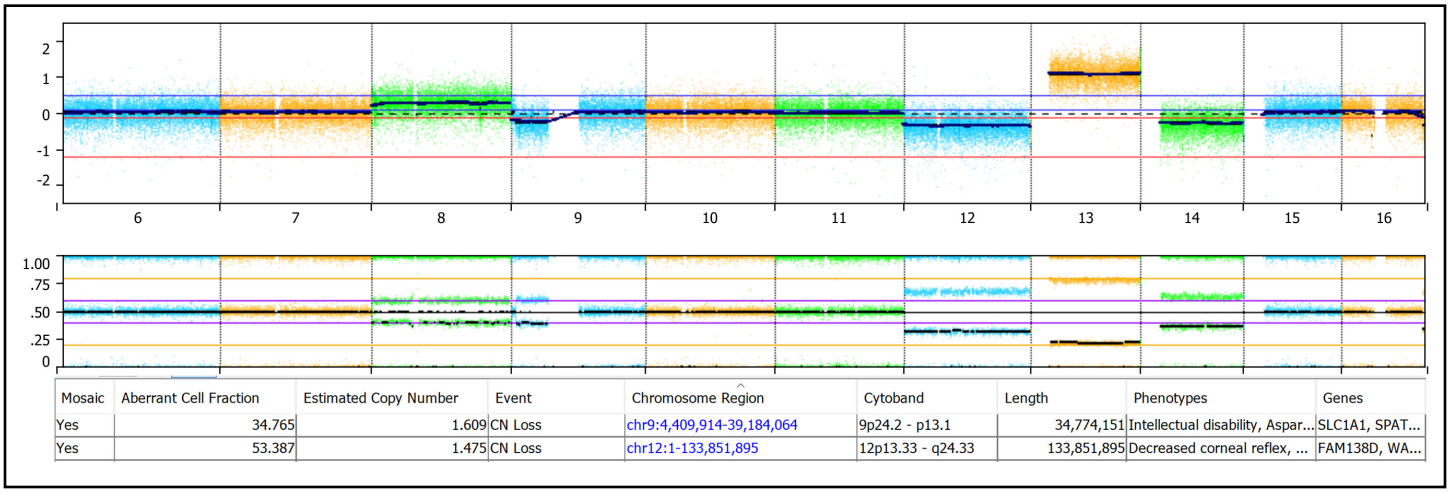
BioDiscovery

$N_X$Clinical is a platform-independent software solution for genetic data analysis, interpretation, management, and reporting for cytogenetic and molecular genetic 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... |

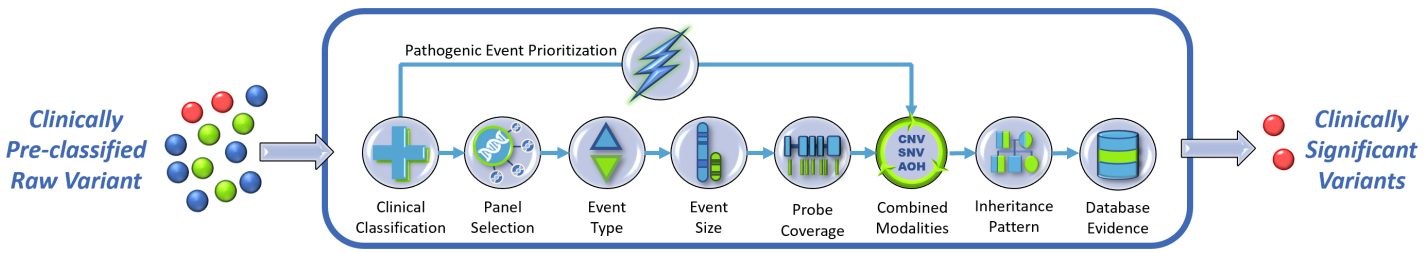
Zoomed in whole-genome view of log ratio (top) and BAF (bottom) plots. Note the different allele patterns on 9p and chr 12 losses indicating different percentages of mosaicism. The report table shows the estimated copy number and aberrant cell fraction which is auto-calculated by $N_X$Clinical and is 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

