641. Evaluation of the FilmArray Pneumonia Panel and Potential Impact of Antimicrobial Use on Patients in a Trauma and Medical Intensive Care Unit

Kathy Krupinski- Shaw, BSc[1]; Lauren Lopez, PharmD, BCPS, BCIDP[2]; Halle Orlinski, PharmD[2]; Patrick Ozbolt, MS, MT(ASCP)[2]; Stella Antonara, PhD, D(ABMM)[2]; [1]OhioHealth Laboratory Services, Columbus, Ohio; [2]OhioHealth, Columbus, Ohio

Session: 67. New Diagnostics
Thursday, October 3, 2019: 12:15 PM

Background. Organisms causing infections of the lower respiratory tract in hospitalized patients can lead to high morbidity and mortality. Identification of the agents of pneumonia allows implementation of appropriate antimicrobial therapy and fast and accurate results are essential for the application of the correct antimicrobial regimen.

Methods. For 6 months results of quantitative bronchioalveolar lavage (Q-BALs) respiratory cultures, ordered as a standard of care for patients in our intensive care unit, were compared with the results obtained by a new multiplex molecular assay for the detection of lower respiratory tract pathogens, the FilmArray pneumonia panel (PP). The panel offers semi-quantitation of the bacterial targets that were compared with the quantitative results of the Q-BALs. Additionally, a retrospective chart review was performed to examine whether there would be any difference in the timing of appropriate antimicrobial therapy if the results of the panel were to be available for those patients. Appropriate antimicrobial therapy was determined according to the institution protocol for treatment of patients for ventilator-associated pneumonia based on the results of the quantitative cultures

Results. Thirty-six unique patients Q-BALs were run and of those there was 82% agreement on the detected targets between cultures and PP. Six targets were not detected by the panel (yeast, *S. maltophilia*, Streptococci, *Salmonella* spp.). *M. catarrhalis*, *S. agalactiae* and 3 viral targets were detected only by the panel. There was 100% agreement between the panel detected resistance markers and the culture isolates susceptibilities. Of the 36 patients, 12 were excluded because their medical records were not available for review. Of the 24 reviewed, 8 (33.3%) would have de-escalation in their antibiotics use at least 24h earlier due to the PP result. Eight (33.3%) would have no potential change in therapy and 8 (33.3%) could have inappropriate escalation or continuation due to reporting of potential pathogens by the PP but recorded as normal flora by cultures.

Conclusion. The use of PP would lead to a reduction of unnecessary antimicrobial therapy in 1/3 of the patients examined. However, quantification of organisms otherwise reported as normal flora may lead to unnecessary treatment and requires education of staff to understand the results of the assay.

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

642. Higher Diagnostic Accuracy with Ultrasensitive Detection of *Helicobacter pylori* Stool Antigen Using Single-Molecule Counting Technology

Phoebe Katzenbach, BS[1]; Gipshu Dave, MS[1]; Ali Mukherjee, PhD[1]; Johanna Sandlund, MD[1]; Joel Estis, MS[1]; Niamh Nolan, MS[1]; Niaz Banaei, MD[2]; Brian Noland, PhD[1]; [1]Singulex, Inc., Alameda, California; [2]Stanford University School of Medicine, Palo Alto, California

Session: 67. New Diagnostics
Thursday, October 3, 2019: 12:15 PM

Background. Current diagnostic methods for *Helicobacter pylori* infection include fecal antigen tests, ^{13}C-urea breath test, and gastric biopsy. The breath test is limited by poor specificity and the fecal antigen tests by poor sensitivity. We have developed a prototype assay for detection of *H. pylori* antigen in human stool, powered by ultrasensitive Single Molecule Counting technology, and compared the analytical performance to a commercially available enzyme-linked immunoassay (EIA) antigen test.

Methods. The Singulex Clarity *H. pylori* antigen assay incubates diluted stool with capture and fluorescent-labeled detection antibodies. After incubation and wash steps, fluorescent molecules are eluted and single-molecule fluorescence measured by detected events (DE′). Analytical performance was compared with a commercial EIA (Premier Platinum HpSA® Plus, Meridian Bioscience, Inc.) using serial dilutions of *H. pylori* control (~37,500–1.7 ng/mL) and high positive stool (signal to noise ratio >2). Clinical performance was evaluated using two cohorts, one had 10 EIA-negative and 10 EIA-positive samples and the other 13 high positives (> 0.500 at 450/630) and 5 low positives near the EIA cutoff (0.100–0.500 at 450/630). One sample was excluded due to discordant EIA results, and three to reader flags.

