**1033. Skin Surface Thermal Imaging to Differentiate Cellulitis and Pseudocellulitis in the Emergency Department**

Michael Pulia, MD, MS[1]; Rebecca Schwei, MPH[2]; Edward Harwick, BS[2]; Ambar Haleem, MD[3]; Jamie Hess, MD[2]; Robert Glinert, MD[2]; Thomas Keenan, MD PhD[2]; Joseph McBride, MD[2]; Robert Redwood, MD MPH[4]; [1]University of Wisconsin School of Medicine and Public Health, Madison, WI; [2]University of Wisconsin Madison School of Medicine and Public Health, Madison, Wisconsin; [3]University of Wisconsin School of Medicine and Public Health, Madison, WI, Madison, Wisconsin; [4]Cooley Dickinson Health Care, Northhampton, Massachusetts

**Session:** P-58. New Approaches to Diagnostics

***Background.*** Cellulitis is misdiagnosed in up to 30% of cases, resulting in overuse of antibiotics. This represents a threat to patient safety and public health. Surface thermal imaging has been proposed as a tool to reduce errors in diagnosing cellulitis. The study objective was to compare skin surface temperature measurements between patients with cellulitis and pseudocellulitis.

***Methods.*** We prospectively enrolled patients presenting to the emergency department (ED) with dermatologic lower extremity complaints that involved visible erythema. Using a thermal imaging camera, the maximum temperature value (Tmax) for the affected area of skin and corresponding area on an unaffected limb were captured. The Tmax gradient between the affected and unaffected limb was calculated. Gold standard diagnosis (cellulitis versus pseudocellulitis) was determined by consensus of a blinded, multidisciplinary physician review panel (two infectious disease, two dermatologists and two emergency medicine). Differences in temperature variables (Tmax and Tmax gradient) between cellulitis and pseudocellulitis were compared using t-tests.

***Results.*** The sample included 204 participants, 59% male with an average age of 57 years. Based on expert panel consensus diagnosis, 92 (45%) of the participants had cellulitis. The cellulitis group had an average Tmax of 33.2°C and 30.2°C for affected and unaffected skin respectively, which was a significant difference of 2.9°C (CI: 2.5 to 3.6; p< 0.001). The difference in the Tmax gradients between patients with cellulitis and pseudocellulitis was 2.08°C (CI: 1.46-2.70; p< 0.001).

***Conclusion.*** This represents the largest validation study of skin surface temperature differences between cellulitis and pseudocellulitis. Significant difference in temperature gradients between cases of cellulitis and pseudocellulitis suggests thermal imaging could be a useful diagnostic adjunct that can help differentiate these conditions. Such a modality could be particularly helpful in the ED setting where providers must balance diagnostic uncertainty with antimicrobial stewardship principles. Future work will identify the best performing temperature variables and determine optimal cutoff values for use in diagnostic algorithms.

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

**1034. FebriDx use in Immunocompromised Patients in a Real-World Hospital Setting during the second (COVID-19) wave in Italy**

FIlippo Lagi, MD, MSc[1]; Alessandro Bartoloni, Prof[2]; Catalina Suarez-Cuervo, MD[3]; [1]Department of experimental and clinical medicine, Florence, Toscana, Italy; [2]Department of Experimental and Clinical Medicine, University of Florence, Florence, Italy, Florence, Toscana, Italy; [3]Lumos Diagnostics, Lakeland, Florida

**Session:** P-58. New Approaches to Diagnostics

***Background.*** The diagnosis of acute respiratory infection (ARI) in patients with immunosuppression secondary to disease or medications is often unclear. Symptoms may be absent or blunted, and acute phase reactants, like procalcitonin (PCT) and C-reactive protein (CRP) may not elevate. For these patients, minor signs or symptoms could lead to hospitalization and antibiotic prescriptions to prevent complications or death. FebriDx® is a rapid, qualitative immunoassay test designed to distinguish between viral or bacterial respiratory infection through simultaneous detection of both CRP and Myxovirus resistance protein A (MxA) from a fingerstick blood sample.

