3rd International Conference on Molecular Microbiology

A multicenter retrospective cohort study evaluated at the clinical impact of metagenomic next-generation sequencing of plasma cell-free DNA for infectious diseases diagnosis.

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Abstract

Background: Metagenomic next-generation sequencing (mNGS) of plasma cell-free DNA has emerged as a promising diagnostic tool for broad pathogen detection, noninvasive sampling, and earlier diagnosis. However, nothing is known regarding its clinical impact in the actual world when employed in everyday practise.

Methods: Over the course of 1.5 years, we conducted a retrospective cohort study of all patients for whom plasma mNGS (Karius test) was performed for all purposes at 5 US hospitals. A thorough analysis of the patient's medical records was conducted, and a standardised assessment of the mNGS' clinical impact was produced based on the treating team's interpretation.

The Stanford University and Columbia University Medical Center Institutional Review Boards (IRBs) gave their approval to this investigation (CUMC). The University of California, Los Angeles (UCLA), the University of Utah (UT), and Children's Hospital of Los Angeles (CHLA) did not need IRB approval for this project (CHLA).

In December 2016, the Karius facility began offering commercial tests. Plasma was separated from whole blood in a K2–ethylenediaminetetraacetic acid or BD Vacutainer PPT tube (Becton Dickinson, Franklin Lakes, New Jersey) and shipped either fresh (within 4 days of blood take) or frozen (within 6 hours of blood draw). All testing was carried out by Karius according to the testing protocol described previously. The Karius Test is a liquid biopsy that can detect over 1000 bacteria that cause both deep-seated and bloodstream infections from a single blood sample non-invasively and quickly. The Karius test, as it is now employed in ordinary clinical practise, has a limited impact in the actual world. More research is needed to identify high-yield patient populations, define the role of mNGS as a complement to traditional microbiological approaches, and figure out how to best integrate mNGS into current testing algorithms.

A total of 82 Karius tests were examined from 39 (47.3%) adults and 43 (52.4%) children, as well as 53 (64.6%) immunocompromised individuals. The positive rate for Karius was 50 out of 82 (61.0%), with 25 (50.0%) revealing two or more organisms (range, 2-8). The Karius test results indicated a positive impact in 6 (7.3%), a negative impact in 3 (3.7%), no impact in 71 (86.6%), and indeterminate in 2 cases (2.4 percent). Bacteria and/or fungi were involved in cases with a positive Karius test and clinical impact, but not DNA viruses or parasites. Only one of the 16 extra tests performed on ten patients was linked to clinical impact. From 1 August 2017 to 31 May 2019, we conducted a retrospective cohort study of patients for all sequential plasma mNGS samples sent out for Karius test from 5 US institutions (CHLA, CUMC, Stanford Health Care [SHC], UCLA, and UT). Each site investigator reviewed all patient records thoroughly, and clinical impact solely based on the treating team's interpretation of Karius results and subsequent management decisions was assessed using predefined objective grading criteria (Table 1) to determine whether the Karius test result had a

positive, negative, or no clinical impact, or if the impact was indeterminate. Because the goal of this study was to assess the Karius test's real-world impact, only the treating team's decisions and actions were considered.

Importance of Research

Metagenomic next-generation sequencing (mNGS) of pathogen nucleic acid in clinical samples has emerged as a promising one-test strategy for diagnosing potentially all infectious etiologies. mNGS may presently

be ordered from plasma cell-free DNA (Karius, Redwood City, California), DNA and RNA in cerebrospinal fluid (CSF) (University of California, San Francisco), and DNA and RNA in respiratory secretions (IDbyDNA, San Francisco, California) at chosen reference laboratories. The Karius test has been

commercially accessible for the longest and is perhaps the most commonly used mNGS send-out test at US institutions (US). The Karius test has been commercially accessible for the longest and is perhaps the most commonly used mNGS send-out test at US institutions (US). This technique has been used to diagnose invasive fungal disease, community-acquired pneumonia and infections in immunocompromised hosts [6, 7], and has been reported to detect and quantify pathogen cell-free DNA from 1250 bacteria, DNA viruses, fungi, and eukaryotic parasites. Because of the noninvasive nature of testing and the possibility to deliver an actionable diagnosis faster than traditional microbiologic approaches, clinical metagenomic cell-free DNA sequencing has piqued the interest of clinical practitioners across disciplines. The clinical significance of mNGS testing when utilised for routine patient care, however, remains unknown.

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Biography

Andressa Dias completed her Ph.D. at the age of 39 years and postdoctoral studies from from University of Liverpool, United Kingdom (Department of Microbiology and Infectious Diseases). she is the head of department of Clinical Microbiology .she has published more than 15 papers in reputed journals and has been in serving as an editorial board member of repute. From 1986 until 1999, she was the Director of the State of Florida and University of Florida Southeastern Florida Regional infectious diseases Program, where she was in charge of converting current scientific research into clinical application and training for South Florida health professionals and patients. she is a well-known and active teacher of medical students and postgraduate physicians, as well as a member of the Division's Fellowship training committee.

The Institution of Liverpool is an English public research university located in Liverpool. It was established as a college in 1881 and received its Royal Charter in 1903, allowing it to confer degrees. It is also one of the six original ‘red brick' civic universities. It is divided into three faculties, each with 35 departments and schools. The university management school is Triple Crown accredited, and it is a founding member of the Russell Group and the N8 Group for research collaboration. The university has nine Nobel Prize winners among its alumni and prior teachers, and it provides over 230 first-year courses in 103 fields. Global Foundries, ARM Holdings, Tesco, Motorola, and The Coca-Cola Company all have CEOs among its alumni. At the Johnston Laboratories, it was the world's first university to create departments of oceanography, civic design, architecture, and biochemistry. The institution was the first in the UK to create an autonomous university in China, Xi'an Jiao tong-Liverpool University, in 2006, making it the first Sino-British University in the world. Liverpool had a profit of £584.7 million in 2019–20, with £95.1 million coming from research grants and contracts. It has the seventh highest endowment of any English institution. The post-nominal letters are used to style university graduates.

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