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Kathy Moran, MBA
kmoran@acmg.net

ACMG Releases Two Important Secondary Findings Policies: Announces Recommendations for Future SF Reporting and New SF v3.0 List, with Plans to Update SF List Annually

BETHESDA, MD – May 20, 2021 | The American College of Medical Genetics and Genomics (ACMG) has just released an updated policy statement and gene list for the reporting of secondary findings (SF). Together, these two documents update the recommendations for SF reporting and unveil the highly anticipated recommended minimum gene list **(SF v3.0)** for reporting secondary findings in clinical exome and genome sequencing. The ACMG also declares its intent to update the SF gene list now annually, with a goal of publishing the updated list each January.

The two papers, "Recommendations for Reporting of Secondary Findings in Clinical Exome and Genome Sequencing, 2021 Update: a Policy Statement of the American College of Medical Genetics and Genomics" and "ACMG SF v3.0 List for Reporting of Secondary Findings in Clinical Exome and Genome Sequencing: a Policy Statement of the American College of Medical Genetics and Genomics," are the culmination of several years of work by the ACMG Secondary Findings Working Group (SFWG) and are being published in ACMG's official journal, *Genetics in Medicine*.

"Our group worked very hard on this update, taking a thoughtful and careful approach that balances the goals of keeping it as a minimum list while also providing results that will impact patients and their families in a positive way," said lead author and co-chair of the ACMG SFWG, David T. Miller, MD, PhD, FACMG.

Guidance from the original ACMG policy statement on incidental (updated later to the current term, "secondary") findings in 2013 established that clinical laboratories performing exome or genome sequencing should report a "minimum list" of known pathogenic or expected pathogenic variants in a defined set of genes considered medically actionable, even when unrelated to the primary medical reasons for testing. Recognizing the need to regularly update the recommended list of genes, the ACMG Board of Directors created the ACMG Secondary Findings Working Group to define and implement a process for updating the Secondary Findings list. The overall goal of the ACMG SFWG is to recommend a minimum list of genes that places limited excess burden on patients and clinical laboratories while maximizing the potential to reduce morbidity and mortality when exome sequencing/genome sequencing (ES/GS) is being performed.

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The ACMG SF v3.0 Includes 73 Genes

The paper also announces the highly anticipated next list of genes for the return of secondary findings, SF v3.0, which now includes 73 genes. It states that the ACMG Secondary Findings Working Group built upon the solid foundation of the earlier policy statements, making adjustments in response to updates in the medical literature and feedback from the medical genetics community. They also outline a new framework to update the ACMG SF list annually, and on a predictable schedule that will facilitate integration into laboratory and clinical workflows.

It is important to note that the ACMG SF gene list is still intended to be a minimum list for the return of SFs that have a high likelihood for reducing morbidity and mortality, and is not an inclusive list for any genetic results that could be actionable.

ACMG also strongly recommends referencing the SF gene list using the version number system (e.g., ACMG SF v3.0 instead of, for example, "ACMG 73"), in order to accurately reflect the genes included and reduce any confusion.

Christa L. Martin, PhD, FACMG and co-chair of the ACMG SFWG explained, "As we plan to update the list more regularly going forward, versioning will help to avoid misunderstandings about what genes were being reviewed at the time a clinical report was issued."

Not Intended for Use in Population Screening

The authors emphasize that the ACMG Secondary Findings (SF v3.0) gene list is not intended for use in population screening, and explain that ACMG also currently has two separate working groups focused on population screening, including the Genomic Screening of Asymptomatic Patients Working Group and the Population Screening Working Group. The ACMG has made it clear that the ACMG SF list was not intended for general population screening. The ACMG, however, is supportive of continued research and discussions around the additional factors to consider in rolling out population screening programs, including the efficacy of using such genomic screening in individuals without other indications for genomic testing.

ACMG Accepts Nominations for the Secondary Findings List: Plans to Update List Annually

The ACMG SFWG has created a mechanism for continued nominations to add a gene to, or remove a gene from, the list. Nominations are accepted not only from ACMG

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members, but also from other professional organizations. Each decision about a gene has unique variables and considerations, and the nomination process engages the community in presenting the supporting evidence to the working group. Dr. Miller stresses that there is "a very high bar for the SF list." He added, "Most of the 'obvious' genes have already been included in the list, so now the decisions get more complicated as time goes on. The SFWG developed a flowchart describing the nomination and review process to try and guide nomination of the most appropriate genes for future consideration."

Finally, the SFWG recommends that the ACMG SF gene list now be updated annually, with intervening updates if any urgent changes are identified that could impact patient care. If new information emerges that might affect the status of any gene on the list, ACMG members or other healthcare professionals are encouraged to submit that information to the SFWG for immediate consideration using the online form on the ACMG website.

The volunteer members of the Secondary Findings Working Group provide their diverse expertise and varying perspectives and have been actively involved in the effort to update the ACMG SF list. The SFWG considers the perspectives of different stakeholders, including patients, clinical laboratories, and clinicians.

The ACMG recognizes the invaluable contributions and hard work of the ACMG Secondary Findings Working Group: Co-chairs David T. Miller, MD, PhD and Christa L. Martin, PhD; and working group members, Kristy Lee, MS; Wendy K. Chung, MD, PhD; Adam S. Gordon, PhD; Gail E. Herman, MD, PhD; Teri E. Klein, PhD; Douglas R. Stewart, MD; Laura M. Amendola, MS; Kathy Adelman; Sherri J. Bale, PhD; Michael H. Gollob, MD; Steven M. Harrison, PhD; Ray E. Hershberger, MD; Kent McKelvey, MD; C. Sue Richards, PhD; Christopher N. Vlangos, PhD; and Michael S. Watson, MS, PhD.

About the American College of Medical Genetics and Genomics (ACMG) and ACMG Foundation

Founded in 1991, the American College of Medical Genetics and Genomics (ACMG) is the only nationally recognized medical professional organization solely dedicated to improving health through the practice of medical genetics and genomics, and the only medical specialty society in the US that represents the full spectrum of medical genetics disciplines in a single organization. The ACMG is the largest membership organization specifically for medical geneticists, providing education, resources and a voice for more than 2,500 clinical and laboratory geneticists, genetic counselors and other healthcare

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professionals, nearly 80% of whom are board certified in the medical genetics specialties. ACMG's mission is to improve health through the clinical and laboratory practice of medical genetics as well as through advocacy, education and clinical research, and to guide the safe and effective integration of genetics and genomics into all of medicine and healthcare, resulting in improved personal and public health. Four overarching strategies guide ACMG's work: 1) to reinforce and expand ACMG's position as the leader and prominent authority in the field of medical genetics and genomics, including clinical research, while educating the medical community on the significant role that genetics and genomics will continue to play in understanding, preventing, treating and curing disease; 2) to secure and expand the professional workforce for medical genetics and genomics; 3) to advocate for the specialty; and 4) to provide best-in-class education to members and nonmembers. *Genetics in Medicine*, published monthly, is the official ACMG journal. ACMG's website, www.acmg.net offers resources including policy statements, practice guidelines, educational programs and a 'Find a Genetic Service' tool. The educational and public health programs of the ACMG are dependent upon charitable gifts from corporations, foundations and individuals through the ACMG Foundation for Genetic and Genomic Medicine.

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