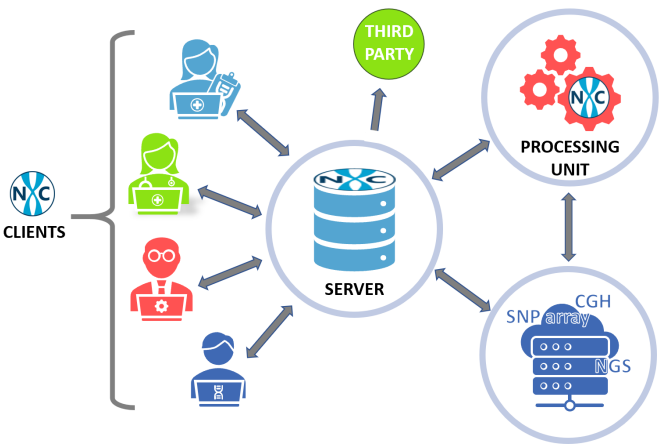


## Accurate reporting with regular annotation and reference data updates

- 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

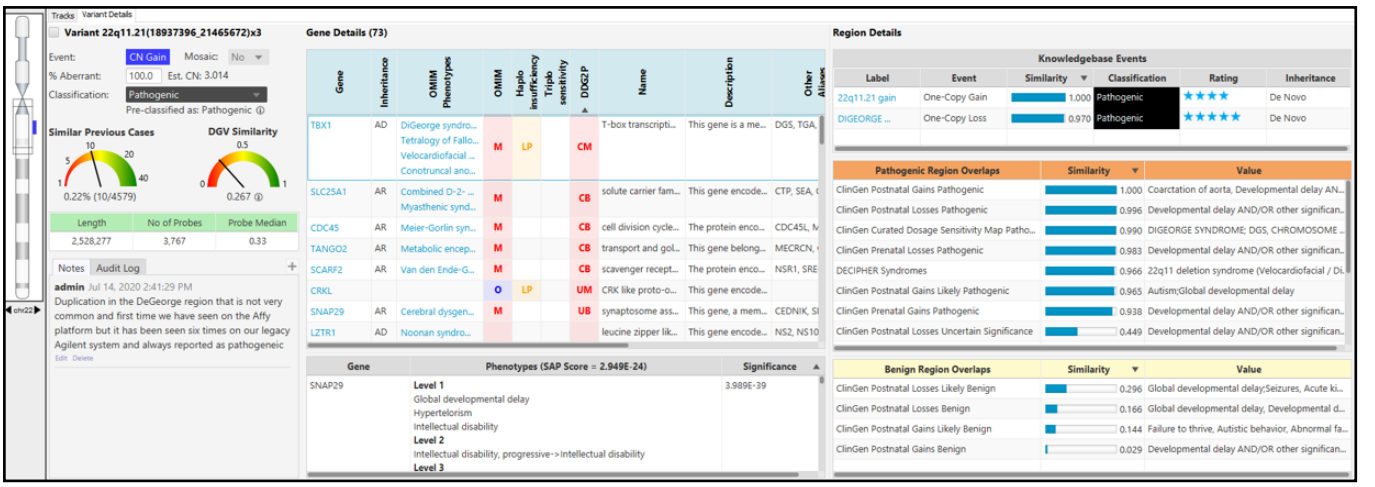
- Family based analysis (duo/trio) with mode of inheritance and parent-of-origin identification
- Mosaicism and aberrant cell fraction analysis with estimated copy number and % aberrant cells
- Virtual gene panels for reviewing specific gene lists or to avoid incidental findings
- Interactive genome 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).

*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.

