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Background: Community-acquired pneumonia (CAP) and hospital-acquired pneumonia (HAP) are the leading causes of death from infection in developed countries. Mannose-binding lectin (MBL) is a C-type serum lectin that plays a central role in the innate pulmonary host defenses against respiratory pathogens. We hypothesized that MBL polymorphisms may increase the risk of developing *Legionella* pneumonia. Therefore, the aim of this study was to evaluate the role of *MBL* polymorphisms in susceptibility to CAP and HAP caused by *Legionella* spp.

Methods: A total of 96 BAL and blood samples collected for routine microbiological analysis from Lithuanian patients presenting with CAP and HAP, were used for this study. *MBL* polymorphisms in the 54 codon (54 G/G, 54 G/A, and 54 A/A) were detected by *Ban*IRFLP. *Legionella* spp. were detected by nested PCR.

Results: Polymorphisms in the 54 codon of *MBL* were determined in 96 patients. Among 96 patients with CAP and HAP, the most commonly observed 54 codon *MBL* variant was 54 G/G (69.8%, $n = 67$), followed by 54 G/A (21.9%, $n = 21$), and 54 A/A (8.3%, $n = 8$). By using nested PCR, *Legionella* pneumonia was detected among 15.6% ($n = 15$) of patients diagnosed with CAP and HAP. *Legionella* spp. were detected among 7 patients with *MBL* 54 codon G/G variant (10.4%), while 3 patients with *MBL* 54 G/A (14.3%), and 5 patients with *MBL* 54 codon A/A variant (62.5%). During this study *Legionella* spp. were detected more frequently ($P < 0.05$) among patients with the A/A variant of the 54 codon vs. those with other variants of *MBL* 54 codon. There were no significant differences found among those with *Legionella* infection and G/A (14.3%) or G/G (10.4%) variants of *MBL* gene 54 codon.

Conclusion: *MBL* gene 54 codon variant A/A polymorphisms may play an important role in increased susceptibility to lower respiratory infectionscaused by *Legionella* spp.

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2601. Identification of *Staphylococcus aureus* Genetic Factors Associatiated with the Subversion of Macrophage Phagosomal Acidification

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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 is demonstrable with impaired acidification and failure of lysosome fusion. Inhibition of phagosomal maturation is dependent upon bacterial factors as it is reversed in heat-killed bacteria. Intracellular survival of *S. aureus* is associated with reduced antimicrobial effectivity and increased complications. Within the intracellular environment, persistence of *S. aureus* is associated with adaptation of gene expression which confers greater resistance to antimicrobial effector mechanisms.

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 derivative of USA300 LAC *S. 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.

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2602. Genetic Basis of *Staphylococcus aureus* Virulence

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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 χ^2 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*, *sep*, *entB*, *lukS*, *lufK, fosB*, *mecA*, and *ermA* 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 *hlY* genes between surveillance and clinical 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 bacteremia, pneumonia, urinary tract infections) these differences in gene frequency may contribute to variation in the clinical manifestations of infections by differing *S. aureus* strains.

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2603. Biofilm Formation as a Predictive Marker of Prognosis for *Escherichia coli* Sepsis

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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.

Clinical Characteristics		Non-Biofilm Forming Isolates	Biofilm Forming Isolates	P-value
Age ,mean (SD)		64 (18)	69.3(14)	0.154
Sex (n=91)	Female	36	27	0.377
	Male	12	14	
Race (n=91)	Caucasian	38	39	0.066
	Non-Caucasian	10	3	
Admission source (n=88)	Healthcare Setting	10	6	0.420
	Home	38	35	
Comorbidities	Congestive Heart Failure	10	18	***0.023***
	Renal Disease	12	17	0.113
	Diabetes	19	19	0.576
Charlson Comorbidity Index,CCI , (mean)		4.4	7.2	**< 0.05**

Table 1. Clinical characteristics of patients with *E. coli* bacteremia isolates based on biofilm production.