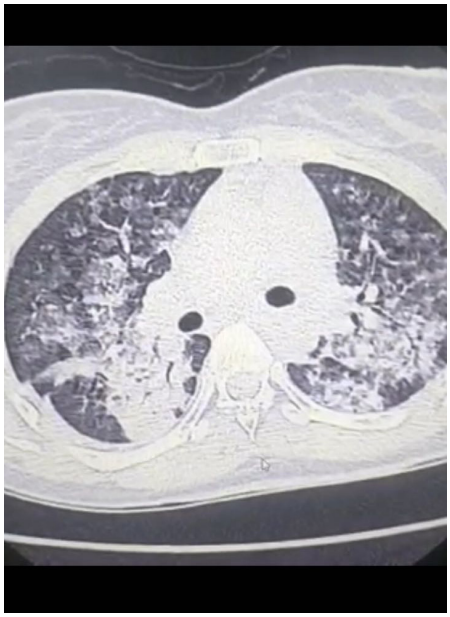

Disclosures. **All authors:** No reported disclosures.

1791. Novel Metabolomics Approach for the Diagnosis of Respiratory Viruses Directly from Nasopharyngeal Specimens

Catherine Hogan, MD, MSc[1]; Anthony T. Le, MSc[1]; Justin Mak, MSc[2]; Malaya Kumar. Sahoo, PhD[1]; Tina Cowan, PhD[1]; Benjamin A. Pinksy, MD, PhD[1]; [1]Stanford University School of Medicine, Stanford, California; [2]Stanford Health Care, Palo Alto, California

Session: 170. Viral Diagnostics
Friday, October 4, 2019: 12:15 PM

Background. Respiratory virus infections are important causes of morbidity and mortality among pediatric and adult patients. These viruses infect respiratory epithelial cells, where they may induce specific metabolite alterations. As a proof-of-concept, we investigate the novel use of liquid chromatography (LC) combined with quadrupole time-of-flight mass spectrometry (Q-TOF) for the study of host cell metabolite alterations to diagnose and differentiate respiratory viruses.

Methods. We studied nasopharyngeal swab samples positive for respiratory viruses by the eSensor Respiratory Viral Panel (GenMark Diagnostics, Carlsbad, CA). Banked, frozen samples (−80°C) stored in viral transport media were retrieved and thawed. Aliquots of 100 µL were centrifuged at 13.3 × *g* for 15 minutes, and the filtrate was analyzed by Agilent 6545 Quadrupole LC/Q-TOF (Agilent Technologies, Santa Clara, CA). Compounds were separated using a novel column arrangement based on hydrophobicity and charge using a quaternary solvent manager, followed by accurate mass analysis by LC/Q-TOF. Agilent Mass Profiler 3D principal component analysis was performed, and compound identification was completed using the METLIN metabolite database.

Results. A total of 235 specimens were tested by LC/Q-TOF, including 195 positive specimens [including adenovirus, coronavirus, influenza A H1N1 and H3N2, influenza B, human metapneumovirus, parainfluenza viruses 1, 2, 3, and 4, respiratory syncytial virus (RSV), and rhinovirus] as well as 40 negative clinical specimens. LC/Q-TOF primary component analysis (PCA) allowed preliminary identification of key metabolites that distinguished all virus-positive specimens compared with the negative group, and differentiated respiratory viruses from one another including between influenza A 2009 H1N1 and H3N2 subtypes (Figure 1).

Conclusion. Preliminary data from our LC/Q-TOF analysis show that respiratory viruses exhibit different host cell metabolomic profiles that allow viral differentiation to the species level, and for influenza A virus, the subtype level. This metabolomic approach has substantial potential for diagnostic applications in infectious diseases directly from patient samples, and may be eventually adapted for point-of-care testing.

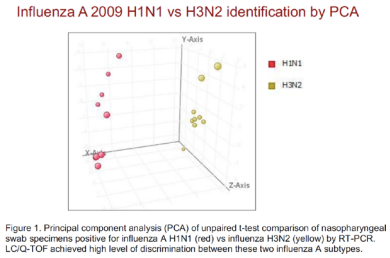

Figure 1. Principal component analysis (PCA) of unpaired t-test comparison of nasopharyngeal swab specimens positive for influenza A H1N1 (red) vs influenza H3N2 (yellow) by RT-PCR. LC/Q-TOF achieved high level of discrimination between these two influenza A subtypes.

