ARLG
Antibacterial Resistance Leadership Group

July 2023
Q3 Newsletter

Welcome to the ARLG Newsletter! Here, you will receive important updates from ARLG regarding recent events, grants, publications, and the committees that help us work toward our mission: to prioritize, design, and execute clinical research that will impact the prevention, diagnosis, and treatment of infections caused by antibiotic resistant bacteria.

Get Involved with ARLG

ARLG continuously accepts proposals for clinical studies designed to prevent, diagnose, treat, or eradicate antibiotic-resistant bacterial pathogens. We also award grants and fellowships to qualified investigators. If you are interested in getting involved with ARLG, apply now or contact us for more information.

Submit a Proposal

Contact Us

News

Tori Kinamon Featured in Duke School of Medicine's *Magnify Magazine*

A recent Magnify Magazine article features ARLG Innovations Working Group member and Duke School of Medicine MD candidate Tori Kinamon. The article highlights her journey from a college athlete who survived a severe Methicillin-resistant *Staphylococcus aureus* (MRSA) infection to an infectious diseases researcher committed to addressing antibacterial resistance with a patient-centered approach.

Kinamon highlights the importance of advancing research development efforts amidst the growing prevalence of antibacterial resistance. She attributes her positive recovery from the infection to the fortunate availability of an effective treatment and expresses a strong determination to extend similar opportunities to future patients.

Read more

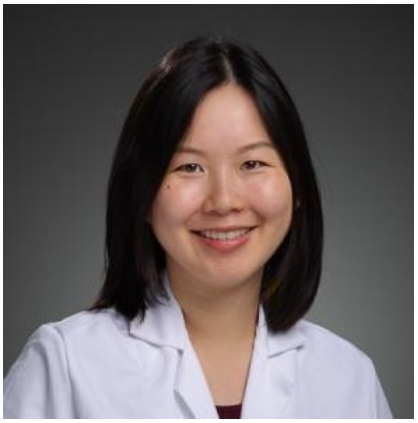
Melinda Pettigrew Appointed Dean of the UMN School of Public Health

We extend our congratulations to Melinda Pettigrew who has been named Dean of the University of Minnesota (UMN) School of Public Health. In this new role, which begins in December 2023, Dr. Pettigrew will serve as the chief executive and chief academic officer.

Dr. Pettigrew is the Chair of the ARLG Diversity Working Group and a member of the **Laboratory Center Consortium Team**. Her research explores the effect of microbiome disruptions on antibacterial resistance and the risk for hospital-acquired infections.

Read more

ARLG Spotlight — Helen Zhang, MD, MSCE



Helen Zhang, MD, MSCE
ARLG Fellow
Duke University

About my role in the ARLG

As an advanced infectious diseases fellow interested in antibacterial resistance research, the ARLG provides me with full salary support to conduct mentored research in antibacterial resistance, as well as support for related training activities. ARLG's support

has given me protected time to focus on building my research skillset and portfolio.

About my research

My research focuses on the epidemiology of infections caused by multidrug-resistant gram-negative bacilli. Specifically, I am investigating risk factors for treatment failure and recurrence among patients with community-onset urinary tract infections caused by extended-spectrum cephalosporin-resistant Enterobacterales.

Why is this research important?

Infections caused by extended-spectrum cephalosporin-resistant Enterobacterales are among the top antibacterial resistance threats in the world. Epidemiologic research on these infections helps to lay the groundwork for future studies aimed at improving their treatment and prevention.

Read More

IDSA 2023 Guidance on the Treatment of Antimicrobial Resistant Gram-Negative Infections

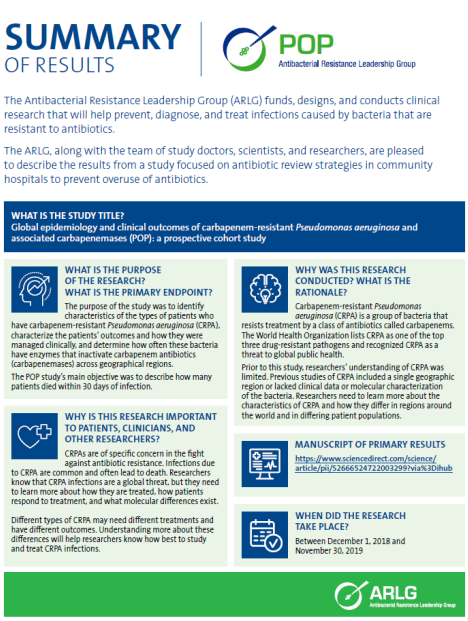
The Infectious Diseases Society of America (IDSA) released new guidance on the treatment of antimicrobial-resistant gram-negative infections. Several ARLG members, including Robert Bonomo, Amy Mathers, David van Duin, Cornelius Clancy, and Pranita Tamma drafted this new guidance with Samuel Aitken.