***Methods.*** FebriDx was evaluated as part of a real-world prospective, observational study in hospitalized patients with symptoms of ARI and suspected COVID-19 in a single tertiary care center in Italy (August, 2020 - January, 2021). A sub analysis of patients with expected reduced host immune responses secondary to immunosuppression by disease or medication was performed. (Classified by treating clinician; patient on high dose steroids/ immunosuppressive therapy, or underlying condition like cancer or autoimmune disease). Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and likelihood ratios were calculated for FebriDx with respect to the final diagnosis.

***Results.*** We included 28 patients from 200 in the study, 16 patients had a final diagnosis of bacterial infection and 12 had viral infection. FebriDx showed a sensitivity of 91.7% to accurately diagnose viral infection and 93.8% for bacterial infection (see tables). Serum CRP was not available for 4 of the patients included (14%) and elevated in the remaining patients. PCT was not available for one patient with viral infection and was elevated in 50.0%.

**Table 1- Results for Viral Infection**

| | Viral Infection | | |
|---|---|---|---|
| **FebriDx Result** | **Present** | **Absent** | **Total** |
| **Positive** | 11 | 0 | 11 |
| **Negative** | 1 | 16 | 17 |
| **Total** | 12 | 16 | 28 |
| **Sensitivity (95% CI)** | 91.67% (61.52 – 99.79% | | |
| **Specificity (95% CI)** | 100% (79.41-100.00%) | | |

**Table 2- Results for Bacterial Infection**

| | Bacterial Infection | | |
|---|---|---|---|
| **FebriDx Result** | **Present** | **Absent** | **Total** |
| **Positive** | 15 | 1 | 16 |
| **Negative** | 1 | 11 | 12 |
| **Total** | 16 | 12 | 28 |
| **Sensitivity (95% CI)** | 93.75% (69.77 – 99.84%) | | |
| **Specificity (95% CI)** | 91.67% (61.52 – 99.79% | | |

FebriDx Performance when compared to Clinical Diagnosis

***Conclusion.*** FebriDx demonstrated a higher accuracy for differentiating bacterial vs. viral infection in an immunocompromised cohort than single biomarkers CRP and PCT. FebriDx demonstrated a high diagnostic accuracy to differentiate viral from bacterial infection in patients with chronic immunosuppressive conditions in a real-world setting and had better performance than standalone CRP and PCT to distinguish viral and bacterial ARI in immunocompromised patients.

***Disclosures.*** **Catalina Suarez-Cuervo, MD**, **Lumos Diagnostics** (Employee)

**1035. Manufacturing Processes of SER-109, a Purified Investigational Microbiome Therapeutic, Reduce Risk of Transmission of Emerging and Undetected Infections in Donor Stool**

Christopher McChalicher, n/a[1]; Ahmad Abdulaziz, MS[1]; Elizabeth Halvorsen, PhD[1]; Mary-Jane Lombardo, PhD[2]; Jonathan Winkler, PhD[1]; Sanabel Almomani, MS[1]; Barbara McGovern, MD[3]; Gregory McKenzie, PhD[4]; David Ege, PhD[1]; John Aunins, PhD[1]; [1]Seres Therapeutics, Cambridge, Massachusetts; [2]Seres Therapeutics, Inc, Cambridge, Massachusetts; [3]Seres Therapeutics, Inc., Cambridge, MA; [4]Seres Therapeutics (Current: Prolacta Biosciences), Cambridge, Massachusetts

