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ADDENDUM

Addendum: Yield of additional genetic testing after chromosomal microarray for diagnosis of neurodevelopmental disability and congenital anomalies: A clinical practice resource of the American College of Medical Genetics and Genomics (ACMG)

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Addendum to: "Yield of additional genetic testing after chromosomal microarray for diagnosis of neurodevelopmental disability and congenital anomalies: A clinical practice resource of the American College of Medical Genetics and Genomics (ACMG)." Darrel Waggoner, MD, Karen E. Wain, MS, Adrian M. Dubuc, PhD, Laura Conlin, PhD, Scott E. Hickey, MD, Allen N. Lamb, PhD, Christa Lese Martin, PhD, Cynthia C. Morton, PhD, Kristen Rasmussen, MS, Jane L Schuette, MS, Stuart Schwartz, PhD, David T. Miller, MD, PhD. *Genetics in Medicine* 20(10):1105–1113 (2018). http://doi.org/10.1038/s41436-018-0040-6, published online 18 June 2018.

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This document was reaffirmed by the ACMG Board of Directors as of 26 August 2024 with the following addendum:

The American College of Medical Genetics and Genomics (ACMG) Professional Practice and Guidelines Committee and the Chromosomal Microarray Additional Testing Reaffirmation Workgroup reviewed this document and voted during their working meeting on 14 August 2024 to reaffirm the Practice Resource with the following considerations that clinical practitioners should be aware of the following:

- The committees unanimously believe that this document remains a useful guide in assessing additional testing options and recurrence risk after chromosomal microarray. Chromosomal microarray continues to be widely used for prenatal and pediatric genetic testing.
- Although the rationale for additional testing remains valid, microarray is no longer the sole first-tier go-to test per ACMG evidence-based clinical guidelines,[1,2] nor is it necessarily the first place to start a diagnostic query, as mentioned in the document. Additional testing after chromosomal microarray remains clinically relevant for disease-specific testing (eg, testing for an autosomal recessive pathogenic variant or uniparental disomy after detection of homozygosity), as well as more general testing recommendations (eg, balanced translocations and insertions).

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- Genetic testing has rapidly evolved in the 6 years since publication of the practice resource to include clinical genome sequencing, long-read sequencing, RNA sequencing, and optical genome mapping. Although these methods have the potential to detect the same copy-number variation captured by a chromosomal microarray, no single method or analysis pipeline will catch all structural variations (SV).[3]
- Genome sequencing, long-read sequencing, and optical genome mapping can detect balanced SV typically cryptic by chromosomal microarray.[4] However, further systematic analyses of the diagnostic yield, clinical utility, and testing merits for balanced translocations, insertions, and other rearrangements is warranted. Sequencing-based methods that simultaneously detect a genome-wide SV and single-nucleotide variation are already clinically available.
- Accordingly, while reaffirming this clinical practice resource, we encourage health care professionals to consult emerging studies when making testing decisions. For this purpose, we also include more recent literature to support this recommendation.[3-6]

Therefore, the ACMG considers it the best practice to reaffirm this document as a Clinical Practice Resource with additional considerations outlined above.

Conflict of Interest

The authors declare no conflict of interest.

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