

C A S E S T U D Y

NxClinical Software Increases Efficiency in the Reporting Process at CombiMatrix | Invitae

NxClinical software significantly improves efficiency and turnaround time at CombiMatrix\Invitae, a clinical diagnostic laboratory, and provides the laboratory a robust system for data management, analysis, and interpretation of genomic changes.

N_xClinical Software Increases Efficiency in the Reporting Process at CombiMatrix / Invitae

Introduction

CombiMatrix is a clinical diagnostic laboratory specializing in cytogenomic testing for prenatal diagnosis, pre-implantation genetic testing, miscarriage analysis, and pediatric developmental disorders. As a full-scale cytogenetic and cytogenomic laboratory, CombiMatrix offers chromosomal microarray analysis, copy number analysis by Next Generation Sequencing (NGS), standard and customized FISH, and high resolution karyotyping. While CombiMatrix uses different technologies such as NGS and SNP arrays, this case study focuses on the Illumina SNP array platform used for their pediatric, prenatal and products of conception (POC) tests.

As a high volume diagnostic laboratory, the clinical team at CombiMatrix processes various sample types for copy number either by microarray or NGS analysis. The array result from each specimen undergoes a multi-tier review by Clinical Laboratory Scientists (CLS), Laboratory Directors, and Genetic Counselors. The company's goals include accurate identification of genomic variants and quick and efficient delivery of results to clients.

Challenge

Prior to implementation of N_xClinical, CombiMatrix's data processing and interpretation workflow was extremely laborious and time consuming, and required many manual quality control steps to ensure accuracy. Additionally, lack of an efficient centralized database system limited the ability to leverage previous case information and share data among all laboratory staff. Finally, the lab required access to up-to-date reference databases which came at a significant cost and required additional man hours to maintain.

CombiMatrix utilized BioDiscovery's Nexus Copy Number software for the secondary and tertiary analysis. The software used well-accepted algorithms for analysis and interpretation but was not designed specifically for use in a cytogenomic laboratory and therefore lacked many features (such as a centralized multi-user database, audit trail recording, and automated workflows following SOPs) that are immensely valuable to such labs.

Quick Glance

N_xClinical software significantly improves efficiency and turnaround time at CombiMatrix, a clinical diagnostic laboratory, and provides the laboratory a robust system for data management, analysis, and interpretation of genomic changes.

Each CLS saved two hours per day after implementation of N_xClinical

Additional Benefits:

- A centralized database system to leverage past cases
- Automated protocol-based data loading and processing that reduced potential human errors
- Extensive audit-trail to track all changes during sample review
- Multi-user access
- Access to up to date OMIM[®] data without additional cost

Each type of test (e.g. pediatric, prenatal, POC) required a different set of processing and analysis parameters which needed to be set manually each time a sample was loaded and processed. This time-consuming process required extensive secondary quality control to ensure that the correct processing settings were applied for each sample type.

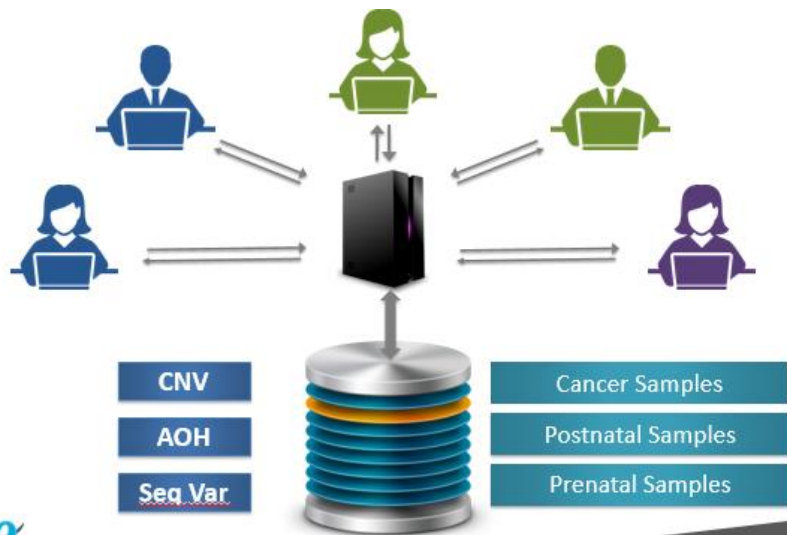
Because each individual user maintained and updated a separate installation of Nexus Copy Number and separate annotation database versions, great care and staff time was expended to ensure all users had the same version of the software and annotation files (e.g. tracks) to avoid any inconsistencies. In addition, the software did not provide updated access to the OMIM® database which was crucial to CombiMatrix's clinical decision process, thus forcing upon the lab additional costs to obtain their own separate license.

