs are inserted into the OM by the β-barrel assembly machinery (Bam). The Bam complex has emerged as a major target for antibiotic development due to its essential role in the OM biogenesis. However, our poor understanding of molecular details of the Bam complex function presents a major roadblock for rational antibiotic design.

The Bam complex consists of BamA, an OMP itself, and four associated lipoproteins, BamB-E. BamA and BamD are the only essential and best-studied core components. BamB,C,E are individually dispensable, but collectively play an essential function in regulating BamAD core. The specific function of each of these components remains elusive. Previously we discovered that BamE plays a specific role in the Bam complex facilitating assembly of the OMP- dependent surface exposed lipoproteins, such as RcsF (a regulator of capsule synthesis protein F. In the absence of BamE, RcsF is stalled on BamA, blocking its function. This the first report that a lipoprotein rather than an OMP substrate can block the Bam complex activity and may provide alternative or additional routes for Bam complex inhibition.

My new unpublished work focuses on elucidation of molecular function of BamE. We report that BamE interacts directly to both BamA and BamD, stabilizing the BamADE complex, and both interactions are required for RcsF/OMP assembly. We propose that BamE is a bifunctional regulator, it directly and indirectly regulates BamA conformations to ensure functional coordination with BamD.

Hypothesis: BamE stabilizes the interactions between two essential BamA and BamD through its direct interaction and plays regulatory role for BamA/D compatibility in Bam mediated RcsF/OMP complex formation

Methods: Affinity purification approach, Invitro interaction assay with purified proteins, Formaldehyde crosslinking, and Growth curve analysis was used for Phenotype screening.

Results: Our *in vitro* and *in vivo* pull-down approach clarifies the molecular interaction in Bam complex, we have successfully shown that the BamE directly interacting with BamA and BamD to stabilizes the BamA-BamD interaction. Our genetic and biochemical analysis show that BamE and BamD interaction is needed for the Bam complex stability. While, the both BamE/BamA and BamE/BamD interaction is compulsory for Bam complex function.

Conclusion: BamE directly influence the confirmation of BamA, and its direct interaction with BamD. We conclude that BamE is a bifunctional regulator, it directly and indirectly controls BamA conformations to confirm functional coordination with BamD.

Acknowledgments: We thank all members of the Konovalova lab for helpful discussions. The research in the A.K. laboratory is supported by National Institute of General Medical Sciences and the Welch Foundation Research.

Poster 48

Conformational Rearrangements in the Sensory RcsF/OMP Complex Mediate Signal Transduction Across the Bacterial Cell Envelope

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Background: Timely detection and repair of envelope damage are paramount for bacterial survival. The Regulator of Capsule Synthesis (Rcs) stress response is a signaling pathway that can detect damage in the outermost layers of a bacterial cell and transduce the stress signals across the multilayered gram-negative cell envelope to regulate gene expression in the cytoplasm. Previous studies defined the overall pathway, which begins with the sensory lipoprotein RcsF interacting with several outer membrane proteins (OMPs). RcsF can also interact with the periplasmic domain of the negative regulator IgaA, derepressing the downstream RcsCDB phosphorelay. However, how the RcsF/IgaA interaction is regulated at the molecular level to activate the signaling in response to stress remains poorly understood.

Hypothesis/Goals: Previous studies established an overall model for Rcs: Rcs activity is regulated at the level of RcsF C-terminal signaling domain availability in the periplasm for IgaA interaction. Our specific hypothesis is that in response by Polymyxin B treatment, the sensory RcsF/OMP complex undergoes a conformational change, allowing the signaling residues of RcsF, which are normally occluded by the OMP, to be exposed for interaction with IgaA, thereby alleviating inhibition of the phosphorelay.

Methods: In this study, we used a site-saturated mutant library of *rcsF* to carry out several independent genetic screens to interrogate the mechanism of signal transduction from RcsF to IgaA. We analyzed several distinct classes of *rcsF* signaling mutants, their impact on RcsF protein interaction with OMPs and IgaA by pull-down and in vivo biochemical crosslinking, and how they alter the ability of RcsF to signal using the Rcs-dependent transcriptional reporter fusion.

Results and Conclusions: We determined the region of RcsF that is critically important for signal transduction. This region is bifunctional as it is essential for RcsF interaction with both IgaA and OMPs. The mutant analysis provides strong evidence for conformational changes in the RcsF/OMP complex mediating signal transduction to IgaA, and the first direct evidence that OMPs play an important regulatory role in Rcs signaling.

Acknowledgments: We thank Dr. Marcin Grabowicz (Emory University School of Medicine) for sharing the MG2201 strain. We thank all members of the Konovalova lab for helpful discussions. This research is supported by the National Institute of General Medical Sciences R01GM133904 and the Welch Foundation Research Grant AU-1998.

Poster 49

Perspectives on Non-prescription Antibiotic Use Among Hispanic Patients in the Houston Metroplex

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Background: Non-prescription antibiotic use includes taking an antibiotic without medical guidance (e.g., leftover prescription antibiotics, antibiotics given by friends or relatives, or antibiotics purchased without a prescription). Studies have found that non-prescription use is prevalent in many Hispanic communities in the US, ranging from 19-66%. Using non-prescription antibiotics may contribute to antimicrobial resistance, adverse drug reactions, interactions, superinfection, and microbiome imbalance.

Goals: Our prior survey data shows that non-prescription antibiotic usage among Hispanics is endemic, even among those who may have healthcare coverage. This qualitative study seeks to understand why Hispanic patients with healthcare coverage use antibiotics without a prescription. We used the Kilbourne Framework for Advancing Health Disparities Research to identify factors influencing patients' non-prescription antibiotic use.

Methods: Our study includes Hispanic primary care clinic patients with different types of health insurance coverage in the Houston metroplex who endorsed non-prescription use in a previous survey. Semi-structured interviews explored the factors driving non-prescription use in Hispanic adults. Interviews were conducted by telephone, in English or Spanish, between May 2020 and October 2021. Inductive coding and thematic analysis identified motives for non-prescription use.

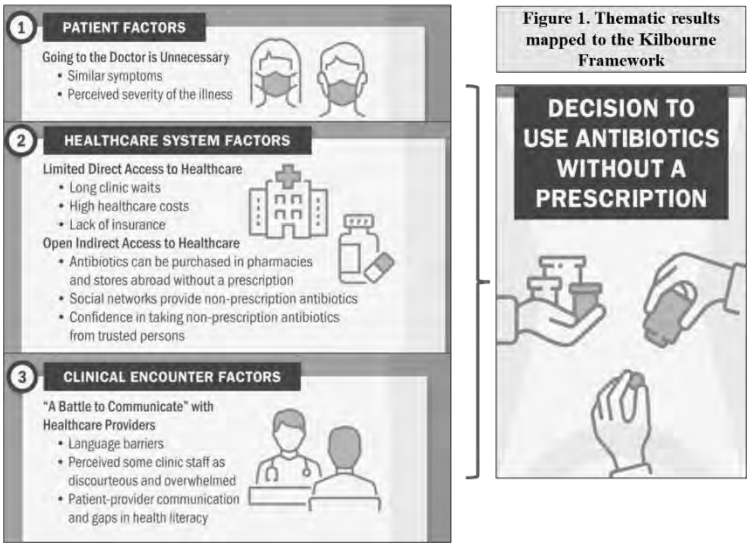

Figure 1. Thematic results mapped to the Kilbourne Framework

Results: Of the 35 participants interviewed, 69% were female. The median age was 48 (range 27-66). Figure 1 shows the thematic results of our interviews mapped to the Kilbourne Framework. Participants reported obtaining antibiotics through trusted persons, buying under-the-counter in US markets, and purchasing without a prescription abroad. Factors contributing to non-prescription use included beliefs that the doctor visit was unnecessary, limited access to healthcare (due to insurance constraints, high costs, and long clinic wait times), and communication difficulties (e.g., language barriers with clinicians and perceived staff rudeness). Participants expressed confidence in medical recommendations from pharmacists and trusted community members, such as community health workers (CHWs) (Figure 1).

Conclusions: Community pharmacists and CHWs may have a pivotal role in delivering a planned future intervention to reduce non-prescription antibiotic use, as they are trusted sources of medical advice. In addition, interventions to improve access to care, address communication barriers, and enhance cultural competency in clinics may promote safe antibiotic use.

Acknowledgments: This work is funded by R01 HS026901 from the Agency for Healthcare Research and Quality and a Ruth L. Kirschstein National Research Service Award (T32HP10031).

Poster 50

An Epidemiologic Exploration of Fidaxomicin Reduced Susceptibility in Clostridioides difficile

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Background: *Clostridioides difficile* infection (CDI) is the most common healthcare associated infection in the USA. The use of the antibiotic fidaxomicin has increased dramatically for the treatment of CDI after a change in the IDSA guidelines placing fidaxomicin as first-line therapy. However, whether antimicrobial resistance to fidaxomicin has increased is unknown.

Hypothesis/Goals: The objective of this study was to assess fidaxomicin susceptibility in *C. difficile* as well as prevalence of *rpoB* mutations at 3428 bp.

Method: A total of 510 samples from hospitalized patients with CDI were obtained from two different healthcare systems between 2016 - 2021. Fidaxomicin minimum inhibitory concentrations (MIC) were determined in accordance with agar dilution method per Clinical and Laboratory Standards Institute (CLSI) guidance. Ribotypes were assessed using fluorescent PCR ribotyping, followed by Sanger sequencing on a subgroup of 40 isolates with elevated MICs to detect SNPs within *rpoB* gene target at position 3428 bp. Growth curves were also performed to analyze the growth patterns of a highly resistant strain (MIC ≥ 64 µg/ml) versus susceptible wildtype strains (MIC ≤ 0.03125).

Results: Fidaxomicin MICs ranged from < 0.03125 - 2 µg/ml with a MIC_{50} of 0.5 µg/ml and MIC_{90} of 1 µg/ml. Ribotype F027 was the most common isolates identified with an MIC range from 0.125 - 2 µg/ml, representing 54% of isolates with MIC of 2 µg/ml. Among 40 isolates, no SNPs were observed at 3428 bp, however, 5 isolates had alternative *rpoB* SNP at other previously unreported base positions. Growth patterns of the highly resistant strain identified a slow and relatively flat curve compared to the competitive and outburst growth of the wildtype isolates.

Conclusion: Fidaxomicin MIC_{50} and MIC_{90} in this study were one dilution higher compared to previous reports. Ribotype F027 represented most of the isolates with MIC of 2 µg/ml. Several new SNPs was observed without any nucleotide change at well-reported 3428 bp position. The study identified that reduced susceptibility isolates may exhibit a fitness cost in growth compared to wildtype isolates.

Poster 51

Activity of Newer Antibiotics Against Carbapenem-Resistant Enterobacterales Isolates - Emory Healthcare, 2016-2021

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Background: Few antibiotics are active against carbapenem-resistant Enterobacterales (CRE), making CRE infections difficult to treat and associated with high mortality. There is limited data on the activity against CRE of 3 newer beta-lactam/beta-lactamase inhibitor (BL/BLI) combinations: imipenem-relebactam [I-R], ceftazidime-avibactam [CZA], and meropenem-vaborbactam [MVB].

Goals: To evaluate rates of resistance and trends over time, to newer BL/BLI in a sample of clinical CRE isolates collected from an academic healthcare system from 2016 to 2021.

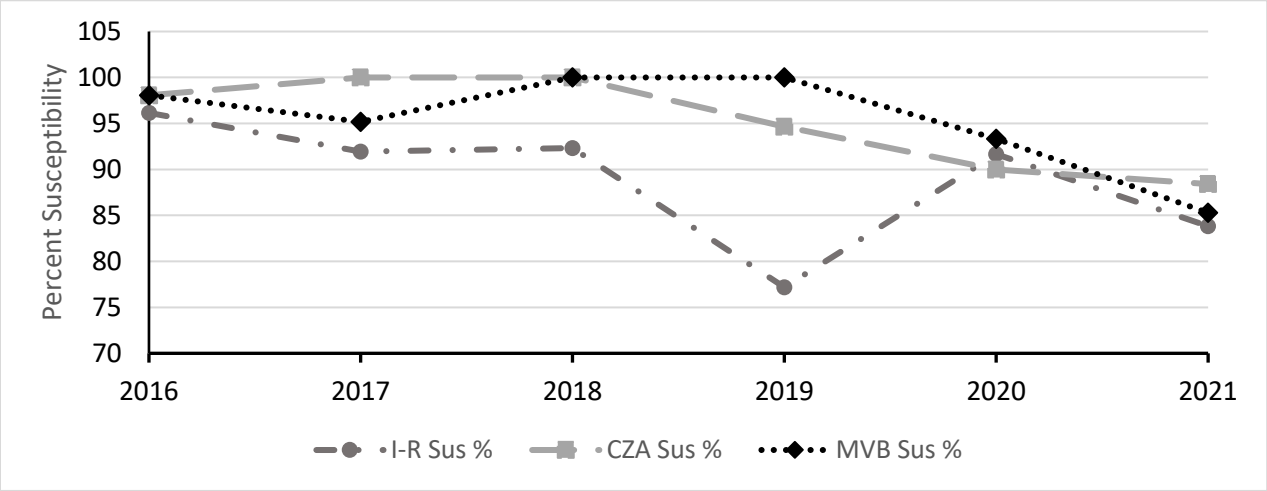
Methods: We created an antibiogram for carbapenem-resistant *Enterobacter cloacae*, *Escherichia coli* and *Klebsiella pneumoniae* isolates collected between 2016–2021 as part of routine clinical care from two > 500-bed hospitals in a single academic healthcare system. The first isolates per patient were tested for susceptibility to I-R, CZA, and MVB by broth microdilution or E-test.