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

1792. Viral DNA Loads in Various Blood Components of Patients with EBV-Positive T/NK Cell Lymphoproliferative Diseases

Jun-ichi Kawada, MD, PhD[1]; Yasuko Kamiya, MD, PhD[2]; Akihisa Sawada, MD, PhD[3]; Keiji Iwatsuki, MD, PhD[4]; Koji Izustu, MD, PhD[5]; Yuka Torii, MD, PhD[1]; Hiroshi Kimura, MD, PhD[6]; Yoshinori Ito, MD, PhD[1]; [1]Nagoya University Graduate School of Medicine, Nagoya, Aichi, Japan; [2]Department of Pediatrics, Nagoya University Graduate School of Medicine, Nagoya, Aichi, Japan; [3]Department of Hematology/Oncology, Osaka Women's and Children's Hospital, Izumi, Osaka, Japan; [4]Department of Dermatology, Okayama University Graduate School of Medicine, Okayama, Japan; [5]Department of Hematology, National Cancer Center Hospital, Tokyo, Tokyo, Japan; [6]Department of Virology, Nagoya University Graduate School of Medicine, Nagoya, Aichi, Japan

Session: 170. Viral Diagnostics
Friday, October 4, 2019: 12:15 PM

Background. Epstein–Barr virus (EBV) is associated with T- and NK-cell lymphoproliferative disorders (EBV T/NK-LPD). For diagnosis of EBV T/NK-LPD, quantification of EBV DNA loads in peripheral blood by real-time PCR has been widely used. However, optimal blood components and cut-off values for diagnosis were not fully evaluated.

Methods. Fifty-nine patients with EBV T/NK-LPD including chronic active EBV infection (CAEBV), severe mosquito bite allergy, hydroa vacciniforme-like lymphoproliferative disorder (HV), and EBV- hemophagocytic lymphohistiocytosis (EBV-HLH) were enrolled. EBV DNA loads were compared among disease categories in each blood component from the same whole blood sample. The association between EBV DNA loads and disease activity were evaluated in CAEBV patients. Furthermore, the diagnostic cut-off value for EBV DNA loads in whole blood from CAEBV patients as compared with infectious mononucleosis patients was determined.

Results. EBV DNA loads in whole blood and peripheral blood mononuclear cells (PBMCs) were not significantly different among disease categories, whereas EBV DNA loads in plasma were significantly higher in EBV- HLH patients than in HV patients. EBV DNA loads in whole blood and PBMCs showed strong correlation (Figure 1). EBV DNA loads in plasma were significantly higher in CAEBV patients with active disease than in those with inactive disease (median: $10^{4.5}$ IU/mL vs. $10^{0.8}$ IU/mL, $P < 0.001$) (Figure 2). Diagnostic cut-off values for whole blood EBV DNA loads of CAEBV patients as compared with those of infectious mononucleosis was $10^{4.2}$ (= 15,800) IU/mL (Figure 3).

Conclusion. Measuring EBV DNA loads in whole blood can be considered as initial evaluation for diagnosis of EBV T/NK-LPD. EBV DNA loads in plasma are more closely related to disease activity of CAEBV than EBV DNA loads in whole blood and PBMCs.