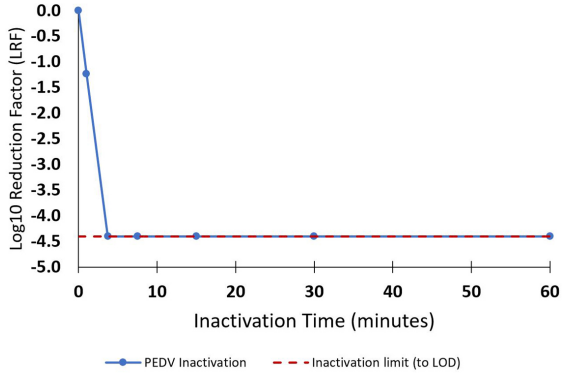
**Session:** P-59. New Drug Development

***Background.*** Fecal microbiota transplantation (FMT) is vulnerable to emerging pathogens due to reliance on donor screening for risk mitigation. These concerns were highlighted by dual FDA safety alerts regarding FMT transmission of bacterial pathogens, which were recognized in hindsight only after hospitalizations and deaths. The FDA also warned of potential risk of SARS-CoV-2 transmission, leading to quarantine of FMT in March 2020, two months after COVID-19 was reported on US soil. Conversely, our development program for SER-109, an oral investigational microbiome therapeutic, was prospectively designed to inactivate organisms of concern, while purifying the hardy Firmicutes spores. We evaluated whether the manufacturing processes for SER-109 inactivate model organisms, including a coronavirus with gastrointestinal tropism, and a representative Gram-negative bacterium.

***Methods.*** Model organisms were selected based on biologic suitability, detectability, and laboratory safety. Porcine Epidemic Diarrhea Virus (PEDV, a coronavirus) was selected to model SARS-CoV-2. Quantitation used a Vero cell tissue culture infectious dose ($TCID_{50}$) assay. For *E. coli*, a rifampicin-tolerant *Salmonella enterica* was selected and quantified with MacConkey lactose agar plus rifampicin. Spiking experiments into representative fecal suspensions were completed to measure inactivation of model organisms. Log-reduction factors (LRF) were calculated based on the drop in organism titer during inactivation. Hold controls in non-ethanolic test matrices were used to confirm specificity of the ethanol inactivation.

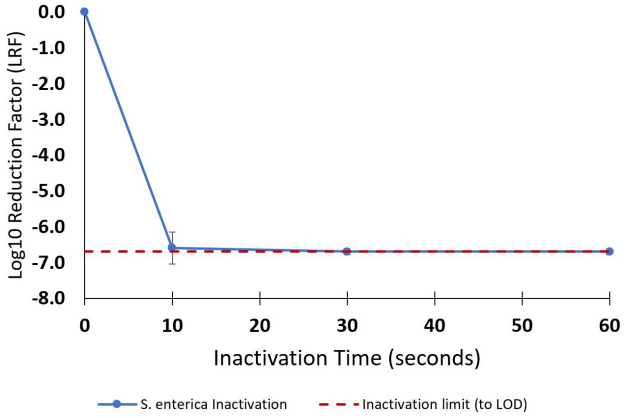
***Results.*** In 70% v/v ethanol, PEDV was inactivated by more than 4.2 $\log_{10}$ (to limit of detection, LOD) within 4 minutes (Fig1). In 50% v/v ethanol, *S. enterica* was inactivated by more than 6.5 $\log_{10}$ (to LOD) within 30 seconds (Fig2).

Figure 1. Inactivation of Porcine Epidemic Diarrhea Virus (PEDV), log10 reduction factor (LRF) versus time




Average of two experiments shown. Also shown is the maximum achievable inactivation based on the limit of detection (LOD).

Figure 2. Inactivation of S. enterica, log10 reduction factor (LRF) versus time.




Average of three experiments with error bars represent 95% CI. Also shown is the maximum achievable inactivation based on the limit of detection (LOD).

***Conclusion.*** These experiments demonstrate substantial inactivation of the model organisms and support the potential benefit of SER-109 manufacturing process to mitigate risks of undetected or emerging pathogens for which reliable screening is limited. Ethanol exposure leads to a purified investigational product of beneficial Firmicutes spores while affording a safety net beyond donor screening alone.

