2011. Identification of *Streptococcus agalactiae* on Human Fetal Membrane Tissues Using Raman Microspectroscopy

Ryan Doster, MD[1]; Oscar Ayala, PhD[2]; Shannon Manning, PhD[3]; David Aronoff, MD, FIDSA[1]; Anita Mahadevan-Jansen, PhD[2] and Jennifer Gaddy, PhD[4]; [1]Medicine, Vanderbilt University School of Medicine, Division of Infectious Diseases, Nashville, Tennessee, [2]Biomedical Engineering, Vanderbilt University, Nashville, Tennessee, [3]Michigan State University, E. Lansing, Michigan, [4]Tennessee Valley Healthcare Systems, Nashville, Tennessee

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Background. *Streptococcus agalactiae*, also known as Group B *Streptococcus* (GBS), colonizes 10–40% of women during late pregnancy and is an important cause of chorioamnionitis, or infection of the fetal membranes, and neonatal sepsis. The CDC recommends third trimester rectovaginal GBS screening, and intrapartum antibiotic prophylaxis for those testing positive. A rapid GBS diagnostic test could provide opportunities to identify GBS colonized women at the time of labor and focus the use of antibiotic therapy. Raman spectroscopy (RS) is an inelastic light scattering technique that provides biochemical spectra and has been used *in vitro* to characterize bacteria at the genus and species level. This study evaluated RS to identify and differentiate GBS, *Escherichia coli*, and *Staphylococcus aureus ex vivo* infection of human fetal membrane tissues.

Methods. Bacterial colonies of GBS, *S. aureus*, and *E. coli* were cultured on Mueller–Hinton agar. In addition, de-identified human fetal membrane tissues (VUMC IRB Approval #131607) were isolated and infected with 10^6 bacterial cells per 12 mm tissue punch for 48–72 hours. Samples from both were characterized using a Raman microscope. Hierarchical cluster analysis was implemented to evaluate principal component scores of Raman spectra from bacterial colonies. For tissue spectra, a machine learning algorithm, sparse multinomial logistic regression (SMLR), was used to determine the ability to discriminate across tissues types and identify biochemical features important for classification. Following RS analysis, scanning electron microscopy was performed to verify the presence of bacterial cells at the site of Raman measurements.

Results. Unique spectral features were identified from colonies grown on agar and infected fetal membrane tissues. Analysis using SMLR accurately identified GBS-infected tissues with 92.2% sensitivity and specificity. Scanning electron microscopy evaluation confirmed the presence of bacterial cells that were structured in biofilms at the site of Raman measurements.

Conclusion. Together, these findings support further investigation into the use of RS as an emerging microbiologic diagnostic tool and intrapartum screening test for GBS carriage.

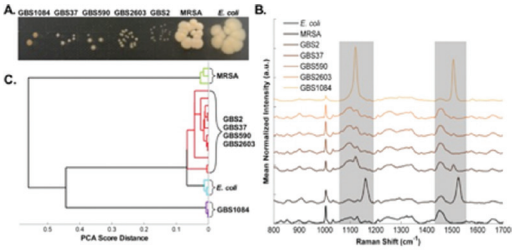

Figure 1: Raman spectra of GBS, *S. aureus*, and *E. coli* bacterial colonies present distinct biochemical features. *A:* Bacterial cells from five GBS strains, *S. aureus* strain USA300 (MRSA), and *E. coli* serotype 075:H5:K1 were grown to steady state, serially diluted, and plated on agar to demonstrate pigmentation differences of the strains. B: Mean ± standard deviation Raman spectra of bacterial colonies cultured on agar. C: Hierarchical cluster analysis (HCA) of bacterial colony measurements based on principal component analysis scores.

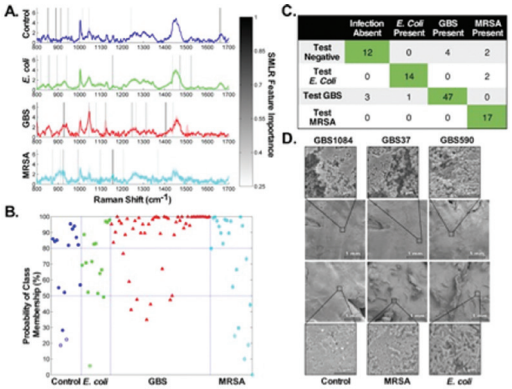

Figure 2: Raman spectroscopy of *ex vivo* infected fetal membrane tissues identifies and differentiates the presence of bacterial cells within tissues. *A:* Mean Raman ± standard deviation spectra for each class (control (uninfected), *E. coli*, GBS, and MRSA) with gray bands representing SMLR feature importance. B: Posterior probability of class membership plot for each tissue type. C: Confusion matrix representing the performance of the SMLR classifier for each tissue type. D: Scanning electron microscopy images of fetal membrane tissues used for Raman analysis to verify the presence of bacteria at the location of Raman measurements. A small cut was made into the membrane tissues to denote the relative location of Raman evaluation. Inserts demonstrate bacterial cells and extrapolymeric substances, suggestive of biofilms, seen in these locations.

