

# BlueFuse™ Multi Analysis Software for Molecular Cytogenetics

A powerful software package designed to detect and display areas of potential chromosomal abnormality within the genome.

#### Highlights

#### · Seamless Data Comparison

All tables and charts linked within the software for easy viewing

#### · Confident Answers

Optimized and validated algorithms and automated analysis provide user-independent results

#### · Scalable Software Platform

Single software package, with multi-user capabilities, provides data and information management solutions

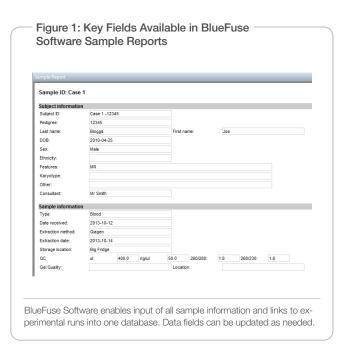
#### Introduction

Developmental delay is a common condition affecting 1–3% of the population¹. A number of causative disorders, including Down, Cri-Du-Chat, DiGeorge, and Williams syndromes, are known to have an associated genetic or chromosomal abnormality. Recent advances in microarray screening technologies have enabled identification of further chromosomal microdeletions and microduplications as the cause of many other developmental delay disorders, expanding our understanding of this complex condition.

To support the study of cytogenomic-relevant genes associated with congenital disorders, Illumina offers the Infinium® CytoSNP-850K BeadChip. Providing a truly complete solution, the BeadChip includes a license for BlueFuse Multi Analysis Software. BlueFuse Software offers automated batch import from the primary scanner files, data processing and segmentation using validated algorithms, and automatic report generation for fast sample turnaround time and confident results reporting.

## **Efficient Multiuser Software**

BlueFuse Multi is a sophisticated software for analyzing and interpreting results from molecular cytogenomic studies. Results of each analysis are stored and accessed in a multiuser shared database. BlueFuse Software supports data import from CytoSNP BeadChips, CytoChip Oligo arrays, and CytoChip Focus arrays for both copy number and AOH (absence of heterozygosity) analysis, if applicable. With automated microarray processing, single-click



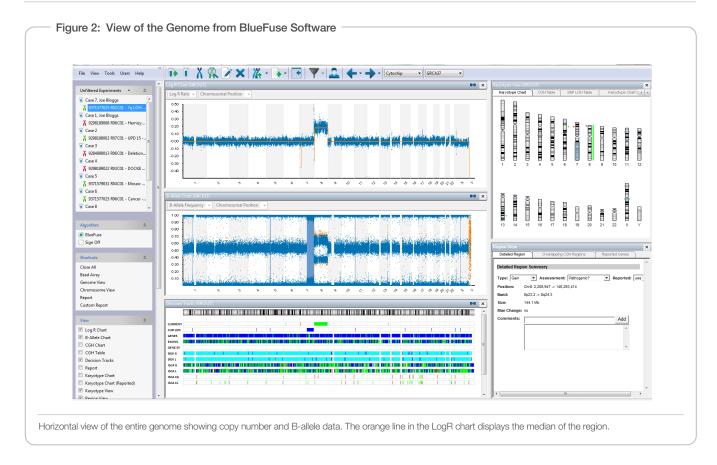
batch import to reporting, and a clear, intuitive user interface, BlueFuse Software generates accurate, user-independent results quickly and efficiently.

# Simple Sample-to-Sample Comparisons

The BlueFuse Software framework enables input of all sample information and provides links to experimental runs into one database (Figure 1). Sample information includes sample type (e.g., blood, CVS, amniotic fluid), date of birth, pedigree number, and phenotype. Related samples can be overlaid for data comparisons and regions of change compared to phenotype.

## Confident Copy Number and AOH Detection

BlueFuse Software uses optimized, validated algorithms to detect copy number changes automatically and display areas of potential abnormality within the genome. For applicable platforms, this includes the ability to detect areas of AOH. Accurate, reliable results are achieved independent of the user.







