# Overview of the Karius Test

KARIUS® clarity at speed™ | TEST

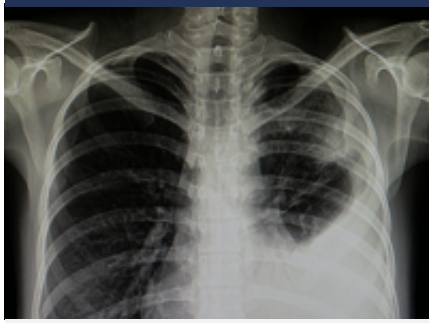
0919-S0043-Rev2

# Karius Inc.

- Life sciences company in Redwood City, CA
- Founded in 2014 based on IP out of Stanford University
- Team of 40+ employees
- CLIA-certified, CAP-accredited laboratory

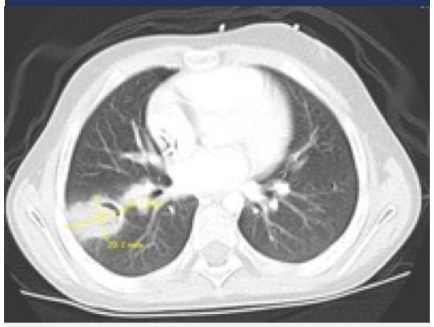
# Challenges of Conventional Infectious Disease Diagnostics

## Low Sensitivity



Unknown pathogen in
- 60% of patients with pneumonia
- 49% of of patients with sepsis

## Invasive



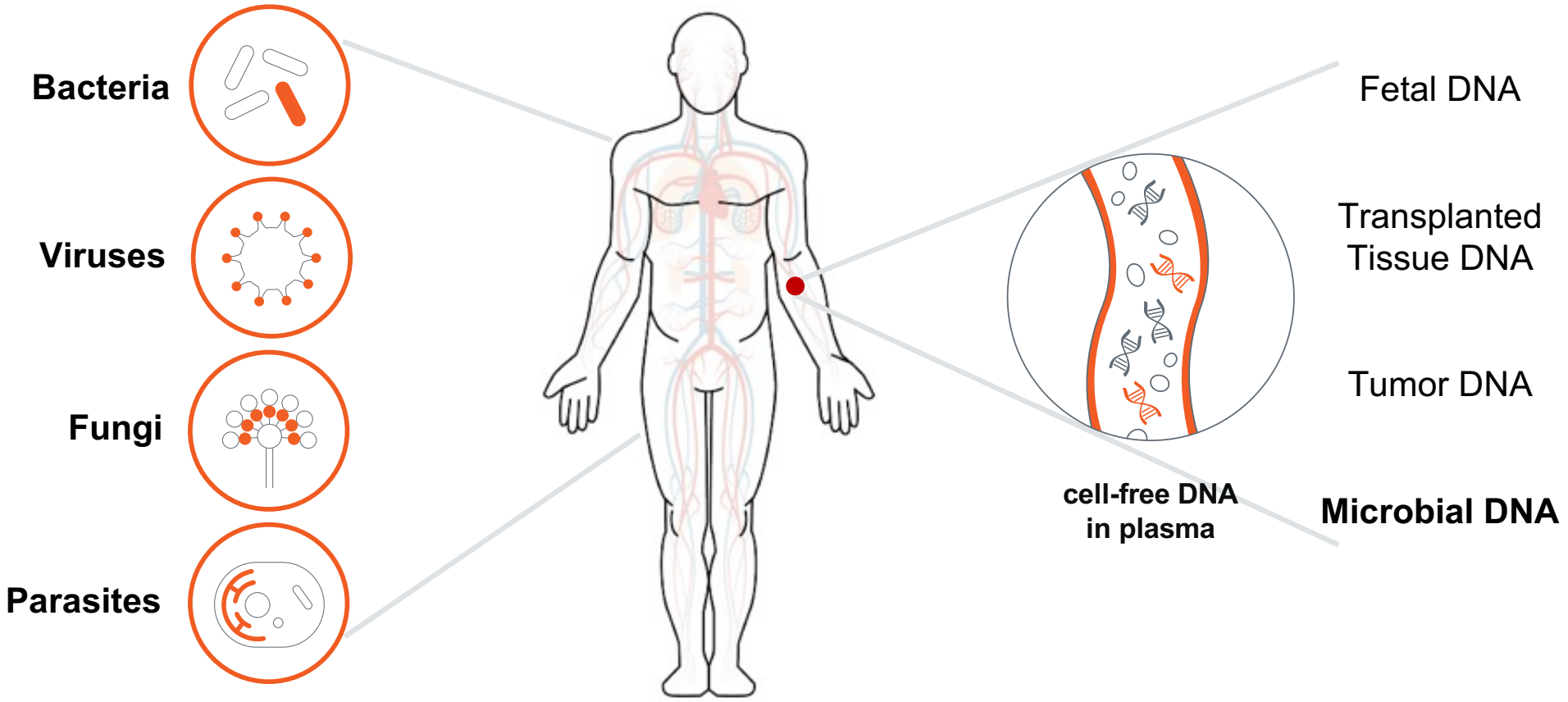
Biopsies often required to identify pathogen in invasive infections

## Narrow Scope

Blood culture, PCR, and serology detect limited pathogens, leading to unnecessary broad spectrum treatment

Jain S., et al., *N Engl J Med.* 2015;373:415-427 I Phua J.,et al., *Crit Care.* 2013;17(5):R202 I Gupta S.,et al., *Chest.* 2016;150(6):1251-1259

# Pathogens Leave Traces of Microbial Cell-Free DNA (mcfDNA) in Blood




De Vlaminck I., et al, *Cell*. 2013;155(5):1178-1187. | Abril M.K., et al, *Open Forum Infect Dis*. 2016;3(3):ofw144. | Blauwkamp T., et al. *Nat. Microbiol*. 2019;4(4):663-674

# KARIUS® TEST

**The Karius Test is a blood test based on next generation sequencing (NGS) of microbial cell-free DNA.**

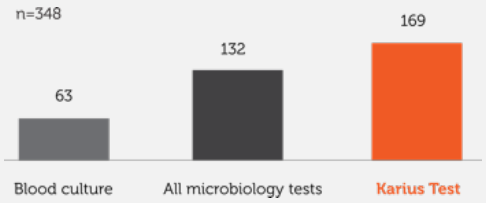
- Comprehensive
  - Over 1,000 pathogens detected from a single blood sample (bacteria, fungi, DNA viruses, eukaryotes, archaea)
- Quantitative
  - Concentration of microbial cell-free DNA is expressed as MPM (molecules per microliter) to quantify/monitor pathogens over time
- Fast
  - Results available the next day*

* >85% of specimens received by 8:30 AM (PT) Monday through Saturday are reported the next day.

# Advantages of mcfDNA in the Diagnosis of Infectious Diseases

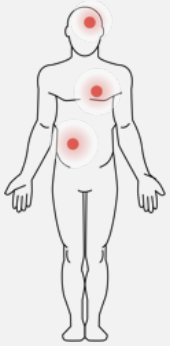
KARIUS® TEST

## Higher Diagnostic Yield



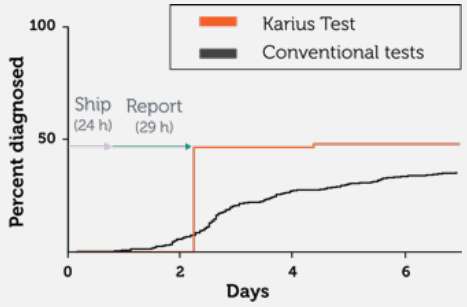

Higher diagnostic yield than conventional tests[1]

## Non-Invasive



mcfDNA generated throughout the body enables detection of both bloodstream and deep infections[1,2]

## Faster Time-to-Diagnosis




Faster time-to-diagnosis than conventional tests[1]

1. Blauwkamp T., et al. *Nat. Microbiol*. 2019;4(4):663-674. 2. Hong D.K., et al, *Diagn Microbiol Infect Dis*. 2018;92(3):210-213.

## Main Clinical Applications of the Karius Test Include:

**Pneumonia**
- Complicated
- Atypical

**Immunocompromised**
- Neutropenic fever
- Invasive fungal infections

**Cardiovascular Infections**
- Endocarditis

# Clinical Data Highlights

**Higher diagnostic yield**

- Karius Test identified **28% more causal pathogens** than standard microbiological testing (169 vs. 132 causal pathogens)[1]
- Karius Test identified a plausible cause of neutropenic fever **2x more often** than standard tests (41 vs. 20)[2]

**Change in antimicrobial management**

- Antimicrobial therapy was changed in **47% (7/15) of patients** based on Karius Test results[3]
- Antimicrobial therapy would have been changed in **47% (26/55) of patients** if results had been available in real-time[2]

**Potential avoidance of invasive biopsies**

- Invasive procedures to diagnose infections could have been avoided in **87%** (34/39) of cases using the Karius Test[4]
- In **7/9 patient cases**, the Karius Test detected the same fungus identified from the biopsy tissue at the species level[5]

1. Blauwkamp T., et al. *Nat. Microbiol.* 2019;4(4):663-674. 2. Benamu E. et al. IDWeek; October 3-7, 2018; San Francisco, CA. 3. Farnaes L., et al. *Diagn Microbiol Infect Dis.* 2019;94(2):188-191.
4. Rossoff, et al. *Open Forum Infect Di.* 2019;6(8):ofz327. 5. Hong D.K., et al, *Diagn Microbiol Infect Dis.* 2018;92(3):210-213.