Results: Of 326 CRE isolates, 73 (22%) were from sterile sites, 151 (46%) from urine, 43 (13%) from the respiratory tract, and 59 (18%) from other non-sterile sites. For *E. cloacae* (n=149), 91% were susceptible to I-R, 95% to CZA, and 99% to MVB. For *E. coli* (n=54), 89% were susceptible to I-R, 94% to CZA, and 93% to MVB. For *K. pneumoniae* (n=123), 85% were susceptible to I-R, 94% to CZA, and 90% to MVB (Table 1). Over time, decreases in the activity of all 3 new BL/BLI were noted. Compared to 2016, the percentage of susceptible CRE isolates decreased by 13% (96% to 83%) for I-R, 10% (98% to 88%) for CZA, and 13% (98% to 85%) for MVB.

Conclusions: From 2016-2021, the most active BL/BLI against CRE was CZA. While newer BL/BLIs remain highly active against most CRE, the observed decrease in susceptibility over time suggests a need for ongoing antibiotic stewardship.

Acknowledgements: Supported by the Stimulating Access to Research in Residency (StARR) of the National Institutes of Health under Award Number R38AI140299 and the Heteroresistance Interdisciplinary Research Unit of NIH/NIAID under Award Number 1U19AI15808-01.

FIGURE 1: Percentage of carbapenem-resistant *Enterobacter cloacae*, *Escherichia coli,* and *Klebsiella pneumoniae* isolates susceptible to three novel beta-lactam/beta-lactamase inhibitor antibiotics, 2016-2021



Poster 52

Reliability of Gram Stain with Culture in Samples Obtained by Cotton Swab with Agar Gel Medium

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Background: In standard practice, Gram stain and culture are regularly done on infected sites and preliminary Gram stain results are often used to inform antibiotic therapy prior to completion of cultures. Prior studies have investigated the congruence of these two techniques, attributing errors to a variety of factors including poor specimen quality, smear preparation, and smear interpretation. However, within specimen quality, the efficiency and precision of individual sampling methods have not been addressed. Sites with concern for infection are often sampled using sterile cotton swabs that are stored in transfer medium; these have been shown to have poor rates of transfer of inoculum because substantial amounts of bacteria remain on the swab and within the agar. As such, it is possible that samples obtained by cotton swab stored in agar medium prior to being sent to the laboratory are particularly likely to result in a mismatch between Gram stain and culture.

Hypothesis/Goals: We hypothesized that Gram stains would be less sensitive than culture in specimens obtained in conventional fashion by cotton swab stored in agar gel.

Methods: In patients referred to the Infectious Disease service for consultation in a 4-week period, we sought patients who had swabs of an infected site sent for Gram stain and culture during that admission. When the same sites showed prior infections, we included samples sent from these subjects within the preceding 3 months. The results of Gram stain or culture were stratified into subgroups by laboratory ratings. For Gram stain, organisms were either present or not seen. For culture, results were categorized by growth in broth only or rare growth, few growth, and moderate or many growth.

Results: In 59 swab samples from 31 patients, 17 samples had completely congruent results of Gram stain and culture. 37 samples had Gram stains that were negative for organisms that grew in culture. 18 of these samples had growth only in broth or rare growth, 14 showed few growth, and 5 showed moderate or many growth. There were 5 samples that showed organisms on Gram stain that did not grow in culture. 1 sample had both discrepancies with different organisms.

Conclusions: Discrepancies between Gram stain and culture can be unexpected and may derail management of infection. We attribute negative Gram stains with positive cultures to problems with specimen collection and positive Gram stains with negative cultures to prior antibiotic therapy. The rate of incongruence between Gram stain and culture for samples obtained with cotton swab warrants further study. A prospective study would likely elucidate these results.

Acknowledgments: None.

Poster 60

Evaluation of Cefazolin High Inoculum Effect in Methicillin-Susceptible Staphylococcus aureus (MSSA) Using Gold standard MICs and Rapid Colorimetric Test (RCT)

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Background: Cefazolin is a 1st generation cephalosporin that has been in use worldwide since the 1970s. It has seen increasing use for the treatment of MSSA infections given its favorable dosing and side effect profile as compared to anti-staphylococcal penicillins. Recent studies suggest that the use of cefazolin for infections with MSSA that exhibit the high-inoculum effect (CzIE) are associated with cefazolin therapeutic failure. The CzIE is defined as an increase in cefazolin MIC (≥16mg/L) at high bacterial inoculum (~$5x10^7$ CFU/ml) while remaining susceptible (≤8 mg/L) at standard inoculum (~$5x10^5$ CFU/ml). A rapid diagnostic CzIE colorimetric test (rCT) was previously developed to detect staphylococcal-β-lactamase activity in supernatant after ampicillin induction.

Hypothesis/Goals: Here, we aim to evaluate the CzIE by gold-standard broth microdilution methodologies and using the rCT.

Methods: We studied 33 isolates of MSSA that were collected from patients with bloodstream infections hospitalized at University of Florida Shands Hospital. Cefazolin MICs were determined by the broth microdilution method using standard and high inocula in Muller-Hinton broth following CLSI recommendation. All samples were evaluated in triplicate. Controls included MSSA strain *S. aureus* TX0117 (harbors a type A BlaZ and exhibits the CzIE.), *S. aureus* strain ATCC 29213 (harbors type A BlaZ but does not exhibit the CzIE) and ATCC 25923 (no BlaZ and negative CzIE). In addition, we performed the rCT using Brain Heart Infusion (BHI) broth (Oxoid limited, UK). Overnight colonies of *S. aureus* strains were inoculated in BHI broth with ampicillin (150 µg/ml). Suspensions were vortexed to mix three times for two minutes, with two incubations (35±1℃) for 10 minutes in between. After the final incubation, samples were centrifuged, and supernatants were mixed with nitrocefin (final concentration 400µM). Samples were incubated at room temperature, protected from light, and monitored for color change every 15 minutes for 2 hours. Data were recorded by 3 different readers.

Results: All of the 33 isolates were susceptible to standard inoculum, yet 3 isolates (9%) displayed the CZIE (MIC ≥16 µg/ml). The rCT test showed sensitivity and specificity of 66.6% and 90%, respectively. 6 % (n=2) of the strains were positive by rCT and exhibited high CzIE by broth microdilution, 9% (n=3) of the strains that were negative for CzIE MICs gold standard and positive by RCT. In addition, 3% (n=1) strain was positive for CzIE by MICs gold standard methodologies and negative by RCT.

Conclusion: The RCT performed similar to reference broth microdilution in this cohort of MSSA bloodstream isolates. The RCT is an inexpensive, easy, and time-efficient method to detect MSSA with the CzIE.

Funding sources: National Institute of Allergy and Infectious Diseases, NIH grants R01AI1346302 to C.A.A.

Poster 54

The Microbiota-Gut-Brain Axis As A Risk Factors For The Development Of Depressive Disorders After Bariatric Surgery

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Background: In the short-term period after the surgical treatment of morbid obesity, most patients experience a reduction in the severity of depressive symptoms. However, they are observed to in-crease after 36, 48, and 60 months after above mentioned surgical treatment.

Goals: The aim of the study was to assess the frequency of depressive disorders among patients after bariatric surgery, as well as: assessment of the diet, assessment of selected parameters of the intestinal barrier integrity, and assessment of the composition of the gut microbiota as potential causes of the development of depressive disorders among patients ≥ 6 months after bariatric surgery using SG and Roux-en-Y gastric bypass (RYGB) methods.

Methods: This study involved 200 adult patients who underwent bariatric surgery. The assessment of mental state was done by using the Beck scale as well as the Hamilton scale The eating habits were analysed by calculating the International Diet Quality Index. The laboratory tests included the assessment of the concentration of zonulin, SCFAs and the composition of the gut microbiota in the stool, LPS, LBP, occludin in the blood.

Results: Depressive disorders were reported in 45% of patients. The composition of the gut microbiota correlated with the intensification of depressive symptoms expressed using the Beck Scale. Microorganisms associated with the occurrence of gastrointestinal symptoms were significantly associated with the increased concentration of isobutyric acid in the faeces of these patients.

Conclusions: In postoperative period, proper balancing of diet should be taken into account in or-der to support the proper functioning of the intestinal barrier and potentially reduce the risk of developing depressive disorders related to the microbiota-gut-brain axis.

Acknowledgements: This research received no external funding.

Poster 55

Penicillin-Susceptibility among* Staphylococcus aureus *Skin and Soft-Tissue Infections in Children: Prevalence and Clinical Impact

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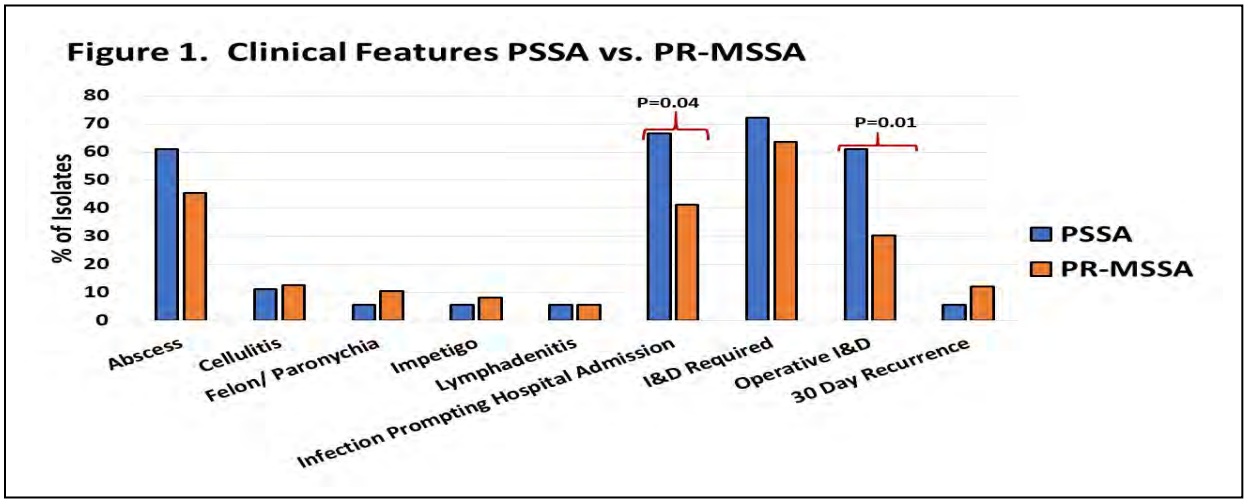
Background: Shortly after its introduction into clinical practice, *Staphylococcus aureus* isolates gained resistance to penicillin via the acquisition of β-lactamases. By the 1960s, these strains became the dominant staphylococci in clinical practice. However, a number of centers have recently described an increase in the proportion of methicillin susceptible *S. aureus* (MSSA) which are also susceptible to penicillin (PSSA). In our center we have recently observed the emergence of PSSA in osteoarticular infections. Little data are available regarding the prevalence or impact of PSSA in pediatric skin-and-soft-tissue infections (SSTI).

Methods: MSSA SSTI isolates were obtained through an ongoing surveillance study at Texas Children's (TCH) from 1/2017-12/2021. Twenty community-acquired MSSA SSTI isolates were chosen at random from every six-month interval during the study period, for a total of 200 isolates to be screened. All isolates underwent PCR for *blaZ* β-lactamase, PVL genes and *agr* group. All *blaZ* negative isolates then underwent penicillin susceptibility testing using macrobroth dilution. Isolates which were *blaZ* negative and had a penicillin MIC ≤ 0.125 μg/ml were regarded as PSSA with the remainder regarded as penicillin-resistant MSSA (PR-MSSA).

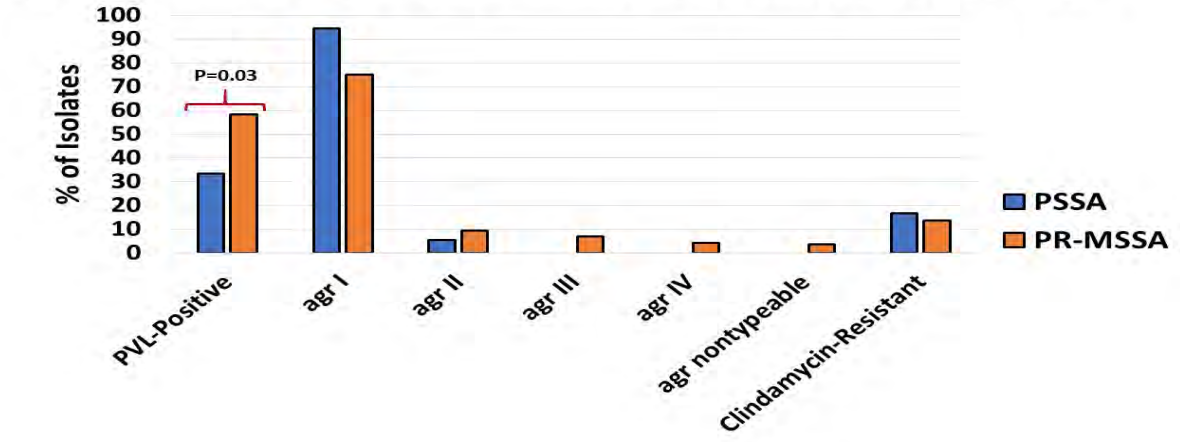
Results: During the study period 1701 MSSA SSTI isolates were collected with 200 examined for penicillin susceptibility. The overall median age of subjects was 4.2 years (IQR: 1.6-10.5). PSSA accounted for 9% of isolates during the study period; the annual frequency of PSSA varied from 5-17.5%. PSSA and PR-MSSA cases were similar with respect to age, demographics, anatomic site of infection and rates of prior antibiotic exposure. Subjects with PSSA SSTI were more often admitted to the hospital and underwent surgical intervention (**Figure 1**) and were less often PVL-positive (**Figure 2**). In multivariable analyses, penicillin susceptibility was independently associated with hospital admission.

Conclusions: PSSA account for a small but significant proportion of MSSA SSTI in children. Clinically distinguishing patients with PSSA and PR-MSSA SSTI is challenging. However, PSSA SSTI were independently associated with higher rates of hospital admission as well as the need for surgical intervention suggesting a significant clinical impact.