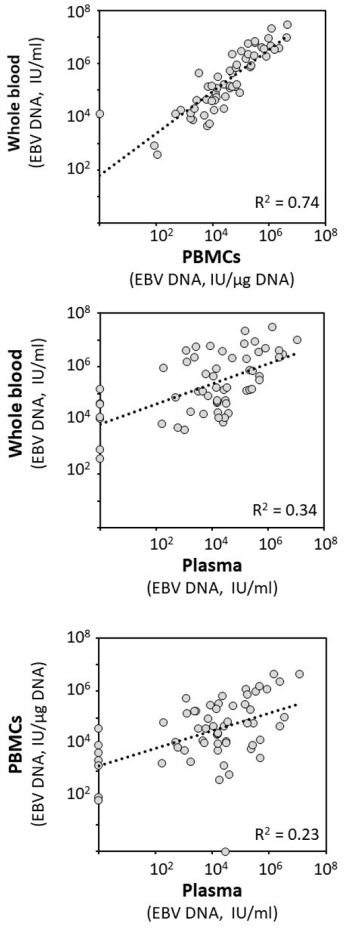

Fig. 1

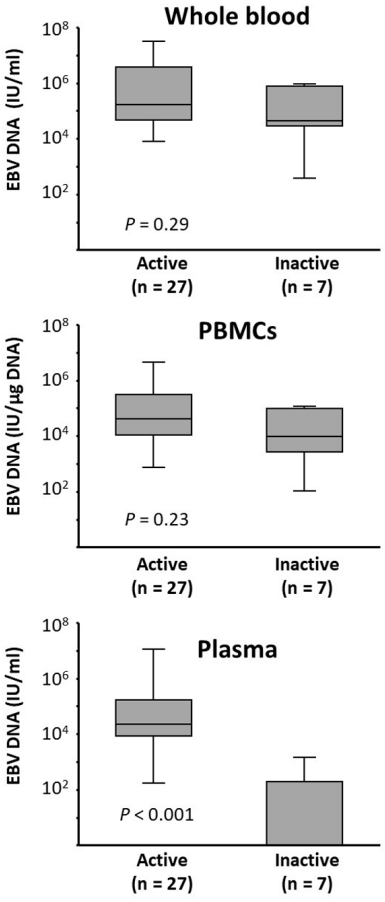

Fig. 2

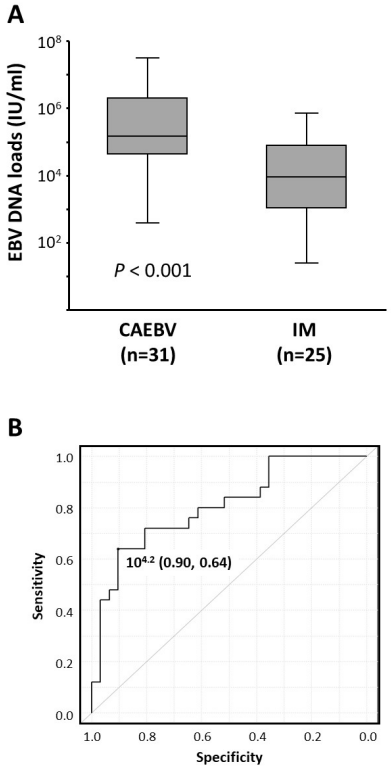

Fig. 3

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

1793. Clinical Outcomes among Febrile Infants Before and After Implementation of BioFire® FilmArray® Panels

Jennifer Crook, BS, BA[1]; Meng Xu, MS[2]; Chris Slaughter, DrPH[1]; Whitney Browning, MD[1]; Cristina Estrada, MD[3]; James Gay, MD, MMHC[1]; Gale Thomas[1]; Criziel Quinn, MT, MB (ASCP) [1]; Alison Benton, MS, MB(ASCP)cm[1]; Jonathan Schmitz, MD, PhD, D(ABMM)[1]; Ritu Banerjee, MD, PhD[1]; Ritu Banerjee, MD, PhD[1]; [1]Vanderbilt University Medical Center, Nashville, Tennessee; [2]Vanderbilt University, Brentwood, Tennessee; [3]Vanderbilt Children's Hospital, Brentwood, Tennessee

Session: 170. Viral Diagnostics
Friday, October 4, 2019: 12:15 PM

Background. The clinical benefits of multiplex polymerase chain reaction panels are not well defined. We evaluated outcomes among infants before and after implementation of the BioFire® FilmArray® Respiratory Panel 2 (RP2) and Meningitis Encephalitis Panel (MEP).

Methods. This single-center study compared outcomes among infants ≤ 90 days presenting to the Emergency Department with fever ($T \geq 38.0$°C) or hypothermia ($T < 35.8$°C) during 3 time periods. P1 (January 1, 2011–December 31, 2014) had batch testing using a Genmark Dx® respiratory viral panel (RVP) and no standardized clinical practice guideline (CPG); P2 (January 1, 2015–April 30, 2018) had the RVP and a CPG; and P3 (May 1, 2018–March 31, 2019) had on-demand RP2 and MEP testing and a CPG. Clinical data were collected from medical records. Statistical analyses were performed using Kruskal–Wallis and Pearson tests.

Results. There were 5195 total patients: 2514 in P1, 2082 in P2, 599 in P3. Groups did not differ in pathogens or antimicrobials used. Testing was faster and performed more commonly in P3 than P1 or P2 (P1, 10%; P2, 6.9%; P3, 71%; Table 1). From P1 to P3 there were significant decreases in length of stay (LOS), % receiving antimicrobials, antibiotic durations, ancillary test use, lumbar punctures (LPs), and chest X-rays (Table 1). In P3 compared with P2, infants more commonly received no antimicrobials (43.1% vs. 32.4%, $P < 0.001$; Figure 1), had fewer median (IQR) number of ancillary tests (5 (5–8) vs. 7 (3–10); $P < 0.001$), and shorter median (IQR) days of antibiotics (2.0 (1.0–2.7) vs. 2.4 (1.1–3.4); $P < 0.001$; Table 1). Among P3 infants, those with positive RP2 and/or MEP results were less likely to receive antimicrobials, be hospitalized or readmitted, had fewer ancillary tests and LPs, and shorter LOS and antibiotic durations than those with negative tests (Table 2).

Conclusion. In this large pre-post intervention study among infants ≤ 90 days with fever or hypothermia, a clinical guideline plus rapid testing with RP2 and MEP was associated with less antimicrobial use and ancillary testing than a clinical guideline alone. Infants with positive RP2 and/or MEP results had fewer admissions, shorter LOS, and less antimicrobial and ancillary test use than those with negative tests. Rapid pathogen testing has benefit for infants.