In its 2019 Strategic Plan, IDSA prioritized the creation and distribution of clinical practice guidelines and other guidance documents as a key initiative. To address the challenge inherent in the traditional process of developing clinical practice guidelines, which involves extensive literature review and rigorous methodology, IDSA endorses creating more focused guidance documents that are updated annually.

The present document focuses on the treatment of infections caused by specific antimicrobial-resistant pathogens, including extended-spectrum β-lactamase-producing Enterobacterales (ESBL-E), AmpC β-lactamase-producing Enterobacterales (AmpC-E), carbapenem-resistant Enterobacterales (CRE), *Pseudomonas aeruginosa* with difficult-to-treat resistance (DTR-*P. aeruginosa*), carbapenem-resistant *Acinetobacter baumannii* species (CRAB), and *Stenotrophomonas maltophilia*. The document provides guidance in the form of answers to clinical questions related to each pathogen, including notable clinical trials, resistance mechanisms, and antimicrobial susceptibility testing methods.

Read more

POP Study Summary Now Available



SUMMARY OF RESULTS

POP Antibacterial Resistance Leadership Group

The Antibacterial Resistance Leadership Group (ARLG) funds, designs, and conducts clinical research that will help prevent, diagnose, and treat infections caused by bacteria that are resistant to antibiotics.

The ARLG, along with the team of study doctors, scientists, and researchers, are pleased to describe the results from a study focused on antibiotic review strategies in community hospitals to prevent overuse of antibiotics.

WHAT IS THE STUDY TITLE?
Global epidemiology and clinical outcomes of carbapenem-resistant *Pseudomonas aeruginosa* and associated carbapenemases (POP): a prospective cohort study

WHAT IS THE PURPOSE OF THE RESEARCH? WHAT IS THE PRIMARY ENDPOINT?

The purpose of the study was to identify characteristics of the types of patients who have carbapenem-resistant *Pseudomonas aeruginosa* (CRPA), characterize the patients' outcomes and how they were managed clinically, and determine how often these bacteria have enzymes that inactivate carbapenem antibiotics (carbapenemases) across geographical regions.

The POP study's main objective was to describe how many patients died within 30 days of infection.

WHY WAS THIS RESEARCH CONDUCTED? WHAT IS THE RATIONALE?

Carbapenem-resistant *Pseudomonas aeruginosa* (CRPA) is a group of bacteria that resists treatment by a class of antibiotics called carbapenems. The World Health Organization lists CRPA as one of the top three drug-resistant pathogens and recognized CRPA as a threat to global public health.

Prior to this study, researchers' understanding of CRPA was limited. Previous studies of CRPA included a single geographic region or lacked clinical data or molecular characterization of the bacteria. Researchers need to learn more about the characteristics of CRPA and how they differ in regions around the world and in differing patient populations.

WHY IS THIS RESEARCH IMPORTANT TO PATIENTS, CLINICIANS, AND OTHER RESEARCHERS?

CRPAs are of specific concern in the fight against antibiotic resistance. Infections due to CRPA are common and often lead to death. Researchers know that CRPA infections are a global threat, but they need to learn more about how they are treated, how patients respond to treatment, and what molecular differences exist.

Different types of CRPA may need different treatments and have different outcomes. Understanding more about these differences will help researchers know how best to study and treat CRPA infections.

MANUSCRIPT OF PRIMARY RESULTS

https://www.sciencedirect.com/science/article/pii/S2666524722003299?via%3Dihub

WHEN DID THE RESEARCH TAKE PLACE?

Between December 1, 2018 and November 30, 2019

ARLG Antibacterial Resistance Leadership Group

A lay summary of results is now available for the **P**rospective **O**bservational ***P****seudomonas* (POP) study on the global epidemiology and clinical outcomes of carbapenem-resistant *Pseudomonas aeruginosa* (CRPA) and associated carbapenemases.

Although the World Health Organization (WHO) lists CRPA as one of the top three drug-resistant pathogens and a threat to global public health, researchers previously had a limited understanding of CRPA. Prior research studies lacked clinical data or molecular characterization of the bacteria or they only included a single geographic region.

The goal of the POP study was to define the characteristics and outcomes of CRPA infections and the global frequency and clinical impact of carbapenemases harbored by CRPA. The study spanned 44 hospitals in the U.S., South and Central America, China, Australia, Singapore, Lebanon, and Saudi Arabia. Researchers followed 972 patients who had CRPA in their bloodstream, respiratory, urinary, or wound cultures. The results from their analyses show that the CRPA genetic characteristics can vary from one region to another, and patients' outcomes may vary as well.

