Table 1. Patient demographics and co-morbidities.

Variable	Total (N=108)
Average Age (years)	58.6
Male – No. (%)	64 (59.2)
Race/Ethnicity – No. (%)	
• White	62 (57.4)
• Black	44 (40.7)
• Asian	2 (1.8)
Immunosuppression – No. (%)	
• Solid malignancy	17 (15.7)
• Hematologic malignancy	6 (5.6)
• SOT	11 (10.2)
• HSCT	3 (2.8)
• Other	17 (15.7)
Diabetes – No. (%)	34 (31.5)
Cardiovascular disease – No. (%)	19 (17.6)
Chronic lung disease – No. (%)	21 (19.4)
CKD – No. (%)	19 (17.6)
ESRD – No. (%)	8 (7.4)
Cirrhosis – No. (%)	13 (12.0)
IVDU – No. (%)	3 (2.8)
Mechanical ventilation – No. (%)	19 (17.6)
Trauma at time of admission – No. (%)	10 (9.3)
Burn at time of admission – No. (%)	1 (0.9)
Pitt Bacteremia Score (Mean)	2.8

Table 2. Gram-negative bacteria frequency.

Gram-negative Bacteria	Total (%)
E.coli	30 (27.8)
Klebsiella pneumoniae	24 (22.2)
Pseudomonas aeruginosa	11 (10.2)
Polymicrobial	11 (10.2)
Enterobacter species	9 (8.3)
Other	7 (6.5)
Not detected	6 (5.5)
Klebsiella oxytoca	4 (3.7)
Serratia marcescens	3 (2.8)
Acinetobacter baumannii	3 (2.8)

Conclusion. The BCID-GN panel enabled earlier time to optimal treatment of highly resistant bacteria as well as multiple opportunities for narrowing gram negative spectrum and a higher degree of certainty in cessation of broad-spectrum gram-positive antibiotics

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1023. Host Gene Expression Biomarkers to Distinguish Between Causes of Acute Respiratory Symptoms in Lung Transplant Recipients

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Session: P-58. New Approaches to Diagnostics

Background. Long-term immunosuppression after lung transplantation increases susceptibility to a variety of respiratory infections that are often difficult to diagnose. Host gene expression patterns in circulating leukocytes may provide additional diagnostic information in these settings.

Methods. 107 lung transplant recipients (79% with cystic fibrosis) were enrolled at Duke University Medical Center over a 2-year period – 59% with acute respiratory symptoms, the remainder as healthy controls. Whole blood was collected by PAXGene for RNA sequencing. Prior to undergoing biomarker analysis, each case was adjudicated to the appropriate clinical phenotype: bacterial infection, viral infection, allograft rejection, and healthy. Logistic regression models were applied to gene expression data to identify classifiers capable of identifying each etiology.

Results. In lung transplant recipients, 117 genes were upregulated at least 2-fold in the presence of viral infection compared to healthy transplant controls. These genes clustered into expected antiviral pathways, including type I interferon signaling, interferon gamma mediated signaling, and defense response to virus, although the magnitude of gene expression was significantly less than that seen in non-transplant cohorts.

Similar results were seen during bacterial infection (defense response to bacterium, antibacterial humoral response) and rejection (upregulation in defensins DEFA3 and DEFA4). Interestingly, despite the presence of immunosuppression, a previously published gene expression signature of respiratory infection (derived from non-immunosuppressed subjects) was able to differentiate between bacterial and viral infection with 100% accuracy.

Conclusion. Even in the presence of systemic immunosuppression and regardless of presence/absence of cystic fibrosis, core canonical components of the host response to infection and rejection are seen. Gene expression signatures based on these conserved components offer the potential for diagnostic capability in the setting of nonspecific respiratory illness in these vulnerable hosts.

Disclosures. **Julie M. Steinbrink, MD**, **CareDx** (Research Grant or Support) **Alice Gray, MD**, **CareDx** (Advisor or Review Panel member, Research Grant or Support, Speaker's Bureau)**Polarean** (Advisor or Review Panel member)

1024. Using DOOR-MAT to Theoretically Compare Three Rapid Diagnostic Tests for Gram-Negative Bloodstream Infections in Immunocompromised Patients

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Session: P-58. New Approaches to Diagnostics

Background. Molecular rapid diagnostic tests (RDTs) for bloodstream infections (BSI) utilize a variety of technologies and differ substantially in organisms and resistance mechanisms detected. RDT platforms decrease time to optimal antibiotics; however, data on RDTs in special populations, such as immunocompromised are extremely limited. This study aimed to compare theoretical changes in antibiotics based on differences in panel identification of organisms and resistance targets among three commercially available RDT panels.

