BlueFuse® Multi Analysis Software for Preimplantation Genetic Screening

A sophisticated multiuser database for storing, analyzing, and interpreting results from preimplantation genetic screening studies.

Highlights

- **Cross-Platform Analysis**
  Supports data from both array and next-generation sequencing studies
- **User-Independent Results**
  Optimized, validated algorithms generate results and reports automatically from barcoded data
- **Fast Sample Turnaround Time**
  Automated batch import and data processing

Introduction

Chromosome aneuploidy (an abnormal number of chromosomes) is a major cause of failure for *in vitro* fertilization (IVF) procedures, as most embryos with aneuploidy will not implant or will miscarry during the first trimester of pregnancy.[1-3] Preimplantation genetic screening (PGS) for euploid embryos, those with a normal number of chromosomes, increases the chance that a viable embryo will be selected for transfer and the likelihood of successful implantation and pregnancy.[4-7]

Illumina offers 2 solutions for comprehensive PGS: the 24sure® array-based technology and the VeriSeq™ PGS Solution, which takes advantage of next-generation sequencing (NGS) technology. Analysis for both platforms is performed using state-of-the-art BlueFuse Multi Analysis Software. BlueFuse Software offers automated batch import and processing of run data using validated algorithms for fast sample turnaround time and confident results reporting.

Cross-Platform Analysis

BlueFuse Multi Analysis Software is a sophisticated multiuser database for storing, analyzing, and interpreting PGS data. By automating microarray processing, from single-click batch import to reporting, BlueFuse Software enables laboratories to process large numbers of samples efficiently. Enabled for both the 24sure assay and the VeriSeq PGS Solution on the MiSeq® System, BlueFuse Software provides a clear, intuitive user interface to deliver user-independent results (Figure 1).

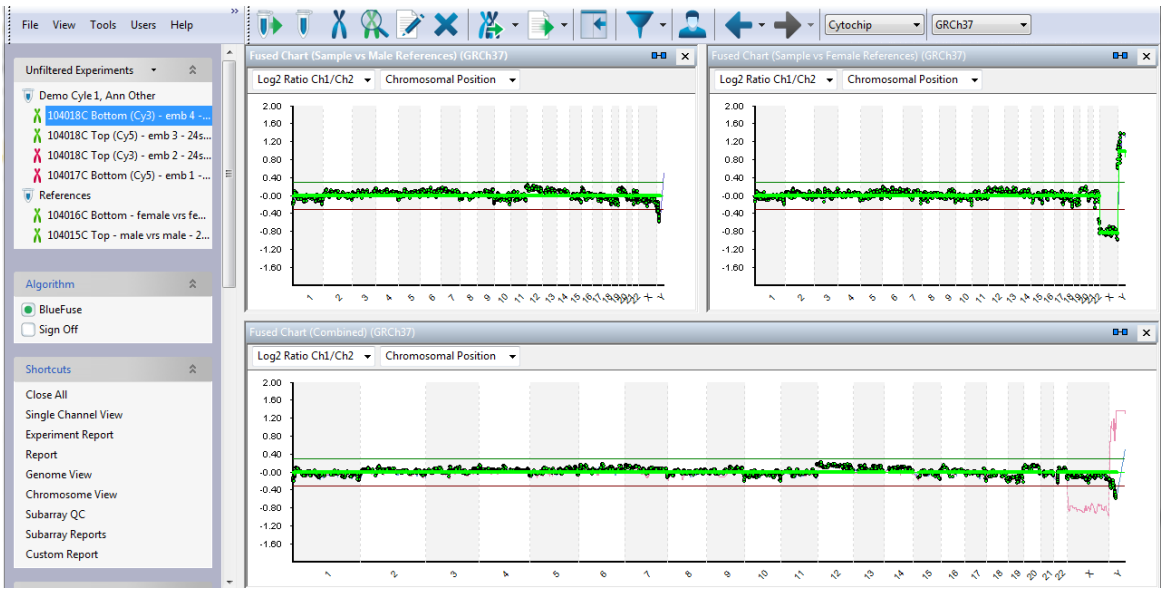

Figure 1: User-Friendly BlueFuse Software Interface for PGS Assays—The integrated approach of BlueFuse Software ensures that laboratories can choose their preferred platform for any run without changing workflows. Generated data from one platform can be analyzed, stored, and viewed alongside data from the other. Data shown is for a euploid male embryo.

