

Background. *Capnocytophaga canimorsus* (Cc) and *Pasteurella multocida* (Pm) are gram negative bacterial commensal pathogens typically from dogs or cats that can cause severe infection in humans when spread through licks, scratches or bites. The diagnosis of these infections can be limited by: (1) their fastidious nature and difficulty to culture; (2) the nonspecific manifestations of the infections; and (3) the unreliability of dog or cat exposure history. Open-ended 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 Cc and Pm were reviewed from August 2017 - present; clinical information was obtained with test requisition or consultation upon result reporting.

Results. KT detected 5 cases of Cc (25,039 MPM +/- 41,062) and 8 cases of Pm (33,264 MPM +/- 69,301) (Table 1). All detections of Cc were in adults (60% male) and included 2 cases of culture-negative endocarditis (one with known liver disease) and one case of sepsis with diffuse rash. Pm detections occurred in 6 adults and 2 children (75% male) and included 2 cases of culture-negative endocarditis, and single cases each of endovascular graft infection, pneumonia, fever of unknown origin, and a cranial dog bite complicated by an abscess. Two patients had immunocompromising conditions including neuroblastoma and aplastic anemia.

Table 1. *Capnocytophaga canimorsus* and *Pasteurella multocida* detections by the Karius Test™

Case	Age	Sex	IC	Liver disease	Exposure	Clinical Context	Karius Test Result	MPM (Rc<10)
1	Adult	M	No	Yes	Dog	Culture-negative native valve endocarditis	<i>Capnocytophaga canimorsus</i>	86,130
2	Adult	M	No	No	No	Culture-negative prosthetic valve endocarditis	<i>Capnocytophaga canimorsus</i>	12,055
3	Adult	F	No	No	Dog	Sepsis with diffuse rash	<i>Capnocytophaga canimorsus</i>	Not available*
4	Adult	F	Unknown	Unknown	Not obtained	Not obtained	<i>Capnocytophaga canimorsus</i>	531
5	Adult	M	Unknown	Unknown	Unknown	Not obtained	<i>Capnocytophaga canimorsus</i>	1,438
6	Adult	M	No	No	No	Endovascular graft infection	<i>Pasteurella multocida</i>	195,385
7	Adult	M	Yes	No	Farm	Fever of Unknown Origin	<i>Pasteurella multocida</i>	99
8	Pediatric	M	Yes	No	No	Pneumonia	<i>Pasteurella multocida</i>	26
9	Adult	F	No	Yes	Cat	Culture-negative prosthetic valve endocarditis	<i>Pasteurella multocida</i>	4,140
10	Adult	M	No	No	No	Culture-negative native valve endocarditis	<i>Pasteurella multocida</i>	774
11	Pediatric	M	No	No	Dog	Dog bite to head complicated by abscess	<i>Pasteurella multocida</i>	27
12	Adult	M	Unknown	Unknown	Unknown	Not obtained	<i>Pasteurella multocida</i>	65,401
13	Adult	F	Unknown	Unknown	Unknown	Not obtained	<i>Pasteurella multocida</i>	261

MPM: Molecules per microliter; Rc: Reference interval which denotes the 97.5% tail of the MPM for each microbe in a cohort of 684 healthy subjects; IC: Immunocompromised *Sample did not meet minimum sequencing depth requirements for quantification

Conclusion. Unbiased, plasma-based mcfDNA NGS provides a rapid, non-invasive test to diagnose diverse clinical infections by Cc and Pm. These cases highlight the potential of the KT to diagnose infections caused by fastidious/unculturable pathogens with non-specific clinical manifestations and broad differential diagnoses.

Disclosures. Nicholas R. Degner, MD, MPH, MS, Karius Inc. (Employee, Shareholder) Ricardo Galvan-Castillo, MD, Karius Inc. (Employee, Shareholder) 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)

1031. Utility of Broad-Range Polymerase Chain Reaction Sequencing for Infectious Diseases Clinical Decision Making: A Pediatric Center Experience
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Background. Broad-range polymerase chain reaction (PCR) sequencing is a promising tool for diagnosis of infectious conditions when traditional microbiologic strategies fail to identify a pathogen. Data on the optimal clinical scenarios in which to use this tool are limited.

Methods. We assessed the rate of organism identification from broad-range PCR testing sent from our quaternary care children's hospital between March 2017 and June 2020. We completed a retrospective chart review to evaluate patients' baseline demographic and clinical features as well as clinical significance of results (defined as influencing antimicrobial management) by specimen type.

