OPTIMIZING EFFICIENCY ACROSS CYTOGENOMIC APPLICATIONS

Illumina's Infinium™ Global Diversity Array with Cytogenetics (GDACyto) Coupled with Bionano's N_xClinical™ Analysis Software

Current ACMG Guidelines recommend microarray as a 1st line test for constitutional genetic abnormalities.[1] As a result, high-density SNP and aCGH arrays are the most common platforms for cytogenetic analyses. Unfortunately, the standard microarray designs being used for cytogenetic analysis today were designed years ago and thus do not represent current clinically relevant knowledge. Figure 1 below shows the continuing changes of new and updated entries in the OMIM Gene Map database over the past twenty years.

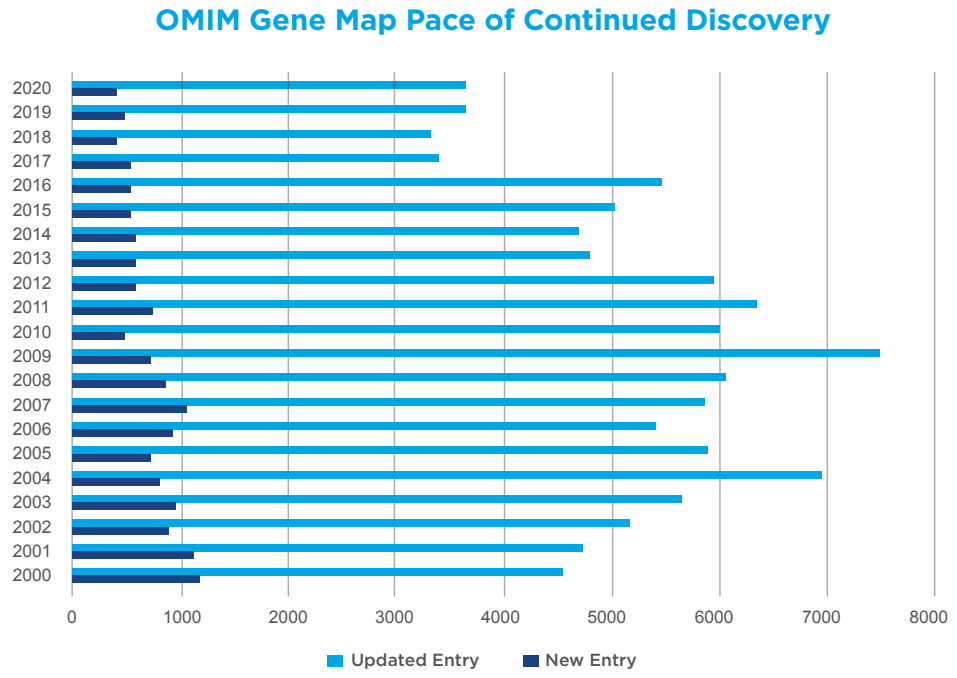


Figure 1: Online Mendelian Inheritance in Man, OMIM®. https://omim.org/statistics/update

[1] *Miller DT, Adam MP, Aradhya S, et al. Consensus statement: chromosomal microarray is a first-tire clinical diagnostic test for individuals with developmental disabilities or congenital anomalies. Am J Hum Genet. 2010.86(5): 749-764. doi:10.1016j.ajhg.2010.04.006*

Design Strategy for GDACyto

The design of the GDACyto array captures the latest insights on gene disease. The array focuses on cytogenetically important genes/regions while providing exon level coverage and a strong backbone from which to make CNV and AOH calls. This single array offers the ability to screen for genetic mutations across a variety of applications including prenatal, postnatal, and oncology. The GDACyto array yields high-quality results from diverse sample types including (but not limited to) blood, prenatal tissues, amniotic fluid, bone marrow, buccal cells, and formalin fixed paraffin embedded (FFPE) tissues. The GDACyto array also serves as a robust complementary assay to next generation sequencing (NGS) results such as whole exome sequencing (WES), whole genome sequencing (WGS), targeted gene panels, or low-pass sequencing.

