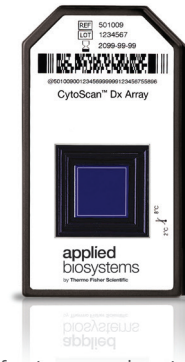




For families struggling with the diagnostic odyssey

The recommended standard in chromosomal
microarray analysis (CMA) testing

Results that matter



Data from the US indicate that the prevalence of developmental disabilities across all racial, ethnic, and socioeconomic groups in US children is 13.87% [1]. Further studies revealed that 1 in 33 babies born in the US have congenital anomalies [2]. Developmental delay/intellectual disability (DD/ID) is frequently accompanied with one or more congenital anomalies or dysmorphic features. These children with special needs can have lifelong challenges, including various medical conditions as well as difficulties with physical movement, learning, and social interaction.

Early intervention is key to providing better outcomes for children with special needs. Despite this, typically, diagnosis of developmental delay in children does not occur until they have reached four years of age [3]. Certain intellectual disabilities are diagnosed much later, often when the child has entered elementary school.

Establishing an underlying diagnosis early can better inform healthcare providers and families of prognosis, recurrence risk, and comorbidity information, all of which have implications beyond medical treatment. However, finding a diagnosis can be an arduous journey, and opportunities for taking early action are often lost during this “diagnostic odyssey”.

While environmental factors and nutritional deficiencies are known causative factors, the largest specific etiology of ID is genetic [4]. When patient history and physical examination do not suggest an obvious syndrome, chromosomal microarray analysis (CMA) is recommended as a first-line test to aid in the diagnostic evaluation of ID by multiple medical societies, including [5,6,7]:

- American Academy of Neurology (AAN)
- Child Neurology Society (CNS)
- American College of Medical Genetics (ACMG)

Medical society guidelines also recommend CMA as a replacement for traditional karyotyping and fluorescence *in situ* hybridization (FISH) because of its:

- Greater sensitivity
- Higher resolution
- Genome-wide capability
- Greater diagnostic yield

The Applied Biosystems™ CytoScan™ Dx Assay was the first FDA-cleared, whole-genome diagnostic test to aid clinicians in identifying the underlying genetic cause of developmental delay, intellectual disability, congenital anomalies, or dysmorphic features in children.



Whole-genome coverage

Designed for today and the future

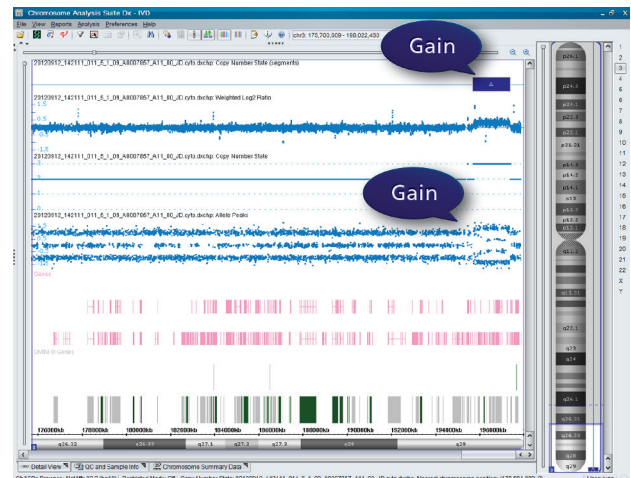
The CytoScan Dx Assay provides high-density whole-genome coverage to deliver higher resolution than karyotyping and more comprehensive coverage than FISH.

- Includes 2.69 million markers for copy number (CN) analysis
 - 750,000 bi-allelic single-nucleotide polymorphism (SNP) probes
 - 1.9 million non-polymorphic markers
- Ensures all genes are covered

Intellectual disability might present itself as the only manifestation of a disease or may be associated with other manifestations causing a clinical syndrome [8]. Techniques like karyotyping, FISH, and array comparative genomic hybridization (aCGH) will miss clinically relevant aberrations.