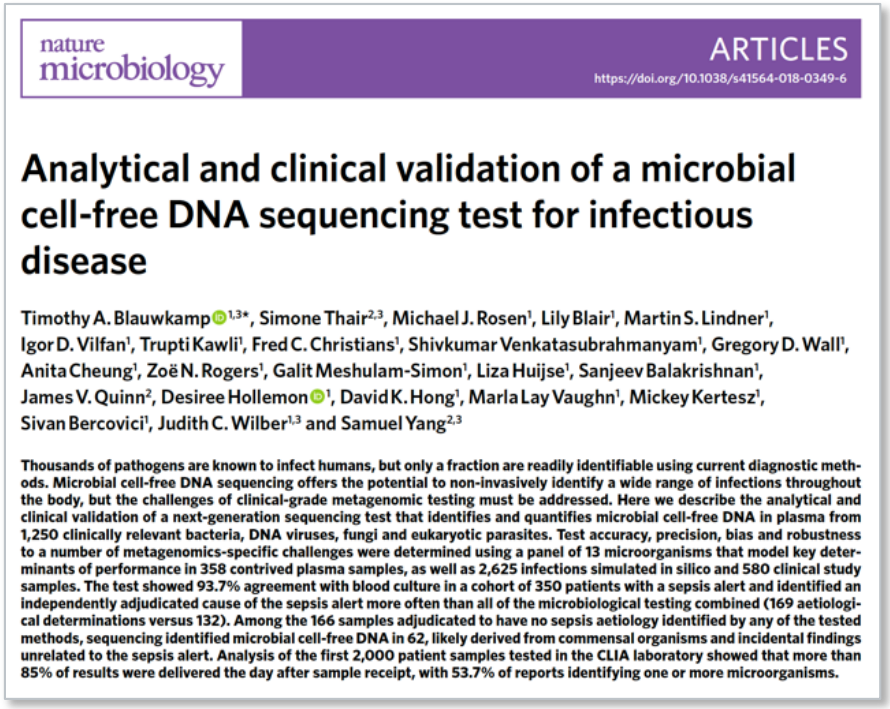
# Analytical and Clinical Validation

KARIUS

# Validation Study for the Karius Test

First study to present a comprehensive and rigorous validation process for a metagenomic infectious diseases diagnostic test for clinical use.

- **Analytical validation:** Accuracy, precision, bias and robustness were determined using a panel of 13 microorganisms that model key determinants of performance in 358 contrived plasma samples, as well as 2,625 computer simulated infections, and 580 clinical study samples.
- **Clinical validation:** The SEP-SEQ study, with 350 patients, compared the performance of the Karius Test to the standard-of-care diagnostic tests in patients with suspected sepsis.



nature microbiology

ARTICLES

https://doi.org/10.1038/s41564-018-0349-6

## Analytical and clinical validation of a microbial cell-free DNA sequencing test for infectious disease

Timothy A. Blauwkamp[1,3*], Simone Thair[2,3], Michael J. Rosen[1], Lily Blair[1], Martin S. Lindner[1], Igor D. Vilfan[1], Trupti Kawli[1], Fred C. Christians[1], Shivkumar Venkatasubrahmanyam[1], Gregory D. Wall[1], Anita Cheung[1], Zoë N. Rogers[1], Galit Meshulam-Simon[1], Liza Huijse[1], Sanjeev Balakrishnan[1], James V. Quinn[2], Desiree Hollemon[1], David K. Hong[1], Marla Lay Vaughn[1], Mickey Kertesz[1], Sivan Bercovici[1], Judith C. Wilber[1,3] and Samuel Yang[2,3]

**Thousands of pathogens are known to infect humans, but only a fraction are readily identifiable using current diagnostic methods. Microbial cell-free DNA sequencing offers the potential to non-invasively identify a wide range of infections throughout the body, but the challenges of clinical-grade metagenomic testing must be addressed. Here we describe the analytical and clinical validation of a next-generation sequencing test that identifies and quantifies microbial cell-free DNA in plasma from 1,250 clinically relevant bacteria, DNA viruses, fungi and eukaryotic parasites. Test accuracy, precision, bias and robustness to a number of metagenomics-specific challenges were determined using a panel of 13 microorganisms that model key determinants of performance in 358 contrived plasma samples, as well as 2,625 infections simulated in silico and 580 clinical study samples. The test showed 93.7% agreement with blood culture in a cohort of 350 patients with a sepsis alert and identified an independently adjudicated cause of the sepsis alert more often than all of the microbiological testing combined (169 aetiological determinations versus 132). Among the 166 samples adjudicated to have no sepsis aetiology identified by any of the tested methods, sequencing identified microbial cell-free DNA in 62, likely derived from commensal organisms and incidental findings unrelated to the sepsis alert. Analysis of the first 2,000 patient samples tested in the CLIA laboratory showed that more than 85% of results were delivered the day after sample receipt, with 53.7% of reports identifying one or more microorganisms.**

# Analytical Validation

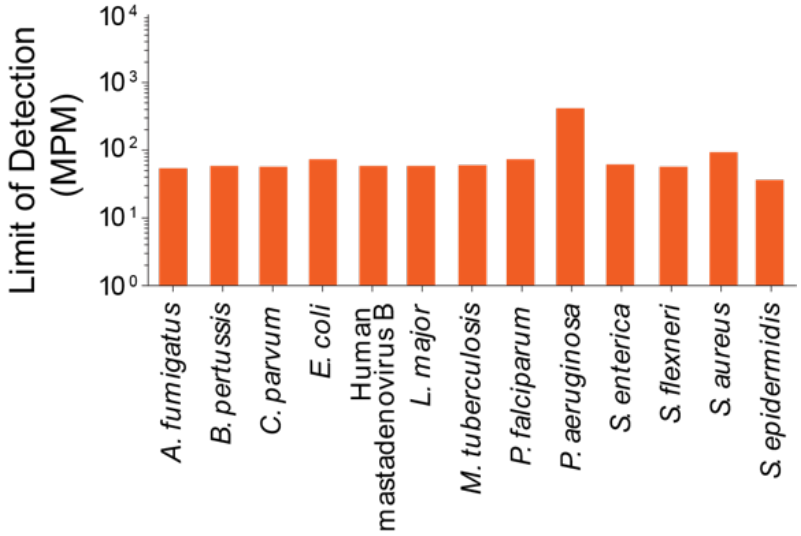
KARIUS

# High Analytical Sensitivity Across a Diversity of Microorganisms Even at Low Concentrations

**Analytical Sensitivity**

**>95% at 50 fragments of cell-free DNA per µL plasma**

Highly optimized processes remove common sources of bias in metagenomic sequencing, resulting in equivalent sensitivity across a wide range of diverse microorganisms.



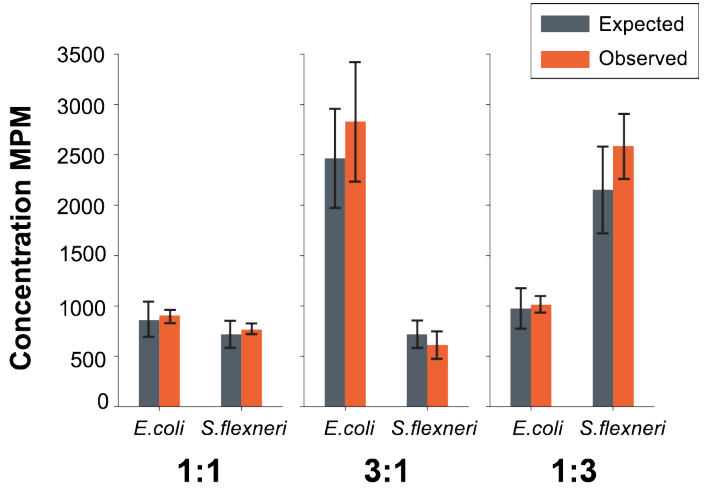

Reference panel of 13 microorganisms representing diversity across superkingdoms, GC-content, and genome length was utilized to reflect the broad range of 1,000+ microorganisms detected by the Karius Test.

Blauwkamp T., et al. *Nat. Microbiol*. 2019;4(4):663-674.

# High Analytical Specificity Ensures Quantitative Accuracy in Coinfections

| | |
|---|---|
| **Analytical Specificity** | 62,449 out of 62,450 expected negative |
| **99.998% per organism** | (Measurements of 1,249 pathogens in 50 measurements of a single sample) |

Analytical specificity of the Karius Test was measured by performing 50 measurements of a single, thoroughly characterized healthy plasma sample.

