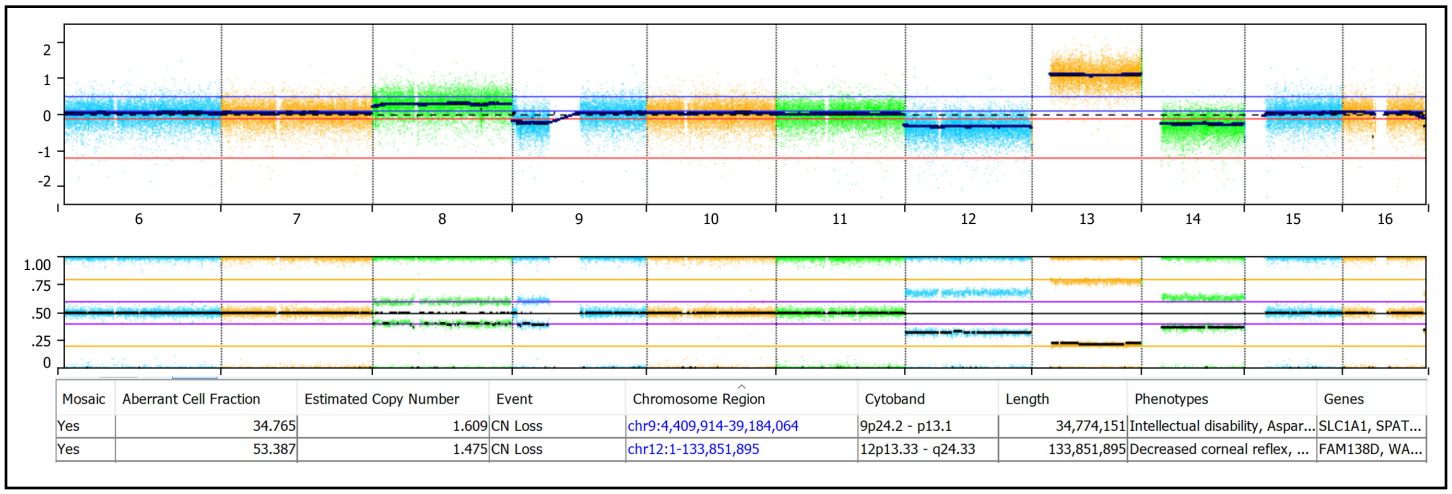
BioDiscovery

N_XClinical is a platform-independent software solution for genetic data analysis, interpretation, management, and reporting for cytogenetics labs. Best-in-class algorithms, customizable settings, efficient processing, fast data retrieval, and automation provide for an accurate and speedy case review process.



Mosaic	Aberrant Cell Fraction	Estimated Copy Number	Event	Chromosome Region	Cytoband	Length	Phenotypes	Genes
Yes	34.765	1.609	CN Loss	chr9:4,409,914-39,184,064	9p24.2 - p13.1	34,774,151	Intellectual disability, Aspar...	SLC1A1, SPAT...
Yes	53.387	1.475	CN Loss	chr12:1-133,851,895	12p13.33 - q24.33	133,851,895	Decreased corneal reflex, ...	FAM138D, WA...

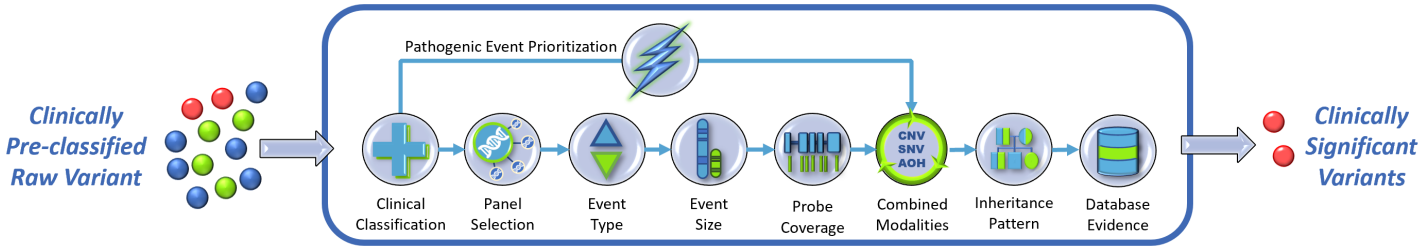
Zoomed in whole-genome view of log ratio (top) and BAF (bottom) plots. Note the different allele patterns on 9p and chr 12 losses indicating different percentages of mosaicism. The report table shows the estimated copy number and aberrant cell fraction which is auto-calculated by N_XClinical and is at about 35% for mosaic deletion 9p24.2p13.1 and about 53% for mosaic deletion of chr12.

