Wisconsin State Laboratory of Hygiene
UNIVERSITY OF WISCONSIN-MADISON

UW Cytogenetics and Molecular Genetics Services

Information for Medical Providers, May 2023

Updated Chromosomal Microarray Platform – Introducing the Illumina Infinium Global Diversity Array with Cytogenetics (GDACyto)!

The GDACyto array is designed to capture the latest insights on genetic disease. The array focuses on clinically important genes/regions (see table below) with strong backbone coverage, enabling accurate detection of small and large aberrations genome-wide. This single array offers the ability to detect genetic disorders across a variety of applications including prenatal, postnatal, and oncology. **The GDACyto array will be available beginning May 8th, 2023.**

Description	Number of Genes	Number of Exons	Exons with ≥1 probe	Exons with ≥3probes
ClinGen pathogenic/likely pathogenic, haploinsufficient and triplosensitive genes	409	6214	>99%	>99%
Developmental disorders gene to phenotype (DDG2P), genes associated with cancer	1254	18,353	>99%	>99%
Input from cytogenetics consortia Mendeliome Panel	2766	36,840	>99%	>60%
OMIM Morbid genes not otherwise included above	456	5434	>99%	>60%

Table 1. Targeted genes and regions on the GDACyto array

Test Performance Characteristics

Analytical Sensitivity: The assay is currently validated for the detection of copy number losses greater than 20-kilobases (kb) in size and copy number gains 50-kb in size (smaller changes may be detected depending on gene content and probe number). Regions of homozygosity greater than 3-Megabases (Mb) will be detected (smaller regions may be detected depending on gene content and probe number). From internal validation studies, abnormalities present in a mosaic state are reliably detected if the mosaicism level (percentage of abnormal cells) is 20% or higher.

Accuracy: Overall accuracy was determined to be 96.6%. Accuracy within the limit of detection was 100% (see Table 2).

Precision: Per manufacturer, reproducibility is 99.99%. The standard deviation and coefficient of variability of internal intra- and inter-precision studies met acceptable criteria (SD<3 and CV<10%).

Reportable Range: Copy number variant classification follows ACMG guidelines (PMID: 31690835). All copy number variants (CNVs) within the limit of detection classified as pathogenic or likely pathogenic will be reported, regardless of size. This includes secondary/incidental findings and probable carrier status (see definitions below). For postnatal specimens, CNVs of uncertain clinical significance will be reported when at least one protein coding gene is involved in a copy number loss greater than 200 kilobases (kb) or a copy number gain greater than 500 kb. Smaller CNVs (less than 200-500 kb) of uncertain significance may be reported based on criteria such as genomic content, published literature,

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public databases and internal lab data, and inheritance pattern/family history. For prenatal specimens (including productions of conception), CNVs of uncertain clinical significance will be reported when at least one protein coding gene is involved in a copy number loss greater than 1 Megabase (Mb) or a copy number gain greater than 2 Mb. Smaller CNVs (less than 1-2 Mb) of uncertain significance may be reported based on criteria such as genomic content, published literature, public databases and internal lab data, and inheritance pattern/family history. Likely benign and benign CNVs are not reported.

Secondary/Incidental findings: these represent copy number variants that are unrelated to the patient's stated reason for referral, but have clear medical relevance for the patient's care.

a. Secondary findings include medically important genes recommended by the ACMG (PMID 34012068).
b. Incidental findings will be limited to pre-symptomatic status for a late-onset disorder (e.g. deletion in tumor suppressor genes).

Probable carrier status: focal deletion of a gene that causes an autosomal recessive or X-linked disorder, where loss of function is a known mechanism of pathogenicity. May also include recurrent deletions that are known to only confer a phenotype in the homozygous state (e.g. STRC/CATSPER, HBA1/HBA2, etc).

Table 2. Comparison of GDACyto to 850k (current platform) for a variety of aberration types.

Aberration type	Aberration description	Number tested	Concordant with current 850k	Accuracy
Sex chromosome CNVs	X and Y chromosome deletions and duplications	9 (4 males, 5 female)	Y	100%
Autosomal losses	Small (<20 kilobases)	7	Y	100%
	Medium (50 kilobases – 1 Megabase)	3	Y	
	Large (>1 Megabase)	1	Y	
Autosomal gains	Small (<30 kilobases)	2	N	87.58%
	Medium (50 kilobases – 1 Megabase)	13	Y	
	Large (>1 Megabase)	1	Y	
Aneuploidy	Triploid, Trisomy 18, Trisomy 21	4	Y	100%
Complex rearrangements	Unbalanced translocations, Ring chromosomes, Pallister-Killian, Turner variant, Pseudo-isodicentric Y	7	Y	100%
Mosaicism	Loss (30%, 55%), Gain (20%, 40%)	4	Y	100%
Regions of homozygosity	Excess homozygosity, UPD4, UPD7, UPD11p, UPD15	7	Y	100%
Total tested		58	56	96.6%
Total within LOD		**56**	**56**	**100.0%**

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Test Information:

Test name: Illumina Microarray Analysis

CPT code: 81229

Specimen Types Accepted: Blood, Saliva, Buccal, Amniotic fluid, Chorionic Villus, Tissue (including products of conception), Skin biopsy, Bone marrow

Turnaround time: Prenatal/infant (0-1 year): approx. 7-10 days; Children >1 year, adult, and products of conception: approx. 12-21 days, with an average of 12 days

Limitations: This assay will detect aneuploidy, deletions, and/or duplications of represented loci, but will not detect point mutations or balanced alterations (reciprocal translocations, Robertsonian translocations, inversions and insertions). The failure to detect an alteration at any locus does not exclude all anomalies at that locus.

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