Update to secondary findings gene list released

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The American College of Medical Genetics and Genomics (ACMG) has released its highly anticipated 2023 update to the recommended minimum gene list for the reporting of secondary findings (SF): "ACMG SF v3.2 List for Reporting of Secondary Findings in Clinical Exome and Genome Sequencing: A Policy Statement of the American College of Medical Genetics and Genomics (ACMG)."

In 2021, the ACMG Board of Directors and Secondary Findings Working Group (SFWG) stated that the College would update the list annually. Today's update (SF v3.2) is being published in *Genetics in Medicine*.

Three new cardiovascular genes, CALM1, CALM2 and CALM3, were added to the SF v3.2 list along with a brief description of the factors considered in adding each of these genes. One gene, ATP7A, was also considered carefully for inclusion but ultimately excluded from the SF v3.2 list. This gene could be reviewed again in the future if new data emerges related to either Menkes disease or other phenotypes associated with ATP7A.

"We continue to balance the goals of providing secondary findings to patients while striving for a minimum list of the most actionable, and impactful, secondary findings," said lead author and co-chair of the ACMG SFWG, David T. Miller, MD, Ph.D., FACMG.

Christa L. Martin, Ph.D., FACMG, co-chair of the SFWG added, "We're excited to continue with our plans to publish updates to the list about one time per year and encourage ACMG members and others to submit nominations as part of this ongoing process."

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 likely pathogenic variants in a defined set of genes considered medically actionable, even when unrelated to the primary medical reasons for testing.

The current ACMG Secondary Findings Working Group includes clinical geneticists, molecular and/or cytogenetics clinical laboratory

directors, genetic counselors, cardiologists, an expert in hereditary cancer predisposition, and a bioethicist.

Note that the versioning nomenclature of the ACMG SF list was designed to differentiate major versus minor revisions. Major revisions include conceptual changes to the categories or genes/variants in the SF list or the removal or addition of a large number of genes in a single update. These major changes are denoted by updating the version number to the next integer, e.g., v4.0 or v5.0. Minor revisions, such as the 2023 release of SF v3.2, reflect the addition or removal of one or a few genes or variants without any significant policy change.

The ACMG SFWG will continue to review the current list of actionable genes, as well as new nominations throughout the course of the year including nominations submitted through representatives of other professional organizations and individuals via the nomination form on the ACMG website.

More information: David T. Miller et al, ACMG SF v3.2 list for reporting of secondary findings in clinical exome and genome sequencing: A policy statement of the American College of Medical Genetics and Genomics (ACMG), *Genetics in Medicine* (2023). DOI: 10.1016/j.gim.2023.100866

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