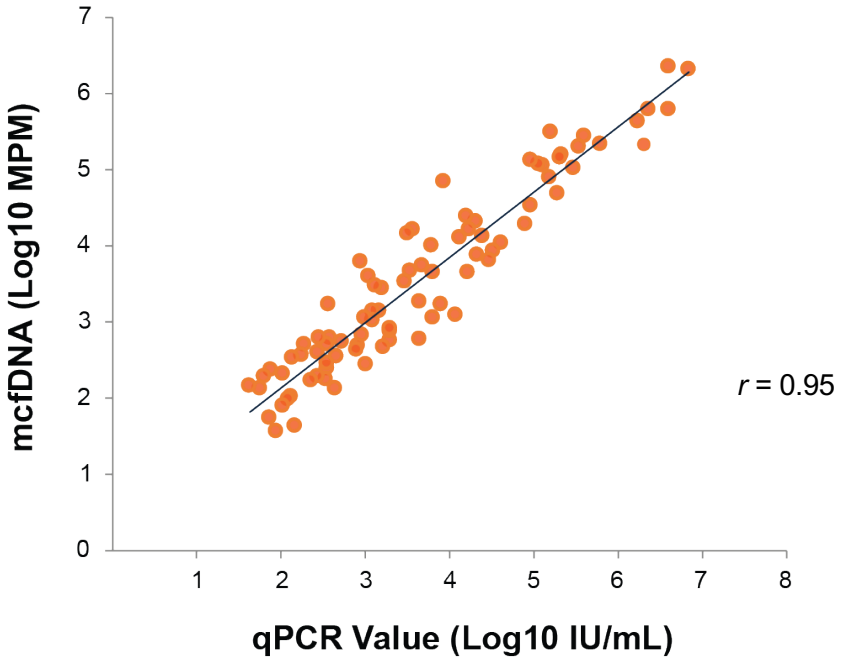



Karius Test can accurately identify coinfections even when microorganisms are genetically similar.

Blauwkamp T., et al. *Nat. Microbiol*. 2019;4(4):663-674.

# High Quantitative Accuracy

Comparison of the Karius Test to Cobas® Blood CMV qPCR in 125 samples



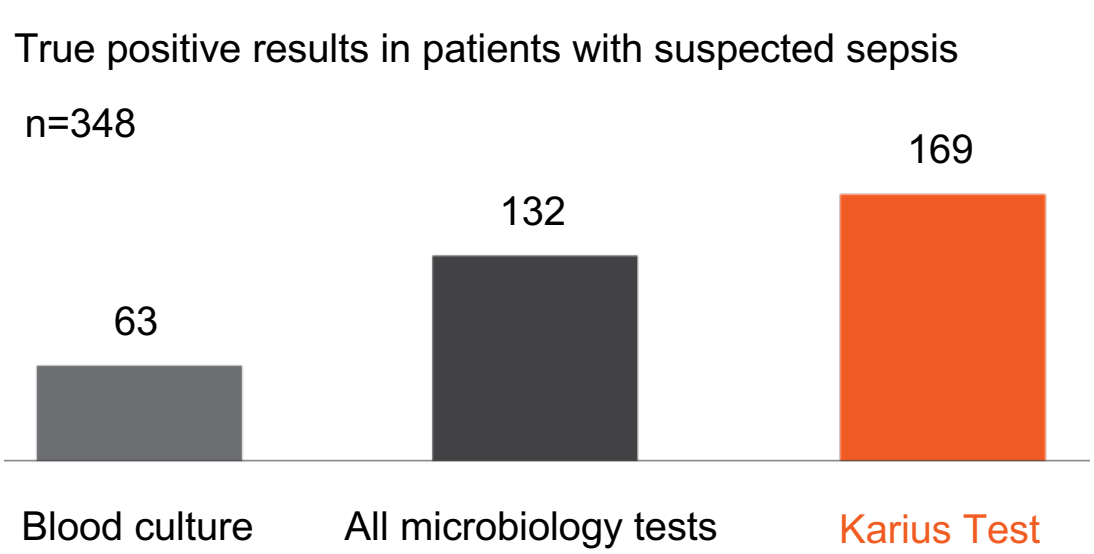

Blauwkamp T., et al. Evaluation of Karius Plasma Next Generation Sequencing of Cell-free Pathogen DNA to Detect and Quantitate Cytomegalovirus, Epstein-Barr Virus, and BK Virus. ASM Microbe, June 23 2019, San Francisco, CA.

# Clinical Validation

KARIUS

# Higher Diagnostic Yield than Conventional Tests

The SEP-SEQ study, with 350 patients, compared the performance of the Karius Test to the standard-of-care diagnostic tests in patients with suspected sepsis.




The Karius Test identified

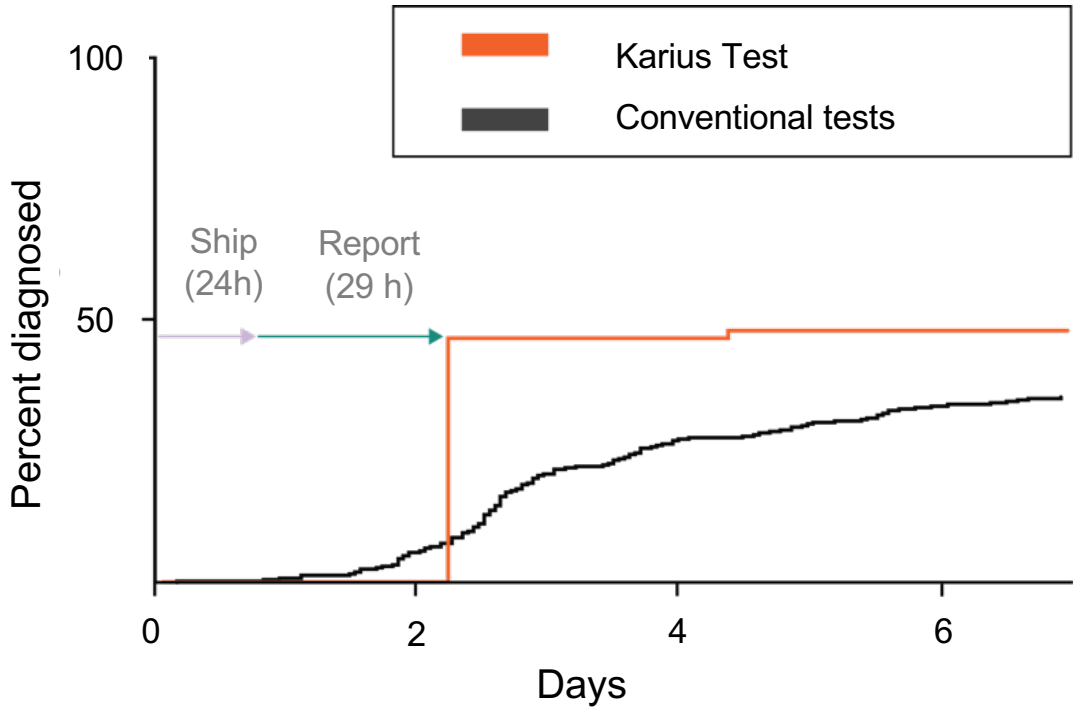
**2.7X** more causal pathogens identified than initial blood culture

**1.3X** more causal pathogens than all microbiological tests

Blauwkamp T., et al. *Nat. Microbiol*. 2019;4(4):663-674.

# Karius Test Shows Potentially Faster Time-to-Diagnosis

**At ~2.5 hospital days (53 hours) the Karius Test could enable significantly more diagnoses than all other microbiological testing.**

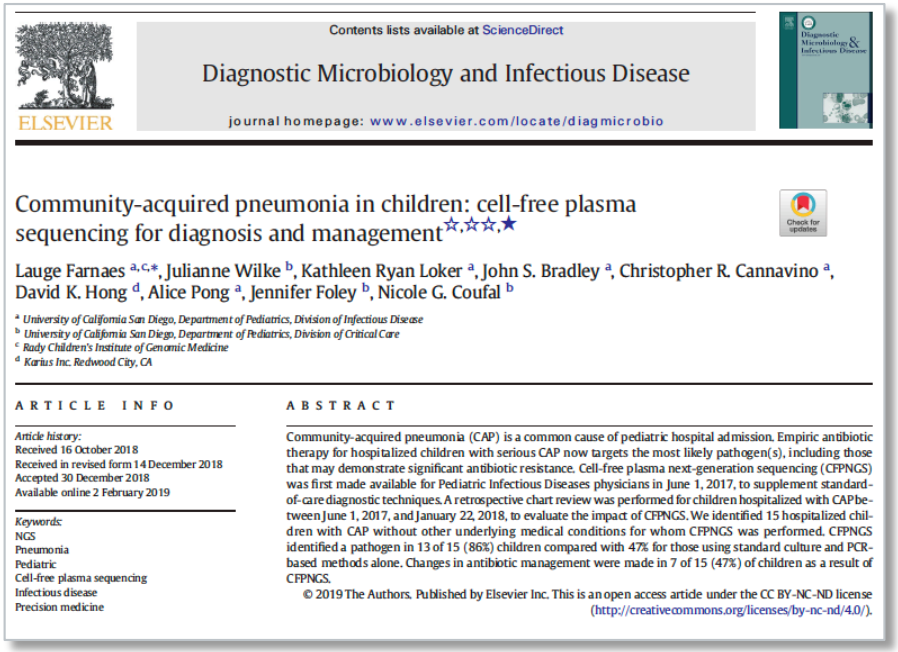



Blauwkamp T., et al. *Nat. Microbiol*. 2019;4(4):663-674.