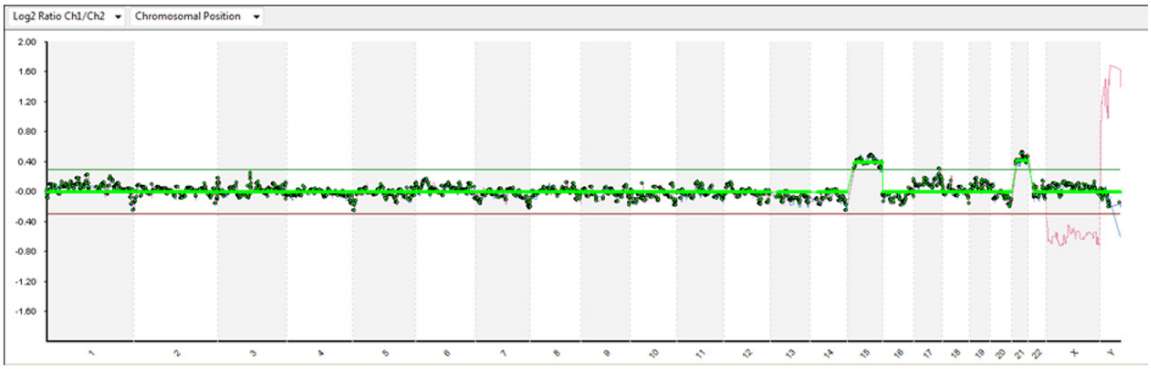

Figure 2: Automated Calling of PGS Data in BlueFuse Software—Genome view of the data showing clear and automatically called trisomies for chromosomes 15 and 21 in a female embryo.

Automated Algorithms for Rapid Interpretation

All PGS data are run through automated, validated algorithms to provide results, independent of user preferences and settings. Sophisticated algorithms calculate and call the status for each chromosome as either euploid or aneuploid, and include an estimate of confidence in the call based on assay noise or underlying ambiguity. Overall euploidy/aneuploidy of the embryo is also provided. In addition to reproducibility and objectivity, this information enables comparison of laboratory results with data published in the literature. The end product is an automated sample and cycle report.

Clear Visualization for Data Confirmation

Key to rapid, confident PGS results interpretation is clear and unambiguous data presentation. BlueFuse Software displays the entire genome along with the automated calling to facilitate user confirmation of the calls (Figure 2). Users can annotate the data manually to note segmental changes or override automated calls.

Automated Report Generation

BlueFuse Software automatically generates individual reports for each embryo and an overall case report. These reports are updated as changes are made to the case, ensuring that the reports are always up to date with the latest experiments.

Single Embryo Reports

A single embryo report provides information regarding the overall status of an individual embryo and each chromosome, including quality control (QC) metrics (Figure 3). Single embryo reports are accessed easily in BlueFuse Software with a single click. Using these reports, users can make an evidence-based decision on the quality of the data for each embryo before making any selections.

Full Cycle Reports

Full cycle reports, generated automatically by BlueFuse Software, show the status of each embryo and the final scores for each chromosome in a single table for analysis. This data enables an embryologist to ascertain which embryos to implant or cryogenically store, and which ones are unsuitable for transfer. Full cycle reports are easily exported or copied to a report to pass directly to the embryologist (Figure 4). Reports are available as Web Reports using a standard internet browser within the institute to maximize availability to all users.*

QC Measures	
SD autosome (Male / Female / Combined):	0.08 / 0.08 / 0.07
% Included clones (Male / Female / Combined):	90.48 / 90.38 / 97.76
% Included reference clones - 104015C Top - male vrs male - 24sure:	92.03
% Included reference clones - 104016C Bottom - female vrs female - 24sure:	90.97
Mean spot amplitude:	1448.21
SBR:	7.35
DLR raw / fused (Male):	0.07 / 0.07
DLR raw / fused (Female):	0.08 / 0.08
DLR fused (combined):	0.07

Figure 3: Key QC Metrics Presented in a Single Embryo Report

Scalable Workflow

BlueFuse Software supports multiple users accessing the database at the same time to ensure the fastest 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 3 levels of user access (Figure 5):

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

BlueFuse Server for Multiuser Write Access

BlueFuse Server is an optional install that enables multiple people to write simultaneously to a central database. If this software is not installed, multiple users can log in with read-only access, but only 1 person can write to the database at any given time.

* When the BlueFuse Server is installed.