***Disclosures.*** **Christopher McChalicher, n/a**, **Seres Therapeutics** (Employee, Shareholder) **Ahmad Abdulaziz, MS**, **Seres Therapeutics Inc.** (Employee, Shareholder) **Elizabeth Halvorsen, PhD**, **Seres Therapeutics** (Employee, Shareholder) **Mary-Jane Lombardo, PhD**, **Seres Therapeutics** (Employee, Shareholder) **Jonathan Winkler, PhD**, **Seres Therapeutics** (Employee, Shareholder) **Barbara McGovern, MD**, **Seres Therapeutics** (Employee, Shareholder) **Gregory McKenzie, PhD**, **Prolacta Bioscience** (Employee) **David Ege, PhD**, **Merck & Co., Inc.** (Shareholder)**Seres Therapeutics** (Employee, Shareholder) **John Aunins, PhD**, **Seres Therapeutics, Inc.** (Employee)

### 1036. *In Vitro* Analysis of AmpC β-lactamase Induction by Tebipenem in *Enterobacterales* and *Pseudomonas aeruginosa*

Rodrigo E. Mendes, PhD[1]; Nicole Cotroneo[2]; Ian A. Critchley, Ph.D.[2]; Brieanna Roth, n/a[1]; S J Ryan Arends, PhD[1]; Mariana Castanheira, PhD[1]; Mariana Castanheira, PhD[1]; [1]JMI Laboratories, North Liberty, Iowa; [2]Spero Therapeutics

**Session:** P-59. New Drug Development

***Background.*** Tebipenem (TBP) is an orally bioavailable carbapenem in clinical development in the US for treating complicated urinary tract infections and acute pyelonephritis. TBP possesses broad-spectrum activity against isolates producing penicillinases, narrow- and extended-spectrum β-lactamases, and AmpC β-lactamases. Exposure to β-lactams has been shown to increase AmpC production and impact susceptibility to β-lactams. This study assessed the induction properties of TBP over AmpC production in Gram-negative organisms.

***Methods.*** Eight *Enterobacterales* species and 1 *P. aeruginosa* isolate were selected for AmpC induction experiments for TBP, imipenem, ertapenem (ETP), and ceftazidime. Induction experiments were performed at 0.25, 1, 4, and 16x MIC. AmpC induction was detected by measuring the intensity of nitrocefin hydrolysis compared to baseline. Isolates where a ≥4x induction of AmpC was detected were tested for susceptibility by the CLSI reference broth microdilution method. A second set of 36 *Enterobacterales* and 32 *P. aeruginosa* isolates with proven overexpression of AmpC by qRT-PCR were tested for susceptibility as well.

***Results.*** In general, TBP and imipenem increased production of AmpC against all *Enterobacterales*, except for *C. koseri* and *S. marcescens* (Table). In contrast, ETP and ceftazidime did not seem to affect production of AmpC among the *Enterobacterales* species tested. All agents but ETP increased the production of AmpC in *P. aeruginosa.* Overall, an MIC increase (i.e., >4-fold) to various β-lactam agents was not observed when tested against isolates that showed an increased production of AmpC after drug exposure. When tested against the second set of *Enterobacterales* that over-produced AmpC, TBP ($MIC_{50/90}$, 0.03/0.25 mg/L) inhibited all isolates at ≤1 mg/L. TBP showed $MIC_{50}$ and $MIC_{90}$ results of 4 and 4 mg/L, respectively, against *P. aeruginosa* isolates that over-produced AmpC.

***Conclusion.*** Among *Enterobacterales*, exposure to either TBP or imipenem, but not ETP or ceftazidime, often resulted in increased measurement of AmpC production. However, increased production of AmpC did not translate into increased MIC values. Finally, TBP showed potent activity against *Enterobacterales* with confirmed overproduction of AmpC.