# Change in Antimicrobial Management

# Karius Test in the Diagnosis and Management of Complicated Pneumonia in Pediatric Patients

The Karius Test was part of the management of community-acquired pneumonia (CAP) in 15 children without other underlying medical conditions at Rady Children's hospital.



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Diagnostic Microbiology and Infectious Disease

journal homepage: www.elsevier.com/locate/diagmicrobio

Community-acquired pneumonia in children: cell-free plasma sequencing for diagnosis and management☆,☆☆,★

Lauge Farnaes [a,c,*], Julianne Wilke [b], Kathleen Ryan Loker [a], John S. Bradley [a], Christopher R. Cannavino [a], David K. Hong [d], Alice Pong [a], Jennifer Foley [b], Nicole G. Coufal [b]

[a] University of California San Diego, Department of Pediatrics, Division of Infectious Disease
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ABSTRACT

Community-acquired pneumonia (CAP) is a common cause of pediatric hospital admission. Empiric antibiotic therapy for hospitalized children with serious CAP now targets the most likely pathogen(s), including those that may demonstrate significant antibiotic resistance. Cell-free plasma next-generation sequencing (CFPNGS) was first made available for Pediatric Infectious Diseases physicians in June 1, 2017, to supplement standard-of-care diagnostic techniques. A retrospective chart review was performed for children hospitalized with CAP between June 1, 2017, and January 22, 2018, to evaluate the impact of CFPNGS. We identified 15 hospitalized children with CAP without other underlying medical conditions for whom CFPNGS was performed. CFPNGS identified a pathogen in 13 of 15 (86%) children compared with 47% for those using standard culture and PCR-based methods alone. Changes in antibiotic management were made in 7 of 15 (47%) of children as a result of CFPNGS.



Farnaes L., et al. *Diagn Microbiol Infect Dis.* 2019;94(2):188-191.

# Karius Test Prompts Change in Antibiotic Management

- Based on Karius Test results, **antibiotic management was changed in 47% of children** (7/15)
- Karius Test **identified a pneumonia-causing pathogen in 87% of children** (13/15) compared with 27% (4/15) for those using bacterial culture (blood, respiratory, pleural)
- Karius Test identified *Streptococcus pneumoniae, Streptococcus pyogenes, Streptococcus intermedius, Fusobacterium nucleatum,* and other bacteria to help guide treatment

Farnaes L., et al. *Diagn Microbiol Infect Dis.* 2019;94(2):188-191.

# Karius Test Performance in Febrile and Neutropenia in Patients with High-Risk Leukemia

# 2294

Correspondence: Esther Benamu: esther.benamu@ucdenver.edu

**Evaluation of the Karius Plasma Next-Generation Sequencing Cell-free Pathogen DNA Test to Determine the Etiology of Infection and Impact on Anti-Microbial Management in Patients with Severe Neutropenia and Fever**

Esther Benamu[1], Kiran Gajurel[2], Jill N Anderson[3], Tullia C Lieb[3], Carlos A. Gomez[3], Hon Seng[4], Romielle Aquino[4], Desiree Hollemon[4], David K Hong[4], Timothy A Blauwkamp[4], Mickey Kertesz[4], Lily Blair[4], Paul Bollyky[3], Bruno C. Medeiros[3], Steven Coutre[3], Simona Zompi[4], José G Montoya[3], Stan Deresinski[3]

[1]Univ. of Colorado, Denver, CO, [2] University of Iowa, Iowa City, IA, [3]Stanford University, Palo Alto, CA, [4]Karius, Inc., Redwood City, CA

Stanford MEDICINE | Infectious Diseases Department of Medicine

KARIUS

This is a prospective, observational study of 57 high-risk leukemia patients who were receiving chemotherapy and presented with febrile neutropenia. The Karius Test was performed within 24 hours of fever onset. Results were compared to blood cultures and clinical diagnosis.

An adjudication panel determined whether antimicrobial therapy could potentially have been changed if Karius Test results had been available in real-time.

Benamu, et al. Evaluation of the Karius Plasma Next-Generation Sequencing Cell-free Pathogen DNA Test to Determine the Etiology of Infection and Impact on Anti-Microbial Management in Patients with Severe Neutropenia and Fever. IDWeek 2018, October 6 2018, San Francisco, CA.

# Karius Test Would Have Changed Antimicrobials for 47% of Patients

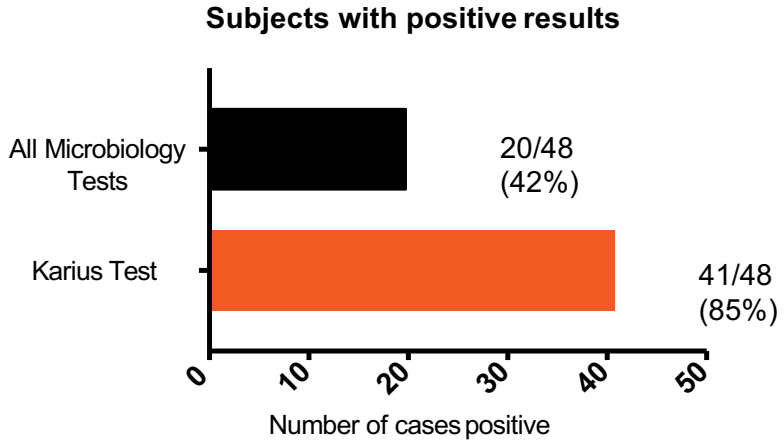
- **Antibiotics narrowed for 20%**
  - MRSA coverage withdrawn for 5%
- Antibiotics added for 20% of patients
- Antivirals added for 15% of patients
- Anti-fungal and -parasitic added for 5% of patients

*Based on an independent panel

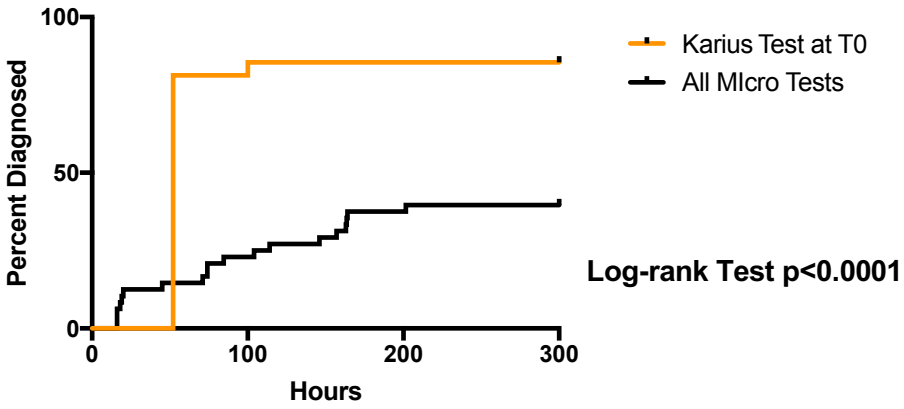
| Antimicrobial Management | Total N=55 |
|---|---|
| Antimicrobial therapy changed if Karius Test results were available in real-time | 26 |
| Antibiotic | 22 |
| Addition | 10 |
| Broadening (non-specified) | 1 |
| **MRSA coverage added** | 1 |
| Anaerobic coverage added | 7 |
| Anti mycobacterial coverage added | 1 |
| Withdrawal | 13 |
| Narrowing (non-specified) | 8 |
| **MRSA coverage withdrawn** | 5 |
| Antiviral | 8 |
| HSV coverage added | 7 |
| CMV coverage added | 1 |
| Anti-parasitic | 1 |
| Anti-parasitic coverage added | 1 |
| Anti-fungal | 2 |
| Anti-fungal coverage added | 2 |

Benamu, et al. Evaluation of the Karius Plasma Next-Generation Sequencing Cell-free Pathogen DNA Test to Determine the Etiology of Infection and Impact on Anti-Microbial Management in Patients with Severe Neutropenia and Fever. IDWeek 2018, October 6 2018, San Francisco, CA.