Poster 55

Figure 2. Molecular and Microbiologic Features PSSA vs. PR-MSSA



Poster 56

Intra-Phylum Differences of the Firmicute polC Gene

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Background: The novel antibiotic, ibezapolstat (IBZ) in clinical development for the treatment of *Clostridioides difficile* infection inhibits the PolC-type DNA Polymerase III (PolC). Present in all Firmicutes, IBZ has been shown to have selective activity against only certain species in this phylum for unknown reasons. We hypothesized that the taxonomic conservation of the Firmicute *polC* may explain the narrow spectrum selectivity of IBZ.

Hypothesis/Goals: The goal of this study was to explore the taxonomic conservation of *polC* across the evolutionary radiance of Firmicutes.

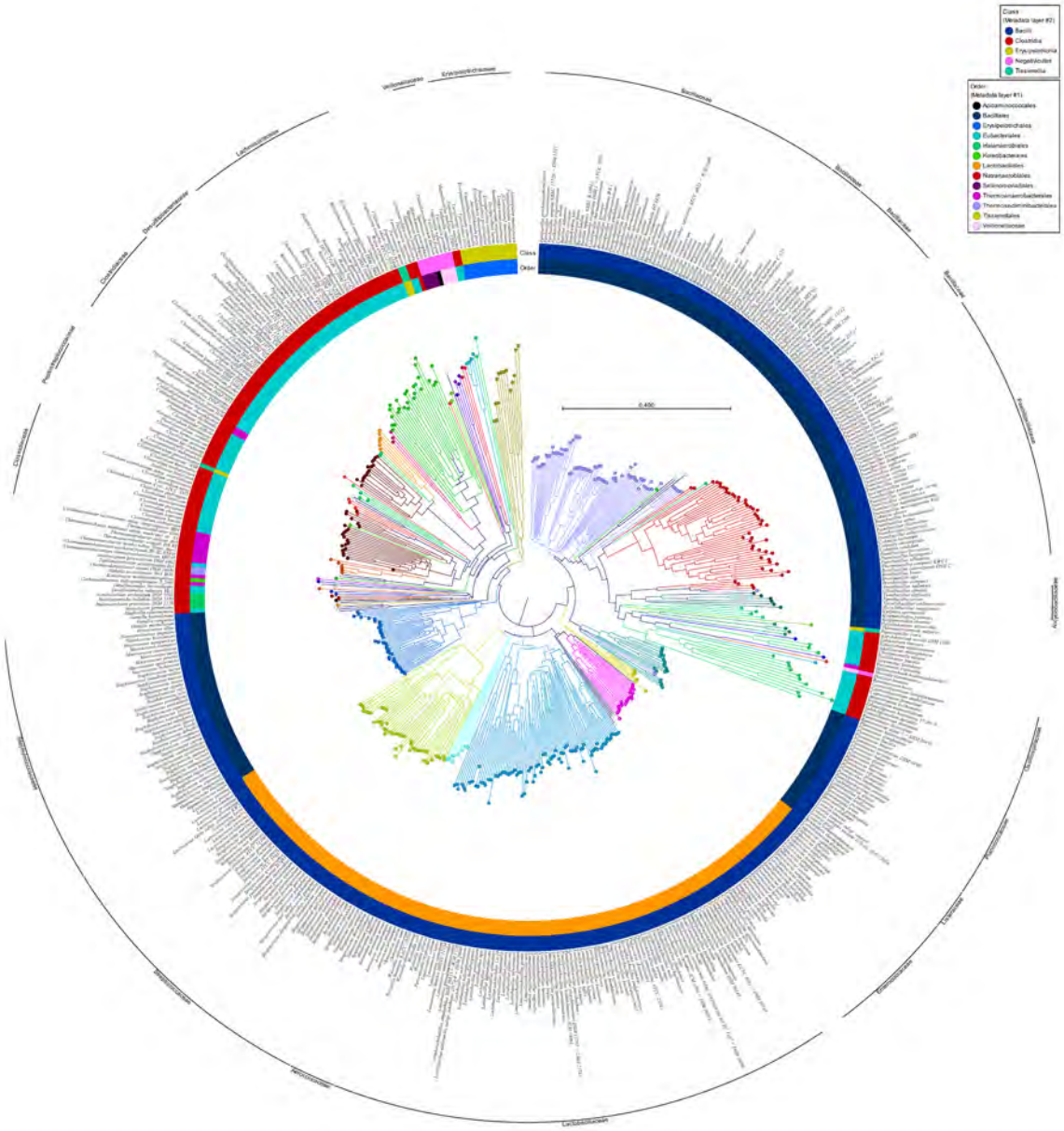
Methods: A Firmicute-specific custom microbial database of 685 representative species' fully annotated genomes was built using CLC Genomics Workbench v.22.0.2. An extraction of '*polC'* annotated regions resulted in 667 genes annotated by automated homology, ab initio prediction, or functionally associated with PolC. Sequences were included if greater than 2400 nucleotides in length and encode PolC. The resulting 542 *polC* nucleotide sequences were analyzed for phylogenetic relatedness by 'Very Accurate' alignment and tree visualization by the Neighbor-Joining algorithm and Jukes-Cantor distance in CLC.

Results: We present the resulting circular phylogenetic tree of 542 Firmicute *polC* sequences, below. We find branch tips cluster according to class (outer ring), order (inner ring) and family (colorized branches) and deep nodes reflect the currently accepted evolutionary radiance of Firmicutes. Within the class Clostridia, we find the Peptostreptococcaceae *polC* node (to which *C. difficile* belongs) inserts within the Clostridiaceae branches. Finally, the Lachnospiraceae *polC* node closely relates to Clostridiaceae and Peptostreptococcaceae *polC,* an interesting finding for further investigation.

Conclusions: We performed the first phylogenetic analysis of the *polC* gene using representative genomes across the entire Firmicute phylum. The *polC* gene has a surprising level of conservation across families within the Firmicutes and may not explain the specificity of IBZ. MIC testing in underway to confirm these results.

Acknowledgements/Funding sources: Acurx Pharmaceuticals

Poster 56



Poster 61

Virulence Factors of Multi-drug Resistant Aeromonas *Isolates Elucidated Using RNA Sequencing*

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Background: *Aeromonas* is increasingly recognized as a formidable human pathogen. It causes a variety of diseases including soft tissue infections, necrotizing fasciitis, and septicemia. Since it has only recently emerged as a globally impactful pathogen, comparatively little is known about the specifics of its virulence or pathogenicity. Its growing propensity for antibiotic resistance including carbapenem resistance poses a huge challenge to public health. There is a need to further our understanding of this pathogen.

Hypothesis/Goals: Using whole genome sequencing (WGS) and RNA sequencing, we seek to measure and compare changes in gene expression *in vivo* verses *in vitro* to identify unique *Aeromonas* virulence factors for future investigation.

Methods: Data from all confirmed *Aeromonas* infections from the Gulf Coast region between January 1, 2008 and December 31, 2021 were collected for analysis. Data include clinical syndrome at presentation, antimicrobial susceptibilities, empiric antibiotics used at treatment, and treatment outcome. *Aeromonas* isolated from three fatal cases which demonstrated multi-drug resistance were selected for full panel antimicrobial susceptibility testing and WGS. RNA sequencing was performed on two of these isolates under both *in vitro* (grown in LB at 37°C incubation) and *in vivo* (grown in previously established mouse infection model. Recovered from peritoneal cavity after 4-6 hours).

Results: 112 isolates from 105 patients were included in the clinical analysis study. Clinical syndromes upon presentation included soft tissue infections (69.52%), traumatic wound infections (27.62%), intraabdominal infections (20.0%), and bacteremia (12.38%). The most frequently used antibiotics for treatment were vancomycin (50.48%), piperacillin-tazobactam (41.9%), and meropenem (12.38%). Infections treated with meropenem and piperacillin-tazobactam showed clinical resistance rates of 58.7% and 28.85%, respectively. ICU admission was required in 32.38% of cases and the case fatality rate was 8.57%. Three isolates from fatal cases which were subjected to full panel antimicrobial susceptibility testing proved resistant to amoxicillin, ampicillin, and cephalosporins. One showed broad spectrum resistance to carbapenems. WGS found the presence of antimicrobial resistance (AMR) genes including mcr-3, blaOXA, and cphA in all three isolates. RNA sequencing data showed a total of 79 potential virulence factors were upregulated *in vivo* at a log fold change of ≥3 in both isolates. Among these virulence factors include genes related to iron uptake/transport, type 3 secretion system, flagellar expression, quorum sensing, and a number of unidentified hypothetical proteins which need further investigation. 12 genes related to cellular export such as macrolide transporter MacAB were also upregulated at a log fold change of ≥3, which may contribute to antibiotic resistance.

Conclusions*:* Recovering and sequencing RNA from a peritoneal mouse infection model has yielded data that has both validated the use of previously established virulence factors and identified new gene targets of investigation.

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Poster 62

***CL Synthases Play Redundant Roles And Are Required for Membrane Remodeling in Daptomycin Resistance* Enterococcus faecalis**

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Background: Daptomycin (DAP) is a lipopeptide antibiotic targeting anionic phospholipids (APLs) at the division septum, and resistance (DAP-R) has been associated with activation of the *E. faecalis (Efs)* LiaFSR response and redistribution of APL microdomains (predicted to contain cardiolipin, CL) away from the septum through the action of an effector protein, LiaY. *Efs* encodes two CL synthase genes, *cls1* and *cls2*. While changes in Cls1 are associated with DAP-R, the exact roles of each enzyme are unknown including their link to the LiaFSR system.

Hypothesis/Goals: This work aims to establish the roles of both enzymes in DAP-R in *Efs* in order to provide insights into cell membrane remodeling associated with the DAP-R phenotype.

Methods: *cls1* and/or *cls2* were deleted from *Efs* OG117 and OG117Δ*liaX* (a DAP-R strain with an activated LiaFSR response). qRT-PCR was used to study gene expression profiles of *cls1* and *cls2* in the *cls* mutants. Membrane lipid content was analyzed using hydrophilic interaction chromatography-mass spectrometry. Mutants were characterized by DAP minimum inhibitory concentration (MIC) using E-test and localization of APL microdomains with 10-N-nonyl-acridine orange (NAO). The bacterial two hybrid system was used to evaluate protein-protein interaction. Fluorescence microscopy was used to evaluate protein co-localization using GFP, mCherry, or tetracysteine tagged proteins of interest (Cls1 and LiaY).

Results: qRT-PCR assays showed upregulation of *cls1* and *cls2* in exponential phase of DAP-R *Efs* OG117Δ*liaX* relative to *Efs* OG117. *cls1* continued to be upregulated in stationary phase. Deletions of either *cls* resulted in upregulation of the remaining *cls* independent of the genetic background. Lipidomics analysis confirmed that deletion of both *cls* is required to completely eliminate CL content. Development of DAP-R resulted in a change of membrane lipid content, of note, an increase in CL with no significant difference in phosphatidylglycerol compared to DAP-S. Evaluation of CL species in DAP-R shows a shift towards species containing longer fatty acid chains and higher unsaturation levels. The double deletion of both *cls* genes lowered the DAP MIC relative to the parent strain and restored septal localization of APL microdomains. Interaction studies confirmed that LiaY interacted with Cls1, but not Cls2. These interactions were then able to be confirmed with fluorescence microscopy demonstration overlay of LiaY-mCherry and GFP-Cls1 at septal regions in the DAP-S strain and non-septally in the DAP-R condition.

LiaY-mCherry and Cls1 containing a tetracysteine tag were independently co-localized to APL microdomains stained with NAO.

Conclusions: While Cls1 is predominantly associated with DAP-R, we show a functional redundancy between Cls1 and Cls2 in both cell membrane homeostasis and in DAP-R. Cls1 interacts with the LiaFSR system, likely through LiaY, and re-localization of both proteins ultimately is responsible for the altered localization of APL microdomains that divert DAP away from its targets at the bacterial division septum.

Acknowledgments: R01 to CAA

Poster 53

Prevalence of Using Antibiotics Without a Prescription in a Pediatric Population

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Background: Non-prescription antibiotic use (taking antibiotics without a prescription) among pediatric populations is understudied in the United States (US). A previous national, internet-based 2018 survey found that 92% of parents had leftover prescription pediatric antibiotics, and nearly 75% reported giving their leftover antibiotics to other children or adults.

Goal: We studied the prevalence of pediatric non-prescription use in a racially and ethnically diverse sample of parents and caregivers of children under 18 years in safety net clinics in the Houston area. We explored the sources whereby parents and caregivers obtained antibiotics without a prescription and investigated the symptoms that drive non-prescription use in children. We also explored the types of antibiotics used, duration of use, and the storage of antibiotics.

Methods: Interviewer-administered surveys were conducted in English and Spanish with parents and caregivers of eligible children receiving care at two Texas Children's Health Plan clinics in Houston, TX. Participant recruitment and interviews occurred from January 2021 to April 2022. Descriptive analysis was used to determine the prevalence of prior pediatric antibiotic non-prescription use, storage practices, and intended reason for antibiotic use (defined as intention to use antibiotics without a prescription or medical guidance for their child).

Results: Of 322 participants surveyed, the majority were female (94%), and the median age was 34 (range 18-69). Participants identified as Hispanic/Latino (51%) and Black/African American (44%). In total, 54 (17%) participants completed the survey in Spanish. Although few participants (n=3) reported previously using non-prescription antibiotics for their children, 21% reported storing antibiotics at home. Commonly stored antibiotics were: amoxicillin (n=52), clindamycin (n=10), cephalexin (n=4) followed by penicillin (n=3) and trimethoprim/sulfamethoxazole (n=2). 46 (14%) of surveyed participants reported intention to give non-prescription antibiotics to their children. When asked whether a given reason would induce them to give antibiotics to their child without a prescription, the most common reasons were ear infection, bronchitis, and sinus infection followed by fever, urinary tract infection, and sore throat (Figure 1).

Conclusions: More than 1 in 5 participants surveyed reported storing antibiotics at home, potentially increasing the likelihood of giving antibiotics to a child without consulting a healthcare provider. Our preliminary findings reveal some of the reasons that may drive parents and caregivers to give non-prescription antibiotics to their child and will help development of an antibiotic stewardship intervention to decrease this unsafe practice.

