**648. Baloxavir Resistance: qPCR Detection of Antiviral Resistance Markers in Influenza A Virus**

Aaron J. Tyler, BS; James Grantham, BS; Manisha Diaz, PhD;
Mauricio Miralles, MS; Katelyn Bartlett, MS; Derek Foland, BS; Amy Berg, BS;
Karen Howard, MS; Donald J. Nelsen, PhD; Jordyn Westergaard, BS;
Mark Wissel, PhD; Steve Kleiboeker, DVM, PhD; Michelle Altrich, PhD; Viracor Eurofins, Lee's Summit, Missouri

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***Background.*** Influenza (flu) infections affect a large subset of the population every year and have significant impacts on the health of patients, especially those with weak or compromised immune systems such as the elderly, children, cancer patients, and transplant recipients. Baloxavir marboxil was approved in October 2018 as a novel antiviral therapeutic for treating flu. During clinical trials, mutations were identified at the I28 codon of the polymerase acidic (PA) protein that greatly increased the resistance of a flu strain to this novel drug. In this study, a qPCR was developed and validated to identify these resistance mutations, allowing for guided therapy based on the resistance profile of the strain.

***Methods.*** Flu A sequences (6,175) of the PA gene from the NCBI Influenza Virus Database collected over the last 5 years were compiled and aligned. Primers and probes were designed to target the I38 codon of the PA gene, and specific probes for each codon yielding a resistant amino acid mutation (I38T, -M, and -F) were designed. Locked nucleic acid (LNA) bases were used to increase the specificity of the probes. A combination of clinical flu specimens, laboratory strains, and synthetic constructs of each potential resistance mutation were used to validate the precision, sensitivity, and accuracy of the assay in nasopharyngeal swabs.

***Results.*** Precision of the cycle threshold (Ct) values for each detector was determined to have a standard deviation of less than 3 for inter-assay and less than 2 for intra-assay replicates. Sensitivity was determined to be 800 copies/mL in nasopharyngeal swabs. Accuracy was found to be 92.3%. A single laboratory strain from the H1N1 2009 epidemic showed cross-reactivity with both wild-type and resistant probes, but no circulating clinical H1N1 samples tested showed this response.

***Conclusion.*** The precision, sensitivity, and accuracy of a qPCR for resistance mutations to baloxavir marboxil support this assay's utility as an aid in the treatment of flu in at-risk patient groups. This assay allows for rapid detection (<24 hours) of resistance markers to aid clinicians in improving flu case outcomes.

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

**649. Prospective Validation of an 11-mRNA Host Immune Signature as a Novel Blood Test for Acute Septic Arthritis**

Blake Schultz, MD[1]; Timothy E. Sweeney, MD PhD[2]; Melissa Remmel, BSc[2];
Uros Midic, PhD[2]; Oliver Liesenfeld, MD[2]; Malcolm DeBaun, MD[1];
Michael Gardner, MD[1]; [1]Stanford University, Stanford, California; [2]Inflammatix, Burlingame, California

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***Background.*** Septic arthritis is an orthopedic emergency requiring immediate surgical intervention. Joint aspirations detect inflammatory cells within hours but often cannot distinguish between infections (e.g., bacterial) or other causes (e.g., gout). Cultures take days, so decisions about surgery are made with incomplete data. Aspirations carry risk and require technical skill and advanced imaging. Novel diagnostics are thus needed. An 11-mRNA host immune blood signature has been validated to distinguish between infectious and noninfectious acute inflammation. It is part of the 29-mRNA HostDx™ Sepsis test that can also distinguish between bacterial and viral infections and predicts severity (currently under development as a rapid point-of-care test). We studied whether the 11-mRNA signature can determine if acute arthritis was due to an infectious cause.

***Methods.*** We conducted a blinded, prospective, noninterventional study on patients undergoing workup for a septic primary joint. Patients received standard-of-care including joint aspiration and lab tests: White Blood Cells (WBC), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and joint fluid analysis. Simultaneously, blood was drawn (PAXgene RNA tubes). mRNAs were measured on NanoString nCounter™ blinded to clinical results.

