2601. Identification of Staphylococcus aureus Genes Associated with the Subversion of Macrophage Phagosomal Acidification
Paul E. R. Morris, MBBCB BA; Stephen Renshaw, MA FRCP PhD; Simon J. Foster, BSc PhD; Andrew Peden, PhD; David Dockrell, MD; The University of Sheffield, Sheffield, UK; 1University of Edinburgh, Edinburgh, UK

Session: 269. Pathogenesis and Host-Response Interactions Saturday, October 5, 2019: 12:15 PM

Background: S. aureus is a major medical pathogen contributing to healthcare-associated costs and mortality. Metastatic S. aureus infection is commonly associated with skin and soft-tissue infections. Macrophages as resident tissue phagocytes are essential for bacterial clearance and effectively phagocytose and kill S. aureus at low inocula. Formation of an intracellular reservoir develops when the capacity for macrophages to eradicate S. aureus is overwhelmed at increased inocula. Phagosomal maturation after bacterial ingestion involves sequential fusion with endosomes and lysosomes, reducing luminal pH, facilitating bacterial degradation. In the context of intracellular S. aureus, incomplete phagosomal maturation demonstrable with impaired acidification and failure of the lytic burst leads to increased bacterial survival. The role of these VFs in bacteremia prognosis is not well characterized. Our study aims to evaluate the clinical characteristics and outcomes of S. aureus bacteremia patients specifically in relation to biofilm forming isolates.

Methods: An ordered mutant library of S. aureus provides the opportunity to give a comprehensive evaluation of gene function. The Nebraska transposon (Tn) mutant library contains 1952 sequence-defined Tn insertion mutants derived of USA300 LA
c aureus, each with a single non-essential gene deletion. The mutants were labeled with a fluorescent stain activated at pH < 6 and challenged against differentiated human monocyte-derived macrophages for 4 hours. A high-content microscopy screen was developed to identify the bacterial genes associated with impairment of phagosomal acidification.

Results: The results of the high-throughput screen indicate the global regulators agr and saeR, hemolysin A and catalase are associated with the inhibition of phagosomal acidification.

Conclusion: The burden of S. aureus bacteremia and metastatic disease makes the targeting of intracellular S. aureus essential. Identification of bacterial factors associated with impaired phagosomal acidification and maturation offers targets to limit S. aureus infections.

Disclosures. All authors: No reported disclosures.

2602. Genetic Basis of Staphylococcus aureus Virulence
Edward W. Adams, III, MD, Doyle V. Ward, PhD, Bruce A. Barton, PhD; Richard T. Ellison, III, MD; Oladapo Okanlawon, MS; University of Massachusetts Medical School, Worcester, Massachusetts

Session: 269. Pathogenesis and Host-Response Interactions Saturday, October 5, 2019: 12:15 PM

Background: Although multiple different virulence factors have been identified for Staphylococcus aureus, there is limited information on genetic variation present between different strains of S. aureus in the clinical setting. To better define whether differing virulence factors could contribute to differing clinical manifestations of S. aureus infections we undertook a comparison of the frequency of virulence and antibiotic resistance genes present in S. aureus isolates from different clinical sites.

Methods: Whole-genome sequencing was performed on a convenience sample of S. aureus isolates from clinical or surveillance cultures obtained at an academic medical center over a 27-month period. Genomic assemblies were generated and annotated to define protein-coding regions. The prevalence of 28 genes previously defined as being associated with S. aureus virulence or antimicrobial resistance, including MSCRAMM genes, was then analyzed in relation to nine specific culture sources including only a single isolate from each culture source per patient using a likelihood ratio χ² analysis.

Results: There were 1286 S. aureus isolates with draft assemblies and annotations, and there was a statistically significant (P < 0.01) difference in gene frequencies between culture sources for 18 genes that included 13 of 19 virulence factors, 4 of 7 antibiotic resistance genes and 1 of 2 MSCRAMM genes. The most notable variation was seen for the presence of the sec, esp, lukS, lukF, fnbA, mecA, and emm4 genes (all with P < 0.0001). There were also significant variations in overall gene frequency patterns between isolates from wound, blood, and respiratory isolates (P < 0.0001), as well as significant differences in the frequency of cna and hlf genes between surveillance and isolates (P < 0.0001).

Conclusion: This study demonstrates a difference in the prevalence of virulence and antibiotic resistance genes in S. aureus isolates based on the culture source. As the culture location can be considered a surrogate for different types of infections (such as bacterial pneumonia, urinary tract infections) these differences in gene frequency may contribute to variation in the clinical manifestations of infections by differing S. aureus strains.

Disclosures. All authors: No reported disclosures.