Table

| | Fold increase in AmpC production after drug exposure at X MIC (mg/L)[a] | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Tebipenem | | | | Imipenem | | | | Ertapenem | | | | Ceftazidime | | | |
| Species | 0.25X | 1X | 4X | 16X | 0.25X | 1X | 4X | 16X | 0.25X | 1X | 4X | 16X | 0.25X | 1X | 4X | 16X |
| *C. freundii* | 3.9 | 5.1 | 5.7 | 6.1 | 7.3 | 5.1 | 5.6 | 1.9 | 0.7 | 0.8 | 0.8 | 0.8 | 0.4 | 0.8 | 0.4 | 0.3 |
| *C. koseri* | 2.1 | 1.1 | 1.0 | 3.3 | 1.7 | 1.4 | 1.3 | 0.2 | 1.0 | 1.0 | 0.8 | 0.8 | 0.8 | 0.7 | 0.4 | 0.5 |
| *E. cloacae* | 3.0 | 7.4 | 4.7 | 0.7 | 2.7 | 9.0 | 22.9 | 27.6 | 1.8 | 1.8 | 1.8 | 1.9 | 2.4 | 0.8 | 0.2 | -0.2 |
| *K. aerogenes* | 1.6 | 5.3 | 7.2 | 0.4 | 2.3 | 12.2 | 14.8 | -1.2 | 0.7 | 0.0 | 0.0 | 0.2 | 0.4 | -0.8 | -3.1 | -0.5 |
| *M. morganii* | 8.0 | 5.6 | 4.8 | 5.5 | 5.6 | 10.6 | 10.4 | 4.0 | 0.5 | 0.6 | 0.7 | 0.6 | 0.7 | 0.5 | 0.7 | 0.9 |
| *P. rettgeri* | 26.1 | 34.0 | 25.9 | 10.4 | 10.6 | 22.6 | 38.6 | 32.4 | -1.9 | -3.6 | 0.0 | -0.4 | -5.2 | -2.1 | -2.4 | -2.8 |
| *P. stuartii* | 12.5 | 40.5 | 5.6 | 12.9 | 12.2 | 11.9 | 7.3 | 3.0 | 0.4 | 1.0 | 0.9 | 0.7 | -0.2 | -0.1 | -0.1 | -1.2 |
| *S. marcescens* | 0.7 | 0.3 | -0.5 | -0.4 | 1.5 | 2.3 | 4.9 | 1.0 | 1.4 | 1.2 | 0.8 | 1.2 | 0.3 | 1.0 | 0.8 | 0.7 |
| *P. aeruginosa* | 82.2 | -1.9 | -1.7 | -19.7 | 363.1 | 13.6 | -25.5 | 1.3 | -1.8 | -8.5 | 2.4 | -22.6 | 5.7 | 24.2 | 53.2 | 125.7 |

[a] The fold increase was measured as the ΔAbsobarnce/minute/mg protein of nitrocefin from cultures exposed to drug divided by ΔAbsobance/minute/mg protein of nitrocefin from a culture without exposure to drug. Induction experiments with >4-fold increase in the production of AmpC are highlighted.