***Results.*** 20 patients were included, of which 10 had infections based on positive synovial fluid cultures. The 11-mRNA blood signature had an area under the ROC curve (AUROC) of 0.87 for separating infectious from noninfectious conditions compared with 0.58 (ESR), 0.60 (CRP), and 0.50 (WBC); AUROC for synovial WBC was 0.54. At 100% sensitivity for infection, specificity of the signature was 40%; thus, a substantial fraction of nonseptic patients could have been ruled out for further surgical intervention.

***Conclusion.*** The 11-mRNA signature showed markedly increased accuracy in predicting septic joints compared with routine diagnostic markers. As a quick point-of-care test this blood RNA signature may be an important tool for early, accurate identification of acute septic joints and need for emergent surgery, thereby improving clinical care and healthcare spending. These findings further add to the generalizability of results obtained in the HostDx Sepsis test.

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**650. Relationship of a Multiplex Molecular Pneumonia Panel (PP) Results with Hospital Outcomes and Clinical Variables**

Kenneth Rand, MD[1]; Stacy Beal, MD[1]; Elizabeth Tremblay, MPH[2];
Herbert Houck, MS[1]; Kylie Weber, M(ASCP)[2]; Christopher Sistrom, MD[1]; [1]University of Florida, Gainesville, Florida; [2]UFHealth Shands Hospital, Gainesville, Florida

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***Background.*** The Pneumonia Panel (PP) (BioFire Diagnostics, Salt Lake City, UT) detects 15 potentially pathogenic bacteria semiquantitatively (copy #/mL), 8 viruses and 7 resistance genes from the lower respiratory tract in ≈1 hour in the laboratory. Since identification and susceptibility take ≈ 2 days, this rapid result time is very attractive; however, the clinical significance of the PP copy #/mL as well as a predictable group of PP positive but culture negative patients is unknown. We retrospectively studied the relationship of 270 PP results to culture results, clinical data and outcomes.

***Methods.*** Bronchoalveolar lavage fluid ($N$ = 197) and endotracheal aspirates ($N$ = 73) submitted to the UF Health Shands Hospital microbiology laboratory from June-September 2018 were frozen at −70°C, until tested on the PP. Patient data were extracted from the inpatient electronic medical record (Epic).

***Results.*** Of 270 patients tested, 111/270 (41.1%) were PP bacteria negative/culture no growth or normal flora (Group 1), 59/270 (21.9%) were PP positive/culture negative (Group 2), and 100/270 (37.0%) were PP positive/culture positive (Group 3) for at least 1 concordant bacterial potential pathogen. Hospital length of stay (LOS), $P$ = 0.0274, ANOVA; ICU LOS $P$ = 0.0007 and BAL % Polys $P$ < 0.0001 were significantly longer/higher in Group 3 than in Groups 1 and 2 (Table 1). Max daily temp on the day of culture in PP-positive groups 2 and 3 was significantly higher than the PP-negative group 1, $P$ = 0.0260, ANOVA, (Table 1). Age, daily WBC, lowest paO2, max FiO2, % on antibiotics ( ≥80% for all groups), and % with viruses in the PP were not significantly different across groups. When all PP pathogens were grouped by copy # /mL, ICU LOS was significantly longer for 10(7) copies/mL ($P$ = 0.0088), as was BAL % polys ($P$ = 0.0006). Max daily temp was almost significantly higher for PP-positive groups 10(5), 10(6), and 10(7) combined compared with the PP-negative group (Table 2, $P$ = 0.0608).

***Conclusion.*** Hospital LOS was significantly longer and BAL %Polys higher in the bacterial pathogen culture-positive/PP-positive group vs. not positive groups. ICU LOS and BAL %Polys were significantly higher for the PP-positive groups vs. PP negative regardless of culture results. PP results (copy #/mL) independently correlated with outcome and clinical measures.

| | Hospital LOS n=270 obs* | ICU LOS n=270 obs | BAL % Polys n=78 obs | Max Daily Temp n=267 obs |
|---|---|---|---|---|
| Group 1 BP negative/culture negative N=111 | 18±16 | 10.8±14 | 44±36 | 99.6±1.4 |
| Group 2 BP positive/culture negative N=59 | 17±13 | 10.9±12 | 71±26 | 100.2±1.6 |
| Group 3 BP positive/culture positive N=100 | 23±18 | 17.9±16 | 81±19 | 100.6±1.5 |
| p-value (ANOVA, SAS) | 0.0274 | 0.0007 | <0.0001 | <0.0001 |