Read More

Events

IDWeek 2023 Late Breaker Abstract Submission Deadline

IDWeek 2023 is just around the corner and it's already shaping up to be an exciting conference! This year's hybrid event will take place October 11-15 in Boston and online. Be sure to **register** if you haven't already.

If you have a late breaker abstract, the submission website is now open. Late breaking abstracts should present high-impact, ground-breaking scientific research

results that were not yet available for the regular abstract submission deadline in May.

The deadline to submit late breaker abstracts is August 16.

Learn more

Past ARLG Grand Rounds Now Available to View

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Have you missed any of the ARLG Grand Rounds events? If so, you're in luck. ARLG's Events page now contains an archive of past presentations. There, you will find information about the topics and speakers along with links to presentation videos and slides.

Here are the Grand Rounds presentations currently available:

Straining For the Best Outcomes: Top Controversies in *C. difficile* Management March 3, 2023	Michael Woodworth, MD, MSc. Assistant Professor, Division of Infectious Diseases Emory University	Sarah Doernberg, MD, MAS Associate Professor in the Division of Infectious Diseases Medical Director, Adult Antimicrobial Stewardship UCSF Medical Center
Dissecting The Epidemics of Multidrug-Resistant Organisms: A Focus on Carbapenem-Resistant *Klebsiella pneumoniae* February 4, 2022	Cesar A. Arias, MD, MSc, PhD Professor of Medicine, Co-director, Center for Infectious Diseases Research Houston Methodist Hospital Weill Cornell Medical College	
The Microbiota and Resistome in Clinical Trials: Opportunities and Challenges May 6, 2022	Melinda M. Pettigrew, PhD Deputy Dean and Anna M. R. Lauder Professor of Epidemiology Yale School of Public Health	

Considerations for the Use of Phages in Clinical Practice November 4, 2022	Gina Suh, M.D. (Mayo Clinic) Thomas Lodise, Pharm.D., Ph.D (Albany College of Pharmacy and Health Sciences) Robin Patel, M.D. (Mayo Clinic)	

We will be adding more presentations to the Events page archive as they become available, so be sure to check back. While you're there, hit the subscribe button to receive notifications of upcoming events.

Read more

Study Milestones

View recent ARLG study updates.

DOTS	**D**albavancin as an **O**ption for **T**reatment of **S**. aureus Bacteremia	Enrollment Complete
FAST	**F**ast **A**ntibiotic **S**usceptibility **T**esting for gram-negative bacteremia	Sites Selected
STEP FMT	**S**train **T**emporal **E**ngraftment and **P**ersistence after **F**ecal **M**icrobiota **T**ransplantation	Data Analysis
OPTIMIZE-GNI	**Optimiz**ation of Beta-lactam Dosing in Critically-Ill Patients with Suspected or Documented Antimicrobial Resistant **G**ram-**N**egative **I**nfections with Cystatin C	Planning

Go to the ARLG Studies page for more milestones and updates!

Learn More

Recent Publications

View the following recent ARLG publications.

Boutzoukas AE, Komarow L, Chen L, Hanson B, Kanj SS, Liu Z, Salcedo Mendoza S,Ordonez K, Wang M, Paterson DL, Evans S, Ge L, Giri A, Hill C, Baum K, Bonomo R, Kreiswirth B, Patel R, Arias CA, Chambers HF, Fowler VG Jr., van Duin D; on behalf of the Antibacterial Resistance Leadership Group and Multi-Drug Resistant Organism Network Investigators. International epidemiology of carbapenemase-producing Escherichia coli isolates. Clin Infect Dis. 2023;ciad288. doi:10.1093/cid/ciad288.

Simner PJ, Dien Bard J, Doern C, Johnson JK, Westblade L, Yenokyan G, Patel R, Hanson KE; for the Antibacterial Resistance Leadership Group. Reporting of Antimicrobial Resistance from Blood Cultures, an Antibacterial Resistance Leadership Group Survey Summary: Resistance Marker Reporting Practices from Positive Blood Cultures. Clin Infect Dis. 2023;76(9):1550-1558. doi:10.1093/cid/ciac952.

Kinamon T, Gopinath R, Waack U, Needles M, Rubin D, Collyar D, Doernberg SB, Evans S, Hamasaki T, Holland TL, Howard-Anderson J, Chambers H, Fowler VG Jr., Nambiar S, Kim P, Boucher HW. Exploration of a Potential DOOR Endpoint for Complicated Intra-Abdominal Infections Using Nine Registrational Trials for Antibacterial Drugs. Clin Infect Dis. 2023 Apr 19;ciad239. doi: 10.1093/cid/ciad239. Online ahead of print.