2603. Biofilm Formation as a Predictive Marker of Prognosis for Escherichia coli Septis
Kathleen Zhang, Bachelor of Science; Daniella Schneider, Masters Physician Assistant; Rakesh Baweja, Medical Degree (MD); Mariana Gomez de la Espriella, IMM/Infectious disease; Jayashrini Rao, PhD; Anthony Baillie-Bonne, Medical Degree (MD); Virginia Tech Carilion School of Medicine, Roanoke, Virginia; College of Health Sciences, Boones Mill, Virginia; Inova Health System, Fairfax, Virginia; Carilion Clinic, Virginia Tech, Blacksburg, Virginia; Virginia Tech School of Medicine, Carilion Clinic, Jefferson College of Health Sciences, Roanoke, Virginia; Carilion Clinic/VTCSOM, Roanoke, Virginia

Session: 269. Pathogenesis and Host-Response Interactions Saturday, October 5, 2019: 12:15 PM

Background: Escherichia coli is the Gram-negative organism most commonly associated with bloodstream infections and death due to sepsis. Timely administration of appropriate antibiotic(s) plays a significant role in improving patient outcomes. E. coli expresses virulence factors (VFs) such as biofilm formation and motility phenotypes which play a role in bacterial attachment and dissemination by enabling immune system evasion and host migration. The role of these VFs in bacteremia prognosis is not well characterized. Our study aims to evaluate the clinical characteristics and outcomes of E. coli bacteremia patients specifically in relation to biofilm forming isolates.

Methods: 91 E. coli bacteremia clinical isolates were consecutively collected from patients between 2013 to 2015. Virulence factor phenotypes were determined by in vitro biofilm formation, motility, and milk hydrolysis. Clinical patient data associated with the isolates were abstracted from the electronic medical records database and blinded from research team throughout characterization. Descriptive statistics were used for clinical variables and analyzed in a dichotomized fashion based on biofilm formation. The chi-square or Fisher exact test were used for categorical data and the Mann-Whitney U or Student T-test for continuous variables as appropriate.

Results: Of the 91 isolates, 41 had a biofilm-forming phenotype. Of the 87 isolates tested for milk hydrolysis and motility a positive finding was seen in 61 (70%) and 67 (77%) isolates, respectively. In the multivariate model, patients with E. coli bacteremia from biofilm producing isolates were at increased risk of death or going into hospice during that hospitalization. ([OR],9.8; 95% CI, 1.1,88.7, P = 0.041).

Conclusion: Patients with biofilm-forming E. coli bacteremia had worse clinical outcomes than their non-biofilm forming counterparts suggesting that this phenotype leads to a more pathogenic organism. A prospective study to confirm this finding is needed as is the design of rapid diagnostics to promptly identify this phenotype in septic patients.

Disclosures. All authors: No reported disclosures.
Disclosures. All authors: No reported disclosures.

2604. Changes in a Fatty Acid Kinase Associated with Daptomycin (DAP) Resistance Lead to Increased Collagen Binding and Biofilm Formation in Enterococcus faecalis
William R. Miller, MD1; Kavindra V. Singh, PhD2; Jinneth Reyes, MSc, PhD2; Barbara E. Murray, MD1; Cesar A. Arias, MD, MSc, PhD, FIDSA3,4; 1Center for Antimicrobial Resistance and Microbial Genomics, UTHealth, Houston, Texas; 2Molecular Genetics and Antimicrobial Resistance Unit and International Center for Microbial Genomics, Universidad El Bosque, Bogota, Distrito Capital de Bogota, Colombia; 3CARMG, UTHealth and Center for Infectious Disease, UTHealth School of Public Health, Houston, Texas; 4Molecular Genetics and Antimicrobial Resistance Unit and International Center for Microbial Genomics, Universidad El Bosque, BOG, COL, Houston, Texas

Session: 269. Pathogenesis and Host-Response Interactions
Saturday, October 5, 2019: 12:15 PM

Background: Enterococci are a major cause of healthcare-associated infections with limited treatment options. We previously identified that mutations in dak (a gene encoding a putative fatty acid kinase), ace (a collagen adhesin) and the YxddK stress response system are associated with DAP resistance (DAP-R) in E. faecalis (Efs) in the absence of a functional LiaFSR system. Here, we examined the role of DAK in pathogenesis by examining the ability of the mutants to produce biofilm and bind to collagen, an important protein of the extracellular matrix.

Methods: Previously, the Efs strain OG1RFΔliaR (inactive LiaFSR system, DAP susceptible) was adapted to make a DAP-R derivative (mutations in isolaR, ace and dak), and the mutant OG1RFΔliaRΔdak, lacking the C-terminal domain of dak, and its complement OG1RFΔliaRΔdak-c-dak were constructed to study the dak mutation in isolation. Biofilm formation (BF) for the above strains was assayed after growth in tryptic soy broth with glucose in 96-well plates at 37°C for 24 hours. Bacteria were fixed with Bouin’s solution OG1RFΔliaRΔdak (P < 0.001), a phenotype which reverted on complementation (7.9 vs. 1.2, P < 0.001). This enhanced biofilm phenotype was also seen in the setting of DAP-R.

Results: When compared with OG1RFΔliaR, the DAP-R derivative exhibited a significant increase in BF (4.6 vs. 2.4, P < 0.001). This enhanced biofilm phenotype was also seen in the setting of DAP-R.