Results. Among 184 total samples, 111 (60%) were obtained from immunocompromised patients. The median age of patients at the time of sample collection was 11.4 years (IQR 6.5-16.0). 128/181 (71%) samples were from patients known to be on ≥ 1 antimicrobial, including prophylaxis, in the 24 hours prior to sample collection. 52/184 (28%) patients ultimately had an infectious disease diagnosed by another testing modality. The most common PCR sample types were bronchoalveolar lavage (BAL) fluid (35), lung tissue (20), and bone (14). An organism was identified from 41 (22%) samples, but positive results for only 8 samples (4%) led to a change in antimicrobial management: addition of agents in 4 cases, cessation of agents in 2, and transition from one agent to another in 2. Negative results for 3 (2%) samples led to discontinuation of antimicrobials. Organisms were identified from 11 (31%) BAL samples, of which only 2 (6%) were judged to be clinically significant. No results from lung tissue, CSF (11), skin biopsies (6), or joint fluid (4) affected antimicrobial management.

	Organism identified, impact on antimicrobial management	Organism identified, no impact on antimicrobial management	No organism identified
Receipt of antimicrobials during 24 hours prior to sample collection, n (%) ^a	6 (4.7%)	24 (18.8%)	98 (76.6%)
Infectious disease diagnosed by other modality, n (%)	2 (3.8%)	12 (23.1%)	38 (73.1%)
Sample Type, n (%) ^b			
Pleural fluid	1 (14.3%)	3 (42.9%)	3 (42.9%)
Cardiac Hardware/ Cardiac Tissue	1 (9.1%)	1 (9.1%)	9 (81.8%)
Abscess	1 (8.3%)	4 (33.3%)	7 (58.3%)
Lymph Node	1 (7.7%)	1 (7.7%)	11 (84.6%)
BAL	2 (5.7%)	14 (40.0%)	19 (54.3%)
Lung	0 (0%)	1 (5.0%)	19 (95.0%)
Bone	0 (0%)	1 (7.1%)	13 (92.9%)
CSF	0 (0%)	1 (9.1%)	10 (90.9%)
Liver Tissue	0 (0%)	1 (11.1%)	8 (88.9%)
Other	1 (1.9%)	7 (13.5%)	44 (84.6%)

a. Three samples were obtained outside of our institution, so data are unavailable on whether the patient was on antimicrobials at the time testing was sent

b. For one sample sent from explanted cardiac hardware, one from bone, and one from liver tissue, antibiotics were stopped after BRPCR did not identify an organism

Conclusion. We found that only 6% of broad-range PCR results influenced antimicrobial management in a diverse pediatric cohort. Our findings suggest that many positive results, especially in BAL fluid, do not lead to changes in antimicrobial management. Additional work is necessary to characterize the ideal clinical scenarios in which broad-range PCR should be used as over a quarter of patients had a causative infectious disease identified by another modality.

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1032. Evaluation of a Multiplex Rapid Diagnostic Panel in Respiratory Specimens from Critically Ill Patients with Hospital-Acquired Pneumonia

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Background. Rapid diagnostic tests can be a valuable aide in clinical decision-making but often cost more than traditional cultures. Prior to its implementation at our institution, we sought to evaluate the potential clinical and financial impact of using the FilmArray® Pneumonia Panel® (FP panel) in patients with hospital-acquired pneumonia (HAP).

Methods. This was a retrospective, observational, comparative study conducted at an 885-bed academic medical center. Respiratory samples obtained by bronchoalveolar lavage or tracheal aspiration from adult intensive care unit (ICU) patients with a diagnosis of HAP from Nov 2019 – Feb 2020 were tested by the FP panel in addition to routine cultures. Medical records were reviewed to determine potential changes in antimicrobial therapy if FP panel results were known by the treatment team in real time. A cost analysis was also performed incorporating the cost of the FP panel and the savings associated with the potential avoidance of antibiotics and other rapid diagnostic tests normalized per patient.

Results. 56 patients met study criteria. FP panel results could have prompted a change in therapy in 36 (64.3%) patients, with a mean reduction in time to optimized therapy of approximately 51 hours. The panel identified 3 cases where the causative pathogen was not treated by empiric therapy and 34 opportunities for antibiotic de-escalation, the most common being the discontinuation of empiric vancomycin. 36 patients had been tested with a Respiratory Virus Panel, which could have been avoided if the FP panel was used. The potential therapy impact based on specific ICU and respiratory culture results is summarized in Table 1. The cost analysis calculated an additional cost of \$10 per patient associated with using the FP panel.

Table 1. Potential Changes in Therapy Based on Patient Location and Culture Result

Location	Potential Therapy Change, n (%)
Medical ICU	13/24 (54.2)
Positive culture	11/20 (55)
Negative culture	2/4 (50)
Surgical ICU	12/20 (60)
Positive culture	9/15 (60)
Negative culture	3/5 (60)
Trauma ICU	11/12 (91.7)
Positive culture	6/7 (85.7)
Negative culture	5/5 (100)

Conclusion. The FP panel could have prompted a change in therapy in about two-thirds of patients studied. Its potential benefits include quicker time to optimized therapy, reduced exposure to and cost of broad-spectrum antimicrobials, and reduced cost of other rapid diagnostic tests.

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