Methodology: The microarray analysis was performed using the Infinium Assay with the Illumina CytoSNP-850Kv1.2 BeadChip platform. This chip contains approximately 846,500 genome-wide markers, an overall average probe spacing of 1.8 kb and an average effective resolution of 18 kb to determine copy number change. Copy number changes ≥10 SNP markers are reviewed for clinical significance. The test is used to identify chromosomal imbalances throughout the human genome. These imbalances include deletions, duplications and aneuploidy. Microarray testing is not designed to detect balanced chromosomal changes, insertions or deletions that are in regions not well covered with markers. Also, it is not used to reliably detect low level mosaicism (<15% of cells with an abnormality). Small genetic alterations, such as point mutations and small deletions within a single gene, may not be detected with the DNA microarray analysis. Polymorphisms (common genetic changes) and rare variants (less common imbalances) with unknown clinical significance may be detected with this technology. Imbalances that are detected in regions of known copy number variation may not be reported if they are considered to be a benign copy number change with no known clinical significance at the time this report is issued. Results are described using the ISCN (2016) guidelines. Linear positions of abnormalities are listed according to the Human Genome Build (GRCh37: Feb. 2009(hg19)). Information regarding genes located within chromosomal regions are obtained from Database of Genomic Variants (http://projects.tcag.ca/variation/), The human genome browser at UCSC http://genome.ucsc.edu/, and the NCBI RefSeq Project (http://www.ncbi.nlm.nih.gov/RefSeq). Detailed methodologies are available upon request.

This test has not been cleared or approved by the United States Food and Drug Administration. The FDA has determined that such clearance or approval is not necessary. This laboratory is certified under the Clinical Laboratory Improvement Amendments of 1988 ('CLIA') as qualified to perform high complexity clinical laboratory testing. The performance characteristics of this test have been developed and validated by CCHMC Cytogenetics Laboratory.

Detailed information about the array composition, sensitivity and reporting protocols is available by request from Cincinnati Children's Hospital Cytogenetics Laboratory (513-636-4474) or visit our website (http://www.cincinnatichildrens.org/cytogenetics).

Methodology References: Genome Res (2009) 16:1682-1690; Am J Hum Genet (2007) 81:768-779; Hum Mol Genet (2007) 16(1):1-14; Genome Res (2006) 16:1136-1148; Nat Genet (2005) 37:549-554; Nat Genet (2004) 36(9):949-51; ISCN (2009): An International System for Human Cytogenetic Nomenclature (2013), L.G. Shaffer, J. McGowan-Jordan, M. Schmid (eds); S. Karger Publishers, Inc., 2013; Gardner and Sutherland, Chromosome Abnormalities and Genetic Counseling, Oxford University Press, Third Edition, 2004.