Methods. Retrospective cohort of immunocompromised patients treated for gram-negative BSI at University of Maryland Medical Center from January 2018 to September 2020. Immunocompromised was defined as active hematologic or solid tumor malignancy at time of BSI diagnosis, history of hematopoietic stem cell transplantation (HSCT) or solid organ transplantation (SOT), or absolute neutrophil count (ANC) < 1000 cells/mm^3 at any time 30 days prior to BSI diagnosis. Verigene BC-GN was performed as standard of care. GenMark ePlex BCID and BioFire FilmArray BCID 2 results were assigned based on respective identifiable organism panels.

An infectious diseases clinician blinded to final antimicrobial susceptibility testing (AST) results used RDT results to assign antibiotic treatments for each platform. Decisions were referenced against *a priori* DOOR-MAT matrices. A partial credit scoring system (0 to 100) was applied to each decision based on final AST results. The mean and standard deviation (SD) were compared across panels using One-Way Repeated Measures ANOVA with modified Bonferroni for multiple comparisons.

Results. A total of 146 patients met inclusion. Baseline characteristics are summarized in Table 1. The mean (SD) DOOR-MAT scores for the three RDT panels were: 86.1 (24.4) Verigene BC-GN vs. 88.5 (22.2) GenMark BCID vs. 87.2 (24.4) BioFire BCID 2. There was no statistically significant difference between the panels for DOOR-MAT score (P=0.6).

Table 1. Baseline Patient Characteristics and Organism Identification

Age; mean (SD), years	57 (15)
Male; n (%)	92(63)
Level of care; n (%)	
Floor	87 (59.6)
IMC	39 (26.7)
ICU	20 (13.7)
Type of immunosuppression; n (%)	
Hematologic malignancy only	45 (30.8)
SOT only	45 (30.8)
Any history of HSCT	44 (30.1)
Hematologic malignancy and history of HSCT	43 (29.5)
Solid tumor malignancy only	12 (8.2)
Solid tumor malignancy and history of HSCT	1 (0.7)
Most common organisms isolated; n (%)	
Escherichia coli	48 (32.9)
Pseudomonas aeruginosa	34 (23.3)
Klebsiella pneumoniae	32 (21.9)

Conclusion. Within an immunocompromised patient population, differences in organism identification between three commercially available RDT panels did not impact theoretical antibiotic prescribing.

Disclosures. **J. Kristie Johnson, PhD, D(ABMM)**, **GenMark** (Speaker's Bureau) **Kimberly C. Claeys, PharmD**, **GenMark** (Speaker's Bureau)

1025. Prediction of Intravenous Immunoglobulin Resistance and Coronary Artery Dilatation in Kawasaki Disease: a Multicenter Study from Oman

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Session: P-58. New Approaches to Diagnostics

Background. Prediction of intravenous immunoglobulin (IVIG) resistance and coronary artery dilatation continues to be a challenge in the management of Kawasaki disease. Significant differences exist among different populations.

Methods. Children < 13 years of age who presented to the two main tertiary care hospitals in Oman (Royal Hospital and Sultan Qaboos University Hospital) between 2008 and 2019 with a diagnosis of Kawasaki disease were included. Diagnosis was confirmed and clinical, laboratory and echocardiography data was systematically collected and checked for accuracy. The primary outcome was the presence of IVIG resistance or coronary artery dilatation at the 6-week follow-up. Bivariate analysis was used to identify significant predictors of the primary outcome, followed by multivariable logistic regression to determine independent predictors. The Muscat Index of Kawasaki disease Severity (MIKS) score was created based on the results.