# Clear Visualization for Rapid Data Confirmation

The key to rapid, confident results interpretation is clear, unambiguous data presentation. In the BlueFuse Software, data can be viewed horizontally or vertically (classical cytogenetics view). The opening view shows the entire genome with the automated calling displayed, facilitating user confirmation of the calls. The user can zoom in to any region on the genome for more detailed analysis at any time by selecting the desired region or abnormality. The user may also annotate the data manually for segmental changes or override the automated calls. The region comments box supplements any changes with an explanation, enabling an audit trail and case history and facilitating the addition of any other relevant information used in the analysis (Figure 2).

#### **Intuitive Navigation**

BlueFuse Software links all data for each view, making navigation as simple as a click of the mouse. For example, click a region in a chart to see specific information in a table format, or click a line in a table to see that data highlighted in the charts (Figure 3).

## **Helpful Data Interpretation**

In addition to clear data presentation, BlueFuse Software helps users understand the significance of any detected changes. This is achieved through the import of a secondary file called the annotation database. The annotation database is comprised of summary information from the key public databases (ISCA, DGV, Ensembl, and Decipher) and is updated regularly. To make sure that the most recent information is used, BlueFuse Software facilitates direct link-out to the live websites for region, gene, and OMIM searches, simply by right-clicking on the

relevant region in the decision track. Laboratories can import custom BED or TXT files to supplement this information. Visualization features in the decision tracks enable data comparison between current experiments and published regions, and a closer look at gene and exon content within each region (Figure 4).

## Full History of Laboratory Data

BlueFuse Software incorporates a number of measures to ensure a transparent audit trail of laboratory data and decisions made regarding data interpretation.

#### **Record of Data Assessment**

The Region View dialog within BlueFuse Software provides a laboratory record of the decisions made for every region identified. Every region can be assigned an assessment of Benign, Probably Benign, Unknown, Probably Pathogenic, and Pathogenic, following ISCA guidelines. Users can add specific comments regarding the assessment, supplying additional support of the decision. This non-deletable audit trail delivers a history of analysis and a paperless format of case management between users. All information appears on the generated report (Figure 5).

# Sample and QC Comparison

Complete information for all samples is stored in a central database. A summary of all regions found in all experiments, including frequency of detection and previous region assessments, is available to guide decisions. Data are permanently available and can be revisited and interrogated at any time ensuring that any follow-up questions can be readily answered. QC metrics for each experiment are also stored

within the database allowing laboratories to perform run-to-run, lot-to-lot, and user-to-user comparisons to aid in the development and optimization of QC\QA processes.

## **Complete Audit Trail**

From a laboratory record perspective, it is essential to track who evaluates experiment performance and when in the process this evaluation occurs. BlueFuse Software provides a "Sign-off" functionality that logs this activity automatically. After a result is reviewed, the user will sign off on that experiment as a pass or a fail. Each inspection includes a user name and time stamp to establish the audit trail. The experiment is then passed to the next user and confirmed before being signed-off by the senior members of the team. This trail cannot be deleted or edited, even by an administrator, providing a robust audit trail of the sample (Figure 6).

#### Scalable Workflow

BlueFuse Software supports multiple users accessing the database at the same time to ensure fast workflows and ease of use. If installed with the recommended (optional) BlueFuse Server, every user

maintains write access to the database for full functionality. There are three levels of user access (Figure 7):

- 1. User-write samples and experiments to the database only
- 2. Supervisor—write, annotate, and delete samples and experiments to the database
- Administrator—write, annotate, and delete samples and experiments to the database; change global database settings

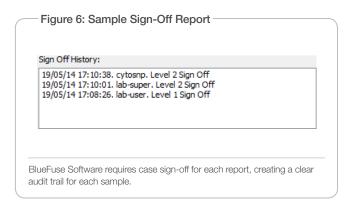
#### **BlueFuse Server for Multi-User Write Access**

BlueFuse Server is an optional install that enables multiple users to write simultaneously to a central database. If this software is not installed, multiple users can log in with read-only access, but only one person can write to the database at any given time.

