CytoScan® Dx Assay
To aid in the diagnosis of developmental delay and intellectual disability

Unrivaled performance. Results that matter.

For In Vitro Diagnostic Use
The prevalence of developmental disabilities in US children is 13.87%,¹ and they occur across all racial, ethnic, and socioeconomic groups. Recently, it has been reported that 1 in 33 babies is born with congenital anomalies in the US.² Frequently, developmental delay and/or intellectual disability (DD/ID) is accompanied with one or more congenital anomalies or dysmorphic features. The affected individuals have lifelong challenges, including various medical conditions and difficulties with physical movement, learning, and social interaction.

Early intervention is key to providing better outcomes for children with special needs. Despite this, on average, diagnosis of developmental delay in children does not occur until they have reached the age of four years old.³ Often, certain intellectual disabilities are diagnosed much later, as late as when the child has entered elementary school.

Establishing an underlying diagnosis early can provide physicians and families with knowledge of which disorder is affecting the child, prognosis, and comorbidity information, all of which have implications beyond medical treatment. However, finding a diagnosis can be a lengthy journey, and opportunities for taking early action are often lost during this so-called “diagnostic odyssey.”

While environmental factors and nutritional deficiencies are known causative factors, the largest specific etiology of ID is genetic.⁴ According to the American Academy of Neurology (AAN), the Child Neurology Society (CNS), the American College of Medical Genetics (ACMG), and the International Collaboration for Clinical Genomics (ISCA/ICCG), a chromosomal microarray analysis (CMA) is considered the first-line genetic test to aid in the diagnostic evaluation of ID when patient history and physical examination do not provide an obvious syndrome diagnosis.⁵, ⁶, ⁷

These guidelines for CMA to replace traditional karyotype and fluorescence in situ hybridization (FISH) as first-line genetic testing for unexplained ID are due to its greater sensitivity, higher resolution, genome-wide capability, and greater diagnostic yield.⁶ CytoScan Dx Assay is the first CMA to receive FDA clearance and CE mark.

CytoScan® Dx Assay is the first FDA-cleared whole-genome diagnostic test to aid physicians in identifying the underlying genetic cause of developmental delay, intellectual disability, congenital anomalies, or dysmorphic features in children.
Whole-genome coverage for today and tomorrow

The high-density, whole-genome CytoScan® Dx Array includes 2.69 million markers for copy number (CN) analysis, with 750,000 bi-allelic SNP probes and 1.9 million non-polymorphic markers. CytoScan Dx Assay with its whole-genome coverage delivers higher resolution than karyotyping and more comprehensive coverage than FISH.

Intellectual disability might be present as the only manifestation of a disease or may be associated with other manifestations causing a clinical syndrome. Some syndromes are genetically heterogeneous and may be caused by aberrations in several genes with distinct roles in common biological pathways like Rubinstein-Taby Syndrome (RTS).

CytoScan Dx Assay detects chromosomal aberrations across the whole genome

- This example illustrates two interstitial duplications: in blue, a 5 Mb duplication in 15q11.2->15q13.1; in red, a 1 Mb hemizygous gain in 16p13.11- >16p13.11.
- Due to the high density of non-polymorphic (copy number) probes and polymorphic (SNP) markers in the array, the copy number changes can be visualized in the Log2 ratio track as well as confirmed in the allelic difference track.
- These microarray findings, in conjunction with clinical evaluation, led to a diagnosis of 15q11 microduplication syndrome.

References
CytoScan® Dx Assay can accurately detect numerous chromosomal variations of different types, sizes, and genomic locations. In addition to identifying copy number changes, CytoScan Dx Assay is capable of detecting allelic imbalances and copy number neutral abnormalities such as AOH/LOH that can be associated with uniparental disomy (UPD) or consanguinity, both of which may pose increased risk for autosomal recessive conditions.