SOURCE	GENES
OMIM Morbid	4192
DDG2P	1036
Oncology	522
ExAC Loss Intolerant	1063
OMIM Non-Morbid	15,228

Table 1: Genes with Disease Associations Covered by GDACyto

A Trusted, Proven Genomics Software Provider

For more than 20 years, software from BioDiscovery, a Bionano Genomics® company, has enabled clinical and research labs around the world to analyze and interpret genomic data all the way through to high-quality reports. Today, N_xClinical software is a comprehensive solution for analysis and interpretation of microarray or NGS generated data by integrating CNV, AOH, and Sequence Variant data into a single comprehensive interface.

Key Benefits of N_xClinical

Platform Versatile	Validated platform for CNV detection of microarray and NGS data
Intelligent Variant Interpretation	***Pre-classification*** rules pre-label variants. *Filtering* rules to streamline review. ***Phenotype Associated Variant Ranking***
SNV/AOH/CNVs	Review sequence variants, AOH and copy number events
Useful Databases	Leverage historical case data & up to date, curated ***clinical variant*** annotations
Consistent, Accurate Results	Industry-standards algorithms, tools, audit trail, and admin controls ensure the highest standard of accuracy
Data Visualization	Best-in-class ***raw data visualization*** down to a single base, customized to fit your workflow

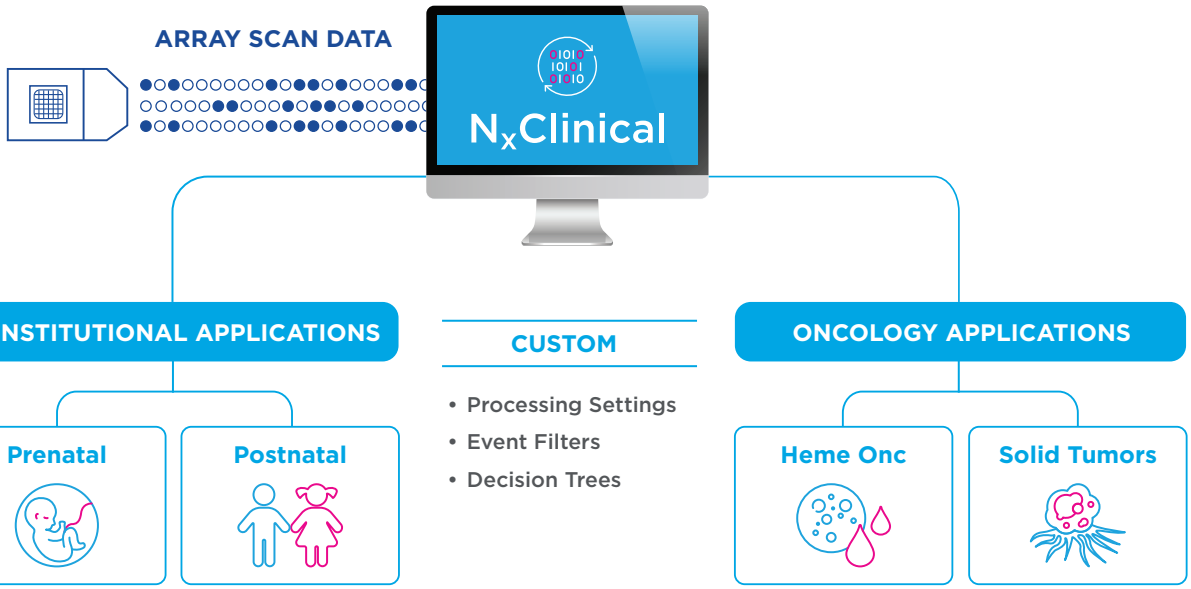
Triaging Sample Processing According to Application

The GDACyto design provides high-resolution analysis across a high breadth of genes relevant to multiple applications, which enables laboratories to benefit from consolidating workstreams to a single array and increase efficiency. Since samples from multiple applications can be combined on a single array run, a different analysis will be required for each sample type. N_xClinical software enables the differential analysis of each sample according to the appropriate processing settings for the respective application type. This ensures that the desired level of resolution is maintained for the sample type. Examples of the broad spectrum of anomalies detected by the combined solution are below.

