

AMP Assesses Clinical Implementation of Past Standards and Guidelines for Interpretation and Reporting of Sequence Variants in Cancer

Multidisciplinary working group consisting of clinical laboratory and oncology experts identifies opportunities for improvement to drive adoption of evidence-based somatic variant classification system

ROCKVILLE, Md. – Dec. 13, 2022 – The Association for Molecular Pathology (AMP), the premier global molecular diagnostic professional society, has published a report that was designed to assess clinical adoption, identify classification inconsistencies, and evaluate implementation barriers for the 2017 report, [“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.”](#) The AMP manuscript, [“Assessments of Somatic Variant Classification Using the AMP/ASCO/CAP Guidelines”](#) was released online ahead of publication in *The Journal of Molecular Diagnostics*.

To help standardize the interpretation and reporting of sequence variants in cancer, the 2017 guidelines were developed by a panel of experts and based on evidence from a comprehensive review of published literature, empirical data, current laboratory practice surveys, feedback from multiple public meetings, and 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

In 2018, the AMP Variant Interpretation Across Testing Laboratories (VITAL) Somatic Working Group was formed to better understand the implementation and utilization of the previous guidelines among laboratories, assess concordance between laboratories, and identify content within the guidelines that may result in variant classification inconsistencies between laboratories. The project involved VITAL Somatic Challenges and an implementation survey.

“Cancer genomics is a rapidly evolving field, and the increasing use of NGS technologies has raised new challenges, especially regarding how somatic variants are interpreted and how molecular results are reported by different clinical laboratories,” said Jane Gibson, PhD, Associate Dean for Faculty Affairs, Chair, Clinical Sciences, and Professor of Pathology at the University of Central Florida College of Medicine, and 2022 AMP Clinical Practice Committee Chair. “As part of our ongoing commitment to improving clinical practice, AMP will continue to reassess and modify our guidelines as needed to address common challenges and improve patient care.”

The VITAL Somatic Challenges demonstrated that 86% of the participants correctly differentiated clinically significant variants from variants of uncertain significance and benign/likely benign variants and most participants (>70%) agreed in judging the potential for germline variants. Meanwhile, the survey showed that 71% of respondents implemented the guidelines for variant classification and more than 90% of them utilized

the recommended tier-based reporting system. The project identified several areas for improvement, including a more granular and comprehensive classification system, more detailed guidelines on interpretation and reporting, and additional educational programs for clinical laboratory professionals and medical oncologists. AMP will continue to collaborate with key stakeholders in the cancer genomics community and will use the results obtained from these studies to help inform future revisions of guidelines.

“We are working diligently to ensure the cancer genomics community has the tools to improve communication between molecular pathologists, oncologists, pathologists, and most importantly, patients,” 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 VITAL Somatic Working Group. “Collectively this study demonstrates that the 2017 guideline recommendations are being implemented, and with modifications based on these challenges, we believe we can achieve standardization and improve consistency for somatic variant interpretation across the globe.”

To read the full manuscript, please visit: <https://doi.org/10.1016/j.jmoldx.2022.11.002>.

ABOUT AMP

The Association for Molecular Pathology (AMP) was founded in 1995 to provide structure and leadership to the emerging field of molecular diagnostics. AMP's 2,900+ members practice various disciplines of molecular diagnostics, including bioinformatics, infectious diseases, inherited conditions, and oncology. Our members are pathologists, clinical laboratory directors, basic and translational scientists, technologists, and trainees that practice in a variety of settings, including academic and community medical centers, government, and industry. Through the efforts of its Board of Directors, Committees, Working Groups, and Members, AMP is the primary resource for expertise, education, and collaboration in one of the fastest-growing fields in healthcare. AMP members influence policy and regulation on the national and international levels, ultimately serving to advance innovation in the field and protect patient access to high-quality, appropriate testing. For more information, visit www.amp.org and follow AMP on Twitter: [@AMPath](https://twitter.com/AMPath).

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