Results. The lower limit of detection of the Clarity *H. pylori* assay was 1.7 ng/mL and the EIA 1,250 ng/mL (IFU: LOD 4.67 ng/mL). A high positive stool sample was detectable by the Clarity *H. pylori* assay diluted 1:10,000,000 and by the EIA 1:10,000. The Clarity *H. pylori* assay showed a 729-fold increase in lower limit of detection and 1,000-fold increase in endogenous antigen lower limit of detection compared with the EIA. Clarity signal ranged from 46–665 DE' for EIA-negative samples and 487,484–576,747 DE' for EIA-positive samples.

Conclusion. The Singulex Clarity *H. pylori* antigen assay may have orders of magnitude higher analytical sensitivity than the commercial EIA and demonstrated 100% positive agreement and 100% negative agreement on detection of *H. pylori* antigen in human stool samples. The ultrasensitive Clarity *H. pylori* assay has the potential for high sensitivity and specificity to improve current diagnostic options for *H. pylori* infection; however, additional multicenter studies are required.

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

643. Comparison of Multiplex Polymerase Chain Reaction (PCR) and Routine Culture for the Detection of Respiratory Pathogens in Pneumonia Patients

Emad Abu Sitta, MD[1]; Nicole Hubbard, MD[2]; Geehan Suleyman, MD[1]; [1]University of Toledo Medical Center, Toledo, Ohio; [2]Promedica Toledo Hospital, Toledo, Ohio

Session: 67. New Diagnostics
Thursday, October 3, 2019: 12:15 PM

Background. The identification of causative pathogens in pneumonia can be challenging, and conventional culture methods can take up to 72 hours. However, rapid microbiologic tests identify organisms within hours. The Biofire®Filmarray ((bioMérieux, North Carolina) Pneumonia Panel was recently approved by the FDA. The multiplex PCR system identifies 33 targets from sputum and bronchoalveolar (BAL) samples, which include 18 bacteria, 8 viruses, and 7 antibiotic resistance genes. The purpose is to compare the panel to routine culture methods for the detection of respiratory pathogens in patients with pneumonia in a 794-bed teaching hospital in northwest Ohio.

Methods. We retrospectively screened all hospitalized intensive care unit patients who met clinical and radiological criteria of pneumonia using electronic medical records between November 2018 and February 2019. Adult patients who had respiratory cultures collected within 7 days were included. Repeat specimens were excluded. Routine cultures were performed using the laboratory's standard procedure, and Pneumonia Panel testing was performed according to manufacturer instructions.

Results. Fifty-nine respiratory or 13 BAL and 46 sputum specimens were evaluated. There was no discrepancy between culture and PCR in 63% (37/59) samples. One (8%) BAL and 10 (22%) sputum specimens had additional pathogens detected by PCR. There was a discrepancy between culture and PCR in four (31%) BAL and seven (15%) sputum samples. The largest discrepancy was noted amongst Serratia marcescens (4/59 or 7%) and Haemophilus influenzae (6/59 or 10%) species. Only one sputum culture had Legionella detected by PCR. Additionally, 17 specimens had a virus detected either alone or with another bacterial pathogen by PCR. For the resistance genes, KPC was detected by PCR but not by Modified Carbapenem Inactivation Method (mCIM) test. The mecA gene was detected in six of seven (86%) of methicillin-resistant *Staphylococcus aureus* (MRSA) isolates. CTX-M was detected in Serratia and *Klebsiella pneunomiae* in two samples; however, the organisms were not isolated in culture.

Conclusion. The Pneumonia Panel can identify additional bacteria that did not grow in culture. This panel can rapidly identify pathogens and potentially reduce unnecessary antibiotic use.