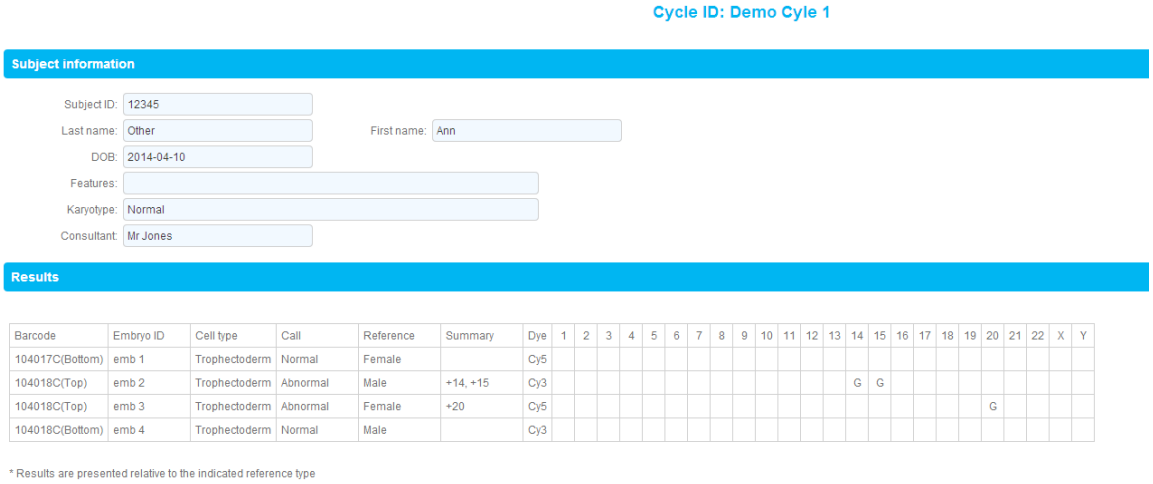

Figure 4: Full Cycle Report for PGS Experiment—Automated cycle report providing the user with an overall summary for each embryo within this cycle. This report is available directly through the software and also in web format if using the server.

Complete Audit Trail through Sample Sign-Off

From a laboratory record perspective, it is essential to track who evaluates experiment performance and when in the process this evaluation happens. 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 build 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).

Searchable Database

Experimental results analyzed using BlueFuse Software are stored in a central database. Data are permanently available and can be revisited at any point in the future for comparison across multiple cycles, which may have a treatment or counseling impact. Data storage also ensures that any follow-up questions can be readily answered. Summary 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.

Integrated Framework

BlueFuse Software offers a single framework for analyzing data for IVF and molecular cytogenetic applications. The software supports analysis and visualization of sequencing and array data on the same platform. This integrated approach enables IVF laboratories to run a suite of technologies and expand their testing portfolios.

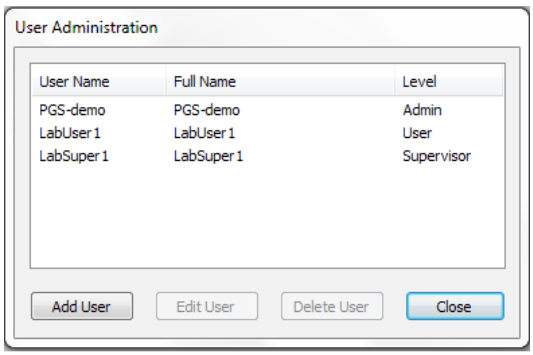

Figure 5: Configuring User Level in the Database—BlueFuse Software ensures access control by assigning 3 user levels with different privileges and functions. The software supports multiple users at each level and administrators can reassign access levels at any time.

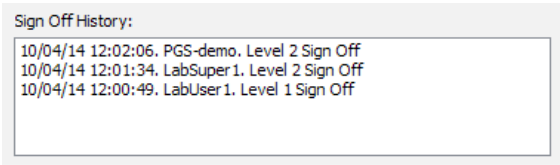

Figure 6: Sample Sign-Off Form—BlueFuse Software requires case sign-off for each report, creating a clear audit trail for each sample.

Summary

BlueFuse Multi Software enables rapid reporting of PGS experiments. Optimized algorithms combined with automated report generation allow laboratories to run multiple tests per day with confidence and minimal hands-on time. The integrated framework ensures that laboratories are able to scale rapidly to higher volumes and offer new tests with minimal staff training. Designated user login and profiles coupled with experiment sign-off requirements provides sample traceability throughout the workflow and institute.

Ordering Information

Access to 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 for laboratory developed tests (LDTs). Download the software from www.illumina.com/clinical/clinical_informatics/bluefuse.html. Contact techsupport@illumina.com for license information.

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