*obs=observations, not all patients had %Polys done or Daily Temps electronically available

| Copies/ml | Hospital LOS n=270 obs* | ICU LOS n=270 obs | BAL % Polys n=78 obs | Max Daily Temp n=267 obs |
|---|---|---|---|---|
| 0 N=111 | 18±16 | 11±14 | 44±36 | 99.6±1.4 |
| 10(4) N=13 | 15±8 | 8±6 | 68±43 | 100.8±1.8 |
| 10(5) N=30 | 22±15 | 16±16 | 72±24 | 100.6±1.6 |
| 10(6) N=26 | 17±13 | 11±12 | 66±19 | 99.9±1.5 |
| 10(7) N=90 | 22±18 | 17±17 | 84±18 | 100.5±1.5 |
| p-value (ANOVA,SAS) | 0.2042 | 0.0088 | 0.0006 | <0.0001 |

*obs=observations, not all patients had %Polys done or Daily Temps electronically available

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**651. Multi-Center Evaluation of the BioFire® FilmArray® Blood Culture Identification 2 Panel for the Detection of Microorganisms and Resistance Markers in Positive Blood Cultures**

Yang Lu, PhD[1]; Joseph Hatch, BS[1]; Kristen Holmberg, Master[1];
Anna Hurlock, PhD[1]; Daria Drobysheva, PhD[1]; Usha Spaulding, PhD[1];
Sophia Vourli, PhD[2]; Spyridon Pournaras, MD/PhD[2]; Kathy Everhart, BS[3];
Amy Leber, PhD[3]; Becki Barr, BS[4]; Judy Daly, PhD[4]; Tai Henry, BS[5];
Amy Johnson, BS[5]; Joan-Miquel Balada-Llasat, PharmD/PhD[5];
Daniel D. Rhoads, MD[6]; Michael Jacobs, MBBS[6]; Kathleen Mc Kinley, BS[7];
Amanda Harrington, PhD[7]; Frank Zhang, BS[8];
Gregory J. Berry, PhD D(ABMM)[8]; Moon Hyung Jeong, BS[9];
Rosemary She, MD[9]; Vittorio Sambri, MD/PhD[10]; Michela Fantini, BS[10];
Giorgio Dirani, BS[10]; Silvia Zannoli, BS[10]; Kevin Bourzac, PhD[1]; [1]BioFire Diagnostics, LLC, Sandy, Utah; [2]National and Kapodistrian University of Athens, Athens, Zakinthos, Greece; [3]Nationwide Children's Hospital, Columbus, Ohio; [4]Primary Children's Hospital, Salt Lake City, Utah; [5]The Ohio State University Wexner Medical Center, Columbus, Ohio; [6]University Hospital Cleveland Medical Center, Cleveland, Ohio; [7]Loyola University Medical Center, Maywood, Illinois; [8]Northwell Health Labs, Little Neck, New York; [9]University of Southern California, Los Angeles, California; [10]The Greater Romagna Area Hub Laboratory, Bologna, Piemonte, Italy

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***Background.*** The BioFire® FilmArray® Blood Culture Identification 2 (BCID2) Panel is a diagnostic test that provides results for 26 bacterial, 7 fungal pathogens and 10 antimicrobial resistance (AMR) genes from positive blood culture (PBC) specimens in about an hour. The BCID2 Panel builds upon the existing BCID Panel with several additional assays that include *Candida auris* and an expanded AMR gene menu that provides methicillin-resistant *Staphylococcus aureus* (MRSA) results plus detection for *mcr-1*, carbapenem resistance, and ESBL. Here, we summarize studies conducted to establish clinical performance using an Investigational Use Only version of the BCID2 Panel.

***Methods.*** Three studies were performed. The first involves prospective collection and testing of an expected ~1,000 residual PBCs at 7 US and 2 EU sites, which began in