Configurable Analysis in N_xClinical Software Optimized for Each Application

Multiple Applications on One GDACyto Beadchip

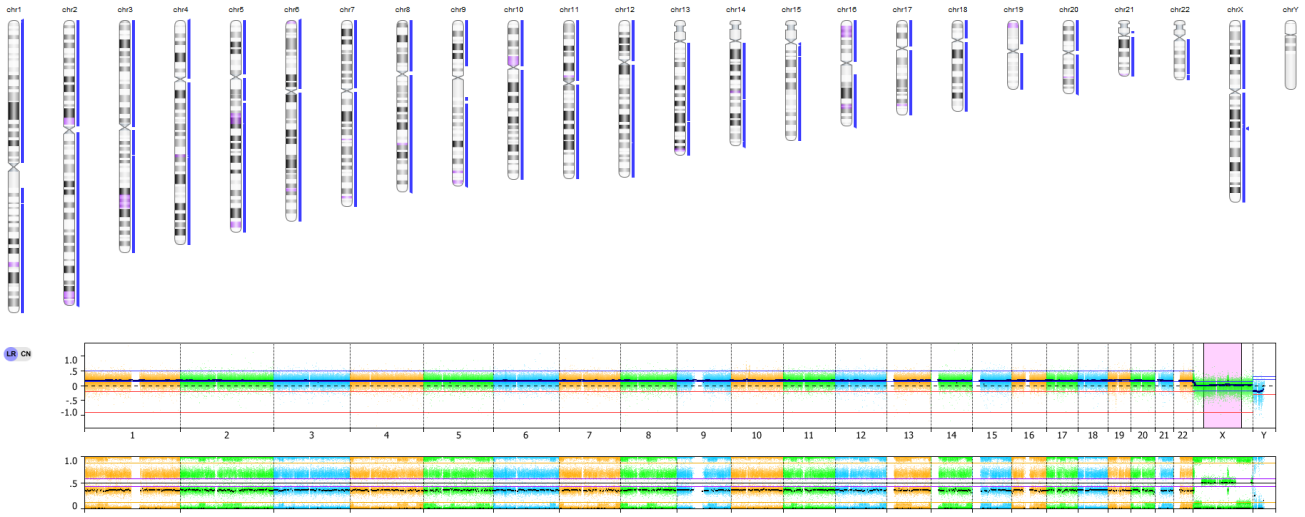
Prenatal | Heme Onc | NGS Confirm
Postnatal | FFPE | WGS QC



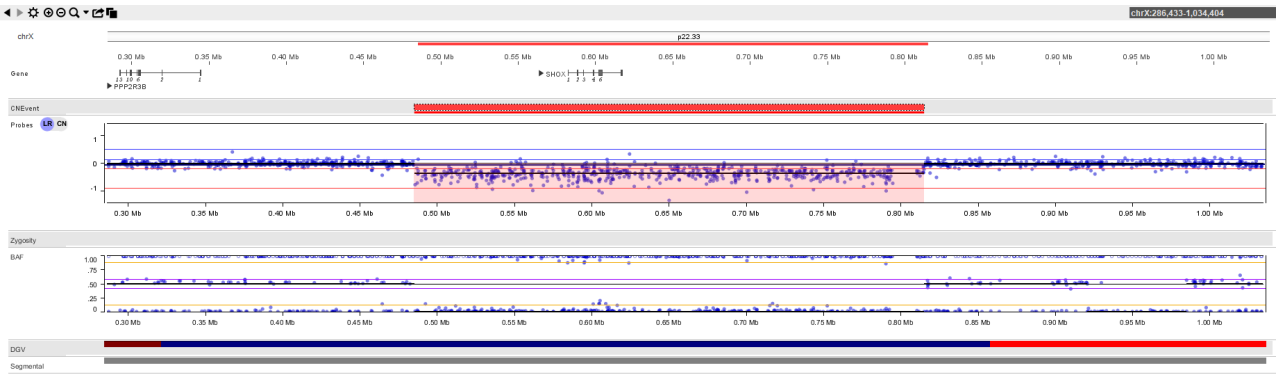
For Research Use Only. Not for use in diagnostic procedures.

