ARLG Update
Antibacterial Resistance Leadership Group

To prioritize, design, and execute clinical research that will reduce the public health threat of antibacterial resistance

ARLG Update

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INSIDE THIS ISSUE

For more information about the ARLG, its leaders, or its current projects, please visit **arlg.org**

ARLG Mentoring Core

Early Stage Investigator Seed Grants

A key component of the ARLG Mentoring Core is the availability of Early Stage Investigator (ESI) Seed Grants. Each grant year, up to $50,000 in direct costs will be provided for up to five ESIs. These ESI Seed Grants allow upcoming investigators, who have been on faculty for less than five years, to generate preliminary data which may lead to additional external funding in any area related to antibacterial resistance. These funds can also be combined with isolates contained in the ARLG Virtual Biorepository, [arlgcatalogue.org], which was deployed on 12/12/14. Potential ESI candidates can apply on the ARLG website:
https://arlg.org/protocol-concept-fellow-and-site-applicants/esi-seed-grant-applicants

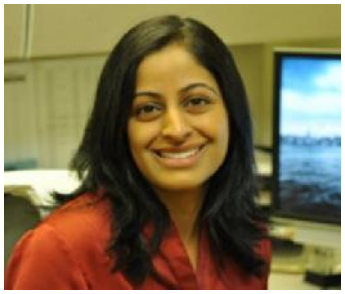
To date, ESI Seed Grants have been awarded to three early stage investigators: Ritu Banerjee, MD PhD, Pranita Tamma, MD MHS, and Jennifer Han, MD.

Ritu Banerjee, MD, PhD of the Mayo Clinic was the first recipient of an ARLG ESI Seed Grant for her project - *Clinical and Economic Impact of Rapid Identification and Susceptibility Testing of Pathogens Growing in Blood Culture Bottles*. Robin Patel, MD of the Mayo Clinic is serving as her mentor.

Ritu Banerjee, MD, PhD

The primary objective of Dr. Banerjee's project is to determine if the BCID test either alone, or in combination with antimicrobial stewardship, will impact the antimicrobial utilization, clinical outcomes, and healthcare costs of patients with bloodstream infections. Dr. Banerjee hypothesizes that among patients with bloodstream infections, use of the BCID test combined with real-time audit of antimicrobial prescribing and feedback to prescribers will improve timely administration of optimal antimicrobial therapy and improve clinical and economic outcomes, compared to use of standard culture and susceptibility testing, or the BCID test alone.

To test this hypothesis, a prospective, randomized controlled trial was conducted comparing clinical and economic outcomes among patients with positive blood cultures who received either: standard culture and antimicrobial susceptibility testing (AST) of positive blood culture bottles as is done today (control), standard culture and AST of positive blood culture bottles plus the FilmArray Blood Culture ID Panel (intervention group 1), or standard culture and AST of positive blood culture bottles plus the FilmArray Blood Culture ID Panel testing along with expert infectious diseases phone consultation (intervention group 2). A manuscript describing results of the study is currently under review.



Pranita Tamma, MD, MHS

Pranita Tamma, MD, MHS of Johns Hopkins University was the second recipient of an ARLG ESI Seed Grant for her project *Development of a Multicenter Gram-negative Database to Establish Clinically Relevant Antibiotic Breakpoint Interpretative Criteria*. Sara Cosgrove, MD, MS of Johns Hopkins University is serving as her mentor.

The primary objective of Dr. Tamma's project is to compare clinical outcomes of adult patients with Gram-negative bacteremia with organisms with minimum inhibitory concentrations (MICs) between 4-8 µg/ml (susceptible using the previous CLSI breakpoint criteria and resistant using the current CLSI breakpoint criteria) who received ceftriaxone compared with broader-spectrum antibiotic agents.

ARLG Mentoring Core

Early Stage Investigator Seed Grants *continued*

Dr. Tamma hypothesizes that there will be no difference in 14-day mortality, 14-day bacteremic relapse, or length of hospital stay between adults receiving ceftriaxone versus broader-spectrum antibiotic agents in adults with Gram-negative bacteremia with organisms susceptible to ceftriaxone using pre-2010 CLSI recommended breakpoints and resistant using post-2010 breakpoints (MICs 4-8 µg/ml).

To test this hypothesis, a retrospective, observational propensity score-matched study of patients ≥18 years of age with monomicrobial Gram-negative bacteremia over a 7-year period is being conducted at 3 academic medical centers, Johns Hopkins University, the University of Maryland, and the University of Pennsylvania.

Jennifer Han, MD MSCE of the University of Pennsylvania was the third recipient of an ARLG ESI Seed Grant for her project *The epidemiology of carbapenem-resistant Klebsiella pneumoniae (CRKP) in long-term acute care hospitals (LTACHs)*. Ebbing Lautenbach, MD, MPH, MSCE of the University of Pennsylvania is serving as her mentor.

Jennifer Han, MD MSCE

The primary objectives of Dr. Han's project are 1) to evaluate risk factors for relatedness of CRKP isolates from LTACH residents and 2) to assess the impact of various resistance mechanisms, virulence factors, and capsular gene types on clinical outcomes in the LTACH setting.

Dr. Han hypothesizes that the presence of indwelling devices (e.g., urinary catheters, central venous lines) will be a significant risk factor for strain relatedness as assessed by whole-genome sequencing. Specifically, that indwelling devices will increase the risk of transmission (e.g., through CRKP colonization/infection) and that the results of whole-genome sequencing will provide high genotype-phenotype concordance and will have a significant impact on clinical outcomes in LTACH residents in association with antibiotic treatment selection.

To test this hypothesis, a clinical epidemiologic and microbiologic study is being conducted building on an existing collaboration that will focus on characterization of CRKP isolates from a network of LTACHs, including linkage to clinical epidemiologic characteristics. Patients will be identified through the clinical microbiology laboratories that process and culture clinical specimens for the respective LTACH.

Publications Update

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