# Karius Test Identifies a Plausible Cause of Neutropenic Fever 2x More Often and Faster Than All Other Standard Tests




Plausible cause of neutropenic fever identified **2x more often** than all other tests



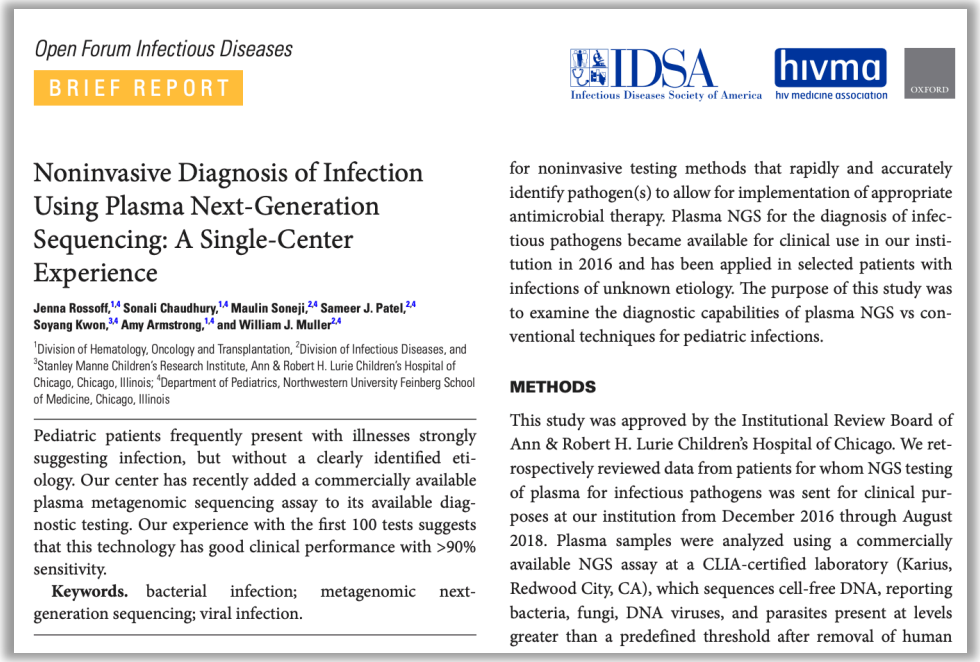

A plausible cause of neutropenic fever identified **faster** than all other standard microbiology tests

Benamu, et al. Evaluation of the Karius Plasma Next-Generation Sequencing Cell-free Pathogen DNA Test to Determine the Etiology of Infection and Impact on Anti-Microbial Management in Patients with Severe Neutropenia and Fever. IDWeek 2018, October 6 2018, San Francisco, CA.

# Concordance with Invasive Biopsies

# Non-invasive Diagnosis of Infections Using the Karius Test: Lurie Children's Hospital Experience

A retrospective study of 79 pediatric patients (100 samples) by the Ann & Robert H. Lurie Children's Hospital of Chicago examined the diagnostic capabilities of the Karius Test versus conventional techniques for pediatric infections.



*Open Forum Infectious Diseases*

BRIEF REPORT

IDSA Infectious Diseases Society of America · hivma hiv medicine association · OXFORD

## Noninvasive Diagnosis of Infection Using Plasma Next-Generation Sequencing: A Single-Center Experience

**Jenna Rossoff,[1,4] Sonali Chaudhury,[1,4] Maulin Soneji,[2,4] Sameer J. Patel,[2,4] Soyang Kwon,[3,4] Amy Armstrong,[1,4] and William J. Muller[2,4]**

[1]Division of Hematology, Oncology and Transplantation, [2]Division of Infectious Diseases, and [3]Stanley Manne Children's Research Institute, Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, Illinois; [4]Department of Pediatrics, Northwestern University Feinberg School of Medicine, Chicago, Illinois

Pediatric patients frequently present with illnesses strongly suggesting infection, but without a clearly identified etiology. Our center has recently added a commercially available plasma metagenomic sequencing assay to its available diagnostic testing. Our experience with the first 100 tests suggests that this technology has good clinical performance with >90% sensitivity.

**Keywords.** bacterial infection; metagenomic next-generation sequencing; viral infection.

for noninvasive testing methods that rapidly and accurately identify pathogen(s) to allow for implementation of appropriate antimicrobial therapy. Plasma NGS for the diagnosis of infectious pathogens became available for clinical use in our institution in 2016 and has been applied in selected patients with infections of unknown etiology. The purpose of this study was to examine the diagnostic capabilities of plasma NGS vs conventional techniques for pediatric infections.

### METHODS

This study was approved by the Institutional Review Board of Ann & Robert H. Lurie Children's Hospital of Chicago. We retrospectively reviewed data from patients for whom NGS testing of plasma for infectious pathogens was sent for clinical purposes at our institution from December 2016 through August 2018. Plasma samples were analyzed using a commercially available NGS assay at a CLIA-certified laboratory (Karius, Redwood City, CA), which sequences cell-free DNA, reporting bacteria, fungi, DNA viruses, and parasites present at levels greater than a predefined threshold after removal of human

Rossoff, et al. *Open Forum Infect Di.* 2019;6(8):ofz327.

# Karius Test Shows Potential to Avoid Invasive Biopsies

- In the 39 invasive procedures performed in patients with diagnosed infections, the Karius Test showed 87% sensitivity versus 67% sensitivity with conventional testing on invasively obtained samples
  - **87% of invasive procedures could have been avoided by the Karius Test**

- 70% of the Karius Test results were positive for ≥1 pathogen
  - 80% (56/70 tests) were deemed clinically relevant
  - 20% (14/70 tests) of the Karius Test results identified a clinically relevant pathogen when all conventional testing was negative

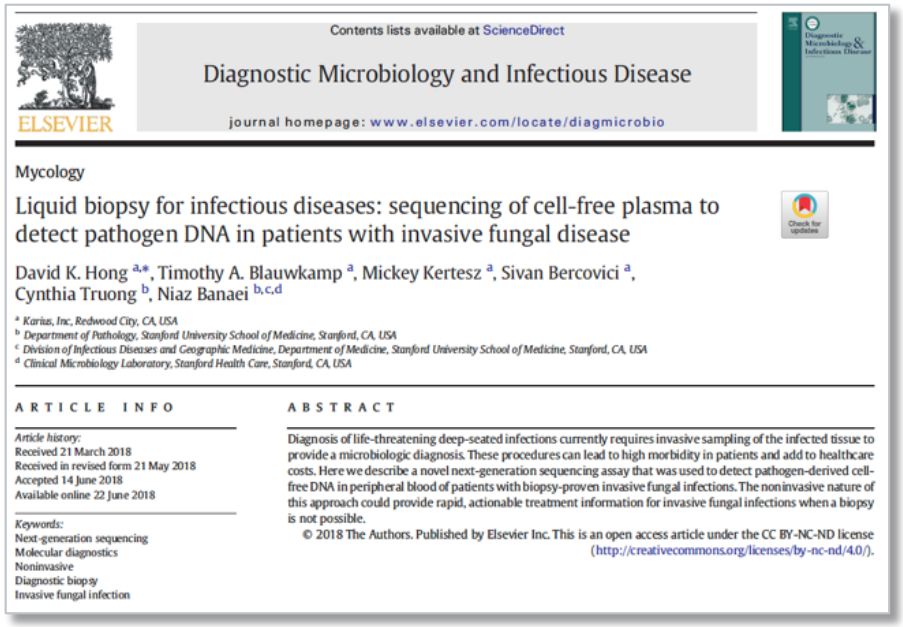
- The Karius Test detected infections in the bloodstream and respiratory tract, and infections isolated to the skin, bone, internal hardware, urinary tract, and CSF

Rossoff, et al. *Open Forum Infect Di.* 2019;6(8):ofz327.

# Karius Test Performance as a Non-Invasive Method in the Diagnosis of Invasive Fungal Infections

A retrospective study of 9 adult patients identified with proven invasive fungal infections.

Patients had documented fungal infections from a variety of sources including lung, peri-pancreatic lymph node, heart, brain, sternum, and small bowel.



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Diagnostic Microbiology and Infectious Disease

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Mycology

## Liquid biopsy for infectious diseases: sequencing of cell-free plasma to detect pathogen DNA in patients with invasive fungal disease

David K. Hong [a,*], Timothy A. Blauwkamp [a], Mickey Kertesz [a], Sivan Bercovici [a], Cynthia Truong [b], Niaz Banaei [b,c,d]

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[b] Department of Pathology, Stanford University School of Medicine, Stanford, CA, USA
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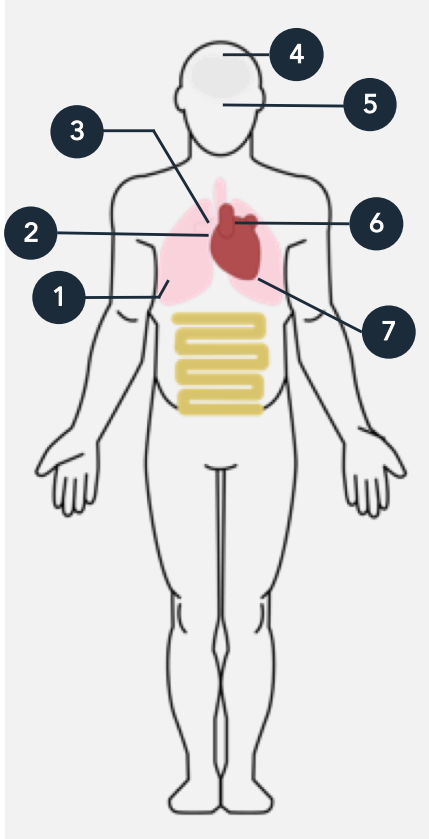
ABSTRACT

Diagnosis of life-threatening deep-seated infections currently requires invasive sampling of the infected tissue to provide a microbiologic diagnosis. These procedures can lead to high morbidity in patients and add to healthcare costs. Here we describe a novel next-generation sequencing assay that was used to detect pathogen-derived cell-free DNA in peripheral blood of patients with biopsy-proven invasive fungal infections. The noninvasive nature of this approach could provide rapid, actionable treatment information for invasive fungal infections when a biopsy is not possible.