Consistency and accuracy in event calling

- CNV calling algorithms for accurate calls even from wavy and noisy data
- Automated pipelines for loading, processing, and pre-classification of different sample types
- Consistency in mosaic calling with ability to adjust the calling algorithm sensitivity
- Platform agnostic to support any array or NGS platform

Faster turnaround time with automation and intelligent filtering

- Variant interpretation assistance system pre-classifies events based on regional guidelines (e.g. ACMG) to speed up the interpretation process
- Intelligent dynamic filtering minimizes false negative results and trims the list of potentially causative variants from thousands to a handful
- Machine learning approach uses classified events in automated case history review to classify new cases
- Phenotype-driven variant prioritization (SAP scoring) using standardized vocabulary (HPO) quickly ranks clinically relevant events

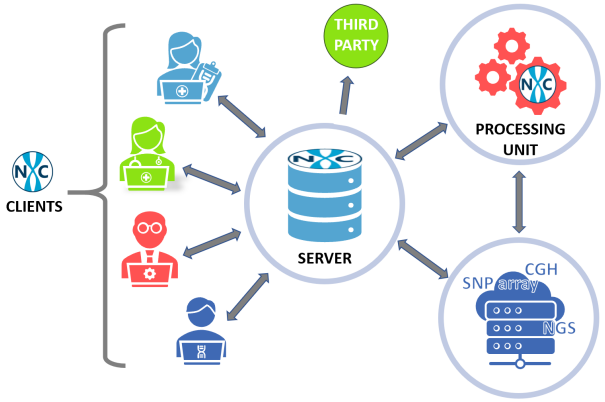


Accurate reporting with regular annotation and reference data updates

- Integration of numerous external databases to aid with interpretation. Databases include OMIM*, DECIPHER, ClinGen (Prenatal, Postnatal, Dosage Sensitive), CIViC, Segmental Duplications, and more
- Clinical databases and internal annotations (e.g. HPO) are regularly updated to provide the latest information for a thorough and accurate review process
- Ability to customize by adding lab specific gene lists

Transparency and traceability

- A single central repository accessible from anywhere
- Efficient retrieval, processing, and display of results
- Multi-user environment with role-based user privileges
- Audit trails (every action is logged with user and timestamp)
- Client-server architecture with unlimited users
- Features enabling compliance with reporting guidelines



Dynamic and interactive visual interpretation tools

- Family based analysis (duo/trio) with mode of inheritance and parent-of-origin identification
- Mosaicism and aberrant cell fraction analysis with estimated copy number and % aberrant cells
- Virtual gene panels for reviewing specific gene lists or to avoid incidental findings
- Interactive genome browser with log ratio, probe plots, similar events in case history, etc.

Trio example: Dup 22q11.21 (highlighted blue region) inherited from a maternal allele (pink SNP probes in the BAF track).

A single integrated solution that saves time, money, and increases diagnostic yield

The N_XClinical system is "future-proof" with numerous features to keep a lab running smoothly today and tomorrow within a fast-paced evolving environment

- Pioneering BAM MSR algorithm for CNV detection from NGS data makes high-fidelity calls from WES, WGS, and targeted panels allowing facility in shifting from microarrays to NGS should the need arise
- Ability to annotate and interpret sequence variants and integrate with CNV and AOH calling for increased diagnostic yield particularly useful for complex and reflexed cases
- Platform agnostic nature allowing easy transition from one array platform to another without having to learn to use and invest in new tools

*This software is designed to assist clinicians and is not intended as a primary diagnostic tool. It is each lab's responsibility to use the software in accordance with internal policies as well as in compliance with applicable regulations.

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