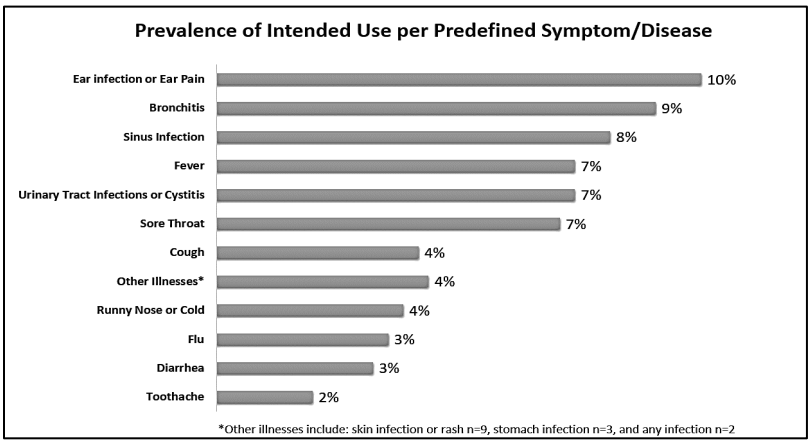

Figure 1. Prevalence of Intended Use per Predefined Symptom/Disease

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Poster 63

***LiaF is necessary for LiaX-mediated resistance against daptomycin and antimicrobial peptides in* Enterococcus faecalis**

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Background: Daptomycin (DAP) resistance in enterococci is mediated by the LiaFSR three-component regulatory system. Mutations in *liaF* have been associated to activate LiaFSR, with increased expression of *liaX*, a major effector of the system leading to DAP resistance. LiaX functions by recognizing DAP in the extracellular medium and serves as a signal transduction molecule. However, the role of LiaF in signaling and its relationship with LiaX are not yet determined.

Methods: A *liaF* mutant in *E. faecalis* OG117 was obtained by adding four stop codons at amino acid positions 11-14 (OG117*liaF**$_{11\text{-}14}$) using a CRISPR-Cas9 system. We complemented the mutant *in cis* by restoring wild-type *liaF* in its chromosomal location (OG117*liaF**$_{11\text{-}14}$::*liaF*). The strains were confirmed with whole genome sequencing (WGS). Anionic phospholipid (AP) microdomain distribution was evaluated by fluorescent microscopy using 10-*N*-nonyl-acridine-orange (NAO). LiaFSR activation was evaluated by surface expression of LiaX via ELISA. DAP MICs were performed by broth microdilution in the presence/absence of exogenous LiaX (eLiaX). Minimal Bactericidal Concentration (MBC) was performed and the killing assays with LL37 (50µg/ml) and DAP (1.5µg/ml) in triplicate was also done in the presence and absence of eLiaX.

Results: Truncation of *liaF* (OG117*liaF**$_{11\text{-}14}$) did not have any effect on DAP MICs compared with the wild type (OG117) and complemented strain (OG117*liaF**$_{11\text{-}14}$::*liaF*). However, the DAP MBC decreased 2 fold in OG117*liaF**$_{11\text{-}14}$ (16 µg/mL vs 32 µg/mL for the wild type and complemented strains, respectively). AP microdomain distribution or LiaX surface expression of the mutant did not show any change compared to wild type and complemented strain. No additional mutations were observed by WGS in the mutant. In the presence eLiaX, DAP MIC increased 8-fold in wild-type OG117 but remained within susceptible range (1 µg/mL) in the mutant OG117*liaF**$_{11\text{-}14}$. Complementation of *liaF* restored the increase in DAP MIC in the presence of eLiaX. In the LL37 killing assay, survival of OG117 was significantly increased with the addition of eLiaX (2.9% vs 11.8%, respectively, *P* 0.005). Addition of eLiaX was unable to rescue OG117*liaF**$_{11\text{-}14}$ in the presence of LL-37 (2.4% vs 2.5% respectively, *P*=0.670), but was able to increase survival in the complemented strain (4.3% vs 10.29%, respectively, *P* 0.029). A similar trend was seen in the DAP killing assay, with increased survival for OG117 (7.1% vs 15.45% (P <0.0001) and OG117*liaF**$_{11\text{-}14}$::*liaF* (1.32% vs 1.31% P 0.925), but not OG117*liaF**$_{11\text{-}14}$ (8.2% vs 15.2% P 0.029).

Conclusion: LiaF is required for the resistance phenotype and tolerance to the cathelicidin LL37 and DAP in *E. faecalis* OG1RF. These results suggest that LiaF is part of signal transduction pathways that involves LiaX, as a part of the LiaFSR stress response.

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Poster 64

Microbial Therapeutics to Prevent ExPEC Colonization and Disease

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Extraintestinal pathogenic *Escherichia coli* **(ExPEC)** are the most common cause of extraintestinal infections worldwide. ExPEC are versatile bacteria, able to infect nearly all sites of the body, including: blood, urinary tract, and the brain. Global rates of ExPEC morbidity and mortality are steadily increasing, predominantly driven by the emergence of multidrug resistant strains. To date, there are no vaccines or non-antibiotic treatments available and novel therapeutic options are gravely needed to combat this emerging threat. ExPEC behave as commensals while in the gastrointestinal tract **(GIT)** and only cause disease upon dissemination. To disseminate to non-intestinal sites and cause infection, ExPEC must first outcompete and coexist with the native microbial community of the GIT. The necessity of GIT establishment as a precursor to extraintestinal infections provides an opportunity to target ExPEC colonization as a preventative measure to disease.

We predict that administration of microbial communities that enhance colonization resistance against ExPEC establishment in the GIT will dramatically reduce ExPEC infections. To achieve these goals, we will use simplified human microbial communities previously generated through dilution of fecal samples. Using a method developed in our laboratory, *in vitro* minibioreactor array **(MBRA)** platforms, we can rapidly screen these simplified microbial communities for inhibition of ExPEC colonization.

To date, we have identified two simplified microbial communities which successful inhibit ExPEC colonization in our MBRAs. These communities will be further tested in a humanized microbiota mouse model of ExPEC colonization. Following identification of simplified communities which successfully and unsuccessfully provide colonization resistance in vivo we will use a comparative genomic sequencing approach to identify the major organisms common among resistant communities. **We hypothesize that select simplified microbial communities will prevent *in vitro* and *in vivo* ExPEC colonization.**

This project is funded by The Gulf Coast Consortia MBID Training Program, NIAID Grant No. T32 AI055449-17

Poster 65

Simplified Microbial Communities as Antibiotic Alternative in Treatment of* Clostridioides difficile *Infection

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Background. Human fecal microbial transplantations (FMT) restore the homeostasis within the gut environment that resists *Clostridioide difficile* and are an effective treatment option in recurrent *C. difficile* infections (CDI). However, safety concerns of FMTs arise due to indications that acute and chronic disease can be transferred and long-term effects on human health remain unknown, in addition, they have yet to be regulated by the Food and Drug Administration (FDA). Due to *C. difficile* being classified as an urgent threat by the Center for Disease Control and Prevention (CDC), there is an immediate need for an alternative treatment option that is safe and does not pose short or long-term adverse outcomes to human health.

Hypothesis/Goals. In this study we identified and are aiming to characterize multiple defined and simple microbial communities originating from the human intestine that are aimed to prevent CDI and disease recurrence.

Methods. Using a dilution/extinction approach coupled with rapid screening of resulting simplified communities in minibioreactor arrays, four simplified human fecal microbial communities consisting of 15-30 members that reduce *C. difficile* invasion were identified. These communities were also tested in an in vivo humanized microbiota mouse model. To get a better understanding of key organisms that are required to resist the invasion to the pathogen metagenomics were compared between invasion reducing communities and invasion sensitive communities.

Results. The four identified communities clustered into distinct community types and shared less than 5 OTUs that were > 0.1% abundant. In the humanized microbiota mouse model, those communities were able to significantly reduce the severity of initial CDI and limit susceptibility to disease relapse. Comparative analysis of fecal microbiomes from treated mice demonstrated that simplified communities accelerated recovery of indigenous bacteria and led to stable engraftment of some of the OTUs from simplified communities. Fourteen key microbes were identified that either positively (four microbes) or negatively (10 microbes) correlated with *C. difficile* abundance. Individual strains have been isolated from the communities and further studies are aimed to characterize each individual isolate and reconstitute the communities one strain at a time.

Conclusions. Using a dilution/extinction approach we narrowed down complex fecal communities that would be administered as FMTs to ten key microbes that can be characterized and vetted for safety to become a microbial therapeutic to prevent *C. difficile* infection and relapse.

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Poster 66

A Novel Model For Rapid Prediction of Antibiotic Susceptibility In Blood Stream Infections Using Direct Sequencing From Blood Cultures Coupled With Neighbour-Typing Prediction Algorithms.

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Background: Increasing rates of antimicrobial resistance (AMR) in Gram-negative bacteria make empiric treatment of patients with infection increasingly challenging. Culture-based techniques form the basis of pathogen and antibiotic susceptibility determination yet are limited by long turn-around-time. Next generation sequencing with the Nanopore MinION platform has been successful in rapidly identifying culprit pathogens after extracting bacterial DNA directly from positive blood cultures. By comparing the derived sequences to databases of known antibiotic resistance genetic determinants, it is possible to anticipate resistance to specific antibiotics. However, inference of resistance by identification of specific resistance loci remains computationally intense, slow, and potentially unreliable, limiting the ability to inform choice of antibiotics in a timely and feasible manner. A more rapid alternative (or complimentary) approach is to use k-mer-based genomic neighbour typing, where isolate identification and antibiotic susceptibility is inferred by comparing the isolate to a reference database of pathogens with known antimicrobial susceptibilities via the previously published resistance-associated sequence elements (RASE) algorithm.

Hypothesis/Goals: We hypothesize that analysis of positive blood cultures containing Gram-negative bacilli with long-read sequencing followed by species identification, sequence typing, and RASE analysis based on local reference databases will be effective in rapidly improving prediction of AMR to specific antibiotics and can inform appropriate antibiotic therapy significantly faster than conventional culture-based techniques.

Methods: We designed a novel metagenomic diagnostic workflow for pathogen identification and inference of antimicrobial susceptibilities based on sequences isolated directly from positive blood cultures. A rapid extraction method is used to purify pathogen DNA from positive blood cultures revealing Gram-negative bacilli. Sequencing library preparation is optimized for rapid throughput using a PCR-free rapid barcoding kit and then sequenced on the Nanopore MinION Mk1c platform. Reads are time stamped to facilitate determination of the average minimum time required for pathogen identification and susceptibility predictions. Pathogen species identification is determined via Kraken2 followed by RASE analysis. Each step in our extraction and sequencing pipeline is assessed for feasibility, speed, and reproducibility.

Results: Components of our diagnostic workflow, specifically extraction, library preparation, sequencing, Kraken2 pathogen identification, and resistance inference via RASE analysis have been piloted and shown to be feasible. Our expected optimized workflow is less than 3 hours from the start of sample preparation. We are in the process of trialing the complete workflow with preliminary results expected in time for the conference reporting.

Conclusions: We have developed a feasible workflow for rapid extraction and sequencing of pathogen DNA directly from positive blood cultures with actionable results anticipated in less than 4 hours from time

of blood culture positivity. In future studies, we will characterize the accuracy of the antimicrobial susceptibility inferences against phenotypic antimicrobial susceptibility testing.

Poster 67

Regulation of Bla Operon is Associated with the Cefazolin Inoculum Effect in Methicillin Susceptible Staphylococcus aureus

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Background. The Cefazolin Inoculum effect (CzIE) is a matter of concern in the use of cefazolin for severe MSSA infections. The CzIE involves the staphylococcal β-lactamase (BlaZ), part of the *bla* operon (*blaI*, *blaR* and *blaZ*). In preliminary data, expression of *bla* operon genes originated from *S. aureus* ATCC29213 (CzIE-negative) and TX0117 (CzIE-positive) suggested that the regulatory genes, which control *blaZ* expression (*blaI* and *blaR*), are key for the CzIE (**Figure 1A**).

Goal. We aimed to determine the transcriptional profile of the *bla* operon in the context of the CzIE in MSSA strains.

Methods. *S. aureus* TX0117 (type A BlaZ, CzIE+) and ATCC 29213 (type A BlaZ, CzIE-) were included. RNA was extracted from independent biological replicates (n=3) from log-phase cultures with and without antibiotic ampicillin [AMP] (150 µg/ml) for 30 min. Expression levels of *blaZ* (β lactamase), *blaI* (transcriptional repressor) and *blaR* (antibiotic sensor transducer) relative to *gyrB* were evaluated using qRT-PCR. Ratios of the fold change were calculated using the Pfaffl method and gene efficiencies. Differences in expression were calculated using t-unpaired test

Results. After AMP induction, the genes of the *bla* operon in TX0117 (CzIE-positive) showed significantly higher expression levels compared to levels in ATCC29213 (CzIE-negative strain) (**Figure 1B**). β-lactamase gene expression considerably increased after AMP exposure (9.7x, $p< 0.001$) in the CzIE+ strain, while the CzIE-negative strain showed no significant increase in *blaZ* expression (1,2x, $p>0.05$). Similarly, transcription of regulatory genes, *blaR* and *blaI*, was found to be upregulated in TX0117 strain after induction (3.4x and 3.3x, respectively), while ATCC29213 showed no significant increase in *blaI* expression (1.5x, $p>0.05$) and even downregulation of the *blaR* transcript levels (0.5x, $p\leq0.01$). Moreover, in the CzIE+ strain, the increase of *blaZ* expression was three times higher than the increase in the expression of the regulatory genes *blaR* and *blaI* (9.7x vs 3.4x and 3.3x) In contrast, there was no significant difference between the transcription of the repressor *blaI* and the effector, *blaZ*, in the CzIE- strain ($p>0.05$).

Conclusions. We found significant statistical differences in expression of the *blaZ* operon genes in CzIE-positive strain TX0117, compared to ATCC 29213**,** after induction with AMP. Our results strongly suggest that expression of the *blaZ* operon plays a critical role in the CzIE.

