MedicalXpress

AMP addresses clinical relevance of DNA variants in chronic myeloid neoplasms

August 22 2018

The Association for Molecular Pathology (AMP), the premier global molecular diagnostics professional society, today published consensus, evidence-based recommendations to aid clinical laboratory professionals with the management of most Chronic Myeloid Neoplasms (CMNs) and development of high-throughput pan-myeloid sequencing testing panels. The report, "Clinical Significance of DNA Variants in Chronic Myeloid Neoplasms (CMNs): A Report of the Association for Molecular Pathology," was released online ahead of publication in The *Journal of Molecular Diagnostics*.

CMNs are a complex group of hematopoietic disorders, encompassing myelodysplastic syndromes (MDS), myeloproliferative neoplasms (MPNs), and the overlap entities (MDS/MPNs), that causes a person's bone marrow to make too many, or too few, red blood cells, white blood cells or platelets. The increasing availability of targeted high-throughput next-generation sequencing (NGS) panels has enabled scientists to explore the genetic heterogeneity and clinical relevance of the small DNA variants in CMNs. However, the biological complexity and multiple forms of CMNs has led to variability in the genes included on the available panels that are used to make an accurate diagnosis, provide reliable prognostic information and select an appropriate therapy based on DNA variant profiles present at various time points. The AMP CMN Working Group was established to review published literature, summarize key findings that support clinical utility and define a minimum set of critical gene inclusions for all high-throughput pan-myeloid sequencing testing panels.

"The molecular pathology community has witnessed a recent explosion of scientific literature highlighting the clinical significance of small DNA variants in CMNs," said Rebecca F. McClure, MD, Associate Professor, Health Sciences North and the Northern Ontario School of Medicine, AMP CMN Working Group Member and Co-lead Author. "AMP's working group recognized a clear unmet need for evidence-based recommendations to assist in the development of the high-quality pan-myeloid gene panels that provide relevant diagnostic and prognostic information and enable monitoring of clonal architecture."

The AMP CMN Working Group proposed the following 34 genes as a minimum recommended testing list: ASXL1, BCOR, BCORL1, CALR, CBL, CEBPA, CSF3R, DNMT3A, ETV6, EZH2, FLT3, IDH1, IDH2, JAK2, KIT, KRAS, MPL, NF1, NPM1, NRAS, PHF6, PPM1D, PTPN11, RAD21, RUNX1, SETBP1, SF3B1, SMC3, SRSF2, STAG2, TET2, TP53, U2AF1, and ZRSR2. The list of genes is meant to aid clinical laboratory professionals with the management of most CMNs and selection of myeloid testing panels.

"While the goal of the study was to distill the literature for molecular pathologists, in doing so we also revealed recurrent mutational patterns of clonal evolution that will aid hematologist/oncologists, researchers, and pathologists understand how to interpret the results of these panels as they reveal critical biology of the neoplasms," said Annette S. Kim, MD, Ph.D., Associate Professor of Pathology at Harvard Medical School and Brigham and Women's Hospital, AMP Hematopathology Subdivision Chair and CMN Working Group Chair.

"This new CMN report is another validation of AMP's commitment to continuously improve clinical practice and patient care," said Mark D. Ewalt, MD, Assistant Professor at University of Colorado, AMP CMN Working Group Member and Co-lead Author. "Moving forward, the AMP CMN Working Group will plan on revisiting and updating the

gene list as insight on specific clinicopathologic characteristics of CMNs accumulates."

More information: Rebecca F. McClure et al, Clinical Significance of DNA Variants in Chronic Myeloid Neoplasms (CMNs): A Report of the Association for Molecular Pathology, *The Journal of Molecular Diagnostics* (2018). DOI: 10.1016/j.jmoldx.2018.07.002

Provided by Association for Molecular Pathology