Hong D.K., et al, *Diagn Microbiol Infect Dis*. 2018;92(3):210-213.

# Karius Test Shows Concordance with Invasive Tests in 7/9 Patients with Invasive Fungal Infections




| | Diagnostic Method | Clinical Diagnosis | Karius Test |
|---|---|---|---|
| 1 | Tissue right lung culture positive | *Cunninghamella* sp. | ***Cunninghamella bertholletiae*** |
| 2 | Sternal tissue culture positive | *Rhizopus* sp. | ***Rhizopus microsporus***, HSV 1, *Staphylococcus epidermidis* |
| 3 | Mediastinal lymph node | *Aspergillus terreus, Pseudomonas aeruginosa, Streptococcus* sp., *Candida* sp. | ***Aspergillus terreus***, *Pseudomonas aeruginosa* |
| 4 | Brain tissue culture | *Scedosporium boydii* | ***Scedosporium apiospermum***, *Pseudomonas pseudoalcaligenes, Mycobacterium mageritense* |
| 5 | R sinus tissue – Fungal sequencing | *Rhizopus oryzae* | ***Rhizopus oryzae var delemar***, CMV |
| 6 | Heart tissue – Fungal culture positive | *Rhizopus* sp. | ***Rhizopus microsporus*** |
| 7 | Sputum culture positive; Galactomannan positive | *Aspergillus fumigatus* | ***Aspergillus lentulus*, CMV** |

Hong D.K., et al, *Diagn Microbiol Infect Dis*. 2018;92(3):210-213.

# Samples where Fungal DNA was Not Detected in Plasma from Patients with Fungal Infection

| Diagnostic Method | Clinical Diagnosis | Karius Test |
|---|---|---|
| Small bowel tissue – Fungal Sequencing | *Aspergillus fumigatus* | ***Mycobacterium abscessus, Staphylococcus epidermidis***[1] |
| Tissue left lung culture | *Aspergillus fumigatus* | ***Negative***[2] |

1. Plasma sample was obtained 20 days after the biopsy procedure, after at least 15 days of anti-*Aspergillus* therapy.
2. *Aspergillus fumigatus* sequences were present in the raw data but abundance was below the threshold required for a positive test result.

Hong D.K., et al, *Diagn Microbiol Infect Dis*. 2018;92(3):210-213.

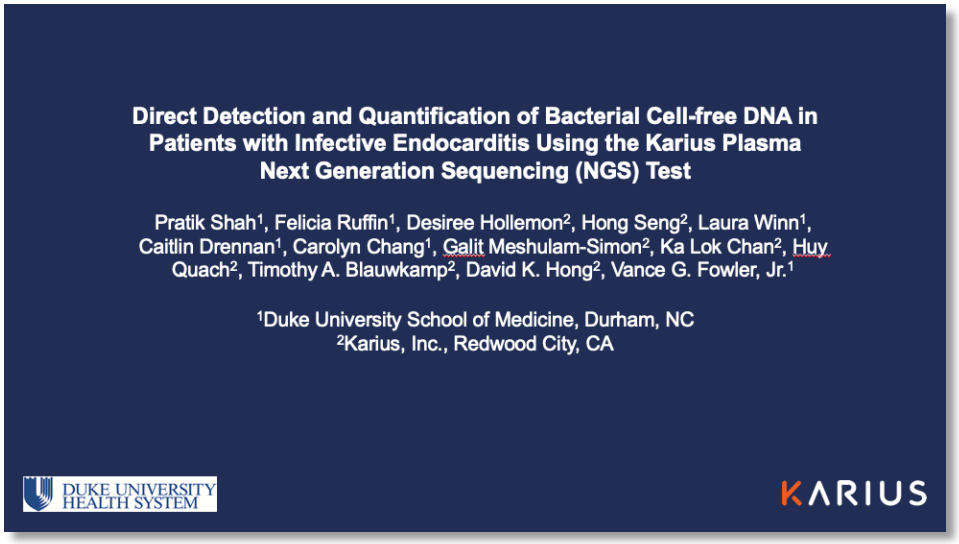
# Diagnosis and Monitoring of Endocarditis

# Karius Test for the Diagnosis and Monitoring of Endocarditis

This is a prospective study of 30 adult patients admitted to Duke University Hospital with suspected infective endocarditis (IE).

Parallel samples for blood culture and the Karius Test were collected within 48-72 hours of enrollment.

Follow-up samples were collected every 2-3 days for a maximum total of 8 samples.



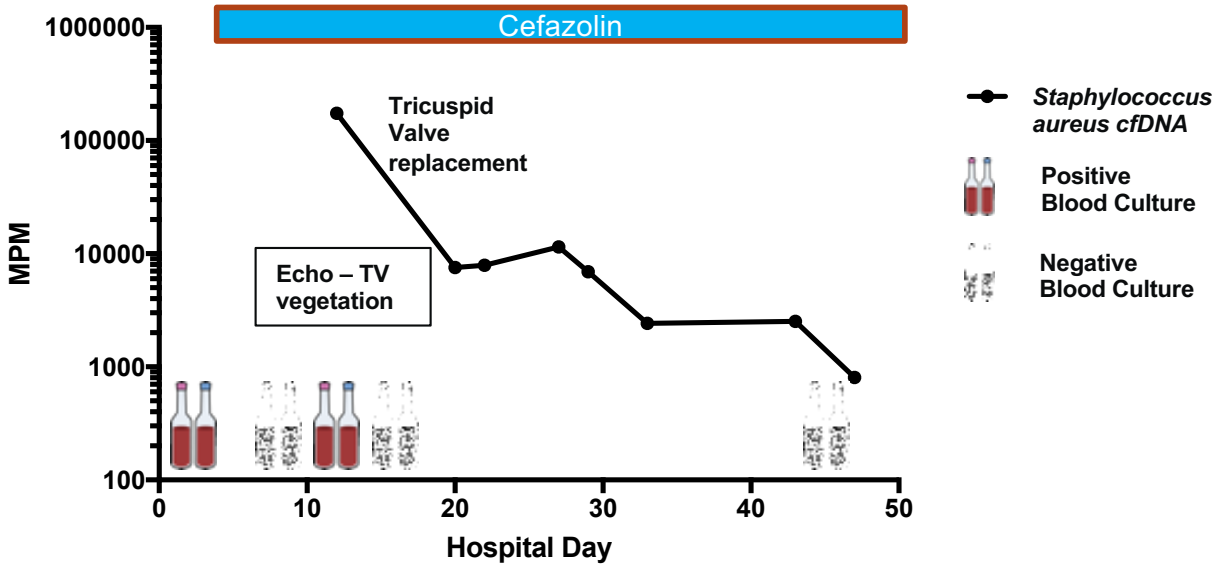

Shah P., Fowler V. et al. Direct Detection and Quantification of Bacterial Cell-free DNA in Patients with Infective Endocarditis (IE) Using the Karius Plasma Next Generation Sequencing (NGS) Test. Talk presented at IDWeek; October 3-7, 2018; San Francisco, CA.

# Karius Test Identifies Nearly all Pathogens in Culture-Positive Infective Endocarditis

- Karius Test correctly **identified a causative pathogen in 95%** (20/21) of patients with blood culture-positive infective endocarditis (IE)
  - Pathogen was identified despite pre-treatment with antibiotics (Median – 7 days; Range 1 – 30 days)
  - 1 Karius Test negative case had received 25 days of antibiotics prior to Karius testing
- Karius Test identified the cause of culture-negative IE in 1 out of 3 cases

Shah P., Fowler V. et al. Direct Detection and Quantification of Bacterial Cell-free DNA in Patients with Infective Endocarditis (IE) Using the Karius Plasma Next Generation Sequencing (NGS) Test. Talk presented at IDWeek; October 3-7, 2018; San Francisco, CA.