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Poster 67

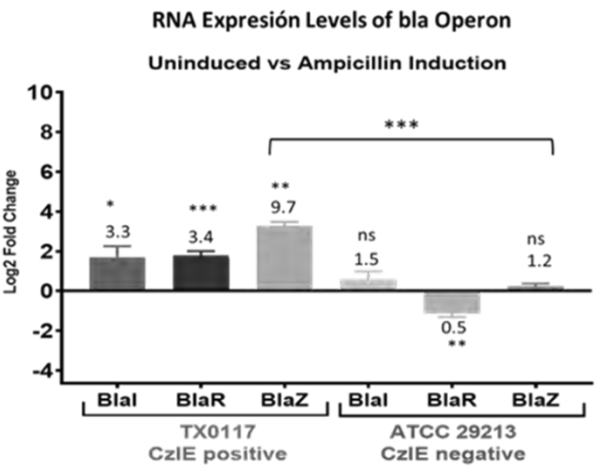
Figure 1

A

Strain	Cz SI-MIC µg/mL	Cz HI-MIC µg/mL
Original Strains		
TX0117	1	64
ATCC29213	0.5	4
Unrepressed *blaZ* expression		
RN4220 pWM401::$blaZ_{TX0117}$	0.5	64
RN4220 pWM401::$blaZ_{ATCC29213}$	0.5	128
Regulatory portions from CzIE (+) TX0117		
RN4220 pWM401::$blaI_{TX0117}$ $blaR_{TX0117}$ $blaZ_{TX0117}$	0.5	64
RN4220 pWM401::$blaI_{TX0117}$ $blaR_{TX0117}$ $blaZ_{ATCC29213}$	0.5	64
Regulatory portions from CzIE (-) ATCC29213		
RN4220 pWM401::$blaR_{ATCC29213}$ $blaI_{ATCC29213}$ $blaZ_{TX0117}$	0.5	8
RN4220 pWM401::$blaR_{ATCC29213}$ $blaI_{ATCC29213}$ $blaZ_{ATCC29213}$	0.5	16

A. Cefazolin (Cz) MIC values after in trans expression of bla operon genes from a CzIE+ and CzIE- strains in a *blaZ* negative strain RN4220. Cz MIC values were measured at Standard (SI-MIC, 10^5 CFU/ml) and High Inoculum (HI-MIC, 10^7 CFU/mL) in transformants after in trans expression of the *blaZ* genes of a CzIE+ (TX0117) and CzIE- (ATCC29213) MSSA strains. The *blaZ* genes were expressed with and without the respective regulatory genes (*blaR* and *blaI*) and the regulatory genes of the counterpart in a *blaZ* negative strain RN4220.

B



B. Transcriptional profile of *bla* operon components after ampicillin induction vs untreated control. Bars and numbers represent the average of fold change from 3 biological replicates (expression was normalized to *gyrB*), error bars show standard error of the mean (SEM) variation of the data. Asterisks indicate significant change in gene transcription (vs untreated control) and (*blaZ* TX0117 vs ATCC29213) by two-tailed Unpaired t-test (ns $p \geq 0.05$, *$p \leq 0.05$, **$p \leq 0.01$, ***$p \leq 0.001$)

Poster 68

Validation of a Rapid Nitrocefin-Based Test for The Detection of the Cefazolin Inoculum Effect (CzIE) in Methicillin-Susceptible* Staphylococcus aureus *In a Colombian Clinical Laboratory

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Introduction. The CzIE is defined as a major increase in the cefazolin MIC (≥16μg/ml) at high bacterial inoculum (10^7 CFU). The CzIE has been associated with therapeutic failure and increased mortality in high-burden MSSA infections. The gold standard to identify the CzIE is broth microdilution at high inoculum. However, this method is cumbersome, laborious, and difficult to implement into the routine clinical laboratory work. Recently, we developed a rapid nitrocefin-based test to identify MSSA exhibiting the CzIE. The test was initially validated in a robust collection of MSSA isolated from the blood of patients in hospitals from Latin-America and the USA. Nonetheless, the performance of the rapid test in a clinical microbiology setting has not been evaluated.

Goal. We aimed to validate the CzIE rapid test under real conditions in a clinical laboratory from a public hospital in Colombia.

Methods. A total of 83 MSSA isolates recovered from bloodstream infections (2011-2019) and previously characterized for the presence of the CzIE were sent to a clinical microbiology laboratory of a public hospital in Pereira, Colombia. After an initial period of training, the laboratory staff performed the rapid test using real conditions, facilities, and equipment available at the site. The staff was blinded to the results of the CzIE performed in a central laboratory using the gold standard (broth microdilution using standard and high bacterial inocula). Well characterized control strains, TX0117 and ATCC29213 (positive and negative for the CzIE, respectively) were included. Performance metrics and agreement (the kappa coefficient) were calculated. Whole genome sequencing of all strains was available. Typing of BlaZ was performed using the genomic information.

Results. The CzIE was identified in 42% (n=35) of the 83 MSSA, and BlaZ A and C were the predominant present in 33% and 34 % of isolates, respectively. Among the MSSA exhibiting CzIE (n=35), types A and C BlaZ were the most frequent in 54% and 43% of isolates, respectively. Overall, the rapid test performed in the clinical microbiology laboratory showed sensitivity of 94% (95% CI= 81-99) and specificity of 92% (95% CI= 80-98), compared to the gold standard. The test accuracy was 93 %, with PPV of 89% (95% CI = 76-95) and NPV of 96% (95% CI= 85-99). No false positives were detected among the *blaZ*-negative isolates (n=10). A strong agreement with the gold standard was observed, kappa= 0.85 (95% CI=0.74-0.97).

Conclusions: The rapid test identified MSSA exhibiting the CzIE using the facilities available in a clinical laboratory in Colombia with an overall accuracy of 93%. The rapid test represents a valuable diagnostic tool to identify a clinically relevant phenomenon in MSSA.

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Poster 6

Daptomycin Induced Expression of the MadR Regulon in E. faecalis *OG1RF is Independent of the MadS Histidine Kinase*

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Background: Daptomycin (DAP) is a lipopeptide antibiotic often used to treat serious enterococcal infections, and the emergence of resistance to this drug in the clinical setting is a major concern. Previous work by our lab described the role of the two-component signaling (TCS) system MadRS in mediating resistance to antimicrobial peptides (AP) and AP-like antibiotics such as DAP in *E. faecalis*. This system is composed of the MadS transmembrane histidine-kinase, which phosphorylates the MadR response regulator, leading to transcriptional activation of components of the MadR regulon involved in AP defense. The target genes include *madEFG*, *madLM*, and the *dlt* operon. Deletion of *madR* in *E. faecalis* OG1RF leads to a decrease in DAP minimum inhibitory concentration (MIC) as well as a decrease in expression of the genes in the MadR regulon as determined by RNA-seq analysis. In contrast, a deletion of the MadS histidine-kinase, responsible for activation of the MadR response regulator, did not lead to a decrease in DAP MIC.

Hypothesis/Goals: We sought to investigate the role of MadS in the expression of the MadR regulon.

Methods: Wild type (WT) *E. faecalis* OG1RF, OG1RFΔ*madR*, and OG1RFΔ*madS* were grown to mid-exponential phase (OD_{600} 0.5-0.7) in tryptic soy broth supplemented with 50 mg/L calcium chloride. Each strain was grown either with or without DAP (½ of the MIC). RNA isolation (PureLink RNA Isolation Kit, Invitrogen) and cDNA synthesis (SuperScript II, Invitrogen) was performed. Expression of *madG*, *madL*, and *dltA* were evaluated by qRT-PCR (SYBR Green) relative to the control strain, OG1RF, without DAP exposure. Values were normalized to the *gyrB* "housekeeping" gene. Fold-change was calculated using the Pfaffl method. Differences in gene expression were determined using two-way ANOVA with Tukey's test for multiple comparisons.

Results: Compared to the control strain, OG1RF (DAP MIC 1.5 µg/mL), the OG1RFΔ*madR* mutant exhibited a lower DAP MIC of 0.38 µg/mL. Conversely, the DAP MIC increased to 4 µg/mL in the OG1RFΔ*madS* mutant. In the absence of DAP exposure, OG1RFΔ*madR* had a statistically significant decrease in expression of *madG* ($p<0.001$) and *madL* ($p=0.003$) as compared to OG1RF (**Fig. 1**). In the presence of DAP, OG1RFΔ*madR* had a significant decrease in expression of *madG* ($p<0.0001$), *madL* ($p<0.0001$), and *dltA* ($p=0.01$) as compared to OG1RF. In the absence of DAP, the OG1RFΔ*madS* mutant also showed a significant decrease in expression for *madG* ($p<0.001$) and *madL* ($p=0.02$), but not *dltA* ($p=0.84$) as compared to OG1RF. Interestingly, when exposed to DAP, expression of *madG*, *madL* and *dltA* in OG1RFΔ*madS* was not significantly different from wild type OG1RF.

Conclusions: The lack of the MadS histidine-kinase in OG1RF did not impair expression of the downstream genes *madG*, *madL*, and *dltA* in the presence of DAP. This finding suggests a MadS-independent mechanism of MadR phosphorylation in *E. faecalis* OG1RF.

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Poster 69

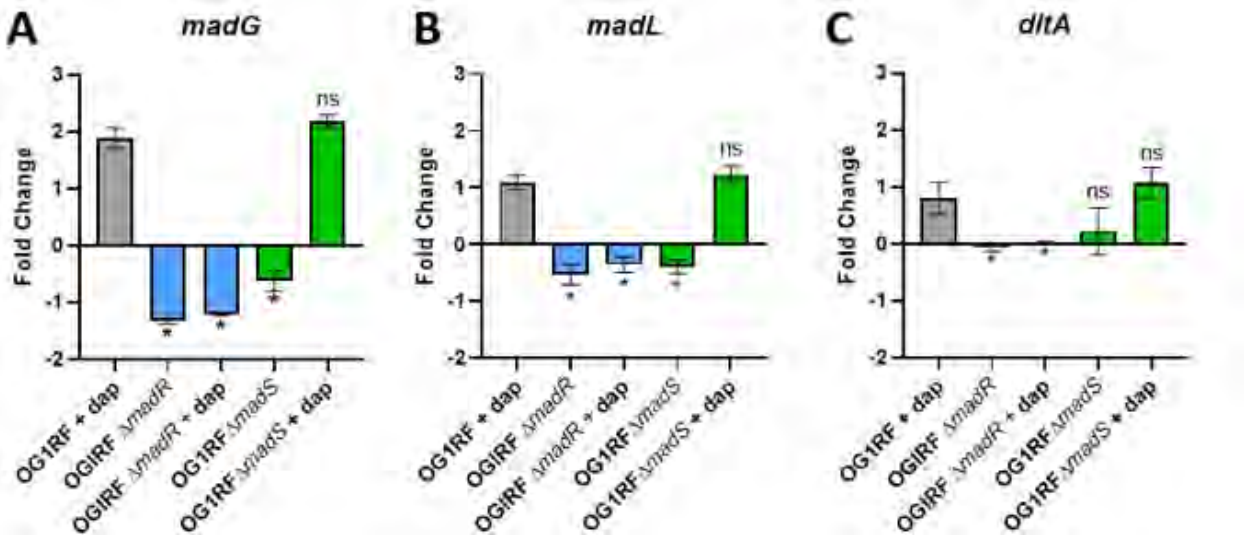

Figure 1. Gene expression in OG1RF, MadR, and MadS knockout strains.

Poster 70

Polymicrobial Communities Contribute to Increased Recalcitrance Towards Hydrogen Peroxide

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Background: Recent advances in sequencing technologies have shown that chronic infections, such as those observed in non-healing wounds, often contain a mixture of microbial species contributing to disease progression. Species interactions within a polymicrobial community can lead to decreases in antimicrobial efficacy through polymicrobial cooperation or increases through polymicrobial competition. Despite the knowledge that polymicrobial communities are common occurrences in persistent infections, current antimicrobial susceptibility testing (AST) is performed on monomicrobial suspensions.

Hypothesis/Goals: Polymicrobial interactions within communities will alter individual antimicrobial susceptibilities to hydrogen peroxide. Understanding how communities change an individual microorganism's susceptibility to this antimicrobial can help us better understand infection dynamics and propose more effective treatments.

Methods: Four relevant chronic wound pathogens (*Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, and *Enterococcus faecalis*) were grown in both monomicrobial and polymicrobial conditions following the procedures outlined in the Clinical and Laboratory Standards Institute (CLSI) guidelines. Changes in individual organism's susceptibilities to hydrogen peroxide were determined by visible turbidity followed by comparing colony counts between the two conditions after plating on selective and differential media.

Results: Hydrogen peroxide (H_2O_2) was determined to be less effective at most concentrations against individual species within a polymicrobial community, as compared to the bacteria grown alone. It was determined that a potential mechanism of decreased susceptibility to hydrogen peroxide within the community was the activation of *E. faecalis*' heme-dependent catalase. *E. faecalis* acquires heme from the other members of the community through cross-feeding, activating the catalase, which neutralizes the hydrogen peroxide, increasing survival rates.

Conclusions: These results demonstrate that the community a microorganism is present in influences its susceptibility to antimicrobials like hydrogen peroxide. Unfortunately, this means that current AST testing, which focuses on determining the one causative agent of disease, may not be truly reflective of the community dynamics found in infection environments. However, by acknowledging the role the community plays in persistent infections, we can prescribe more effective treatments and improve patient care.

Acknowledgements: I would like to thank my graduate mentor, Caroline Black, as well as Dr. Catherine Wakeman for their guidance. I would also like to thank the rest of the Wakeman lab for their support, as well as our funding sources: NIH/NIGMS (R15GM128072) and a TTU Mid-career grant.