Table 1: Outcomes among infants ≤90 days (n=5195)

Outcome	P 1 n=2514	P 2 n=2082	P 3 n=599	p-value
Readmission within 30 days, number (%)	140 (5.6)	89 (4.3)	33 (5.5)	0.117
Deaths within 30 days, number (%)	1 (0.0)	2 (0.1)	0 (0.0)	0.602
Admitted[1], number (%)	1610 (64.0)	1332 (64.0)	367 (61.3)	0.422
Inpatient LOS[1,2,3] (days)	1.9 (1.6-2.6) n=1517	1.8 (1.3-2.4) n=1276	1.7 (1.2-2.3) n=367	<0.001*
Antimicrobial usage				
No antimicrobials received[4], number (%)	785 (31.2)	674 (32.4)	258 (43.1)	<0.001*
Single Dose of 1-2 Antimicrobials[5], number (%)	244 (9.7)	284 (13.6)	63 (10.5)	<0.001*
Antibiotic duration[2,5] (days)	3.5 (2.0-4.2) n=1464	2.4 (1.1-3.4) n=1096	2.0 (1.0-2.7) n=271	<0.001*
Antiviral duration[2,6] (days)	1.4 (0.9-1.9) n=584	1.0 (0.6-1.7) n=338	1.0 (0.6-1.7) n=97	<0.001*
Number of ancillary tests per patient[2,7]	7 (4-10)	7 (3-10)	5 (3-8)	<0.001*
Received Chest Xray, number (%)	687 (27.3)	350 (16.8)	66 (11.0)	<0.001*
Received Lumbar Puncture, number (%)	1529 (60.8)	1169 (56.1)	313 (52.3)	<0.001*
Test Time-to-Results[2] (hours)	RVP: 29 (20.25-47.5) n=244	RVP: 26 (19.6-37.5) n=142	RP2: 1.7 (1.3-2.7) n=392 MEP: 3.6 (2.5-7.1) n=172	

[1]Considered inpatient if discharged from inpatient unit
[2]Median (IQR)
[3]Excludes 93 patients in Period 1 and 56 patients in Period 2 with incomplete data
[4]Antimicrobials include acyclovir, ampicillin, cefepime, cefotaxime, ceftriaxone, gentamicin, oseltamivir, penicillin, and vancomycin
[5]Among patients receiving more than a single dose of 1-2 antibiotics
[6]Among patients receiving more than a single dose of 1-2 antivirals
[7]Includes LP, CBC, BMP, urinalysis, CSF cell count and chemistries, enterovirus PCR, RSV antigen, influenza antigen, HSV PCR, AST, ALT, total and direct bilirubin, and bacterial cultures

Table 2: Outcomes among P3 patients receiving BioFire RP2 or MEP (n=424)

Outcome	Positive test n=230	Negative test n=194	p-value
Readmission within 30 days, number (%)	8 (3.5)	18 (9.2)	0.014*
Deaths within 30 days, number (%)	0 (0.0)	0 (0.0)	-----
Admitted[1], number (%)	139 (60.4)	160 (82.5)	<0.001*
Inpatient LOS[1,2], days	1.5 (1.1-2.0) n=139	1.9 (1.5-2.3) n=160	<0.001*
Antimicrobial Usage			
No antimicrobials received[3], number (%)	101 (43.9)	43 (21.9)	<0.001*
Single Dose of 1-2 Antimicrobials[3], number (%)	37 (16.1)	15 (7.7)	0.008*
Antibiotic duration[2,4] (days)	1.8 (1.0-2.3) n=91	2.4 (1.3-2.8) n=137	<0.001*
Antiviral duration[2,5] (days)	1.0 (0.6-1.2) n=22	1.1 (0.6-1.7) n=54	0.377
Number of ancillary tests per patient[2,6]	5 (4-8)	7 (5-9)	<0.001*
Received Chest Xray, number (%)	36 (15.6)	22 (11.3)	0.184
Received Lumbar Puncture, number (%)	130 (56.5)	148 (75.5)	<0.001*

[1]Considered inpatient if discharged from inpatient unit
[2]Median (IQR)
[3]Antimicrobials include acyclovir, ampicillin, cefepime, cefotaxime, ceftriaxone, gentamicin, oseltamivir, penicillin, and vancomycin
[4]Among patients receiving more than a single dose of 1-2 antibiotics
[5]Among patients receiving more than a single dose of 1-2 antivirals
[6]Includes LP, CBC, BMP, urinalysis, CSF cell count and chemistries, enterovirus PCR, RSV antigen, influenza antigen, HSV PCR, AST, ALT, total and direct bilirubin, and bacterial cultures