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

644. Comparative Evaluation of ETEST® ERV bioMérieux with the CLSI Broth Microdilution Method for Eravacycline MIC Determination

Veronique Sauvonnet[1]; Corey Fyfe, MS[2]; Diane Halimi[1]; Roland Martelin[1]; Gilles Zambardi[1]; [1]Biomerieux, La Balme Les Grottes, Rhone-Alpes, France; [2]Tetraphase Pharmaceuticals, Watertown, Massachusetts

Session: 67. New Diagnostics
Thursday, October 3, 2019: 12:15 PM

Background. Eravacycline (XERAVA™) is a novel, FDA and EMA-approved fully-synthetic fluorocycline antibiotic developed by Tetraphase Pharmaceuticals Inc. for the treatment of complicated intra-abdominal infections (cIAI) including those caused by multidrug-resistant (MDR) pathogens that have been highlighted as urgent public health threats by the US CDC and the WHO.

The new ETEST ERV strip (MIC range 0.002 – 32 µg/mL) has been developed by bioMérieux and calibrated vs. the broth microdilution reference method (BMD) as described by the Clinical and Laboratory Standards Institute (CLSI) to determine the minimal inhibitory concentration (MIC) of eravacycline against Enterobacterales and *Enterococci.* The aim of the study was to compare ETEST ERV to the CLSI BMD method on a panel of 166 strains comprising 131 Enterobacterales and 35 *Enterococci.*

Methods. Quality control was performed with the CLSI QC strains *E.coli* ATCC 25922 and *E.faecalis* ATCC 29212. The ETEST ERV strip was applied on a Mueller–Hinton agar plate previously seeded with a 0.5 McF bacterial suspension. After incubation for 16–20H at 35°C, the reading was performed using the bacteriostatic mode i.e.,80% of growth. The FDA-approved breakpoints were applied (S≤0.5µg/mL for Enterobacterales and S ≤0.064 µg/mL for *Enterococci*).

Results. The MIC essential agreement was 99.4% at ±1 dilution for the whole panel and the category agreement was 96.4% with 4.8% Major Errors (1 *E. coli*, 2 *K. pneumoniae,* 1 *K.aerogenes,* 1 *C. koseri*, 1 *E. faecalis*), all at ±1 dilution around the single breakpoint. No Very Major Error (VME) was observed.

Conclusion. In this study, the new ETEST ERV strip has been found to be substantially equivalent to the CLI reference method. MIC end-points appear easier to read in comparison to the reference method. With a 15-dilution MIC range and simplicity of use, ETEST ERV could represent a valuable tool for MIC determination and an alternative to the BMD reference method. ETEST ERV will undergo clinical studies to seek IVD FDA clearance and CE marking. For Research Use Only. The performance characteristics of this product have not yet been established.

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

645. Singulex Clarity Norovirus Assay (In Development) Provides Ultrasensitive Detection of Norovirus Genogroups I and II

Gipshu Dave, MS[1]; Phoebe Katzenbach, BS[1]; Johanna Sandlund, MD[1]; Joel Estis, MS[1]; Ali Mukherjee, PhD[1]; Niamh Nolan, MS[1];

Anna Almazan, MS[1]; Orr Hadass, MS[1]; Brian Noland, PhD[1];
Jeffrey J. Bishop, PhD[1]; Niaz Banaei, MD[2]; Diana K. Riner, PhD[3]; John Todd, PhD[1]; [1]Singulex, Inc., Alameda, California; [2]Stanford University School of Medicine, Palo Alto, California; [3]Michigan Department of Health and Human Services, Lansing, Michigan

Session: 67. New Diagnostics
Thursday, October 3, 2019: 12:15 PM

Background. Commercially available enzyme immunoassays (EIAs) for detection of norovirus antigen have poor sensitivity and are limited to use in investigations of a gastroenteritis outbreak. Hence, there remains a need for a standalone high-sensitivity assay that enables rapid and accurate detection of norovirus antigen.

Methods. The Singulex Clarity norovirus assay is currently in development for use on the Singulex Clarity® system (Singulex Inc., Alameda, CA, USA), a fully-automated platform powered by Single Molecule Counting technology (registered with the FDA and CE marked). The assay uses paramagnetic microparticles bound to capture antibody and a fluorescently labeled reporter antibody to detect virion capsid protein of norovirus genogroups I (GI) and II (GII) in the stool. For the development of Clarity Norovirus assay, diagnostic performance of 4 antibody pairs (as Capture and Detection reagent) were evaluated by testing 137 stool samples from patients with suspected norovirus infection. Samples were sourced from three providers: (1) 90 genotyped samples of which 75 were positive (19 different genotypes) and 15 were negative by the CDC assay, (2) 3 samples positive and 5 samples negative by the BioFire® FilmArray® Gastrointestinal Panel, and (3) 39 samples negative by a lab-developed test using Cepheid reagents (SmartCycler®).