Poster 71

Finding Additional Surface-Exposed Lipoprotein Substrates of the Bam Complex

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Background. Surface-exposed proteins play an important role in bacterial physiology and pathogenesis. Surface-exposed proteins of gram-negative bacteria are associated with the outer membrane (OM) and belong to two main classes: integral membrane β-barrel proteins, known as OMPs, and peripheral lipoproteins anchored to a membrane by a N-terminal lipid moiety. OMPs are inserted into the OM by the essential β-barrel assembly machinery (Bam), and the mechanisms behind lipoprotein targeting to the cell surface are poorly understood. Our laboratory discovered that the Bam complex plays a role in surface localization of OMP-dependent lipoprotein RcsF in *E. coli*. Because the Bam complex is highly conserved and assembles all OMPs, it likely plays a critical role in the localization of other OMP-dependent surface-exposed lipoproteins (SLPs) across Gram-negative bacteria.
Our lab's work on the mechanism of RcsF/OMP assembly by the Bam complex in *E. coli,* and revealed that BamE plays a critical role in SLP biogenesis. In the absence of *bamE*, RcsF is stalled on BamA, blocking the activity of the Bam complex. Indeed, many of the *bamE*- phenotypes, including its conditional essentiality, are caused by the inability to assemble RcsF. While RcsF/OMP remains the only known substrate that requires BamE activity, BamE is more widely conserved suggesting the presence of additional substrates.

Hypothesis and goals. The goal of the project is to identify these new SLPs substrates of the Bam complex. We chose three genetically tractable representatives from α-, β- and γ- Proteobacteria that encode BamE but not RcsF homologues: *Caulobacter crescentus, Burkholderia thailandensis,* and *Pseudomonas aeruginosa*, respectively. In *P. aeruginosa* and *B. thailandensis*, *bamE* was proposed to be essential based on various transposon sequencing (Tn-seq) experiments, while in *C. crescentus bamE* mutant was reported to have severe growth defects. Our hypothesis is that, like in *E. coli*, growth phenotypes of *bamE* mutants are caused by SLP stalling on BamA.

Methods. We used complementary genetic and biochemical approaches. First, we aim to generate *bamE* mutants to properly test for the essentiality of *bamE*, then identify suppressors of *bamE* mutant by Tn-seq. We also aim to identify the SLP substrate of the Bam complex using protein co-purification and mass spectrometry, approaches that had been successful for studies of RcsF.

Results and Conclusions. My preliminary results suggest that *bamE* in *C. crescentus* is essential. I am currently optimizing conditions for use of a xylose- inducible promoter to regulate *bamE* expression. Likewise, I was not able to generate *bamE* knock-out in *P. aeruginosa*, however, this finding is potentially complicated by *bamE* ORF overlapping with the promoter of an essential gene nearby. I have developed strategy for introducing a point mutation that disrupt *bamE* expression to test for its essentiality. While this project is in early-stage, it is obvious that BamE plays a more important role in viability in various gram-negative bacteria than we anticipated based on the research in *E. coli* as a model.

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Poster 72

Title: Clinical Epidemiology of Bacterial Infections in Critically Ill Patients: A Prospective Cohort Analysis 2020-2022

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Background: Bacterial infections are among the most common causes for admission to the intensive care units (ICU). Severe infections can be complicated and evolve to sepsis which is associated with high mortality and morbidity. Understanding the local microbiological distribution of pathogens based on type of unit is essential to establish local protocols of effective empiric antibiotic therapy.

Hypothesis/Goals: To describe the microbiological epidemiology and clinical outcomes of participants by ICU type on the setting of the DYNAMITE study. The purpose of DYNAMITE is to elucidate the dynamics of colonization and infection by multidrug-resistant pathogens in immunocompromise and critically ill patients.

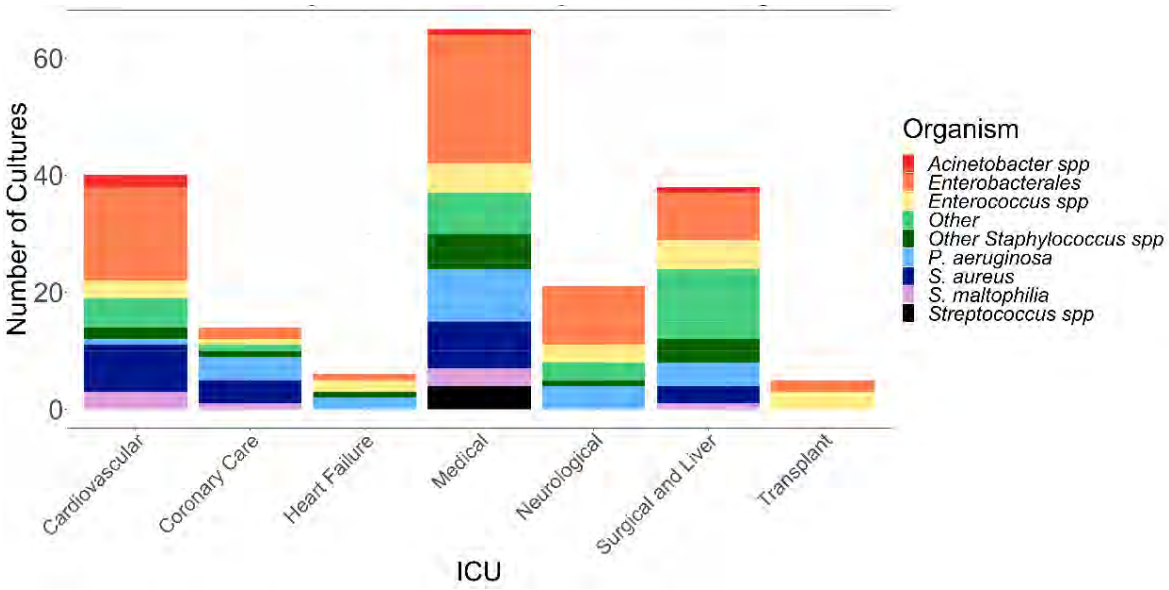
Methods: A prospective cohort study of adults admitted to the ICUs in two Houston hospitals, was conducted from 12/2020 to 11/2022. Subjects were recruited within their first 24 hours from ICU admission. Patients with gastrointestinal derivation, inflammatory bowel disease, and pregnancy were excluded. Variables included clinical and demographic characteristics of patients in the ICUs and bacterial isolates. Bacterial cultures were collected as clinically needed. Repeated positive isolates from the same source or species were not counted. We analyze data on ICU type: medical (MICU), surgical and liver (SLICU), cardiovascular (CVICU), cardiac (CICU), neurological (NICU), heart failure (HF) and transplant. Data were extracted from the electronic medical records. Descriptive statistics were performed using RStudio and Jamovi v18.

Results: A total of 159 subjects admitted to the ICU were included. 55 (35%) and 102 (65%) were from each hospital, respectively. Most patients were male (56%), white (67.9%), and had a median age of 62 years old. Hypertension (57.7%), heart failure (37.1%) and liver disease (27.2) were the most common comorbidities. The main cause of admission was respiratory disease (22%). A total of 189 positive bacterial isolates were collected from 87 subjects. Most common source of isolation were the respiratory tract (26.5%), urine (20.6%) and blood (19.6%). MICU patients had the highest proportion of patients with a positive culture (n=65; 34.4%). In contrast, the HF unit had the lowest number of cultures (n=6; 3.2%). Enterobacterales 61(32.3%) including, *E. coli* (n=22; 11.6) and *K. pneumoniae* (n=14; 7.4%), were the most prevalent microorganism, followed by *P. aeruginosa* (n=24 ; 12.7%), *Staphylococcus aureus* (n=23; 12.2%), *Enterococcus* species (n= 22; 11.6%), other *staphylococci* (n=15; 7.9%), *Stenotrophomonas maltophilia* (n=7; 3.7%), *Acinetobacter* species (n=4; 2.1%), and *Streptococcus* species 4 (2.1%). The overall median hospital length of stay (LOS) was 18 days (11-35). CVICU had the longest LOS with a median of 31 days (16-49) ($p<0.001$). The overall Hospital mortality was 20.1%.

Conclusions: Enterobacterales was the most common bacteria isolated in all the ICUs types. These results could reassure clinicians the need to start empiric Gram-negative coverage in critically ill patients with a suspected infection.

Acknowledgements: Sponsor by the National Institutes of Health/National Institute for Allergy and Infectious Diseases.

Figure 1. Bacterial isolates by ICU type



Poster 73

Genomic Characterization of Extended-Spectrum β-lactamase producing **Klebsiella pneumoniae** *Bacteremia at MD Anderson Cancer Center*

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Background: Extended-spectrum β-lactamase producing *Enterobacterales* (ESBL-*E*) are among the multi-drug resistant (MDR) bacteria considered to be a serious public threat. ESBL-*E* infections are particularly prevalent and difficult to treat in immunocompromised populations. *Klebsiella pneumoniae (Kp)* is the second most common *Enterobacterales* causing ESBL-*E* infections at the University of Texas MD Anderson Cancer Center (MDACC), which has a high density of severely immunocompromised persons. We sought to dissect the genomic factors responsible for ESBL *K. pneumoniae* (ESBL-*Kp*) bacteremia at our institution.

Methods: ESBL positivity was defined as either testing positive for ESBL production in the clinical microbiology laboratory or being ceftriaxone resistant. The proportions of ESBL-*Kp* bacteremia between 2016 and 2022 were abstracted from Epic electronic health record software. 215 ESBL-*Kp* bacteremia isolates were subjected to whole-genome sequencing through Illumina NovaSeq 6000. After quality control and adaptor removal, the genomes were assembled using SPAdes.v3.13. The genome assemblies were assessed for contiguity and contamination through tools such as BUSCO-v.5.4 and CheckM-v1.2. The maximum likelihood phylogeny was constructed through Iqtree2-v1.6 using the core gene alignment obtained from Roary-v3.1.

Results: A total of 554 *K. pneumoniae* bacteremia episodes occurred during the study period. The annual proportion of ESBL positive isolates ranged from 25 to 41%. Out of 215 ESBL-*Kp* isolates subjected to sequencing, all passed quality control with coverage depth of ~250x indicating high confidence in our downstream analyses. 142 of the 215 isolates were from unique patients with the remainder being recurrent isolates. Among the 142 unique ESBL-*Kp* at MDACC, a total of 63 different sequence types (STs) were found with only four STs having more than 5 isolates. ST307 was the most common ST identified (n= 38, 27%) whereas the elsewhere commonly observed ST258 was identified only twice. With regards to ESBL genes, $bla_{\text{CTX-M-15}}$ was the the most commonly observed, being present in 76% of isolates. A total of 7% of isolates were also resistant to carbapenems with $bla_{\text{KPC-2}}$ being the predominant carbapenemase gene (n = 5). Given their prominence, we further analyzed the ST307 strains through a core gene phylogeny and found that most ST307 strains at MDACC (34/38) belong to what has been previously described as a "non-Texas" lineage. The remaining four ST307s carried the distinct markers of the "Texas lineage" of ST307 including a double fluroquinolone resistant (FQR) mutation pattern *gyrA* 83I + 87N in addition to the presence of multiple copies of $bla_{\text{CTX-M-15}}$. In contrast, the non-Texas ST307s causing the majority of disease at MDACC appear to have achieved FQR though acquisition of the plasmid mediated FQR gene *qnrB.*

Conclusions: ESBL-*Kp* bacteremia at MDACC is caused by a diverse array of STs with ST307 being most common and the pandemic ST258 clone being quite rare. Unexpectedly, we found that ST307 strains causing disease at MDACC rarely belonged to the "Texas" lineage suggesting that MDACC patients may be either uniquely exposed to or uniquely susceptible to the "non-Texas" lineage of ST307. We are currently seeking to better understand the factors leading to this surprising finding.

Poster 74

Using Whole Genome Sequencing to Genetically Profile and Analyze **Escherichia coli** *Isolates with Varying Resistance to β-Lactam/β-lactamase Inhibitor Combinations*

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Background: Whole-genome sequencing has gained interest for assessing antimicrobial resistance (AMR). However, multiple studies have shown a poor correlation between the β-lactam/β-lactamase inhibitor (BL/BLI) phenotype and β-lactamase gene presence/absence. In a recent publication, we found that amplification of β-lactamase encoding genes potentially contribute to BL/BLI resistance and here we explore if gene amplifications allow for better BL/BLI genotype/phenotype correlations.

Methods: We selected 109 *E. coli* bacteremia isolates and performed ETests (bioMerieux, Inc) to determine AST profiles using the following BL/BLI antibiotics: ampicillin/sulbactam (SAM), amoxicillin/clavulanic acid (AMC), and piperacillin/tazobactam (TZP). CLSI M100 guidelines (2018) were used to stratify isolates into 4 groups: SAM/AMC/TZP susceptible (Group 1), SAM resistant only (Group 2), SAM/AMC resistant (Group 3), and SAM/AMC/TZP resistant (Group 4). Short-read whole genome sequencing was performed on these isolates and analyzed by identifying AMR genes, establishing multi-locus sequence type (MLST), estimating copy number variants (CNV), and investigating $bla_{\text{TEM-1}}$ promoter regions in relation to phenotype. A t-Distributed Stochastic Neighbor Embedding (t-SNE) clustering method and a core-genome, maximum-likelihood phylogeny was generated to group isolates based on AMR gene content and CNV data.

Results: We found 34 different MLST groups with the three most common sequence types ST131 (n=41), ST1193 (n=12), and ST648 (n=6). Group 1 and Group 2 isolates had similar copy number estimates of β-lactamase $bla_{\text{TEM-1}}$ (1.8X and 1.5X respectively) while there was an increase for both Group 3 (3.7X) and Group 4 (8.2X) isolates (Table 1). Additionally, $bla_{\text{OXA-1}}$ was primarily present in Group 4 isolates (63%) with elevated copy numbers (5.2X). We did not observe associations of $bla_{\text{TEM-1}}$ promoter regions with each of the BL/BLI Groups. Our t-SNE analysis shows that Group 1, Group 3, and Group 4 isolates cluster independently.

Conclusions: There is a clear delineation between fully susceptible and fully resistant BL/BLI *E. coli* isolates when gene amplification and presence/absence of narrow-spectrum β-lactamases are considered, which should be considered for BL/BLI resistance prediction models.