## Rapid and Consistent Reporting

BlueFuse Software automatically generates annotated reports for each experiment. Reports contain a breakdown for every copy number and AOH region, including user assessment and associated comments

Figure 5: Region View in BlueFuse Software × Detailed Region Overlapping CGH Regions Reported Genes Detailed Region Summary ▼ Reported: yes ▼ Type: Loss Assessment: Pathogenic Position: Chr9: 259,822 -> 299,315 Band: 9p24.3 -> 9p24.3 Size: 39.5 Kb Man Change: yes Comments: Add 14/05/14 14:47:54. cytosnp. ensured that this was highlighted in report Ε 14/05/14 14:47:17. cytosnp. changed status to pathogenic 14/05/14 14:45:57. cytosnp. Deletion and disruption of the DOCK8 associated with mental retardation and The Region View shows information regarding data assessment, including the region type, call assessment, reported status, location of the variation, and any user comments. The additional tabs of "Overlapping CGH Regions" and "Reported Genes" enable rapid assessment of the region.



plus details of the Human Genome Organisation Gene Nomenclature Committee (HUGO/HGNC)² and Online Mendelian Inheritance in Man (OMIM)³ genes, overlapping Database of Genomic Variants (DGV) entries⁴, and International Standards for Cytogenomic Arrays (ISCA) database of consensus regions⁵. Reports are updated when any changes to the case are made, ensuring the reports are always up-to-date based on the latest experiment actions and changes. In addition, reports can be customized to make sure that only the desired information is reported outside of the laboratory. All reports are easily exported or copied to a laboratory-specific report as required. Reports are also available as Web Reports using a standard internet browser within the institute to maximize availability to all users\*.

## **Integrated Framework**

BlueFuse Software offers a single framework for analyzing data for IVF and molecular cytogenetic applications. Developed by the clinical genomics community for the clinical genomics community, the clear intuitive interface ensures that the unique needs of these laboratories are met. In addition, the software supports analysis and visualization of sequencing and array data on the same platform. This integrated approach enables molecular cytogenetic laboratories to run a suite of technologies and expand their testing portfolios.

Figure 7: Configuring User Level in the Database User Administration User Name Full Name Level cytosnp lab-super lab-super Supervisor lab-user lab-user User Add User Edit User Delete User Close

## Summary

BlueFuse Multi Software enables rapid, accurate molecular cytogenetics analysis. The ability to visualize and report copy number and AOH data quickly and reliably allows laboratories to run multiple tests per day with confidence and minimal hands-on time. In addition, the integrated framework ensures that laboratories are able to scale to higher volumes and offer new tests with minimal staff training. Designated user login and profiles coupled with experiment sign-off requirements allows the lab to control and track data throughout the workflow and institute.

BlueFuse Software supports multiple user access levels.

## **Ordering Information**

BlueFuse Software is available free of charge to users of Illumina cytogenetic and IVF technologies with unlimited licenses per site. The software is not available as an open platform to other vendors or LDTs. Download the software from www.cambridgebluengome.com/software. For license information, contact techsupport@illumina.com.

<sup>\*</sup> When BlueFuse Server is installed.

### References

- 1. Michelson DJ, Shevell MI, Sherr EH, Moeschler JB, Gropman AL, et al. (2011) Evidence Report: Genetic and metabolic testing on children with global developmental delay. Report of the Quality Standards Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Service. Neurology 77(17): 1629–1635.
- 2. HGNC Home Page (wwwdev.genenames.org/) Accessed 09 June 2014.
- 3. OMIM Online Mendelian Inheritance in Man (omim.org/) Accessed 09 June 2014.
- 4. Database of Genomic Variants (dgv.tcag.ca/dgv/app/home) Accessed 09 June 2014.
- 5. Welcome to the ISCA Consortium web site (www.iscaconsortium.org/) Accessed 09 June 2014.

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