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New Assay Shows Promise to Advance Personalized Therapy for Cancer Patients

NCI-MATCH next-generation sequencing assay for detecting genetic mutations in tumors is sensitive, specific, and reproducible, reports The Journal of Molecular Diagnostics

Philadelphia, PA, February 7, 2017 – One of the most promising areas of cancer research is personalized therapy using precision medicine. The National Cancer Institute's NCI-MATCH (Molecular Analysis for Therapy Choice) is a large, ongoing clinical trial that matches tumors to therapies based on the tumor's genetic characteristics. This effort addresses therapeutic efficacy across multiple tissues, but also adds data as to the clinical value of broad-based screening panels versus disease-specific assays. A report in *The Journal of Molecular Diagnostics* confirms that the assay tailored for this trial is highly sensitive for detecting genetic mutations from a variety of tumor tissue and, for the first time, has been reproduced with accuracy by multiple clinical laboratories, laying the groundwork for future clinical utility.

These results are noteworthy because, to date, concerns have been widely expressed about the complexity, accuracy, and reproducibility of next-generation sequencing (NGS) for application in clinical trials. These results clearly show that locked and controlled procedures permit reliable, accurate, and reproducible use of NGS for clinical purposes.

Ultimately, the NCI-MATCH trial aims to evaluate tumor biopsy specimens from about 6,000 patients. The NGS technology used in the trial (the OncoPrint Cancer Panel assay and the Personal Genome Machine from Thermo Fisher Scientific) is able to detect more than 4,000 pre-defined genomic variations across 143 genes, including single nucleotide variants (SNVs), insertions/deletions (indels), copy number variations (CNVs), and gene fusions. Levels of evidence were developed to select a subset of specific actionable genomic variants to be used for treatment matching.

The investigators report that the assay was highly sensitive (96.98% for 265 known mutations), with 99.99% specificity. Since one feature of the NCI-MATCH trial is the wide variety of tumors examined, including solid tumors and lymphomas that no longer respond to standard therapy, the assay used must

be able to analyze specimens from different tissues. Importantly, the NCI-MATCH NGS assay was able to accurately determine genetic abnormalities in biopsies from the pancreas, melanoma, bone, and skin.

One-hundred and eighty-six samples and 12 cell lines were tested at four different laboratories. Steps were taken to maximize standardization, including development of standard operating procedures, use of the same commercial assay and instruments, and face-to-face discussions. The investigators found that the assay results were highly reproducible, with the same results across multiple laboratories. This is critical for future clinical use leading to improved patient outcomes.

“The validation study reported by Williams and colleagues is another step moving the field closer to the time when precision medicine will generate the expected benefits in improved clinical outcomes,” commented Elizabeth R. Unger, PhD, MD, of the Division of High-Consequence Pathogens and Pathology, Centers for Disease Control and Prevention (Atlanta, GA). “Although the success of the NCI-MATCH trial cannot be assured, linking precision laboratories to precision medicine trials assures that data used for drug assignment will be reliable. Further, the use of a commercial platform and integrated analysis and reporting pipeline will greatly facilitate broader translation of any successes.”

Notes for Editors

The article is “Analytical Validation of the Next Generation Sequencing Assay for a Nationwide Signal-Finding Clinical Trial: Molecular Analysis for Therapy Choice Clinical Trial (NCI-MATCH, EAY131),” by Chih-Jian Lih, Robin D. Harrington, David J. Sims, Kneshay N. Harper, Courtney H. Bouk, Vivekananda Datta, Jonathan Yau, Rajesh R. Singh, Mark J. Routbort, Rajyalakshmi Luthra, Keyur P. Patel, Geeta S. Mantha, Savitri Krishnamurthy, Karyn Ronski, Zenta Walther, Karin E. Finberg, Sandra Canosa, Hayley Robinson, Amelia Raymond, Long P. Le, Lisa M. McShane, Eric C. Polley, Barbara A. Conley, James H. Doroshow, A. John Iafrate, Jeffrey L. Sklar, Stanley R. Hamilton, and P. Mickey Williams (<http://dx.doi.org/10.1016/j.jmoldx.2016.10.007>). It will be published in *The Journal of Molecular Diagnostics*, volume 19, issue 2 (March 2017) by Elsevier.

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Full text of this study is available to credentialed journalists upon request; contact Eileen Leahy at +1 732-238-3628 or jmdmedia@elsevier.com. Journalists wishing to reach the authors should contact P. Mickey Williams, PhD, at mickey.williams@nih.gov. Elizabeth R. Unger, PhD, MD, may be reached for comment at eunger@cdc.gov

About *The Journal of Molecular Diagnostics*

The Journal of Molecular Diagnostics (<http://jmd.amjpathol.org>), the official publication of the Association for Molecular Pathology, co-owned by the American Society for Investigative Pathology, and published by Elsevier, Inc., seeks to publish high quality original papers on scientific advances in the translation and validation of molecular discoveries in medicine into the clinical diagnostic setting, and the description and application of technological advances in the field of molecular diagnostic medicine. The editors welcome review articles that contain: novel discoveries or clinicopathologic correlations, including studies in oncology, infectious diseases, inherited diseases, predisposition to disease, or the description of polymorphisms linked to disease states or normal variations; the application of diagnostic

methodologies in clinical trials; or the development of new or improved molecular methods for diagnosis or monitoring of disease or disease predisposition.

The Journal of Molecular Diagnostics, with an Impact Factor of 5.201, ranks 7th among 78 journals in Pathology, according to *2015 Journal Citation Reports*® Thomson Reuters, 2016.

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