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

2012. FilmArray® Measurement of Host Response Signatures RapidLy Discriminates Viral, Bacterial, and Non-infectious Etiologies of Illness

Ephraim L. Tsalik, MD, MHS, PhD[1,2,3]; Ricardo Henao, PhD[3]; Mert Aydin, MSc[3]; Charles Bullard, MBA[3]; Jesse Montgomery, PhD[4]; Jeff Nawrocki, MS[4]; Maxcén Deneris, AS[4]; Craig Gritzen, MS[4]; Jay Jones, MS[4]; Robert Crisp, PhD[4]; Micah T. Mcclain, MD, PhD[3,5,6]; Thomas Burke, PhD[3]; Geoffrey S. Ginsburg, MD, PhD[3,7]; Andrew Hemmert, PhD[4] and Christopher W. Woods, MD, MPH, FIDSA[2,3,8]; [1]Emergency Department Service, Durham Veterans Affairs Healthcare System, Durham, North Carolina, [2]Division of Infectious Diseases and International Health, Department of Medicine, Duke University, Durham, North Carolina, [3]Center for Applied Genomics and Precision Medicine, Duke University, Durham, North Carolina, [4]BioFire Diagnostics, LLC, Salt Lake City, Utah, [5]Veterans Affairs Medical Center, Durham, North Carolina, [6]Division of Infectious Diseases, Duke University Medical Center, Durham, North Carolina, [7]Director, Center for Genomic Medicine in the Duke Institute for Genome Sciences and Policy, Duke University, Durham, North Carolina, [8]Section of Infectious Diseases, Durham Veteran's Affairs Medical Center, Durham, North Carolina

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Background. The inability to reliably discriminate bacterial, viral, and non-infectious illness has led to an epidemic of antibiotic overuse and rising rates of antimicrobial resistance. Host gene expression provides a powerful approach to distinguish infection etiologies and guide appropriate therapy. However, existing platforms for transcriptomic analysis are not amenable for clinical application. The FilmArray platform is a sample-to-answer multiplex RT-PCR system that automates transcriptomic analysis including sample preparation and data analysis. Here we report the validation of a host gene expression FilmArray test to discriminate bacterial, viral, and non-infectious etiologies of illness.

Methods. Research use only (RUO) FilmArray pouches were manufactured with 45 host response assays previously shown to discriminate bacterial, viral, and non-infectious illness. These pouches were tested on whole blood samples from 226 patients with acute respiratory illness (ARI). Using clinical adjudication as the reference standard, there were 52 bacterial, 100 viral, and 75 non-infectious cases. Quantification cycles were recorded for each assay and normalized to an internal control. A logistic regression model generated probabilities of each condition, which were used to classify subjects.

Results. Beginning with 100 µL of blood, the FilmArray host response panel provided results in ~45 minutes from sample to answer. Overall accuracy for bacterial ARI relative to clinical adjudication was 85% with an area under the receiver operating characteristic curve (AUC) of 0.92. Accuracy and AUC for viral infection were 85% and 0.91, respectively. Ill patients without infection were correctly identified 86% of the time with an AUC of 0.88.

Conclusion. These results show that the FilmArray system can rapidLy measure host gene expression to accurately discriminate bacterial, viral, and non-infectious illness. The development of such a system creates a new option to mitigate inappropriate antibiotic use. It also presents opportunities to use host gene expression as a diagnostic modality for a variety of disease states.

Disclosures. **E. L. Tsalik**, Host Response, Inc.: Founder, Equity. **J. Montgomery**, BioFire Diagnostics: Employee, Salary. **J. Nawrocki**, BioFire Diagnostics, LLC.: Employee, Salary. **M. Deneris**, BioFire Diagnostics, LLC.: Employee, Salary. **C. Gritzen**, BioFire Diagnostics, LLC.: Employee, Salary. **J. Jones**, BioFire Diagnostics, LLC.: Employee, Salary. **R. Crisp**, BioFire Diagnostics, LLC: Employee, Salary. **G. S. Ginsburg**, Host Response Inc: Board Member, Founder, Scientific Advisor and Shareholder, Stock (currently worth < $100). **A. Hemmert**, BioFire Diagnostics, LLC.: Employee and Investigator, Salary. **C. W. Woods**, Host Response, Inc.: Founder, Equity.

2013. Procalcitonin Current State Evaluation Within a Large Health System

Kelsey Pena, PharmD[1]; Mandelin Cooper, PharmD, BCPS[2]; Nickie Greer, PharmD, BCPS[3]; Ty Elders, MS, CHDA[4] and Edward Septimus, MD, FIDSA, FSHEA[5]; [1]University of Tennessee/HCA Healthcare/HealthTrust, Nashville, Tennessee, [2]Clinical Services Group, HCA Healthcare, Nashville, Tennessee, [3]HCA TriStar Division, HealthTrust Supply Chain, Nashville, Tennessee, [4]Clinical Analytics, HCA Healthcare, Nashville, Tennessee and [5]Population Medicine, Harvard Medical School, Houston, Texas

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Background. Procalcitonin is a hormone precursor that has been identified as a marker for bacterial infections. Procalcitonin increases as the body mounts an inflammatory response against infection, then returns to its normal range once the response subsides. Studies have shown that reduced procalcitonin levels may support antibiotic discontinuation. The purpose of this study was to determine how procalcitonin is being utilized at facilities within a large health system.

Methods. From August 1, 2016 through July 31, 2017 facilities with a minimum of 30 procalcitonin levels were assessed. Patients who received antibiotics, with and without procalcitonin levels, were evaluated. The primary outcome was the frequency of multiple procalcitonin levels drawn 24–72 hours apart. Secondary analysis included baseline procalcitonin timing, antibiotic discontinuation based on procalcitonin thresholds (<0.5 or 80% reduction from a peak level), and monitoring patterns related to outcomes such as hospital length of stay (LOS), intensive care unit LOS, antibiotic duration of therapy, and hospital-onset *Clostridium difficile* infections. Data were