Enhanced Visualization of Prenatal, Postnatal, Heme Onc, and FFPE Sample Data

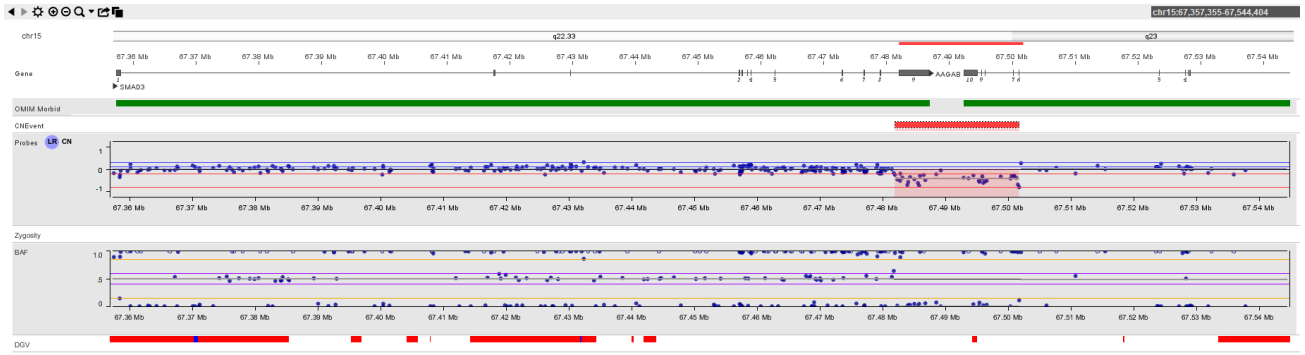
GDACyto example of a prenatal product of conception specimen clearly displaying a 69, XXY triploid genome pattern.



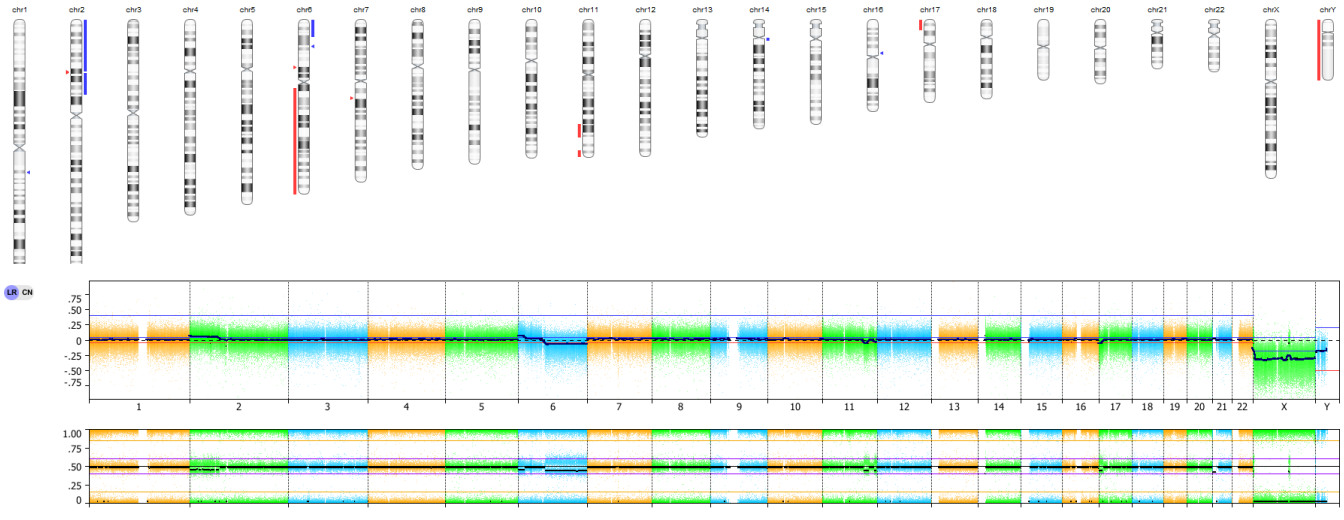
GDACyto example of a peripheral blood specimen demonstrating a ~330kb deletion of the SHOX gene on the PAR1 region of chromosome X, associated with the X-linked dominant disorder Leri-Weill dyschondrosteosis.