Table 1: Narrow Spectrum β-lactamase Characteristics Across ESRI Group Spectrum				
	Group 1 (n=26)	Group 2 (n=28)	Group 3 (n=28)	Group 4 (n=27)

bla$_{\text{TEM-1B}}$ (n; %)	13 (50)	27 (96.4)	26 (92.9)	15 (55.6)
Copy Number (mean; sd)	1.9 (0.7)	1.5 (0.7)	3.7 (4.5)	8.2 (12.1)
bla$_{\text{OXA-1}}$ (n; %)	0 (0)	0 (0)	1 (3.6)	17 (63.0)
Copy Number (mean; sd)	NA	NA	0.8 (NA)	5.2 (4.8)
Other *bla* (n; %)	2 (8)	3 (11)	2 (7)	5 (19)
Copy Number (mean; sd)	12.5 (15.26)	2.0 (1.7)	2.4 (0.8)	4.3 (4.5)

Poster 75

Elucidation of Molecular Mechanisms Underlying Successful Adaptation to Carbapenem Antimicrobials in High Risk Carbapenem Resistant* Escherichia coli *Lineages

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Background: *Escherichia coli* is a leading cause of human infection and a major contributor to the epidemic of antimicrobial resistant (AMR) bacteria. AMR *E. coli* infections that are resistant to carbapenems, which are considered as last-resort antibiotic treatments, are among the most challenging to resolve in hospital settings. Despite extensive research on carbapenem resistant *E. coli* mechanisms, there remains a knowledge gap of how high-risk *E. coli* lineages, such as sequence type (ST) 131, adapt to initial antibiotic exposure, which can be conceptualized as a 'pre-resistant' phase.

Objectives: Our goal is to investigate the evolutionary trajectory of ST131 under initial carbapenem exposures. We hypothesize that AMR gene amplifications and outer membrane porin genomic changes will occur prior to fully carbapenem resistant phenotypes with sub-clades of ST131 more likely to adapt to carbapenem exposures.

Methods: We employed a combination of a novel micro-fluidics system along with standard batch culture passaging to analyze the adaptive strategies of the carbapenem-susceptible, $bla_{\text{CTX-M-15}}$-positive ST131 strain MB1860 to increasing amount of carbapenems over time. Daily aliquots of MB1860 isoforms were subjected to whole genome sequencing including copy number variation assessment using the novel computational biology tool CONVICT. Targeted analyses of porin presence were assessed using Western immunoblots. Relative mutational frequency of 10 unique, genetically diverse ST131 ESBL isolates during carbapenem exposure was determined using a modified Luria-Delbruck assay.

Results: MB1860 developed carbapenem resistance significantly faster (~11 days) in standard batch culture relative to the micro-fluidics system (~52 days). In both systems, we identified that MB1860 rapidly responded to carbapenem exposure by increasing the copy number of the β-lactamase encoding genes $bla_{\text{CTX-M-15}}$ and $bla_{\text{OXA-1}}$ which are co-located on the chromosome in the setting of transposable elements capable of mediating gene amplification. Additionally, in both systems, we found by Western blot down-regulation of porins which would be predicted to reduce carbapenem entry into the *E. coli* cell. Importantly, these changes occurred prior to fixed genetic mutations in porin encoding genes that were ultimately detected in fully carbapenem-resistant strains. When analyzing a broad array of ST131 strains, we identified significant variance in carbapenem adaptive capacity with particularly high rates observed for strains of the recently emerging C1-M27 clade which carry $bla_{\text{CTX-M-27}}$.

Conclusions: Using complementary strategies, we have identified that *E. coli* initially adapts to carbapenem exposure through amplification of non-carbapenemase β-lactamase encoding genes and down-regulation of porin production through non-fixed genetic mechanisms. These findings challenge the current dogma that strains with pre-existing mutations in porin encoding genes are selected for during carbapenem exposure. Additionally, we have identified significant variance in the rates at which ST131

strains adapt to carbapenems with ongoing work focused on understanding factors driving the ‘pre-resistant’ adaptation to carbapenem selective pressures.

Poster 76

Clinical and Genomic Characterization of Persistent Enterococcal Bacteremia in the VENOUS Cohort

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Background. It has been shown that patients with persistent enterococcal bacteremia are at a greater risk of adverse outcomes, including mortality. We have identified a subset of patients in the 2016-2021 Vancomycin Resistant Enterococcal Bacteremia Outcome Study (VENOUS) cohort experiencing persistent bacteremia for further clinical and genomic characterization.

Hypothesis/Goals. This analysis aims to describe clinical and genomic features that may be associated with persistent bacteremia in hospitalized patients.

Methods. Patients with persistent enterococcal bacteremia were defined as having two blood cultures positive for enterococci of the same species and MLST sequence type (ST) ≥ four days apart in the same hospitalization period. Clinical data were collected from electronic medical records at each institution and managed using REDCap. Short- and long-read whole genome sequencing was performed for all isolates. Clinical data was analyzed using R.

Results. A total of 36 persistent infections from 35 patients at 6 study sites have been analyzed from the VENOUS cohort. Of these, 21 (58.3%) were *E. faecium* and 15 (41.7%) were *E. faecalis*. A total of 16 (44.4%) index isolates harbored either *vanA* (13; 36.1%) or *vanB* (3; 8.3%). There was no predominant MLST sequence type observed amongst either species, indicating that persistence of bacteremia in this cohort is not ST-specific and instead seems to be driven by the underlying population structure of enterococcal isolates found at each institution. Interestingly, 3/36 (8.3%) infections developed resistance to vancomycin over the course of bacteremia. Median length of hospitalization after first positive blood culture was 17 days (range: 4, 272). Lastly, 15/35 (42.9%) of patients had a positive culture within 48 hours of admission, and 12/31 (39%; n = 5 missing mortality data) died during hospitalization.

Conclusions. Overall, enterococcal isolates causing persistent enterococcal bacteremia in the VENOUS cohort appear to be genomically diverse, indicating that ST-specific genomic signatures are not significant drivers of persistence in either *E. faecalis* or *E. faecium*. Surprisingly, the majority of these infections were not resistant to vancomycin, suggesting that there may be factors other than resistance to enterococcal

therapies contributing to persistence of infection. More work will be done to further characterize the clinical and genomic determinants of prolonged infection in this cohort.

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Poster 77

Genetic Screen Suggests Pyocins Contribute to **Pseudomonas aeruginosa** *Strain Dominance in Blood Stream Infections*

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Background: Our previous research highlighted *Pseudomonas aeruginosa* multi-locus sequence type (ST) 111, which dominated human blood stream infections (BSI). ST111 alone took up about 40% of *P. aeruginosa* infections in hematologic malignancy and hematopoietic stem cell transplant patients. This project aims to identify specific mechanisms of ST111 dominance. Preliminary experiments suggested ST111 dominance is due in part via their production of >100kDa, protease-sensitive, secreted effector(s) that inhibited a panel of other sequence types found in BSI patients (e.g. ST233, ST234, and ST299). Importantly, PA14 cell-free spent media (filtrate), like ST111 filtrate, contained effector(s) with similar properties that inhibited this same panel of non-ST111 isolates.

Hypothesis/Goals: Noting similar properties of PA14 and ST111 filtrate, this project aimed to develop a PA14 transposon-insertion (tn) mutant library screen to identify genes necessary for inhibition a non-ST111 sensor strain. Genes verified in the PA14 screen could then be tested for relevance in ST111 strain dominance.

Methods: The primary screen was developed to bypass the time-consuming filtration step. PA14 tn mutants were grown in 96 deep well plate. PA14 cultures were then suppressed with meropenem before being added to meropenem-resistant "sensor" strain M0104 (ST233), a member of non-ST111 panel earlier described. M0104 was also transformed with dsRed to track its growth even in mixed culture thorough fluorescence measurements. Screen hits were thus defined as PA14 tn mutants that permitted M0104 growth greater than the plate average plus three standard deviations after 6 or 18 hours incubation at 37ºC. The secondary screen, testing far fewer mutants, permitted the use of PA14 filtrate. The effect of primary screen hits' filtrate on M0104 growth, as well as growth of the rest of the non-ST111 panel, was determined by kinetic OD600 measurements at 37ºC.

Results: The primary screen yielded 45/5810 hits (0.77%). The ongoing secondary screen has confirmed 13 hits so far. Of these, 5 are "strong" hits that result in near-complete abolishment of PA14's inhibition against all 3 isolates on the non-ST111 panel. The "strong" hits are also all R-pyocin-related genes. R-pyocins, a class of bactericidal protein-complexes, match the properties of the unknown ST111 effector(s). Furthermore, ST111 filtrate was able to suppress the growth of a specialized R-pyocin sensor strain, indicating that ST111, like PA14, produces R-pyocins.

Conclusions: PA14 and ST111 both inhibit a panel of non-ST111 BSI isolates via a large, protein-based, secreted effector. A PA14 library screen suggests it inhibits this panel through R-pyocins. ST111 also produce R-pyocins, suggesting the phage-like particle may contribute to its dominance in BSI's. Because of differences between PA14 and ST111 R-pyocin genes, future research aims to clarify whether ST111 R-pyocins can inhibit other BSI isolates.

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Poster 78

A Retrospective, Observational Study of 12 Cases of Expanded Access Phage Therapy

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Background The emergence of antibiotic resistance is threatening to undermine modern medicine. Dire predictions claim 10 million deaths per year by 2050 at a cost of trillions to governments and healthcare. The problem is compounded by the inherent adaptability of bacteria in the face of intense selective pressures. Bacteriophages (phages) – viruses that infect bacteria and are diverse and evolvable themselves – have been proposed as a possible solution for this crisis.

Methods Here, we detail progress following the formation of TAILΦR, a phage center that provides personalized treatment for compassionate-use cases. We report the discovery, characterization, pipeline, and process of phage selection and purification, as well as clinical course and outcomes.

Results TAILΦR responded to 48 requests for a phage hunt, for which we received 40 clinical isolates and generated 150 novel phages against 11 bacterial species. Most common indications requested were urinary tract infection/prostatitis, left-ventricular assist device infections, and bacteremia. From those 40 cases, 12 patients received treatment. Several patients demonstrated bacterial eradication (5/12) and/or clinical improvement (7/12) up to a year post-treatment.

Conclusions The true potential of phage therapy will not be realized until discovery, manufacturing, and regulatory efforts harmonize to rapidly deliver personalized cocktails in a manner that curtails real-time evolution. TAILΦR is addressing barriers by developing good manufacturing practices (GMP) to

significantly reduce time-to-treatment and curating cocktails that anticipate bacterial resistance. Worldwide networks of phage centers will fill a critical treatment void while fueling antibacterial innovation for the most complex and challenging patient cases.

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Poster 57

The Future Direction Of Multidrug-Resistant Tuberculosis With The Latest Treatment Guidelines

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Background: In May 2022, World Health Organization (WHO) released new treatment guidelines for multidrug-resistant tuberculosis (MDR-TB) which consists of a 6-month oral BPaLM regimen (bedaquiline, pretomanid, linezolid, and moxifloxacin). This is a key change from the previous guidelines issued in 2020 which is a longer regimen along with injection. The new guideline is timely and necessary, as only 1 in 3 cases out of 500,000 new cases of MDR-TB each year receive treatments. Furthermore, the COVID-19 pandemic may have also contributed to the further spread of MDR-TB.[1]

Goals: The goals were to review recent literature and data from clinical trials evaluating the efficacy of BPaLM regimen as a treatment for MDR-TB compared to the previous standard of care, as well as barriers to accessing this new regimen.

Methods: We performed a keyword search of medical literature using the search terms "BPaLM" and "MDR-TB". Relevant articles and data were reviewed and selected for inclusion in this report.

Results: We found substantial clinical evidence supporting the efficacy of BPaLM regimen which dramatically promotes safer outcomes with reduced side effects. A recent clinical trial done by TB-Practecal evaluating the safety and efficacy of BPaLM regimen compared to the previous standard of care has shown a 37% increase in successful outcomes from 52% to 89% when treating MDR-TB patients with BPaLM regimen. The same study also shows a 39% decrease in side effects with the new regimen from 59% to 20% and death counts decreasing from 2 to 0.[2]

Conclusions: The results support WHO's new guidelines recommending a shorter, improved, and better-tolerated treatment regimen for MDR-TB compared to the previous standard of care. The practical use of this new and improved guideline with shorter regimen has the potential to significantly save millions of dollars each year which can bridge the gap in TB care. However, financial barriers continue to be a constraint on increasing the uptake of BPaLM regimen in high-TB-burden countries, particularly in developing countries. Therefore, despite the groundbreaking results, we will only see meaningful changes if treatment becomes more affordable.

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Poster 80

Qualitative Analysis of a Twitter-Disseminated Survey Reveals New Patient Perspectives on the Impact of Urinary Tract Infection

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Background: Urinary tract infections (UTIs) are one of the most common infectious reasons for ambulatory care visits. Prior qualitative studies have sought to understand patients' lived experiences with UTI through interviews, but few studies have harnessed social media or online platforms to explore patients' experiences with UTI.

Hypothesis/Goals: We aimed to capture perspectives on the impact of UTI and suggestions for future research from individuals with UTIs using a Twitter-disseminated survey to enhance freedom of responses that traditional interviews may not capture.

Methods: The survey posed three qualitative questions inquiring about the impact of UTIs, greatest UTI management hurdle, and research suggestions. We also asked participants to rate how seriously others perceive UTIs and the importance of UTIs in their life (scale: 1-100 (highest)). The study period spanned from January to June 2021. Coding of qualitative responses was performed in duplicate, followed by thematic analysis.

Results: Of the 466 participants from 22 countries, 128 considered their UTIs recurrent (n=43) or chronic (n=85). Six major themes emerged: UTIs drastically impact (1) physical and (2) mental health, and (3) cause severe limitations in life activities. Patients reported (4) perceived inadequate treatment and management, (5) a lack of knowledge and awareness surrounding UTIs, and (6) research gaps in UTI diagnostics and treatment (Figure). Participants considered UTIs extremely important (median: 100, IQR: 90-100), but characterized others' perceptions of UTIs as less serious (median: 20, IQR: 10-30).