Case #1: Previously missed clinically relevant aberrations can now be identified

- A 14-year-old female with microcephaly, mild right exotropia, mild ID, ADHD, and a family history of ID presented to the clinic [9]
- Previous testing including aCGH, karyotype, FISH for 22q11, and FMR1 was normal
- CytoScan Dx Assay identified a 1.66 Mb heterozygous gain of chromosome 3q29
- These microarray findings, in conjunction with the clinical evaluation, led to the diagnosis of 3q29 microduplication syndrome, ending the diagnostic odyssey for this family



Helps improve diagnostic yield

More answers

An incremental 12.5% diagnostic yield beyond traditional techniques is possible with CytoScan Dx Assay, allowing for accurate detection of numerous chromosomal variations of different types, sizes, and genomic locations.

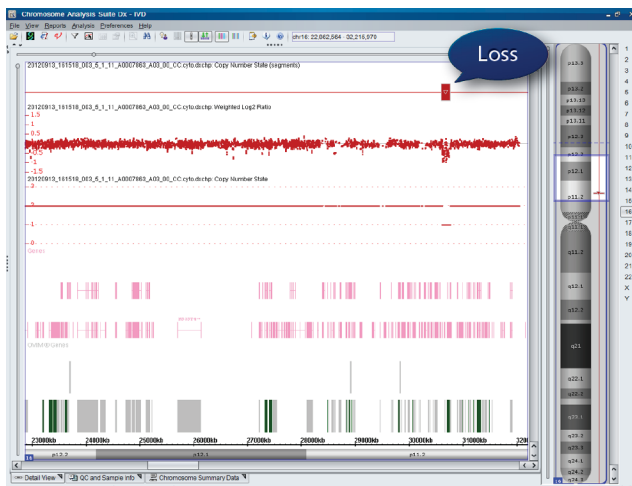
In addition to identifying CN changes, the CytoScan Dx Assay is capable of detecting allelic imbalances and copy-neutral aberrations (e.g., loss of heterozygosity (LOH)), which can be associated with uniparental disomy (UPD) or consanguinity, both of which may pose increased risk for autosomal recessive conditions.

Case #2: The power of high resolution detects small aberrations

- A 2-year-old male with speech delay, development delay (DD), broad nasal bridge, failure to thrive, and abnormal gait (dragging of the left leg) presented to the clinic [9]
- Previous testing including aCGH, karyotype, FISH for 7q11, and FMR1 was normal
- CytoScan Dx Assay identified a 156 kb heterozygous deletion of chromosome 16p11.2
- These microarray findings, in conjunction with the clinical evaluation, led to the diagnosis of Floating-Harbor syndrome

Case #3: SNP probes are informative for copy-neutral aberrations such as LOH

- A 7-year-old female with overgrowth, speech delay, learning disability, fine motor delay, seizures, and a wide mouth presented to the clinic [9]
- aCGH testing was normal
- CytoScan Dx Assay identified a 79.69 Mb region of LOH on chromosome 15q
- These microarray findings, in conjunction with the clinical evaluation, led to the diagnosis of Prader-Willi syndrome



Unrivaled performance

CytoScan Dx Assay



Benefits of CytoScan Dx Assay

Benefit	Description
First-of-its-kind diagnostic test	FDA-cleared and CE-marked postnatal blood test to aid in the diagnosis of: <ul style="list-style-type: none">• Developmental delays• Intellectual disabilities• Congenital anomalies• Dysmorphic features
Analyze the patient's entire genome with one test	Detect numerous chromosomal variations of different types, sizes, and genomic locations at higher resolution than karyotyping and more comprehensively than conventional FISH.
Exceptional performance	Achieve high specificity, sensitivity, accuracy, and resolution across the genome.
Designed for today and the future	The design of the CytoScan Dx Assay, which includes 2.69 million CN markers across the entire genome, helps ensure all genes are represented, not only those identified as currently relevant.
Dual-probe content with high-density SNPs	Containing both CN and SNP probes, the CytoScan Dx Assay elucidates allelic imbalances and identifies LOH which can be associated with UPD or consanguinity, both of which increase the risk of recessive disorders. SNP patterns also provide confirmation of CN changes.

Ask your sales representative about the CytoScan Dx Assay today.

Find out more at thermofisher.com/cytoscandx

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