Rapid, Non-invasive Detection of Infection Using Plasma-based Next-Generation Sequencing for Microbial Cell-free DNA in Individuals Testing Negative for SARS-CoV-2 in a Pandemic Setting

IDWeek Abstract: 395

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Background

The clinical presentation of patients with severe COVID-19 infection can be protracted and deteriorate to ARDS and multi-organ dysfunction with prolonged fever.[1] As such, there is clinical overlap with many infectious diseases especially those that cause pneumonia. Due to of the prevalence of COVID-19 illness amidst the pandemic, concerns about testing sensitivity and the attendant risk to health care personnel (HCP) delivering care, patients are frequently tested multiple times to ascertain that they are truly SARS-CoV-2 negative.[2-4] Often, alternative diagnoses are not considered because some diagnostic modalities—such as bronchoalveolar lavage (BAL)—pose an unacceptable risk to the patient and/or HCP.[5]

Methods

We interrogated plasma for microbial cell-free DNA from 81 patients who were known to be SARS-CoV-2 negative. Clinical information is taken from information submitted with the test requisition or obtained at the time of result reporting from clinical consultations with the ordering provider. In each case, a plasma sample was analyzed with the Karius Test (KT). The KT was developed and validated in Karius' CLIA certified/CAP accredited lab and detects microbial cell-free DNA (mcfDNA), which can assist with the diagnosis of deep-seated infections. After mcfDNA is extracted and NGS performed, human reads are removed and remaining sequences are aligned to a curated database of >1000 organisms. Organisms present above a statistical threshold are reported. For > 85% of test results the time to result reporting is 24 hours from sample receipt. (see Figure 1)

Results

In a subset of 30 samples, we detected a broad range of pathogens in both pediatrics and adults. *Pneumocystis jirovecii* was the most common pathogen detected. We identified detections that were either unexpected in many of the patients or unable to grow or detect with standard of care lab tests. (see Table 1)

Figure 1. Karius Workflow Process[6]

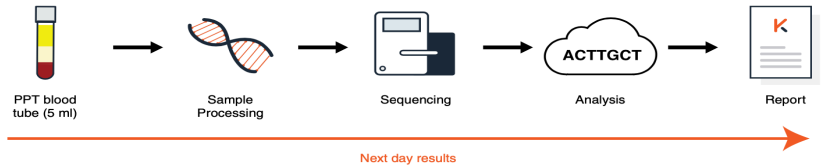
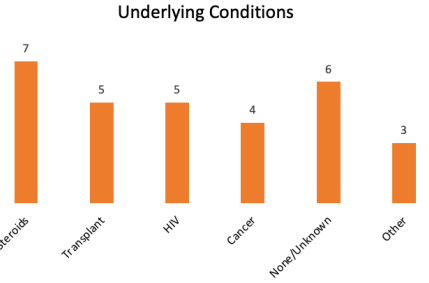


Table 1. Broad Range of Karius Detected Pathogens

Case	Age Group	Detected Organism(s)	Type of Infection	Underlying Condition
1	Pediatric	*Aspergillus fumigatus*	Pneumonia	Chronic corticosteroids
2	Pediatric	*Cunninghamella*	Pneumonia	Aplastic anemia
3	Pediatric	*Fusobacterium necrophorum*	Pneumonia	None
4	Pediatric	*Fusobacterium nucleatum*	Pneumonia	None
5	Pediatric	*Leptospira kirschneri*	FUO	None
6	Pediatric	*Mucor indicus*	FUO/sinusitis	Stem cell transplantation
7	Pediatric	*Pneumocystis jirovecii*	Pneumonia	Acute Lymphocytic Leukemia (ALL)
8	Pediatric	*Pneumocystis jirovecii*	Pneumonia	Leukemia
9	Pediatric	*Pneumocystis jirovecii*	Pneumonia	Chronic immunosuppression
10	Adult	*Aspergillus calidoustus*	Nodular pneumonia	Fever/neutropenia
11	Adult	*Aspergillus fumigatus*	Nodular pneumonia	Solid Organ Transplant (SOT)
12	Adult	*Aspergillus fumigatus*	Pneumonia	Chronic immunosuppression
13	Adult	*Burkholderia gladioli*	Pneumonia	Lung Transplant
14	Adult	*Coxiella burnetii*	FUO	None
15	Adult	*Histoplasma capsulatam*	Nodular pneumonia	HIV (new Dx)
16	Adult	*Legionella jordanis*	Pneumonia	Solid Organ Transplant (SOT)
17	Adult	*Legionella micdadei*	Multifocal pneumonia	Chronic corticosteroids
18	Adult	*Mycobacterium avium complex*	FUO/necrotic pulmonary lesions	Unknown
19	Adult	*Mycobacterium kansaii*	Cavitary pulmonary lesions	None
20	Adult	*Nocardia veterana*	Pneumonia	Interstitial Lung Disease (ILD)
21	Adult	*Pneumocystis jirovecii*	Pneumonia	HIV
22	Adult	*Pneumocystis jirovecii*	Pneumonia	HIV (new Dx)
23	Adult	*Pneumocystis jirovecii*	Pneumonia	Multiple Myeloma
24	Adult	*Pneumocystis jirovecii*	Pneumonia	HIV
25	Adult	*Pneumocystis jirovecii*	Pneumonia	HIV (new Dx)
26	Adult	*Pneumocystis jirovecii*	Pneumonia	Chronic corticosteroids
27	Adult	*Pneumocystis jirovecii*	Pneumonia	Immunocompromised NOS
28	Adult	*Pneumocystis jirovecii*	Pneumonia	Polymyalgia rheumatica on steroids
29	Adult	*Rhizopus oryzae*	Fever w/ lung mass	Stem cell transplantation
30	Adult	*Human papillomavirus*	Pulmonary/endocardial mass-due to viral driven tumor	Myelodysplastic syndrome

FUO=Fever of Unknown Origin; NOS = Not Otherwise Specified

Results



Conclusion

Open-ended, plasma-based NGS for mcfDNA with the KT provides a rapid, non-invasive method to diagnose deep-seated infection like pneumonia. This broad-based test detected a wide range of pathogens – many unsuspected – in patients with severe pneumonia and other invasive infections during the COVID-19 pandemic. These detections highlight the utility of the test enabling improvements in patient management, earlier time to diagnosis with avoidance of additional workup and initiation of targeted antibiotic therapy.

References

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