Tsalik EL, Rouphael NG, Sadikot RT, Rodriguez-Barradas MC, McClain MT, Wilkins DM, Woods CW, Swamy GK, Walter EB, El Sahly HM, Keitel WA, Mulligan MJ, Tuyishimire B, Serti E, Hamasaki T, Evans SR, Ghazaryan V, Lee M, Lautenbach E, and the TRAP-LRTI Study Group, on behalf of the Antibacterial Resistance Leadership Group. Efficacy and safety of azithromycin versus placebo to treat lower respiratory tract infections associated with low procalcitonin: a randomised, placebo-controlled, doubleblind, non-inferiority trial. Lancet Infect Dis. 2023 Apr;23(4):484-495. doi: 10.1016/S1473-3099(22)00735-6. Epub 2022 Dec 13.

Sivapalan P, Staehr Jensen J-U. Procalcitonin to reduce antimicrobial overuse in patients with lower respiratory tract infection: time for re-evaluation of our prescription culture? Lancet Infect Dis. 2023 Apr;23(4):390-391. doi: 10.1016/S1473-3099(22)00757-5. Epub 2022 Dec 13.

Patel R, Tsalik EL, Evans S, Fowler VG Jr., Doernberg SB. Clinically Adjudicated Reference Standards for Evaluation of Infectious Diseases Diagnostics. Clin Infect Dis. 2023 Mar 4;76(5):938-943. doi: 10.1093/cid/ciac829.

Reyes J, Komarow L, Chen L, Ge L, Hanson BM, Cober E, Herc E, Alenazi T, Kaye KS, Garcia-Diaz J, Li L, Kanj SS, Liu Z, Onate JM, Salata RA, Marimuthu K, Gao H, Zong Z, Valderrama-Beltran SL, Yu Y, Tambyah P, Weston G, Salcedo S, Abbo LM, Xie Q, Ordonez K, Want M, Stryjewski M, Munita JM, Paterson DL, Hill C, Baum K, Bonomo RA, Kreiswirth BN, Villegas MV, Patel R, Arias CA, Chambers HF, Fowler VG, Doi Y, van Duin D, Satlin MJ; for the the Prospective Observational POP Study Investigators and the Antibacterial Resistance Leadership Group. Global Epidemiology of Carbapenem-resistant Pseudomonas aeruginosa and Associated Carbapenemases (POP): a Prospective Cohort Study. Lancet Microbe. 2023 Mar;4(3):e159-e170. doi: 10.1016/S2666-5247(22)00329-9. Epub 2023 Feb 9.

Howard-Anderson J, Hamasaki T, Dai W, Collyar D, Rubin D, Nambiar S, Kinamon T, Hill C, Holland TL, Doernberg SB, Chambers HF, Fowler VG Jr., Evans SR, Boucher HW; on behalf of the Antibacterial Resistance Leadership Group. Improving Traditional Registrational Trial Endpoints: Development and Application of a Desirability of Outcome

Ranking (DOOR) Endpoint for Complicated Urinary Tract Infection Clinical Trials. Clin Infect Dis. 2023 Feb 8;76(3):e1157-e1165. doi: 10.1093/cid/ciac692.

Anesi JA, Lautenbach E, Thom KA, Tamma PD, Blumberg EA, Alby K, Mitchell SL, Bilker WB, Werzen A, Ammazzalorso A, Tolomeo P, Omorogbe J, Pineles L, Han JH. Clinical Outcomes and Risk Factors for Carbapenem-resistant Enterobacterales Bloodstream Infection in Solid Organ Transplant Recipients. Transplantation. 2023 Jan 1;107(1):254-263.

Lodise TP, O'Donnell JN, Balevic S, Liu X, Gu K, George J, Ghazaryan V, Beresnev T, Raja S, Guptill JT, Saharoff S, Schwager N, Fowler VG Jr., Wall A, Wiegand K, Chambers HF, Antibacterial Leadership Resistance Group. Pharmacokinetics of Ceftazidime-Avibactam in Combination with Aztreonam (COMBINE) in a Phase 1 Open, Labeled Study of Healthy Adults. Antimicrob Agents Chemother. 2022;66(12):e0093622. doi:10.1128/aac.00936-22.

Lodise TP, O'Donnell N, Raja S, Guptill JT, Zaharoff S, Schwager N, Fowler VG Jr., Ghazaryan V, Beresnev T, Knisely JM, Norice-Tra CT, Wall A, Wiegand K, Serti Chrisos E, Balevic S, Chambers HF, Antibacterial Resistance Leadership Group. Safety of Ceftazidime-Avibactam in Combination with Aztreonam (COMBINE) in a Phase I, Open-Label Study in Healthy Adult Volunteers. Antimicrob Agents Chemother. 2022 Dec 20;66(12):e0093522.