***Disclosures.*** **Rodrigo E. Mendes, PhD**, **AbbVie** (Research Grant or Support)**AbbVie (formerly Allergan)** (Research Grant or Support)**Cipla Therapeutics** (Research Grant or Support)**Cipla USA Inc.** (Research Grant or Support)**ContraFect Corporation** (Research Grant or Support)**GlaxoSmithKline, LLC** (Research Grant or Support)**Melinta Therapeutics, Inc.** (Research Grant or Support)**Melinta Therapeutics, LLC** (Research Grant or Support)**Nabriva Therapeutics** (Research Grant or Support)**Pfizer, Inc.** (Research Grant or Support)**Shionogi** (Research Grant or Support)**Spero Therapeutics** (Research Grant or Support) **Nicole Cotroneo**, **Spero Therapeutics** (Employee, Shareholder) **Ian A. Critchley, Ph.D.**, **Spero Therapeutics** (Employee, Shareholder) **Brieanna Roth, n/a**, **Spero Therapeutics** (Research Grant or Support) **S J Ryan Arends, PhD**, **AbbVie (formerly Allergan)** (Research Grant or Support)**GlaxoSmithKline, LLC** (Research Grant or Support)**Melinta Therapeutics, LLC** (Research Grant or Support)**Nabriva Therapeutics** (Research Grant or Support)**Spero Therapeutics** (Research Grant or Support) **Mariana Castanheira, PhD**, **AbbVie (formerly Allergan)** (Research Grant or Support)**Bravos Biosciences** (Research Grant or Support)**Cidara Therapeutics, Inc.** (Research Grant or Support)**Cipla Therapeutics** (Research Grant or Support)**Cipla USA Inc.** (Research Grant or Support)**GlaxoSmithKline** (Research Grant or Support)**Melinta Therapeutics, Inc.** (Research Grant or Support)**Melinta Therapeutics, LLC** (Research Grant or Support)**Pfizer, Inc.** (Research Grant or Support)**Qpex Biopharma** (Research Grant or Support)**Shionogi** (Research Grant or Support)**Spero Therapeutics** (Research Grant or Support) **Mariana Castanheira, PhD**, Affinity Biosensors (Individual(s) Involved: Self): Research Grant or Support; Allergan (Individual(s) Involved: Self): Research Grant or Support; Amicrobe, Inc (Individual(s) Involved: Self): Research Grant or Support; Amplyx Pharma (Individual(s) Involved: Self): Research Grant or Support; Artugen Therapeutics USA, Inc. (Individual(s) Involved: Self): Research Grant or Support; Astellas (Individual(s) Involved: Self): Research Grant or Support; Basilea (Individual(s) Involved: Self): Research Grant or Support; Beth Israel Deaconess Medical Center (Individual(s) Involved: Self): Research Grant or Support; BIDMC (Individual(s) Involved: Self): Research Grant or Support; bioMerieux Inc. (Individual(s) Involved: Self): Research Grant or Support; BioVersys Ag (Individual(s) Involved: Self): Research Grant or Support; Bugworks (Individual(s) Involved: Self): Research Grant or Support; Cidara (Individual(s) Involved: Self): Research Grant or Support; Cipla (Individual(s) Involved: Self): Research Grant or Support; Contrafect (Individual(s) Involved: Self): Research Grant or Support; Cormedix (Individual(s) Involved: Self): Research Grant or Support; Crestone, Inc. (Individual(s) Involved: Self): Research Grant or Support; Curza (Individual(s) Involved: Self): Research Grant or Support; CXC7 (Individual(s) Involved: Self): Research Grant or Support; Entasis (Individual(s) Involved: Self): Research Grant or Support; Fedora Pharmaceutical (Individual(s) Involved: Self): Research Grant or Support; Fimbrion Therapeutics (Individual(s) Involved: Self): Research Grant or Support; Fox Chase (Individual(s) Involved: Self): Research Grant or Support; GlaxoSmithKline (Individual(s) Involved: Self): Research Grant or Support; Guardian Therapeutics (Individual(s) Involved: Self): Research Grant or Support; Hardy Diagnostics (Individual(s) Involved: Self): Research Grant or Support; IHMA (Individual(s) Involved: Self): Research Grant or Support; Janssen Research & Development (Individual(s) Involved: Self): Research Grant or Support; Johnson & Johnson (Individual(s) Involved: Self): Research Grant or Support; Kaleido Biosceinces (Individual(s) Involved: Self): Research Grant or Support; KBP Biosciences (Individual(s) Involved: Self): Research Grant or Support; Luminex (Individual(s) Involved: Self): Research Grant or Support; Matrivax (Individual(s) Involved: Self): Research Grant or Support; Mayo Clinic (Individual(s) Involved: Self): Research Grant or Support; Medpace (Individual(s) Involved: Self): Research Grant or Support; Meiji Seika Pharma Co., Ltd. (Individual(s) Involved: Self): Research Grant or Support; Melinta (Individual(s) Involved: Self): Research Grant or Support; Menarini (Individual(s) Involved: Self): Research Grant or Support; Merck (Individual(s) Involved: Self): Research Grant or Support; Meridian Bioscience Inc. (Individual(s) Involved: Self): Research Grant or Support; Micromyx (Individual(s) Involved: Self): Research Grant or Support; MicuRx (Individual(s) Involved: Self): Research Grant or Support; N8 Medical (Individual(s) Involved: Self): Research Grant or Support; Nabriva (Individual(s) Involved: Self): Research Grant or Support; National Institutes of Health (Individual(s) Involved: Self): Research Grant or Support; National University of Singapore (Individual(s) Involved: Self): Research Grant or Support; North Bristol NHS Trust (Individual(s) Involved: Self): Research Grant or Support; Novome Biotechnologies (Individual(s) Involved: Self): Research Grant or Support; Paratek (Individual(s) Involved: Self): Research Grant or Support; Pfizer