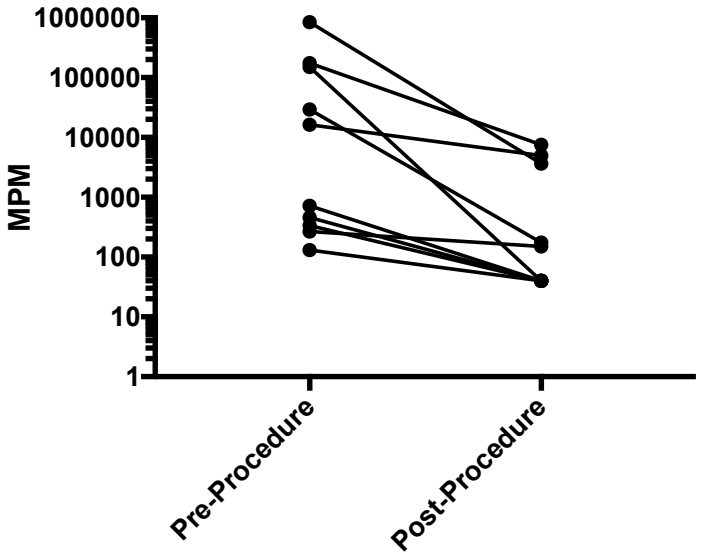
# Pathogen DNA Quantity in Karius Test Correlates with Clinical Course, Including Antibiotic Treatment and Valve Surgery




Shah P., Fowler V. et al. Direct Detection and Quantification of Bacterial Cell-free DNA in Patients with Infective Endocarditis (IE) Using the Karius Plasma Next Generation Sequencing (NGS) Test. Talk presented at IDWeek; October 3-7, 2018; San Francisco, CA.

# Pathogen DNA Quantity in Karius Test Correlates with Clinical Course, Including Antibiotic Treatment and Valve Surgery

Patients with Definite IE who had a plasma sample available before and after source control procedure




Shah P., Fowler V. et al. Direct Detection and Quantification of Bacterial Cell-free DNA in Patients with Infective Endocarditis (IE) Using the Karius Plasma Next Generation Sequencing (NGS) Test. Talk presented at IDWeek; October 3-7, 2018; San Francisco, CA.

# About the Karius Test

# Karius Test Process

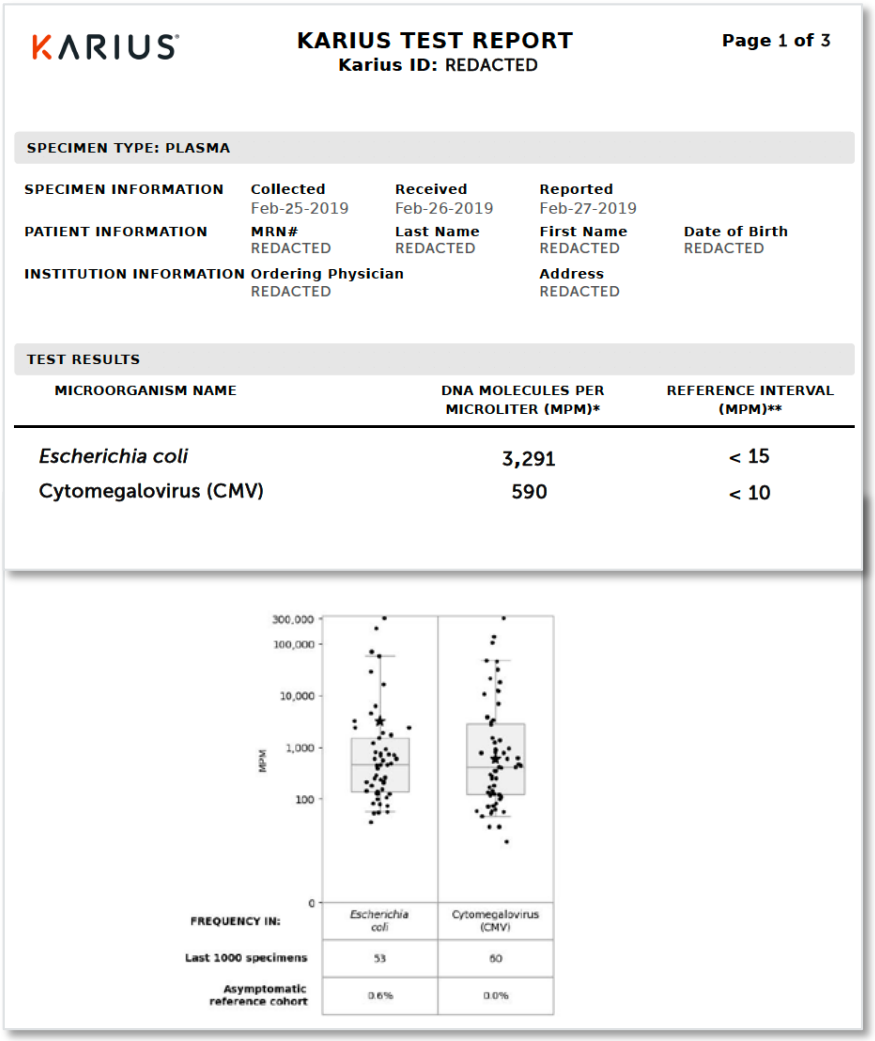
**Reports are typically available one day after specimen receipt***


**5 ml Blood PPT Tube** → **Specimen Processing** → **Sequencing** → **Analysis** → **Report**

* >85% of specimens received by 8:30 AM (PT) Monday through Saturday are reported the next day.

# Karius Test Report

- **Relevance:** Pathogens present in statistically significant amounts are reported
- **Quantification:** Concentration of microbial cfDNA is expressed as MPM (molecules per microliter) to quantify/monitor pathogens
- **Reference range:** Reference interval determined from 167 asymptomatic donors
- **Consultation:** Clinical consultation available with board-certified infectious disease physicians



KARIUS

**KARIUS TEST REPORT**
**Karius ID:** REDACTED

Page 1 of 3

**SPECIMEN TYPE: PLASMA**

| | | | | |
|---|---|---|---|---|
| **SPECIMEN INFORMATION** | **Collected** Feb-25-2019 | **Received** Feb-26-2019 | **Reported** Feb-27-2019 | |
| **PATIENT INFORMATION** | **MRN#** REDACTED | **Last Name** REDACTED | **First Name** REDACTED | **Date of Birth** REDACTED |
| **INSTITUTION INFORMATION** | **Ordering Physician** REDACTED | | **Address** REDACTED | |

**TEST RESULTS**

| MICROORGANISM NAME | DNA MOLECULES PER MICROLITER (MPM)* | REFERENCE INTERVAL (MPM)** |
|---|---|---|
| *Escherichia coli* | 3,291 | < 15 |
| Cytomegalovirus (CMV) | 590 | < 10 |

# Over 1,000 Pathogens Detected from Blood

## Bacteria – 850+

- *Mycoplasma pneumoniae*
- *Mycobacterium tuberculosis* complex
- *Mycobacterium avium* complex
- *Listeria monocytogenes*
- Fastidious or unculturable bacteria

## DNA Viruses – 100+

- Herpesviruses – VZV, EBV, CMV, HHV6
- BK and JC polyomaviruses
- Human papillomavirus
- Adenovirus

## Fungi/Molds and Other Parasites – 450+

- *Aspergillus* species *(42)*
- *Candida* species *(33)*
- *Cryptococcus neoformans*
- *Mucor and Rhizopus* species
- *Coccidioides immitis*
- *Histoplasma capsulatum*
- *Pneumocystis jirovecii*
- *Toxoplasma gondii*
- *Trypanosoma cruzi*

Full list of pathogens can be found at:
https://www.kariusdx.com/pathogenlist

# Karius Experience and Evaluation Program (KEEP)

# KEEP Program

The Karius Experience and Evaluation Program (KEEP) is an opportunity for institutions to gain direct experience with the Karius Test.

The goals of this program are to enable:

- An understanding of the appropriate use of the Karius Test in the management of serious infections
- An understanding of what the results of the test mean and how they are used when developing treatment plans
- A clinical partnership with the laboratory diagnostic stewardship team with the common goal of developing test algorithms to guide proper utilization of the Karius Test including patient selection, disease state, and timing of specimen collection
- A clinical partnership between Karius Medical Affairs team and physicians using the test, providing real time guidance for interpretation of test results
    - An institutional partnership for development of a business case based on agreed upon measurable outcome metric(s) such as
        - length of overall stay,
        - length of critical care unit stay,
        - effect on downstream testing (laboratory, radiology, and pharmacy),
        - effect on downstream antimicrobial usage