Results. 156 children with Kawasaki disease were included. Median age was 2.1 years (IQR 0.9-3.8), and 64% were males. All patients received IVIG, 26 (17%) received steroids, and one received infliximab. Coronary dilatation was identified in 41 (26%) patients on initial echocardiogram, and 26 (18%) at the 6-week follow-up visit. Variables significantly associated with the primary outcome were age ≤15 months (P=0.031), hemoglobin (P=0.009), WBC count (P=0.002), absolute neutrophil count (P=0.006), and CRP ≥150 mg/L (P=0.015). These variables in addition male gender (P=0.058), ALT >80 IU/L (P=0.10) and serum sodium (P=0.10), were entered into multivariable logistic regression. A predictive model based on CRP ≥150 mg/L (LR=2.2, P=0.049), male gender (LR=2.1, P=0.095) and WBC (LR=1.1, P=0.017) resulted, and it was used as basis for the MIKS score (Table 1). The MIKS score performed favorably to the Kobayashi score in its sensitivity to predict the primary outcome and its separate components (Table 2). Combining the MIKS score with other high-risk criteria had a sensitivity of 95% in predicting the primary outcome and a specificity of 56%.

Table 1. Calculation of the Muscat Index of Kawasaki disease Severity (MIKS) score

Criteria	Score
C-reactive protein ≥150 mg/L	2
WBC	
≥13.5 x10^9/L	1
≥19 x10^9/L	3
Male gender	2
Maximum score	7

Table 2. Sensitivity, specificity and P value for the Kobayashi, MIKS, and combined high risk criteria in predicting IVIG resistance, coronary dilatation at 6 weeks, separately or in combination, among patients with Kawasaki disease. MIKS: Muscat Index of Kawasaki disease Severity. *High risk: presence of coronary artery dilatation on initial echocardiogram or age <1>

	IVIG resistance			Coronary dilatation at 6 weeks			IVIG resistance or coronary dilatation at 6 weeks		
	Sens.	Spec.	P value	Sens.	Spec.	P value	Sens.	Spec.	P value
Kobayashi ≥4	53%	78%	0.014	38%	75%	0.22	40%	78%	0.054
MIKS ≥4	72%	69%	0.001	62%	69%	0.006	65%	74%	<0.001
High risk* or Kobayashi ≥4	83%	51%	0.010	89%	56%	<0.001	85%	60%	<0.001
High risk* or MIKS ≥4	100%	47%	<0.001	92%	50%	<0.001	95%	56%	<0.001

Conclusion. The MIKS score predicts IVIG resistance and coronary artery dilatation in Kawasaki disease in our setting, with favorable performance compared to the Kobayashi score.

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

1026. Following the Hoof Prints: Detecting *Coxiella* and *Brucella* infections with A Plasma-based Microbial Cell-Free DNA Next-generation Sequencing Test

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Session: P-58. New Approaches to Diagnostics

Background. *Coxiella burnetii* and *Brucella spp*. are zoonotic bacterial pathogens responsible for Q fever and Brucellosis, respectively. Both pathogens have a global distribution and Brucellosis is the most common zoonosis in the world. However, the CDC reports only 80-120 cases of human brucellosis and ~150 cases of acute Q fever annually. The diagnosis of these infections can be limited by: (1) their difficulty to culture; (2) the insensitivity and nonspecificity of serology; (3) the clinical overlap with other infections; and (4) the unreliability of epidemiological exposure history for these zoonoses. Unbiased microbial cell free DNA (mcfDNA) next-generation sequencing (NGS) offers a potential solution to overcome these limitations.

Methods. The Karius Test™ (KT) developed and validated in Karius's CLIA certified/CAP accredited lab in Redwood City, CA detects mcfDNA in plasma. After mcfDNA is extracted and NGS performed, human reads are removed, and remaining sequences are aligned to a curated database of > 1500 organisms. McfDNA from organisms present above a statistical threshold are reported and quantified in molecules/µL (MPM). KT detections of *Coxiella* and *Brucella* were reviewed from August 2017 - present; clinical information was obtained with test requisition or consultation upon result reporting.

Results. KT detected 8 cases of *Coxiella burnetii* (1735 MPM +/- 3000) and 5 cases of *Brucella melitensis* (avg 296 MPM +/- 223) (Table 1), representing approximately 1-2% of all detections in the US during this period. All of the Coxiella detections were in adults (100% male) with 5 cases of fever of unknown origin, 2 cases of culture-negative endocarditis and one case of endovascular graft infection. *Brucella* detections occurred in 3 adults and 2 children (60% male), 3 with exposure to unpasteurized dairy and included 3 cases of spine infection (2 vertebral osteomyelitis, 1 epidural abscess).