## Increase the efficiency of your case review using the new Variant Details Tab

- This view presents all the important information needed in evaluating an event together on a single screen to allow quick and confident interpretation of variants
- The layout automatically adjusts to the type of variant (e.g. CNV vs. Seq Var) as well as test type (Oncology vs. Constitutional)

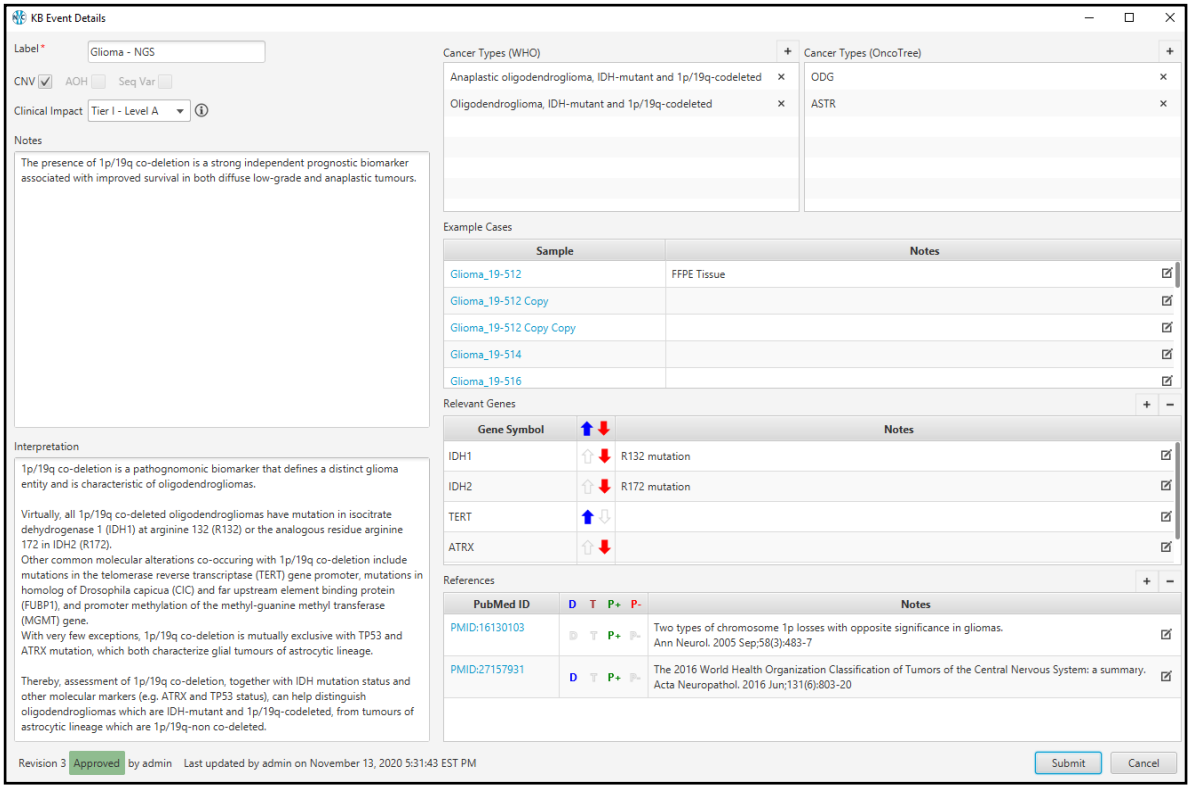



Variant Details Tab - Constitutional Sample - CNV Event. The Variant Details Tab is also available for Oncology tests.

