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AMP issues joint guideline to standardize interpretation and reporting of sequence variants in cancer

December 16 2016

The Association for Molecular Pathology (AMP), the premier global, non-profit molecular diagnostics professional society, today published guideline recommendations for both clinical laboratory professionals and oncologists that assess the status of next-generation sequencing (NGS)-based cancer tests and establish standardized classification, annotation, interpretation, and reporting conventions for somatic sequence variants. The new guideline was developed by a Working Group comprised of representatives from major professional associations whose members provide professional testing and treatment services to cancer patients.

The guideline, "Standards and Guidelines for the Interpretation and Reporting of Sequence Variants in Cancer: A Joint Consensus Recommendation of the Association for Molecular Pathology, American Society of Clinical Oncology, and College of American Pathologists" was released online ahead of publication in the January issue of *The Journal of Molecular Diagnostics*.

"Cancer genomics is a rapidly evolving field, so the clinical significance of any variant in therapy, diagnosis, or prognosis should be reevaluated on an ongoing basis by all of the key stakeholders," said Marina N. Nikiforova, MD, Professor of Pathology at University of Pittsburgh Medical Center, Working Group member, and 2016 AMP Clinical Practice Committee Chair. "These new recommendations resulted from

the successful ACMG, AMP, and CAP efforts on germline variant interpretation and were additionally informed by the diverse perspectives expressed at the ASCO, AMP, and CAP Genomic Roundtable stakeholder discussions."

The increasing use of NGS technologies has raised new challenges, especially regarding how cancer-associated sequence variants are interpreted and how molecular results are reported by different clinical laboratories. To help standardize this process, AMP convened a panel of experts to develop a new set of guidelines based on evidence from a comprehensive review of published literature, empirical data, current laboratory practice surveys, feedback from multiple public meetings, and their own professional experiences. The report proposed a four-tiered system to categorize somatic sequence variations based on their clinical significance in cancer diagnosis, prognosis, and/or therapeutics:

- Tier 1: Variants with strong clinical significance
- Tier 2: Variants with potential clinical significance
- Tier 3: Variants of unknown clinical significance
- Tier 4: Variants deemed benign or likely benign

"This joint consensus recommendation represents a significant step forward in this era of precision medicine and our fight against cancer," said Marilyn M. Li, MD, Vice Chief of the Division of Genomic Diagnostics and Director of Cancer Genomic Diagnostics at Children's Hospital of Philadelphia, AMP Member, and Chair of the multidisciplinary Working Group. "We worked diligently to ensure the cancer genomics community was well represented and it is our hope that we will soon see the widespread adoption of these guidelines leading to improved communication between molecular pathologists, oncologists, pathologists, and most importantly, patients."

More information: Marilyn M. Li et al, Standards and Guidelines for

the Interpretation and Reporting of Sequence Variants in Cancer, *The Journal of Molecular Diagnostics* (2017). DOI: 10.1016/j.jmoldx.2016.10.002