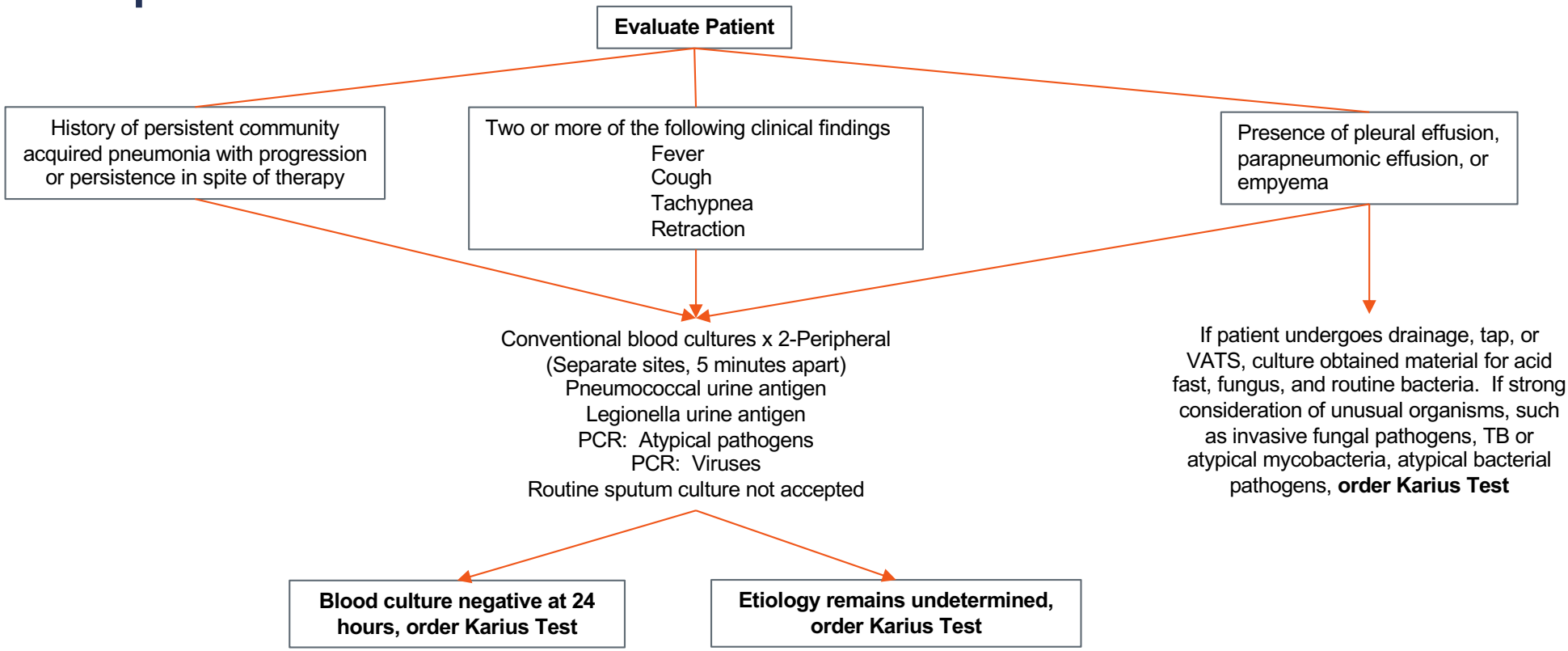
# Disease States

- Complicated pneumonia
- Infections in immunocompromised patients
- Invasive fungal infections
- Endocarditis
- Sepsis

# Laboratory Test Algorithms – Promote Diagnostic Stewardship

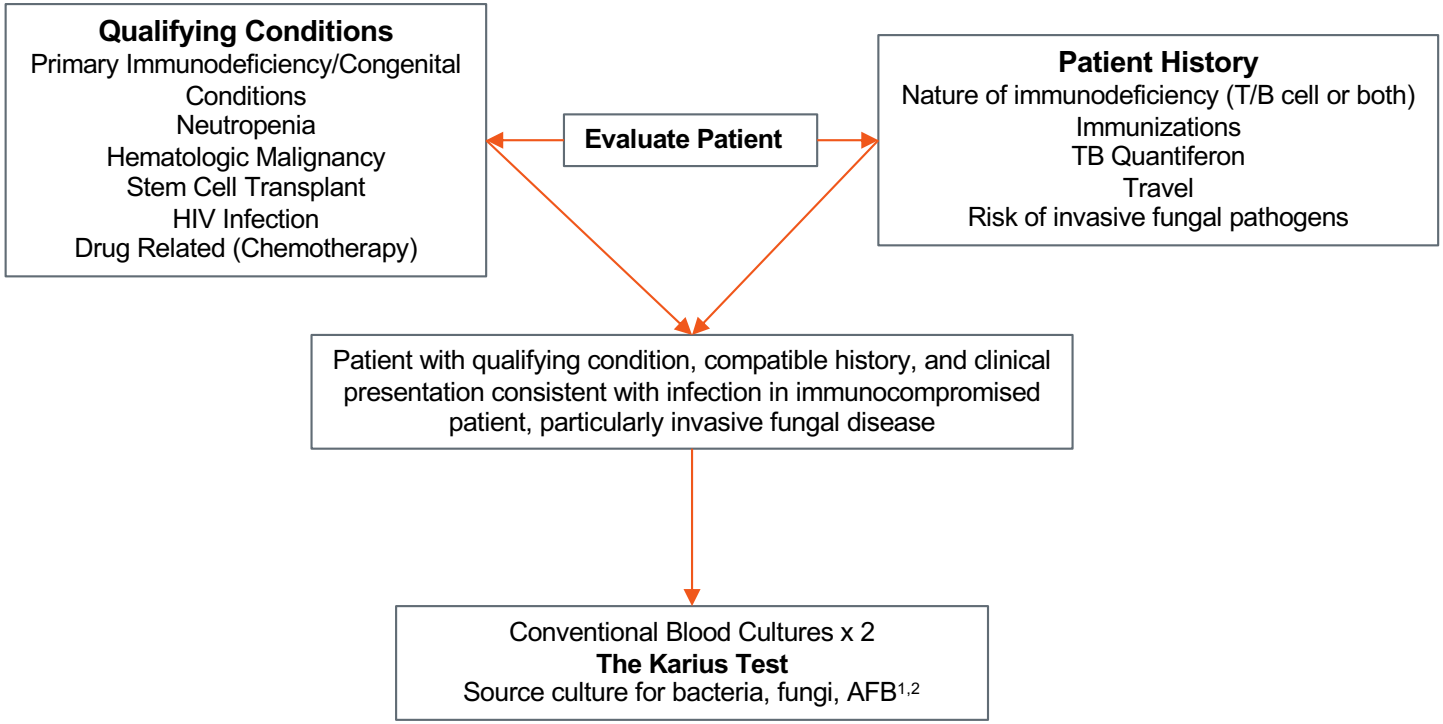
- Enable the use of the right test for the right patient
- Generate accurate clinically relevant results within the time to treat
- Influence optimized clinical care
- Conserve the healthcare dollar
- Utilize advanced technology when it is appropriate and cost efficient

# Laboratory Test Algorithm Example: Complicated Pneumonia




1. This algorithm is an example and can be used as a guide to the development of an institution specific algorithm.

# Laboratory Test Algorithm Example: Immunocompromised Patient




1. Avoid invasive diagnostic procedures if possible, such as biopsy, until Karius Test has been performed and results available.
2. The patient's clinical picture may be related to organisms which are difficult to demonstrate using conventional technology, or infection may be polymicrobial.

This algorithm is an example and can be used as a guide to the development of an institution specific algorithm.

# Sample Digest Report

KARIUS

# Test Results at a Glance

**7**

Samples
7 Patients

**57%**

Positive for one or more microorganisms

**100%**

Reported within 1 Day if received by 8:30 AM Mon-Sat

**0%**

No Results

**4**

Clinical consultations

# Clinical Cases

**Total Cases: 7**

**Clinical Scenarios:** Where Karius Test was ordered and where the information was known based on medical consultations with Karius

- Culture-negative endocarditis
- FUO
- Discitis

**Clinical consultations:** Completed for 4 cases

**# of tests with positive results: 4**

*# of results with 1 pathogen: 2*
*# of results with 2 pathogens: 1*
*# of results with 3 or more pathogens: 1*

# Organisms of Interest Found by the Karius Test

## Bacteria (7)

- *Escherichia coli*
- *Streptococcus salivarius*
- *Helicobacter pylori*
- ***Staphylococcus epidermidis***
- ***Bartonella henselae***
- *Prevotella melaninogenica*
- *Vellonella dispar*

## DNA Viruses (1)

- CMV

## Fungi (0)

# Medical Consultation Highlights

| Patient Information (Report Date) | Results (Potential utility) | Consultation Notes |
|---|---|---|
| 24 yo<br>Otherwise health patient presenting with drenching night sweats and fevers. Treated with antimicrobials. | ***Bartonella henselae*** (188 MPM)<br>*Escherichia coli* (56 MPM)<br><br>**(Diagnosis)** | Karius Test result provided a diagnosis ahead of pending serological tests and allowed for more targeted antibiotic treatment. |
| 84 yo<br>Patient admitted with pacemaker infection. Karius Test sent on the day the device was removed. The explanted device grew *Staph epi* while blood cultures remained negative. Treatment with Vancomycin. | *Staphylococcus epidermidis* (5015 MPM)<br>(Confirmation) | Karius Test result confirmed the testing from the explanted device even though cultures were negative and can potentially provide a way to monitor efficacy of treatment with repeat tests. |
| 80 yo<br>Patient with concern for CIED infection and endocarditis with negative TEE test. Treated with antimicrobials for 6-7 days prior to Karius Test. | *Helicobacter pylori (91 MPM)*<br><br>****Staphylococcus equorum*** (54MPM)<br><br>**(Potential diagnosis)** | Karius Test result did not detect anything significant above the reportable threshold - possibly due to pre-treatment with antimicrobials.<br><br>Raw data revealed a coag-negative staph which could be significant for endocarditis |

# More Information about KARIUS

**Information about the Karius Test:**
www.kariusdx.com

**Clinical Consultation:**
medical@kariusdx.com

**Contact Information:**

**Email**: help@kariusdx.com
**Phone**: 1-866-4KARIUS (1-866-452-7487)