KARIUS™

KARIUS TEST REPORT

Karius ID: REDACTED

SPECIMEN TYPE: PLASMA

SPECIMEN INFORMATION	**Collected**	**Received**	**Reported**	**Specimen ID**
	Jan-08-2018	Jan-09-2018	Jan-10-2018	REDACTED
PATIENT INFORMATION	**MRN#**	**Last Name**	**First Name**	**Date of Birth**
	REDACTED	REDACTED	REDACTED	REDACTED
INSTITUTION INFORMATION	**Ordering Physician**	**Address**		
	REDACTED	REDACTED		

TEST RESULTS

MICROORGANISM NAME	DNA MOLECULES PER MICROLITER (MPM)*	REFERENCE INTERVAL (MPM)**
Klebsiella pneumoniae	55,882	< 10
Staphylococcus epidermidis	122	< 104

* Molecules per microliter = number of DNA fragments present in one microliter of plasma

** Reference Interval = the 97.5th percentile MPM concentration detected in PPT plasma from a cohort of asymptomatic donors

Karius Medical staff are available to answer any questions about these results: Phone: (866) 452-7487 | Email: medical@kariusdx.com

TEST DESCRIPTION

The Karius Test can identify:

Bacteria:	762	**DNA viruses:**	102	**Archaea:**	1	**Fungi:**	393	**Eukaryotes:**	62

Full list of organisms is found at: https://kariusdx.com/pathogen-list/dc3.1.1

The Karius Test for infectious disease detects microbial cell free DNA (cfDNA) in plasma from bacteria, DNA viruses, fungi and protozoa using next-generation sequencing (NGS) [1]. The test reports the presence and abundance of microbial cfDNA when statistically significant levels of the associated cfDNA are detected above background.

Microbial cfDNA may be found in plasma when viable microorganisms are not detected in blood by other methods [2]. It can be detected from localized infections [3] or during effective antimicrobial treatment [4]. The reported microorganism(s) may or may not be the cause of patient infection. Results should be interpreted within the context of clinical data, including medical history, physical findings, epidemiological factors, and other laboratory data.

[1] Data on file, Analytical Validation (March 2018)

[2] De Vlaminck, et al. (2013). Cell, 155(5)

[3] The SEP-SEQ Trial: Clinical Validation of the Karius Plasma Next-Generation Sequencing Test for Pathogen Detection in Sepsis (Late-breaking oral session, IDWeek 2017)

[4] Abril, et al. (2016 Jul 12) Open Forum Infect Dis, 12;3(3):ofw144

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CLIA # 05D2121236 | CAP # 9497749 | Lab Director: Judith Wilber, PhD, D(ABMM)

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PERFORMANCE DATA

Analytical Performance Specifications		
Sensitivity	95% at 41 MPM	
Specificity	Per microorganism	> 99.99%
	Per report	98%

For a summary of the analytical validation see: kariusdx.com/validation

Clinical Validation in the SEP-SEQ Trial (N=350) [1,2]		
Positive Agreement	Blood Culture (N=63)	93.7%
Diagnostic Sensitivity	Composite Gold Standard (All microbiology tests and clinical adjudication)	92.9%
Diagnostic Specificity	Composite Gold Standard (All microbiology tests and clinical adjudication)	63%*

*Discordant Karius results included clinically-relevant pathogens such as *Helicobacter pylori*, EBV, and CMV that were determined not to be the primary cause of sepsis via adjudication.

MPM interpretation: Positive results will display the concentration of pathogen cfDNA detected in units of **M**olecules of cell-free DNA fragments of a pathogen **P**er **M**icroliter of plasma (abbreviated MPM). The MPM value may be used to infer the amount of microorganism cfDNA present in an individual. If a report includes multiple microorganisms, they are listed in the order of high to low MPM. Several variables impact the MPM value, including the location of infection, prior or ongoing antimicrobial treatment, and genome size of the microorganism. In cases where multiple microorganisms are reported, comparison of MPM values across organisms in the context of etiology should be done with caution.

Reference Interval: The reference interval is derived from a study of 167 asymptomatic adults. Specific reference intervals are calculated using the MPM value reported for the 97.5th percentile for each microorganism. For example, the reference range of *E. coli* has an MPM value of < 15, which means that across asymptomatic individuals the 97.5th percentile of *E. coli* quantitations was 15 MPM. MPM values reported below the corresponding reference interval may be the cause of infection, for example due to antibiotic pre-treatment or locus of infection.

[1] SEP-SEQ Trial. Determining the Etiology of Sepsis Using an Infectious Disease Diagnostic Sequencing Assay, Data on File (2018)
[2] ClinicalTrials.gov Identifier: NCT02730468

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