Results. From all the antibody pairs tested, one of the pairs had best performance with the area under the receiver operating characteristic (AuROC) curve demonstrating a C-Statistic of 0.959 (95% CI 0.921–0.997), compared with AuROC C-statistic of 0.943 (95% CI 0.896–0.990), 0.871 (95% CI 0.807–0.936), and 0.914 (95% CI 0.863–0.964) for the three other pairs. The Clarity assay detected all 19 different genotypes tested (figures).

Conclusion. The ultrasensitive and rapid Clarity norovirus assay (in development) for detection of GI and GII demonstrated excellent performance with one of the antibody pairs tested and detected all 19 tested genotypes. The Clarity assay may offer a standalone solution for norovirus diagnostics.

Figure 1. Diagnostic performance of antibody pairs tested.

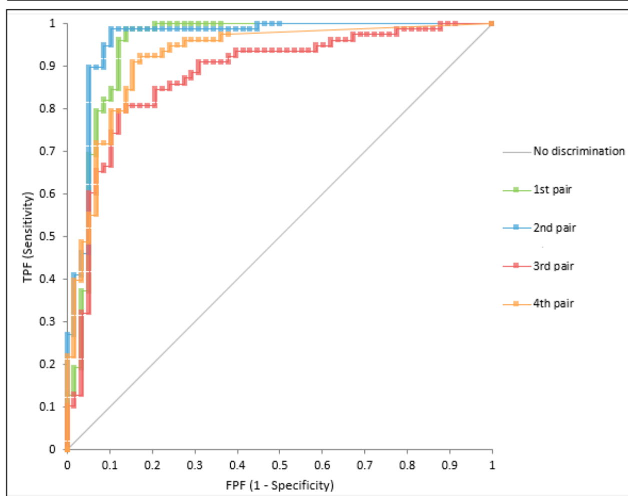
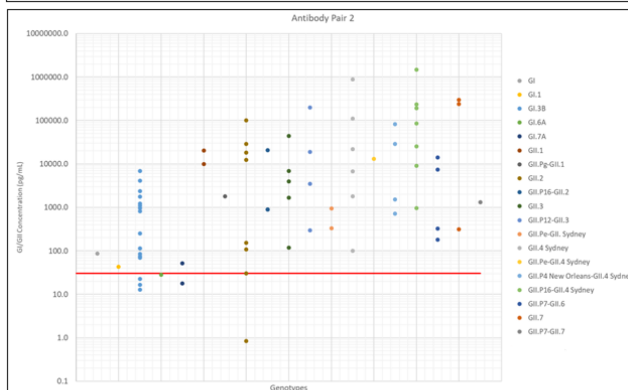


Figure 1: Dot-plot distribution of interpolated concentrations of norovirus-positive and genotyped samples. Antibody pair 2 detected all the tested genotypes with a preliminary cutoff at 30.4 pg/mL.



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

646. Evaluation of the Utility of a New Comprehensive Molecular Assay to Test for the Common Pathogens that Cause Lower Respiratory Tract Infections and its Potential Impact on Antibiotic Therapy

Thomas M. Tarro, MD[1]; Susan Bulter-Wu, PhD [2]; Andrea Kovacs, MD[2]; Mikhaela Cielo, MD[2]; [1]Children's Hospital Los Angeles, Los Angeles, California; [2]Keck School of Medicine, University of Southern California, Los Angeles, California

Session: 67. New Diagnostics
Thursday, October 3, 2019: 12:15 PM

Background. Lower respiratory tract infection (LRTI) has high mortality among critically ill patients. The current standard of care for diagnosing bacterial causes of LRTI is respiratory culture, which is time consuming and insensitive. The FilmArray Pneumonia Panel (FA-Pneumo) (Biofire Diagnostics, Salt Lake City, UT) is FDA-cleared for the detection of lower respiratory tract pathogens (bacteria, atypical bacteria, and viruses) directly from lower respiratory tract specimens. Here, we evaluated the performance of the FA-Pneumo assay in bronchoalveolar lavage (BAL) samples and assessed its potential impact on antibiotic therapy.