Solution and Implementation

CombiMatrix needed a much more robust system with centralized system management, multi-user access, and a streamlined workflow for maximum efficiency. The features that were most important to CombiMatrix included

- A database for sample management and quick retrieval
- Automation for data loading and processing
- Multi-user access with audit trail
- Up-to-date reference data such as the OMIM database

“We had been using Nexus Copy Number for the past ten years for its ease of use and accurate calling. When we first chose that software, we evaluated several other products and Nexus Copy Number was the best product available at the time,” said Dr. Karine Hovanes, Laboratory Director and Vice President of Scientific Advancement at CombiMatrix. “We had been very happy with the results provided by this software but needed additional features to improve the overall efficiency and experience in the lab. We decided to utilize NxClinical because it provided additional valuable features to improve our processes.”



Implementation of NxClinical was a straight forward and quick process as it required two weeks to set up the system and perform validation. After installation and initial configuration, CombiMatrix's entire historical case database was loaded into the NxClinical database over a period of two days. An additional day was utilized to set up sample types and their associated processing settings and workflows within the Administrator account. Once configured for

analysis, the software clients were installed on the lab workstations as well as Directors' computers. This process was quick and clients were up and ready to use NxClinical immediately without requiring additional configurations.

Software validation was performed by re-analyzing raw data for 20 samples and comparing to original results. After data verification yielded equivalent data quality and equivalent calling algorithm results, a multi-day side by side validation was performed using clinical runs with hundreds of samples, where raw data was analyzed on prior software and NxClinical. Validation results indicated accurate, reproducible, and high quality results. Training the operation staff was a quick process as well, since most of the analysis was automated and hands-off process.

Results

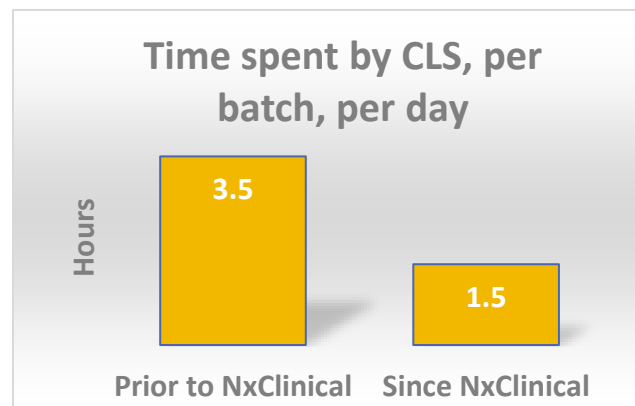
Once NxClinical was successfully deployed into CombiMatrix's production line, the entire process was much more efficient, providing savings in time and money.

Enhanced Sample Management

A secure NxClinical database now houses all samples and allows easy retrieval by searching based on sample name, type, aberration, etc. In addition to being able to query and filter samples, a huge amount of time is saved as there is no need for creation of a complex folder structure and extensive QC in the data organization effort.