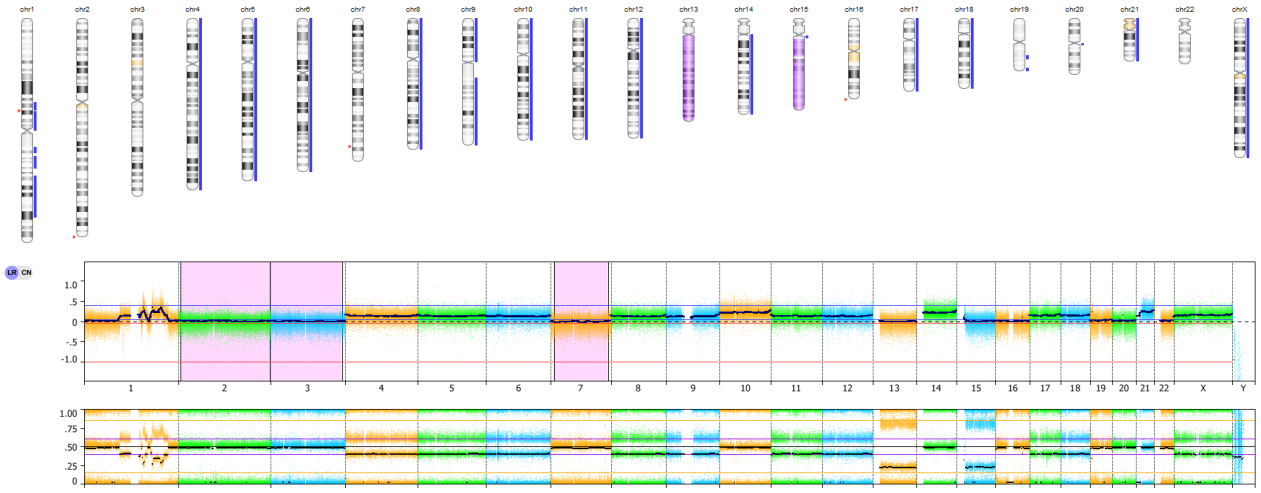
GDACyto example of a peripheral blood specimen from a pediatric constitutional sample demonstrating a 20kb copy number loss resulting in the partial deletion of genes SMAD3 and AAGAB.



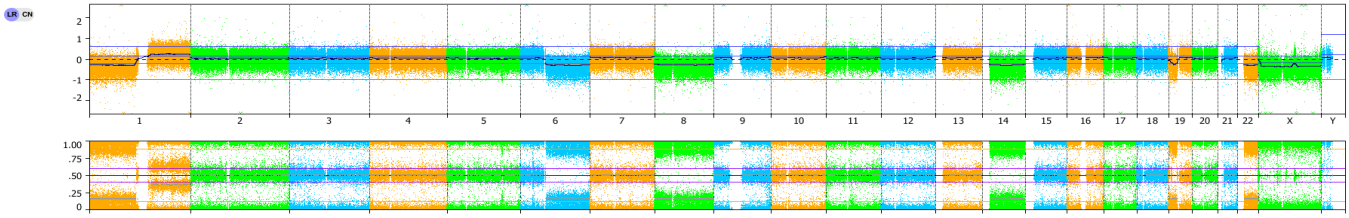
GDACyto example of a bone-marrow specimen indicated for B-Cell Acute Lymphoblastic Leukemia demonstrating multiple chromosomal abnormalities at ~30% aberrant cell fraction.



GDACyto example of a bone-marrow specimen indicated for demonstrating genomic hyperploidy. The highlighted purple shaded areas were selected for manual recentering of the genomic profile.



Formalin-fixed paraffin-embedded solid tumor DNA restored with Illumina's Infinium FFPE DNA Restoration Solution and processed on the GDACyto in N_xClinical showing multiple chromosomal anomalies.



Summary

GDACyto offers genome-wide coverage at exon resolution across high-value clinical regions, and when coupled with N_xClinical software, enables laboratories to review cases faster and remain more economical than current workflows.

For general information about N_xClinical 6.2, please contact:

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