**For improved diagnostic yield, detect more chromosomal aberrations at high resolution in a single assay**

CytoScan Dx Assay detects chromosomal aberrations of different sizes

This example shows two samples each with a hemizygous loss of 515 kb and 83 kb in cytoband 16p13.3 (indicated by red segments) that included the CREBBP OMIM gene. Both of these patients were diagnosed with Rubinstein-Taybi syndrome (RBS) based on clinical evaluation and CMA findings.

CytoScan Dx Assay detects copy-neutral chromosomal aberrations

- Left, a sample with many LOH/AOH regions larger than 3 Mb, which may reflect consanguineous origin.
- Right, a clinically diagnosed Angelman syndrome sample with a typical LOH/AOH block, which is often caused by iso-UPD in this syndrome. In this particular case, the LOH/AOH spans the whole q-arm and is 79 Mb long.
- Individuals with large blocks of LOH/AOH may be at an increased risk for autosomal recessive conditions.
Unrivaled performance
CytoScan® Dx Assay

First of-its-kind diagnostic test
FDA-cleared and CE marked postnatal blood test to aid in the diagnosis of developmental delay, intellectual disabilities, congenital anomalies, or dysmorphic features.

Analyze the patient’s entire genome with one test
Accurately detect numerous chromosomal variations of different types, sizes, and genomic locations at higher resolution than karyotyping and more comprehensively than conventional FISH.

Exceptional performance
High specificity, sensitivity, accuracy, and resolution across the genome.

Designed for today and the future
The design of CytoScan Dx Assay, which includes 2.69 million functional markers across the entire genome, ensures that most genes are represented, not only those identified as currently relevant.

Dual probe content with high-density SNPs
Containing both CN and SNP probes, CytoScan Dx Assay can elucidate allelic imbalances and identify LOH/AOH that can be associated with uniparental disomy or consanguinity, both of which increase the risk of recessive disorders. SNP patterns also provide confirmation of copy number changes.

Streamlined data analysis
Chromosome Analysis Suite Dx (ChAS Dx) Software has an intuitive graphical interface for streamlined analysis workflows, ISCN 2013 array nomenclature, and links to databases* to support data analysis workflows.

*Links in ChAS Dx Software to external databases such as Database of Genomic Variants (DGV) have not been evaluated or curated by Affymetrix, Inc.
GeneChip® System (GCS) 3000Dx v.2
Flexible, proven, powerful

GeneChip® System (GCS) 3000Dx v.2 is the most robust system for clinical research and the only FDA-cleared, IVD and CE marked microarray system for RNA- and DNA-based clinical tests. This industry-leading GeneChip® instrumentation system combined with innovative assays provides a complete platform for hybridizing, washing, staining, and scanning of microarrays. CytoScan® Dx Assay must be run on GeneChip System 3000Dx v.2. GeneChip System (GCS) 3000Dx v.2 includes GeneChip® Scanner 3000Dx v.2 with AutoLoaderDx, GeneChip® Fluidics Station 450Dx v.2, and Workstation with Affymetrix® Molecular Diagnostic Software (AMDS). A hybridization oven that meets specifications is available through Affymetrix.

- Easy-to-use system for rapid adoption of both RNA and DNA applications
- Automated processing for increased data reproducibility and reduced hands-on time
- Cost-effective approach enabling multiple assays on a single flexible system

Ordering information

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<tr>
<td>902420</td>
<td>CytoScan® Dx Assay Kit</td>
<td>Sufficient for 24 samples</td>
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<tr>
<td>902450</td>
<td>CytoScan® Dx Training Kit</td>
<td>Includes arrays, reagents, and control samples necessary to perform the CytoScan® Dx Assay Training</td>
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World-class support

Affymetrix offers an expanding portfolio of customer support and services—from training and instrument maintenance to consulting—led by our world-class team of multilingual technical experts, field application scientists (FAS), and regional field service engineers (FSE). For more information please visit www.affymetrix.com/service.

WARNING: This device is not intended to be used for standalone diagnostic purposes, pre-implantation or prenatal testing or screening, population screening, or for the detection of, or screening for, acquired or somatic genetic aberrations. Interpretation of assay results is intended to be performed only by healthcare professionals, board certified in clinical cytogenetics or molecular genetics.