Raw Data to Reporting in Less than Half the Time

Time savings were noted immediately across different areas. Previously a batch of 32 samples took 3.5 hours of a CLS's time each day. With NxClinical, it now takes only 1.5 hours, a savings of two hours per day. CombiMatrix's Manager of Research and Development, Natasa Dzidic added, "Time savings here are immensely valuable to us as CLSs are expensive and must perform certain steps in the workflow. CLS can now process more samples in the same amount of time allowing us to easily scale up our operation."



Access to Updated OMIM Database

With NxClinical, several public databases (e.g. ClinGen and OMIM®) are available and routinely updated. One such dataset that was critical to CombiMatrix was the OMIM database. Prior to NxClinical, inquiring the OMIM database was laborious since access to the live database was associated with a significant cost. NxClinical solved the problem in not only providing the updated OMIM data that was critical but it also eliminated CombiMatrix having to manage updates of this data.

Simultaneous Access to Software

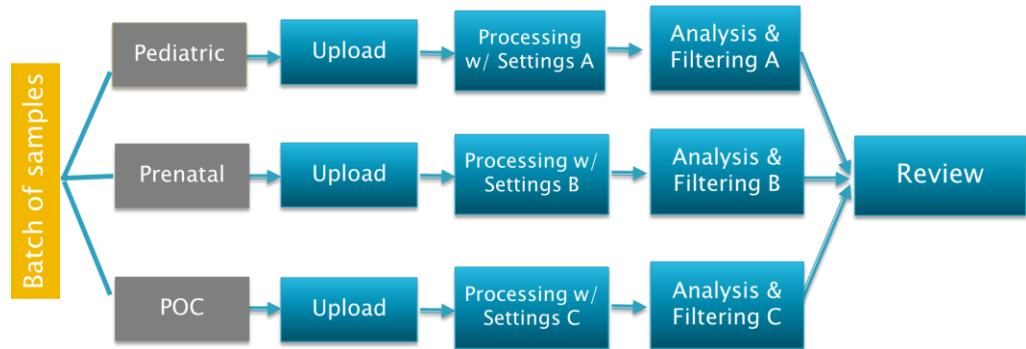
Users no longer have to wait for software to be available to continue with their work. With the server-based NxClinical system, all users at CombiMatrix can concurrently access the system from any location for no additional charge. With the extensive audit trail features, each reviewer can see exactly what changes/comments another reviewer has made.

Reduction in Errors with Automated Loading and Processing

NxClinical eliminated many repetitive and manual tasks that were prone to human error. Now that a single Administrator sets the processing protocol for each sample type based on the type of test and array platform, the CLS does not have to change parameters each time a sample is uploaded. This enables

1. Consistency - samples of the same type have the same parameters applied to them.

2. Accuracy - the settings are automatically applied based on the sample type, so no human error is introduced.



3. Multi-tasking - processing occurs automatically; moreover, the software is available for other tasks during the processing time.

Ease in Managing and Updating Software

Previously, maintaining consistency in software versions and annotations across workstations was time consuming, as each workstation needed to be updated separately. Now the NxClinical Administrator controls installation and updates and only one data repository is maintained which also holds all the annotation files. The Administrator decides when to update the server and then deploys updates to all users automatically so that everyone is working with the same software version and same annotation files.

Looking Forward

In the short time since deployment, CombiMatrix has made impressive gains in efficiency. A batch of samples now takes two hours less to process, the lab can easily and confidently adhere to its SOPs, more samples can be processed in the same amount of time without the need for increased personnel, and the team is less taxed with the effortless workflow provided by NxClinical. The lab isn't yet using NxClinical's capabilities fully. "We have been extremely pleased with the results since deploying NxClinical and our next plan is to implement the Variant Interpretation Assistance feature in NxClinical. By entering our lab-specific rules to automatically pre-classify the commonly detected events via the decision tree, we will save time during data interpretation and reporting. I'm confident that we will gain additional efficiency." said Natasa Dzidic.