## Create your own bespoke Knowledgebase to store variant and genomic region information

Allow the laboratory to collect, organize, and use CNV and AOH events from its own constitutional or oncology case history to create consistent interpretations and reports

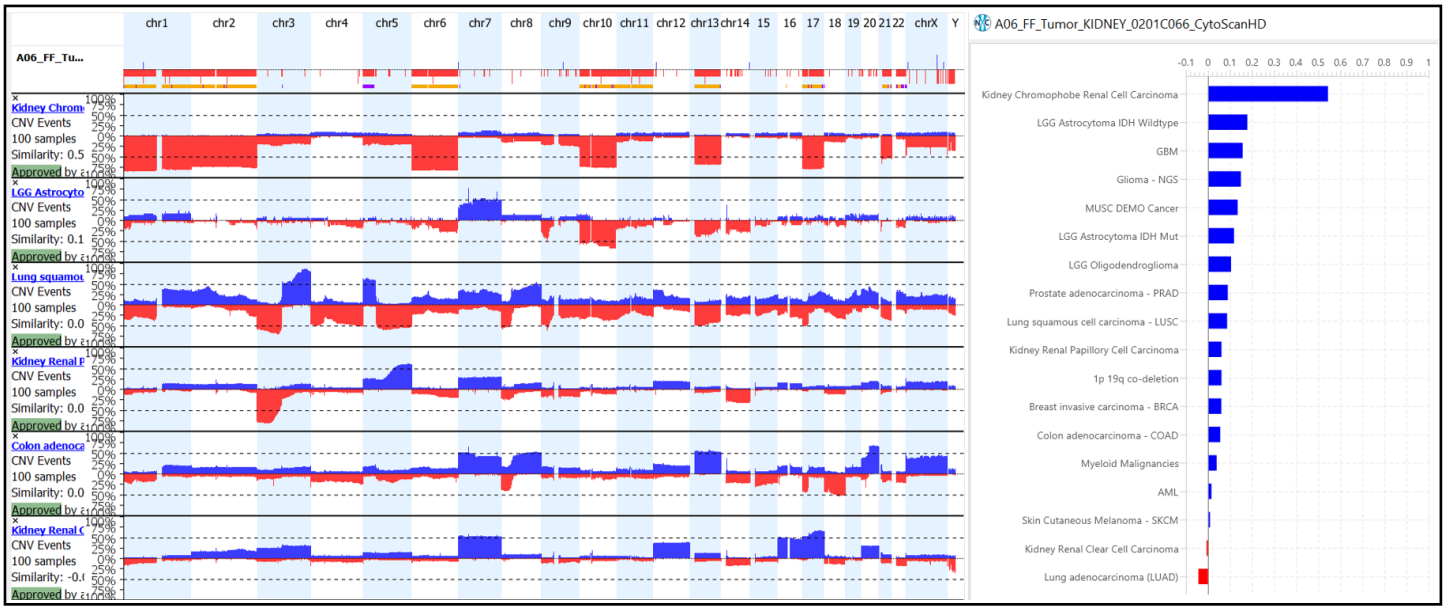
- The KB supports two distinct types of tests - "Oncology" and "Constitutional" - each containing fields unique to the specified test type
- For Constitutional tests, the KB holds information such as relevant genes in the region, mode of inheritance, publication IDs and notes for each publication, interpretation texts, general comments, classification, etc. (see view below)
- For Oncology tests, the KB holds information such as classification based on the AMP guidelines, interpretation, notes, associated PubMed IDs, whether the event is diagnostic, prognostic, or therapeutic, etc. (see view below)




Oncology Knowledgebase entry example. The Knowledgebase is also available for Constitutional tests.

## Build and utilize genome-wide CNV and AOH profiles for different cancer types to assist in tumor diagnosis and interpretation

- Enable the creation of genome-wide CNV and AOH "profiles" in the knowledgebase with associated interpretation, publication links, and relevant gene content.
- Compare a sample under review with all other profiles stored in the knowledgebase using unique genome-wide similarity metric to gauge similarity to other cancer types




(Left image) Profile Comparison window shows genome-wide CNV/AOH pattern of a single sample compared aggregate profile for different sample cohorts

(Right image) Global Similarity function compares a sample against all saved profiles to generate following plot

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

The $N_X$Clinical 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