Conclusions: Our Twitter-disseminated survey revealed a patient population struggling with UTI, particularly chronic UTI, who feel neglected and unheard by the medical establishment. Our survey highlighted perceived shortcomings in current UTI treatment and diagnostic modalities among this group.

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Poster 80

Representative Quotes from the Six Major Themes	
1. Physical Health	➢ "Day to day, I am in pain. It burns when I wee, which is often, and I find it difficult getting up and about because I am in so much pain. I find it difficult to sleep. I am irritable, angry and incredibly sad. I have dyspareunia, depression and my BMI [body mass index] is over what it should be for someone of my height and age due to UTIs." (United Kingdom)
2. Mental Health	➢ "At the age of 23 I feel like my life has ended before it's even properly started. Suicide is on my mind most days. Most of the things I enjoyed in life I cannot do. I feel like a shell of the person I used to be." (United Kingdom)
3. Limitations	➢ "Every aspect of my life is affected. My social relationships, intimacy, work-life, life as a mother, my diet, overall health, as well as my mental health." (United States)
4. Treatment/ Management	➢ "Finding a doctor to prescribe appropriate medication. Three or five days [of antibiotics] has never been enough and has always caused me reoccurrence." (Ireland) ➢ "Not having support from your doctor is the biggest hurdle. They are meant to help and being looked at like you're a loonie and it's all in your head because their medical education contradicts your experience is soul destroying." (Australia)
5. Knowledge and Awareness	➢ "It's poorly understood, not taken seriously enough, and I've not been given a diagnosis, as there is too much ambiguity around bladder pain…so I don't feel like I'm getting anywhere." (United Kingdom)
6. Research Gaps	➢ "safer and more sustainable treatments for the treatment of chronic UTI, as long-term antibiotics are undesirable for a number of reasons (although for those of us with chronic UTI, long-term antibiotics are currently our only option)." (United Kingdom)

Poster 81

Antimicrobial and Antibiofilm Activities of Endemic Plant Species of Cyprus on Drug Resistant Clinical* Staphylococcus aureus *Isolates

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Background: Globally, healthcare systems rely on antibiotics. However, overuse, misuse and abuse of antibiotics promote the spread of antibiotic resistance. As bacteria gain antimicrobial resistance or recalcitrance, utilization of novel approaches for new therapeutics is becoming critical. The island of Cyprus hosts a large and diverse flora of endemic plants with medicinal significance. These plants that grow only on the island of Cyprus were demonstrated to have antimicrobial and anticancer activities.

Hypothesis/Goals: In this study, our goal was to assess whether extracts from two endemic plants species of Cyprus, the understudied *Allium autumnale* and *Posidona oceanica,* with medicinal properties, have antimicrobial activities against drug resistant clinical *S. aureus* isolates from urine or urinary catheter samples and breast implants.

Methods: Plant extracts were made via ethanolic extraction of *Allium autumnale* bulbs and *Posidona oceanica* rhizomes using a rotary evaporator. Antimicrobial activities of the extracts were assessed using minimum inhibitory concentration assays. Additionally, inhibition of biofilm formed by clinical isolates by the extracts was assessed using biofilm assays. The contents of extracts were detailed using GC-MS to reveal the types and amounts of bioactive molecules in their composition.

Results: *P. oceanica* and *A. autumnale* ethanolic extracts were initially tested on an established methicillin resistant *Staphylococcus aureus* (MRSA) skin isolate termed JE2. While JE2 revealed to be resistant against standard doses of ciprofloxacin, 400µg/ml of *P. oceanica* and 1.2mg/ml of *A. autumanle* revealed to be inhibitory against this bacterium. Next, we tested various uncharacterized *S. aureus* isolates obtained from urinary samples or urinary catheters. These isolates are termed HUC97-02, a clinical isolate from patient urinary catheter that is ciprofloxacin resistant; HUC111-01u and HUC111-01c *S. aureus* urine (u) and catheter (c) isolates from the same patient; HUC95 a urinary catheter isolate; and HUC 86-07u and HUC86-07c urine (u) and urinary catheter (c) isolate from the same patient. Both extracts revealed inhibition of all tested clinical isolates at 100-400µg/ml range for *P. oceanica* and 1.2-3.2mg/ml range for *A. autumnale*. Biofilm inhibition assays revealed that, at sub-MIC concentrations, *A. autumnale* also inhibited biofilm formation of clinical isolates HUC97-02 and HUC95. Notably, the well characterized skin isolate JE2 was inhibited by both *P. oceanica* and *A. autumnale* at sub-MIC concentrations. We further evaluated the antimicrobial and antibiofilm activities of *P. oceanica* and *A. autumnale* extracts against drug recalcitrant *S. aureus* breast implant isolates termed BISA1 and BISA2. BISA1 and BISA2 were inhibited by *P. oceanica* extract at 50 and 200µg/ml concentration, respectively. A statistically significant reduction of biofilm formation in these isolates were also observed with *A. autumnale* against BISA2. GC-MS investigation of the extracts revealed the presence of several bioactive molecules with predicted/established antimicrobial and/or antibiofilm activities.

Conclusions: *P. oceanica* extracts exerted potent antimicrobial activity compared to *A. autumnale* in all tested clinical isolates, even those that exhibited antimicrobial resistance. More potent biofilm inhibitory activity was observed with *A. autumnale* against tested clinical isolates. These studies suggest the compounds within these extracts may be developed for the treatment of drug-resistant infections.

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Poster 82

A Novel Type of Cytotoxic Membrane Vesicles Produced by **Pseudomonas aeruginosa**

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Background: *Pseudomonas aeruginosa* is a Gram-negative opportunistic human pathogen that can cause a variety of nosocomial infections. Alarmingly, multidrug-resistant isolates are frequently observed and have been classified as a serious threat by the CDC and WHO. *P. aeruginosa* possesses a large armamentarium of acute and chronic virulence factors. Previously, our lab found that the bacteria-free spent media (filtrate) from *P. aeruginosa* showed toxicity towards murine macrophages. This cytotoxicity was independent of pyoverdine, a toxin commonly secreted by *P. aeruginosa* strains, but was associated with membrane vesicles (MVs). MVs can be generated by Gram-negative bacteria through blebbing of either the outer membrane or both membranes. Transmission electron microscopy (TEM) micrographs of purified MVs showed a class of membrane vesicles, which are around 35 nm on average and have a single-layered membrane around them. The primary objective of the work is to characterize these small MVs, evaluate their toxicity in different models, and elucidate the mechanism for MV production and their role in *P. aeruginosa* infection.

Hypothesis: The membrane vesicles we purified from bacterial filtrate may belong to a novel type with unique characteristics and play an important role in *P. aeruginosa* infection.

Methods: Current pipeline for MV purification is mainly based on macromolecule precipitation and density gradient ultracentrifugation. The cytotoxicity of purified vesicles was measured in murine macrophages, human lung epithelial cells, and other bacterial species. The characteristics of these vesicles were further investigated using biochemical and cell biological methods, including particle measurement via NanoSight, and TEM, protein analysis via SDS-PAGE, and interaction tracking (between cells and MVs) via fluorescence microscopy. In addition to the standard lab strain *P. aeruginosa* PA14, a panel of 68 clinical isolates from pediatric patients with cystic fibrosis (CF) was used in order to better understand vesicle production and the role of MVs in infection.

Results: Purified MVs have shown toxicity towards bacterial cells, mammalian cells, and non-cellular vesicles (giant plasma membrane vesicles (GPMVs)), despite the difference in membrane composition amongst these targets. TEM micrographs of murine macrophages exposed to MVs revealed that cellular damage occurs within minutes after treatment. Cytotoxicity shown in macrophages was strongly correlated with MV concentration in bacterial filtrate, which has been validated in the supernatant from 68 clinical isolates. Interestingly, the strong cytotoxicity exhibited by the MVs we purified has not been previously observed, suggesting that these MVs may belong to a novel type with unique characteristics.

Conclusions: The strong correlation between MV production and filtrate cytotoxicity indicates a potential role for MVs in infection, although the mechanism is still unclear and thus needs more research. Better understanding the role of these MVs may yield to identification of potential treatment targets for *P. aeruginosa* infections.

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Poster 83

The Mechanisms of the Long-term Dominance of Pseudomonas aeruginosa *Isolates in Patients*

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Background: An epidemiological study uncovered that fluoroquinolone (FQ) neutropenic prophylaxis in hematopoietic cell transplant and hematologic malignancy (HCT/HM) patients was associated with breakthrough *Pseudomonas aeruginosa* bloodstream infections (BSIs). Data showed that over 80% of FQ-breakthrough BSIs in HCT/HM patients were due to ST111 and ST446 strains. The mechanisms of ST111/ST446 dominancy have been investigated in this project. Whole genome sequence (WGS) results revealed 1) inactivating mutations in the carbapenem entry protein OprD in most of ST111 and all ST446 strains; 2) a premature stop codon at amino acid position 152 in the major quorum sensing regulatory gene *lasR* in almost all ST111 clinical isolates; 3) several mutations on lipopolysaccharides (LPS) genes in non-ST111/ST446 strains.

Hypothesis/Goals: We hypothesized that these genomic alterations may confer an advanced fitness to ST111 and ST446 strains in competition with other *P. aeruginosa* sequence types.

Methods: WGS was performed on *P. aeruginosa* bloodstream isolates from HCT/HM patients at the OHSU Clinical Microbiology Laboratory. We assessed the colonization capacity, biofilm formation ability, and pyocin susceptibility of clinical isolates, *P. aeruginosa* reference strain PA14, PA14*ΔoprD,* PA14 *ΔoprD* or PA14 *ΔoprD ΔlasR*.

Results: ST111-type strains, but not other *oprD*-deficient, meropenem-nonsusceptible clinical strains, were found to have a colonization advantage over PA14 in *C. elegans* and to outcompete PA14 in *in vitro* co-culture assays. Further, we found that loss of the quorum sensing (QS) regulator LasR may contribute to increased fitness and attenuated virulence seen in ST111. All ST111 and ST446 strains were able to produce the functional bacteriocin (R-pyocin) which caused the killing of other strains during competition. The abundance of LPS may increases the biofilm formation ability of ST111 strains, leading the resistance to pyocin. The deficiency of LPS makes non-ST111/ST446 vulnerable to pyocin instead.

Conclusions: The dominance of ST111 strains may be explained by a relative fitness advantage over other clinical strains which at least in part may be the presence of lasR mutation resulting in social cheating and R-pyocins that have bactericidal properties. ST111 and ST446 strains act as a predator in the pyocin-mediated inter-strain competition, but additional work is necessary to better understand the factors driving their dominance and persistence.

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Poster 84

Flagellin Modulates Regulation of Clostridiodes Difficile *Pathogenesis in The Absence of Motility*

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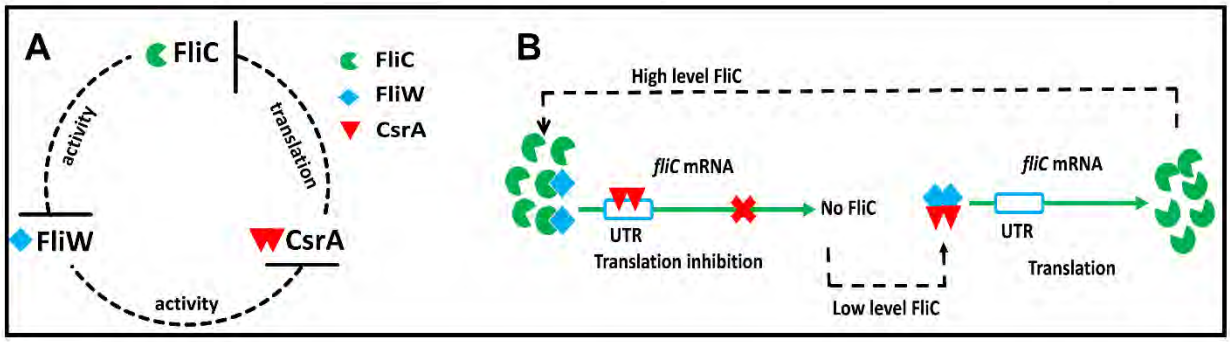
Background: *Clostridioides difficile* is a leading cause of nosocomial antibiotic-associated diarrhea in developed countries with many known virulence factors. In several pathogens, motility and virulence are intimately linked by regulatory networks that allow coordination of these processes in pathogenesis and physiology. *C. difficile* flagellin (FliC) is associated with toxin gene expression, bacterial colonization and virulence, and is also involved in pleiotropic gene regulation during *in vivo* infection. However, how *fliC* expression is regulated and how FliC modulates *C. difficile* pathogenicity remain unclear. In other bacterial species, FliC participates in a regulatory network with FliW and CsrA to regulate motility. Currently, studies investigating the role of *fliC* in *C. difficile* physiology were performed with motile strains. Despite its canonical role in motility, we found *fliC* is highly conserved in non-motile *C. difficile* strains that have jettisoned most flagellar assembly genes. We therefore investigated the roles of *fliC* in pathogenesis and physiology in the non-motile clade 5 ribotype 078 strain *C. difficile* 1015 (CD1015).

Hypothesis: Flagellin Modulates Regulation Of *Clostridiodes Difficile* Pathogenesis In The Absence Of Motility.



Methods: We deleted *C. difficile* 1015 *fliC-fliW-crsA* genes with CRISPR-Cas12a and evaluated the mutants toxin production and pathogenicity *in vitro* and *in vivo*.

Results: We determined that *fliC* was expressed in CD1015 and the regulatory role of *fliC* on toxin production is independent of functional flagella and motility. We showed protein-protein interactions between FliW-FliC and FliW-CsrA using a bacterial two-hybrid system and identified the required binding site for CsrA post-transcriptional regulation in the 5' untranslated region of the *fliC* transcript. Analysis of mutations in *fliC*, *fliW* and *csrA* (and all combinations) on *C. difficile* pathogenesis indicated that FliW plays a central role in *C. difficile* virulence as animals infected with strains carrying a deletion of *fliW* showed decreased survival and increased disease severity.

Conclusions: Our highlights that key proteins involved in flagellar biosynthesis retain their regulatory roles in pathogenesis independent of their functions in motility.

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