Table 1. *Coxiella burnetii* and *Brucella melitensis* detections by the Karius Test™

Case	Age	Sex	IC	Exposure	Clinical Context	Karius Test Result	MPM (RI<10)
1	Adult	M	No	No	Endovascular graft infection	*Coxiella burnetii*	8,262
2	Adult	M	No	Livestock	Fever of Unknown Origin	*Coxiella burnetii*	776
3	Adult	M	No	No	Fever of Unknown Origin	*Coxiella burnetii*	202
4	Adult	M	No	Livestock	Fever of Unknown Origin	*Coxiella burnetii*	2,468
5	Adult	M	No	No	Fever of Unknown Origin	*Coxiella burnetii*	165
6	Adult	M	No	No	Fever of Unknown Origin	*Coxiella burnetii*	217
7	Adult	M	No	No	Culture-negative native valve endocarditis	*Coxiella burnetii*	53
8	Adult	M	No	No	Culture-negative prosthetic valve endocarditis	*Coxiella burnetii*	Not available*
9	Pediatric	M	No	Unpasteurized dairy	Fever of Unknown Origin	*Brucella melitensis*	Not available^
10	Adult	F	No	Unpasteurized dairy	Vertebral osteomyelitis and bacteremia	*Brucella melitensis*	569
11	Adult	M	No	Unpasteurized dairy	Epidural abscess	*Brucella melitensis*	374
12	Pediatric	F	Unknown	Unknown	Not obtained	*Brucella melitensis*	182
13	Adult	M	No	No	Vertebral osteomyelitis	*Brucella melitensis*	59

MPM: Molecules per microliter; RI: Reference interval which denotes the 97.5th %tile of the MPM for each microbe in a cohort of 684 healthy subjects; IC: Immunocompromised
*Initial version of the test that did not offer quantification ^Sample did not meet minimum sequencing depth requirements for quantification

Conclusion. Open-ended, plasma-based mcfDNA NGS provides a rapid, non-invasive test to diagnose diverse clinical manifestations of zoonotic infections such as Q fever and Brucellosis against competing broad differential diagnoses. Furthermore, these cases highlight the potential of the KT to diagnose infections caused by fastidious/unculturable pathogens with cryptic clinical presentations.

Disclosures. **Nicholas R. Degner, MD, MPH, MS**, **Karius Inc.** (Employee, Shareholder) **Ricardo Castillo-Galvan, MD MPH**, **Karius Inc.** (Consultant) **Jose Alexander, MD, D(ABMM), FCCM, CIC, SM, MB(ASCP), BCMAS**, **Karius** (Employee) **Aparna Arun, MD**, **Karius** (Employee) **Ann Macintyre, DO**, **Karius, Inc.** (Employee) **Bradley Perkins, MD**, **Karius, Inc.** (Employee) **Asim A. Ahmed, MD**, **Karius, Inc.** (Employee) **Matthew Smollin, PharmD**, **Karius, Inc.** (Employee)

1027. Earlier Is Better: Progress Toward Decreased Time to Optimal Therapy and Improved Antibiotic Stewardship for Gram-positive Bloodstream Infections Through Use of GenMark Dx ePlex system

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Session: P-58. New Approaches to Diagnostics

Background. The ePlex BCID Gram-Positive (GP) panel utilizes electrowetting technology to detect the most common causes of GP bacteremia (20 targets) and 4 antimicrobial resistance (AMR) genes in positive blood culture (BC) bottles. Rapid detection of intrinsic vancomycin resistance and acquired resistance genes (*mecA, mecC, vanA, vanB*) enables early optimization of antimicrobial therapy whereas early detection of common contaminants is expected to decrease unnecessary antibiotic utilization and hospitalizations.

Methods. In this prospective study, aliquots of BC bottles with GP bacteria detected on Gram stain (GS) (n=101) received standard of care (SOC) culture and antimicrobial susceptibility testing (AST). Additionally, samples were evaluated with the BCID-GP panel but only SOC results were reported in the EMR and available to inform clinical decisions. Patients were excluded if the sample was a subsequent culture in a persistent episode of bacteremia (n=17) or if the assay failed (n=4). Chart review