Methods. A total of 61 BAL samples collected for respiratory culture from intensive care unit patients aged 18 years and older who had symptoms consistent with LRTI were included in the study. Remnant BAL samples were tested using the FA-Pneumo and results were compared with standard of care respiratory culture results. We then conducted a chart review to determine the potential impact of FA-Pneumo results on antibiotic therapy.

Results. The results of 48 out of 61 BAL samples (78.7%) were the same when comparing FA-Pneumo with a standard of care respiratory culture. Two patients grew *Stenotrophomonas maltophilia* and 1 patient grew *Achromobacter*. Importantly, neither of these organisms is targeted by the FA-Pneumo assay. Three patients (4.9%) had viral LRTI, with 9 patients (14.8%) having bacterial/viral co-infection. A total of six patients with methicillin-susceptible *Staphylococcus aureus* (MSSA) remained on vancomycin therapy for a median of 1.5 days (range 0–7 days) and all three patients with viral LRTI remained on broad-spectrum antibiotic therapy for a median of 4 days (range 3–13 days). All three patients with ESBL-positive *Enterobacteriaceae*detected by FA-Pneumo and culture were not started on appropriate antibiotic therapy until >48 hours after the FA-Pneumo would have been resulted.

Conclusion. The FA-Pneumo assay has the potential to lead to earlier discontinuation of vancomycin for patients with MSSA LRTI and earlier broadening of therapy for ESBL LRTI. Providers should be aware of the inability of the FA-Pneumo to detect *S. maltophilia* and *Achromobacter* species.

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

647. Diagnoses Associated with Temperature ≥104°F in Adults

Sharon Chi, DO[1]; Gary Simon, MD, PhD[1]; Amy Weintrob, MD[2]; [1]The George Washington University, Washington, DC; [2]Washington DC VA Medical Center, Arlington, Virginia

Session: 67. New Diagnostics
Thursday, October 3, 2019: 12:15 PM

Background. Temperature ≥104°F ($T \geq 104$) is uncommon in adults. The diagnoses and clinical characteristics were reviewed for patients with $T \geq 104$.

Methods. Infectious disease physicians reviewed charts of patients with $T \geq 104$ seen at the Washington DC Veterans Affairs Medical Center from 2009 to 2018. The following was collected: demographics, past medical history, medications, WBC, maximum temperature, time to defervescence, etiology of $T \geq 104$, and death.

Results. Less than 0.01% of all patient encounters were associated with $T \geq 104$. Of the 60 most recent patients with $T \geq 104$ (from 2014 to 2018), the median age was 63.5 years (range 23–97), 65% were African American, 88% were male. 82% of those with $T \geq 104$ were hospitalized; 76% of those had the $T \geq 104$ on or within 72 hours of admission. 25% of the 60 patients had underlying cancer, 10% HIV, 30% DM, 13% CKD, and 13% were on steroids/immunosuppressants/biologics. The median peak temperature was 104.3°F (interquartile range 104.0 – 104.7); maximum was 106.8°F. 82% had $T \geq 104$ for only 1 day and the median time to defervescence was 2 days. There were 55 diagnoses amongst 48 patients; 12 had no identifiable etiology of $T \geq 104$. Of the identifiable diagnoses, there were 45 (81.8%) infections, 4 (7.3%) metastatic malignancies (1 Hodgkin's lymphoma, 1 small cell carcinoma, 1 squamous cell carcinoma, 1 unknown primary), 2 (3.6%) intracranial bleeds, 2 (3.6%) GI bleeds, 1 (1.8%) mixed collagen vascular disease, and 1 (1.8%) neuroleptic malignant syndrome. The most common infections were 15 cases of pneumonia including 2 Legionella, 8 complicated UTI/pyelonephritis, 3 primary bacteremia, 2 West Nile virus, 2 influenza, and 2 cholangitis with bacteremia. The median WBC of infectious diagnoses (9.8) was significantly higher than noninfectious diagnoses (5.8, $P = 0.006$, T-test). Of the 60 patients, 20% died within 30 days of $T \geq 104$ including 2 patients who died of sepsis. 67% of those who died were receiving hospice care.

Conclusion. $T \geq 104$ is rare in adults and is usually associated with bacterial infections such as pneumonia (including Legionella), complicated UTIs/pyelonephritis, and primary bacteremia but may also be seen with viral infections such as West Nile virus and influenza. Mortality is high.

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